JURNAL LOCUS: Penelitian & Pengabdian
Volume 4 No. 5 May 2025
E-ISSN 2829-7334| P-ISSN 2829-5439
Hompage: https://locus.rivierapublishing.id/index.php/jl

MAPPING THE RESEARCH LANDSCAPE OF NATURAL COMPOUNDS FOR TUBERCULOSIS TREATMENT: A BIBLIOMETRIC APPROACH

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Abstract:
Tuberculosis (TB) remains a global health crisis, exacerbated by rising drug resistance in Mycobacterium tuberculosis. While conventional therapies like BPaL/BPaLM regimens and shorter rifapentine-based treatments show promise 11–33, the need for novel anti-TB agents persists. Natural compounds, particularly from biodiverse regions like Indonesia 77, offer untapped potential, yet prior bibliometric analyses lack comprehensive integration of computational and multi-omics approaches to guide future research. This study maps the research landscape of natural compounds for TB treatment (2015–2025) through bibliometric analysis, identifying gaps and proposing AI-driven, multi-disciplinary strategies to accelerate drug discovery. PubMed-derived data (23 articles) were analyzed using VOSviewer to visualize co-authorship, keyword co-occurrence, and thematic clusters. Trends in authorship, geographic contributions, and research foci (e.g., molecular docking, drug resistance) were evaluated. China dominated research output (11/23 studies), with clusters emphasizing computational methods (e.g., virtual screening), bacterial enzymes, and animal models. Keyword analysis revealed a strong focus on drug resistance and synergism, yet limited exploration of AI, multi-omics, or ethnopharmacology. Notably, studies like Romulo et al. (2018) highlighted Indonesian plants' anti-TB potential 77, but systematic integration with modern technologies remains underexplored. This study identifies a critical gap: the need to merge traditional natural compound research with AI-aided drug design, multi-omics (e.g., transcriptomics 1616), and nanodelivery systems. By proposing a framework that bridges computational predictions (e.g., molecular docking 1515) with experimental validation, this research advances a novel, scalable approach to combat drug-resistant TB, leveraging global biodiversity and cutting-edge technologies.

Keywords: natural compound, TB, bibliometric analysis

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INTRODUCTION

Tuberculosis (TB) remains a global health threat with treatment challenges such as long duration, side effects, and increasing drug resistance (Bai & Bai, 2023; Ghanem, 2015; Nichols & Devlin, 2022) . Recent developments in TB treatment regimens show new promise. For drug-sensitive TB, a shorter 4-month regimen with rifapentine and moxifloxacin is now recommended (Brinkmann & Ritz, 2015; Graciaa et al., 2023; Jha et al., 2023; Pai & Rodrigues, 2015). Meanwhile, for drug-resistant TB, shorter and better-tolerated regimens such as BPaL and BPaLM have shown promising results in increasing efficacy and reducing side effects (Acuña-Villaorduña et al., 2023; Bereda, 2022; Qiao et al., 2022). National guidelines from the Indonesian Ministry of Health and recommendations from the Indonesian Pulmonologist Association (PDPI) also provide important guidance on the diagnosis and management of TB in Indonesia (Acosta et al., 2023; da Silva et al., 2016a, 2016b; Davtyan et al., 2019). While these advances are important, the need for new drugs with innovative mechanisms of action to

overcome resistance and shorten treatment duration remains urgent (Mrunalini et al., 2023; T. Singh et al., 2020; V. Singh & Chibale, 2021).

In this context, the potential of natural compounds as alternative sources of anti-TB drugs becomes increasingly relevant (Hossain et al., 2022; Maiolini et al., 2020; Ndjoubi et al., 2020; Yadav et al., 2022). Indonesia's biodiversity, which is rich in traditional medicinal plants, holds great potential for the discovery of new antimycobacterial agents. In vitro studies of plants used in traditional medicine have identified several species with promising activities. For example, a study by Romulo et al. (2018) examined 49 ethanol extracts from 37 Indonesian plant species and found that several extracts, including those from Orthosiphon aristatus and Woodfordia floribunda, showed significant antimicrobial activity against a variety of bacteria and fungi. Such studies underscore the potential of traditional medicinal plants as sources of active compounds with mechanisms of action that may differ from existing anti-TB drugs, thus potentially being effective against resistant strains and contributing to the development of more innovative therapies (Dzoyem et al., 2016; Liu et al., 2020).

Given the complexity of TB treatment challenges and the vast potential of natural compounds, further research is needed to identify the most promising areas of focus. Therefore, the purpose of this paper is to conduct a bibliometric analysis of the existing scientific literature on tuberculosis and active substances from natural materials. This analysis aims to map current research trends, identify research gaps that have not been explored in depth, and project the potential for future research development. By understanding the existing research landscape, it is hoped that this bibliometric analysis can provide valuable insights for researchers, policymakers, and related parties in prioritizing and directing research efforts for the discovery of new TB drugs based on natural materials that are more effective and innovative.

This study aims to map publications focusing on natural compounds in the treatment of tuberculosis. Unlike prior reviews Maiolini et al. (2020) 66), this study uniquely synthesizes bibliometric trends with actionable, technology-driven strategies (AI, multi-omics) while grounding findings in underutilized natural resources.

METHODS

The database used in the search for articles related to the topic of natural compounds for TB treatment comes from PubMed. The keywords used in the search for articles are "(Tuberculosis AND (Natural compound". The inclusion criteria used are articles published in the last 15 years (2010-2025). Bibliometric analysis includes mapping co-authorship networks through data visualization and cluster analysis as well as keyword networks (co-occurrence) using VosViewer

RESULTS AND DISCUSSION

Publication Trend, Author, and Affiliation Country

Based on the research, 23 articles were found related to the use of natural compounds for the treatment of tuberculosis (TB). The most articles published in 2023 were 7 articles [figure 1]. The publication trend varies but has started to increase in the last three years (2023-2025). This shows that this topic is still interesting to study further, although the number of research studies related to this topic is still minimal. Several studies have stated that there is a trend of increasing and changing use of natural compounds for health after the COVID-19 pandemic (Khmyz, 2023; Lee & Kwon, 2022; Ma & Kwon, 2021; Oprișan et al., 2022; Pranskuniene et al., 2022).

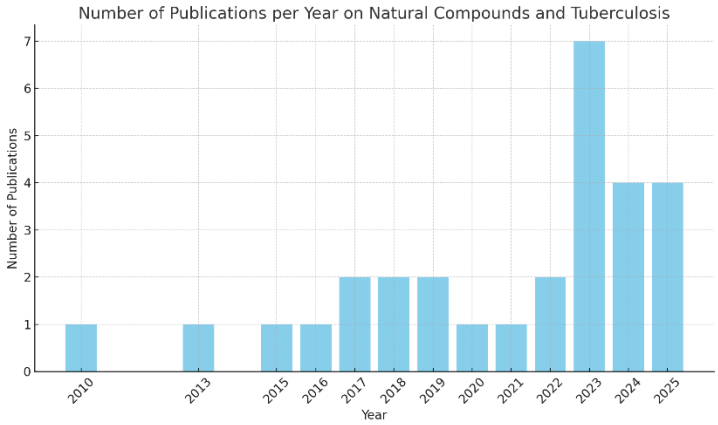


Figure 1. Number of publication per year on Natural Compound for Tuberculosis Treatment

(Source: https://pubmed.ncbi.nlm.nih.gov)

Based on the analysis results, it was found that China is the country with the largest number of publications in the field of research on natural compounds and tuberculosis, namely 11 publications. The second position is occupied by India with 6 publications, and Italy and Malaysia, each with 3 publications. The dominance of China and India shows the high attention of Asian countries to the development of alternative therapies and the search for bioactive compounds to overcome tuberculosis, which is still a major health problem in the region [figure 2]. This also shows the significant contribution of research institutions and universities in developing countries to innovation in the fields of pharmacy and biotechnology.

The presence of other countries such as Italy and Malaysia in the top five positions shows that global collaboration and interest in this topic is quite broad, not limited to countries with a high TB burden, but also include countries with strong research capacity. Although in some countries, such as Italy, the problem of TB is often associated with immigrants or foreign-born people (FBP) (Andreoni et al., 2021; Ingrosso et al., 2014; Mussini et al., 2021; Scotto et al., 2009).

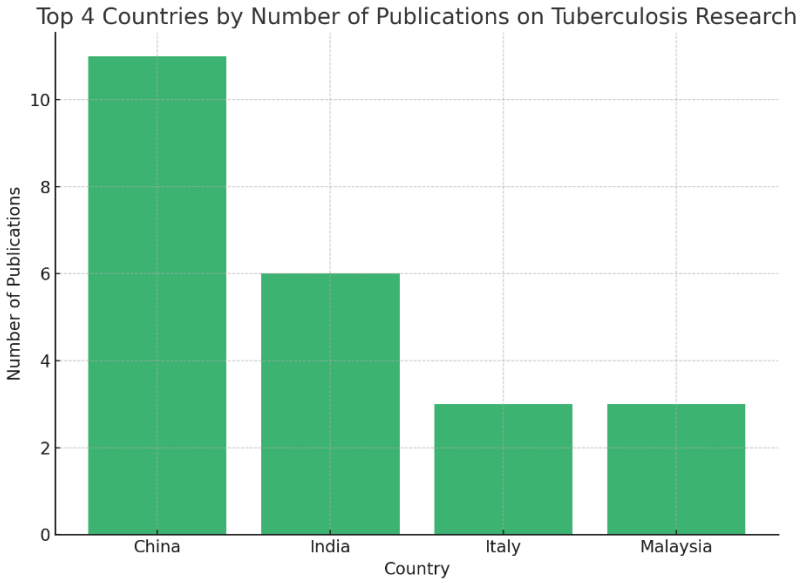


Figure 2. Top 4 Countries by of Publication on Tuberculosis

Based on the results of bibliometric analysis of publications discussing the potential of natural compounds in the treatment of tuberculosis, there are ten top authors with the most contributions including Wu Zhili, Wu Yuchen, Niu Yanhong, Hu Qianfang, Jiang Qihua, Yang Xiaolan, Li Li, Alimu Ayiguli, Zhong Xuemei, and Yang Boyi. All of these authors are from China and have equal productivity, each has published 2 articles, and the publications are collaborative and not centralized on one individual or a particular research group (table 1).

Table 1. Top ten author with the highest number of publications

No.	Author Name	Number of Publications
1	Hu, Qianfang	2
2	Wu, Yuchen	2
3	Jiang, Qihua	2
4	Yang, Xiaolan	2
5	Niu, Yanhong	2
6	Wu, Zhili	2
7	Alimu, Ayiguli	2
8	Zhong, Xuemei	2
9	Yang, Boyi	2
10	Zou, Xiaoguang	2

Co-author mapping

The relationship between several researchers can be seen in the co-author map below (figure 3). This indicates that research on natural compounds for tuberculosis therapy is multidisciplinary. Based on the co-author analysis, Alimu ayiguli is the center of the network because he is in the middle with many connections. This shows that the author has extensive

collaboration with almost all other authors. In addition, authors such as Gong hui, and Zhong xuemei also have many connections, indicating that they actively collaborate in this team.

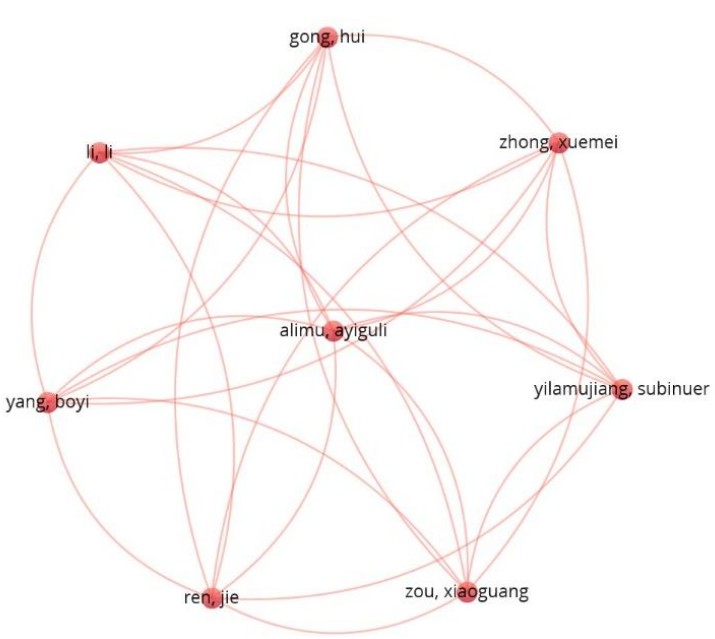


Figure 3. Co-author mapping
(Source: https://www.vosviewer.com/)

Co-occurance mapping

In clustering based on keyword closeness, 5 clusters were found with 5 main focuses, namely drug and molecular simulations, molecular biology and bacteria, drug and animal model testing, impact on humans, and resistance and sensitivity (table 2).

Table 2. Cluster based on co-occurance mapping

Cluster	Color	Main Focus	Keywords
Cluster 1	Red	Drugs & Molecular Simulations	drug discovery, drug resistance, molecular docking simulation, virtual screening
Cluster 2	Green	Molecular Biology of Bacteria	bacterial proteins, catalytic domain, enzyme inhibitors
Cluster 3	Blue	Drug and Animal Model Testing	antitubercular agents, animals, natural compounds
Cluster 4	Purple	Impact on Humans	Humans, oxidative stress
Cluster 5	Yellow	Resistance and Sensitivity	drug synergism, microbial sensitivity tests

In the co-occurrence map, the main topic, Mycobacterium tuberculosis, is at the center of the entire network, indicating that this is the main focus of research. The presence of several keywords indicates a multidisciplinary approach, such as computational techniques, biological

assays, and clinical studies. In the research trends, there is a strong tendency towards in silico (computational) approaches in drug discovery [figure 4].

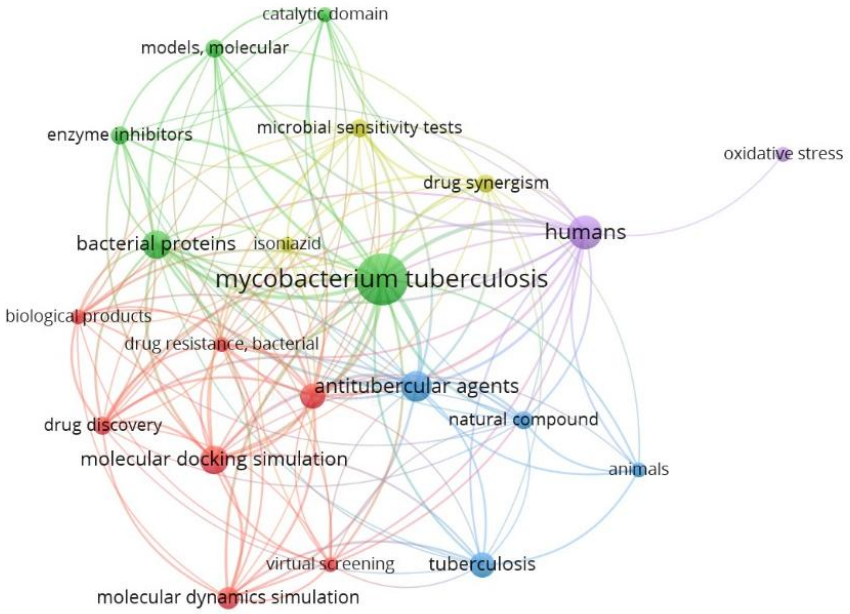


Figure 4. Co-occurance mapping
(Source: https://www.vosviewer.com/)

The emphasis on drug resistance is seen in the keywords drug resistance, drug synergism, and sensitivity tests, indicating that the problem of resistance to anti-TB drugs is a major issue in current research. In addition, the potential for developing new drugs is still wide open, with keywords related to natural compounds, enzyme inhibitors, and antitubercular agents indicating a major focus in the search for new therapies, both from natural sources and molecular design.

In silico strategies can be applied at various stages of the drug discovery paradigm to accelerate the identification of new anti-TB therapies, especially related to the compound nature. The presence of drug resistance, and the application of effective computational tools at various stages of TB drug discovery, when combined with traditional biochemical methods (Cheng et al., 2022; Jagadeb et al., 2019; Macalino et al., 2020). The research approach is multidisciplinary, indicating the need for cross-disciplinary collaboration to understand and treat TB comprehensively.

CONCLUSION

A bibliometric analysis of 23 articles on natural compounds and tuberculosis (TB) reveals that research is predominantly focused on *Mycobacterium tuberculosis*, with key themes including molecular docking, virtual screening, bacterial enzymes, animal model testing, clinical impacts (e.g., oxidative stress), and drug resistance. This highlights a shift toward integrating computational and experimental approaches to understand molecular mechanisms, develop new drugs, and combat resistance. To advance this field, future research should leverage AI-driven drug discovery, multi-omics (transcriptomics, proteomics, metabolomics), and systems biology to identify novel natural anti-TB compounds, optimize synergies with existing drugs, and explore underexplored sources (e.g., marine organisms,

ethnopharmacology). Additionally, nanodelivery systems and PK/PD modeling could enhance clinical translation, bridging the gap between computational predictions and real-world applications to accelerate the development of effective, resistance-proof TB therapies. This integrated approach promises faster drug discovery, improved resistance management, and personalized treatments, advancing global TB eradication efforts.

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