PLANT SCIENCE TODAY
Vol 12(sp2): 1-8
https://doi.org/10.14719/pst.4991

eISSN 2348-1900

REVIEW ARTICLE

Medicinal plants potential as anti-mycobacterial and mechanisms behind their active metabolites

Urvashi Goyal[1], Manish Kumar[2], Deen Dayal[3], Kundan Kumar Chaubey[4*], Divya Sharma[5], Ashwani Kumar Sanghi[6], Nandita Jha[7], Shailendra Thapliyal[8], Shalini Sharma[9], Krishna Dutta Rawat[10], S Y Mukartal[11], Niraj Kumar[12], Ajar Nath Yadav[13] & Anish Kumar Pal[14]

[1]Department of Microbiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226 014, India
[2]Animal Physiology and Reproductive Division, Central Institute for Research on Goats, Makhdoom, Farah, Mathura 281 122, India
[3]Department of Biotechnology, GLA University, Mathura 281 406, India
[4]Department of Biotechnology, School of Basic and Applied Sciences, Sanskriti University, Mathura 281 401, India
[5]Department of Biotechnology, St. John's College, Dr. Bhim Rao Ambedkar University, Agra 282 002, India
[6]School of Allied Health Sciences, MVN University, Palwal 121 105, India
[7]Department of Botany, Lucknow University, Lucknow 226 007, India
[8]Uttaranchal Institute of Management, Uttaranchal University, Arcadia Grant, P.O. Chandanwari, Premnagar, Dehradun 248 007, India
[9]Division of Veterinary Physiology and Biochemistry, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, Jammu 180 009, India
[10]Department of Bio and Nanotechnology, Guru Jambheshwar University of Science and Technology, Hisar 125 001, India
[11]Department of Veterinary Microbiology, Veterinary College, Karnataka Veterinary, Animal and Fisheries Sciences University, Bidar, Athani, Belagavi 591 230, India
[12]Department of Electronics and Communication Engineering, Graphic Era Deemed to be University, Dehradun 248 002, India
[13]Department of Genetics, Plant Breeding and Biotechnology, Dr. Khem Singh Gill Akal College of Agriculture, Eternal University, Baru Sahib, Sirmour 173 101, India
[14]Environmental laboratory, Indian Register of Shipping (IRClass) Systems and Solutions Pvt Ltd, Jaipur 302 017, India

*Correspondence email - kundan2006chaubey@gmail.com

Received: 08 September 2024; Accepted: 17 March 2025; Available online: Version 1.0: 08 June 2025

Cite this article: Urvashi G, Manish K, Deen D, Kundan KC, Divya S, Ashwani KS, Nandita J, Shailendra T, Shalini S, Krishna DR, Mukartal SY, Niraj K, Ajar NY, Anish KP. Medicinal plants potential as anti-mycobacterial and mechanisms behind their active metabolites. Plant Science Today. 2025; 12(sp2): 1-8. https://doi.org/10.14719/pst.4991

Abstract

Tuberculosis (TB) is a contagious disease caused by the bacterium *Mycobacterium tuberculosis*, which most often affects the lungs, specifically pulmonary tuberculosis. One of the leading opportunistic diseases globally, affecting one-third population and resulting in approximately 1.5 million deaths annually. A weakened immune system against mycobacterial diseases has contributed to over 1.1 million people being co-infected with other life-threatening diseases, such as Human Immunodeficiency Virus (HIV). Abundant research highlighted the biotherapeutic potential of naturally occurring compounds against mycobacterial disorder. The increasing cases of MDR/XDR-TB are mainly derived from tuberculosis, coupled with the emergence of extensively drug-resistant (XDR) and multidrug resistance (MDR) strains, have made treatment more challenging. The condition emphasized the crucial requirement for novel plant-derived anti-TB medications. The persistence and latency of *M. tuberculosis*, along with drug resistance, have made tuberculosis treatment increasingly challenging. This review aims to comprehensively examine tuberculosis disease including current standard treatment, promising new drugs under development and the potential of medicinal plants and their bioactive compounds as alternative or supplementary therapies to combat mycobacterial infections, specifically focusing on the potential of plant-derived metabolites to act as effective antimycobaterial agents. It specifically highlights the role of plant-derived metabolites as effective antimycobacterial agents.

Keywords: antimycobacterial agents; drug resistance; MDR/XDR-TB; mycobacterial infection; plant-derived metabolites

Introduction

Tuberculosis (TB), one of the oldest known diseases affecting humans, is caused by the bacterium *Mycobacterium tuberculosis* (MTB) and remains a leading cause of death worldwide (1). About one-fourth of the world's population is infected by *M. tuberculosis*, leading to 10 million active tuberculosis cases and 1.5 million deaths annually (2). However, only 5 to 15 % of infected individuals develop active tuberculosis, while the majority remain in a stage of clinical latency (3). *M. tuberculosis* is an acid-fast bacterium and a member of the *M. tuberculosis* complex, which also includes *Mycobacterium africanum, M. bovis* and *M. microti.* The primary treatment for TB includes rifampicin, ethambutol, isoniazid and pyrazinamide. However, these drugs are

becoming less effective, more expensive and associated with significant side effects (Fig. 1). The TB-affected nation's scenario has worsened due to the emergence of drug-resistant and geographically distinct TB pathogenic strains, highlighting the urgent need for new treatment strategies, particularly those involving medicinal plants. Medicinal plants are widely available, cost effective and associated with fewer side effects, offering a promising avenue for the development of alternative TB treatments. Additionally, addressing drug resistance, plant-derived medications may help combat region-specific TB strain aetiologies.

To reduce TB-related mortality, it is crucial to develop effective alternative anti-TB therapies, especially plant-based ones (4). Patients with TB or multi-drug resistance TB (MDR-TB) require prolonged multidrug chemotherapy, lasting a minimum of six months to a maximum of two years. However, the high toxicity and severe side effects of these medications pose significant health risks. Reported the rise of MDR-TB and extensively drug-resistant (XDR-TB) strains, the global search for novel anti-TB therapeutics is more critical than ever. Diverse bioactive compounds of medicinal plants have played a pivotal role in drug discovery and represent a valuable resource for developing new anti-TB actions. They are also known to be rich sources of metabolites with potent antimycobacterial properties (5).

Varied drugs have been used to treat tuberculosis over decades. Around 1950s, vital drugs including isoniazide, pyrazinamide, cycloserine and kanamycin were discovered. Nevertheless, the emergence of multidrug resistance in *M. tuberculosis* (MDR-TB) led to the adoption of combination therapy, extending treatment durations to 18 months or more. The primary drugs used for tuberculosis treatment include isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide, all of which exhibit strong bactericidal activity. The dosage for each patient varies based on factors such as weight, age, gender and body mass index. Patients are required to take their prescribed medication daily for at least six months. However, long treatment durations, severe side effects including liver toxicity and high medication costs often lead many patients to discontinue treatment prematurely. Drug resistance in *M. tuberculosis* has become a major challenge in tuberculosis treatment. One of the primary reasons for drug resistance is genetic mutations, resulting in a heritable decrease in antibiotic susceptibility. These mutations typically occur in the drug's target or activator regions. Tuberculosis drugs act slowly, giving the bacterium enough time to develop resistance. MDR-TB is resistant to two of the main TB drugs isoniazide (INH) and rifampicin (RMP). Second-line drugs are used to treat such patients. MDR -TB treatment is more challenging due to the limited effectiveness and higher toxicity of these alternative drugs (6).

Limitations of using medicinal plants as anti-mycobacterial agents

Medicinal plants offer abundant potential as a source of novel anti-mycobacterial agents. Nevertheless, their application is hindered by several limitations. One significant challenge is the variability of extraction methods, as inconsistent techniques across studies can impact the potency and reliability of plant extracts. Additionally, the lack of standardization regarding dosage, administration routes and treatment duration makes it difficult to compare findings across different studies.

Another major concern is the lack of comprehensive safety data, with many studies failing to provide detailed toxicity profiles, thereby restricting their progression to clinical use. Moreover, crude plant extracts are complex mixtures containing multiple bioactive compounds, making it challenging to identify the specific molecules responsible for their anti-mycobacterial properties. Bioavailability issues further limit their effectiveness, as some plant-derived compounds may not be readily absorbed or may degrade rapidly in the body.

Potential interaction with other medications also raises concerns, necessitating careful evaluation of plant-based treatments when used alongside conventional drugs. Additionally, regulatory hurdles vary across different countries, further complicating the approval and commercialization of these therapies. Despite these challenges, medicinal plants remain a promising area of research for anti-mycobacterial, emphasizing the need for further scientific investigation and development.

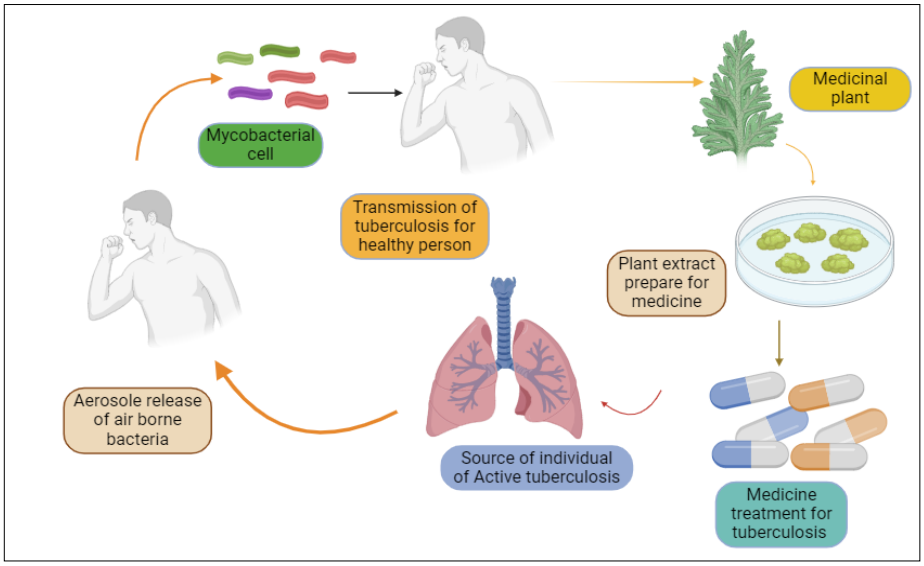

Fig. 1. Medicinal plant extract from plant materials prepared for the treatment of tuberculosis and patients cure.

Drugs currently used for tuberculosis treatment

Tuberculosis treatment typically involves taking multiple medications over an extended period, usually lasting six to nine months. Commonly, more frequently first-line medications used include ethambutol, rifampicin, pyrazinamide and isoniazid. Among them, isoniazid and rifampicin are the primary medications, often prescribed throughout the entire treatment due to their potency bactericidal properties. During the initial intensive phase, pyrazinamide and ethambutol are introduced to assist reduce the bacterial load more rapidly and prevent the development of resistance. For MDR-TB, second-line medications involve injectable drugs such as amikacin or capreomycin, along with fluoroquinolones like levofloxacin and moxifloxacin. They are often combined with newer medications such as bedaquiline and delamanid. Managing drug-resistant tuberculosis, a more complex and prolonged treatment regimen, necessity careful monitoring to ensure adherence and minimize adverse effects. The drugs currently available for tuberculosis treatment are widely used and are summarized in Table 1.

Potential medicinal plants' active metabolites and their mode of action

For centuries, medicinal plants have been utilized to treat infections and prevent diseases, including epidemics. Traditional herbal medicine relies on crude plant extract to manage infectious diseases in humans. In certain countries, plants serve as a valuable source of antibacterial agents. Researchers' studies aim to identify the chemical composition of these plant-derived antimicrobials and understand the mechanisms by which they inhibit microbial growth, either independently or in combination with conventional antibiotics. In various situations, plant-based products may effectively suppress microbial growth (Fig. 2). Since the dawn of human civilization, plants have been used for therapeutic purposes. Infectious diseases remain a major cause of morbidity and mortality, particularly in developing countries (7). Numerous phytochemicals found in plants, such as tannins, terpenoids, alkaloids and flavonoids, have been demonstrated *in-vitro* antibacterial activity (8) (Fig. 3).

Table 1. Currently available drugs for treatment

Type of Drug	Drug name	Nature /Mechanism of action	Side effects	Reference
First line drugs	Isoniazide	Bactericidal/interacts with NADH and inhibits mycolic acid synthesis. Also inhibits cytochrome P450	GIT reaction, nausea, vomiting, liver toxicity, aplastic anemia, insomnia, headache.	Quémard, et al. (15)
	Rifampicin	Bactericidal/inhibits DNA dependent RNA polymerase.	Nausea, vomiting, fever, headache, darkened urine.	Campbell et al. (16)
	Ethambutol	Bacteriostatic/inhibits cell wall synthesis by inhibiting arabinosyltransferase	Headache, upset stomach, vomiting, nausea, joint pain, gout, dizziness.	Goude et al. (17)
	Streptomycin	Bactericidal/ interferes with formyl-methionyl-tRNA by binding to 16SrRNA	Headache, upset stomach, vomiting, nausea, fever, edema, vertigo	Garvin et al. (18)
	Pyrazinamide	Bacteriostatic/ disrupts pH balance causing FAS -1 inhibition.	Joint pain, fatigue, nausea, stomach upset, loss of appetite.	Zhang et al. (19)
Second line drugs	Capreomycin	Bacteriostatic/ Interacts with 30Ssubunits ribosome hence inhibits RNA synthesis.	Nausea, vomiting, vertigo, fever, itching, drowsiness, edema, increased thirst.	Lin et al. (20)
	Streptomycin	Bactericidal/ Interferes formyl-methionyl-tRNA binding to 16SrRNA	Headache, upset stomach, vomiting, nausea, fever, edema, vertigo.	Sagho et al. (21)
	Para-amino salicylic acid	Bactericidal/ Prodrug Inhibits Dihydrofolate reductase enzyme as it acts as antagonist.	Persistent nausea, diarrhoea, may cause hypothyroidism and hepatitis.	De Chiara et al. (23)
	Cycloserine	Bactericidal/ inhibits alanine recemase and Dalanine: D-alanine ligase, causing cell biosynthesis inhibition.	Headache, drowsiness, tremor, hallucination, depression, tiredness, thoughts of suicide, seizures and numbness.	De Chiara et al. (23)
	Thionamide	Bactericidal/Inhibits mycolic acid synthesis, isoniazideanalog	Negligible side effects.	North et al. (24)
	Ofloxacin	Bactericidal (Fluoroquinolone)/Inhibits DNA synthesis by inhibiting DNA gyrase and Topoisomerase II and IV	Nausea, vomiting, mild diarrhoea, headache, dizziness, vaginal itching.	
	Amoxicilin	Bacteriolytic (Fluoroquinolone)/ 6-APA (Aminopenicillanic acid) derivative, inhibits cell wall synthesis	Nausea, vomiting, diarrhoea, headache, dizziness, vaginal itching, swollen back.	Shams et al. (25)
	Clarithromycin	Bacteriostatic (Fluoroquinolone)/ Binds to 50S ribosome, cause inhibition of protein translation	Nausea, vomiting, mild diarrhoea, headache, insomnia, vaginal itching, taste change.	
Third line drugs	Para-amino salicylic acid.	Bactericidal/ Inhibits Dihydrofolate reductase enzyme as it acts as antagonist.	Persistent nausea, diarrhoea, may cause hypothyroidism and hepatitis	Zheng et al. (22)
	Thionamide	Bactericidal/ Inhibits mycolic acid synthesis, isoniazideanalog	Negligible side effects	North et al. (24)
	Streptomycin	Bactericidal/ Interferes formyl-methionyl-tRNA binding to 16SrRNA	Headache, upset stomach, vomiting, nausea, fever, edema, vertigo	Sagho et al. (21)
	Cycloserine	Bactericidal/ Inhibits alanine recemase and Dalanine:D-alanineligase, causing cell biosynthesis inhibition.	Headache, drowsiness, tremor, hallucination, depression, tiredness, thoughts of suicide, seizures and numbness.	De Chiara et al. (23)
	Ethambutol	Bacteriostatic/ Inhibits cell wall synthesis by inhibiting arabinosyltransferase	Headache, upset stomach, vomiting, nausea, joint pain, gout, dizziness.	Goude et al. (17)
New Drugs	Bedaquiline	Bacteriostatic/ adenosine triphosphate synthase inhibition	Increased blood amylase, hemoptysis, nausea, vomiting, dizziness and headache	Field et al. (26)
	Delamanid	Bactericidal/ Inhibiting the synthesis of mycobacterial cell wall components, methoxy mycolic acid and ketomycolic acid.	Headache, dizziness and nausea. Other side effects include QT prolongation	Khoshnood et al. (27)

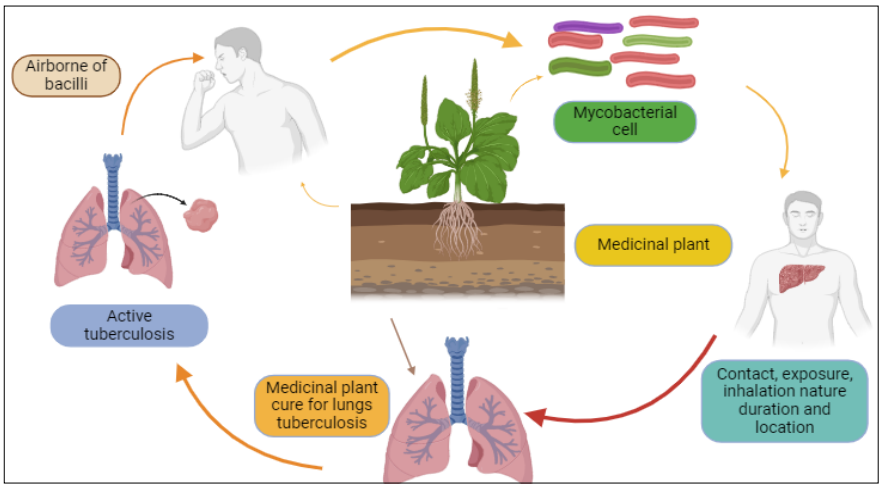

Fig. 2. Medicinal plant treatment of *Mycobacterium tuberculosis.*

Plants serve as vital sources of numerous biologically active compounds and play a crucial role in treating various human diseases. Phytochemicals derived from plants have a long history of providing much needed novel therapies. Several plant secondary metabolites have been extensively considered for their broad-spectrum therapeutic effects against human disease, including alkaloids, coumarins, flavonoids, polyphenols, terpenoids, triterpenoids, quinines, plumbagin, maritinone, 3,3'-biplumbagin, aloe-emodin, epigallocatechin and umckalin. One critical strategy for addressing the rising global tuberculosis burden involves targeting essential enzymes required for critical cellular processes, thereby weakening the survival mechanisms of mycobacteria within the host system (9).

A wide range of phytocompounds found in plants contribute to the prevention and treatment of numerous diseases and health conditions. Plant-based medicinal remedies have been used for centuries and are incorporated into various preparations, including tinctures, extracts, decoctions, infusions, herbal tea and powder. Therapeutic phytochemicals are extracted from different plant parts such as exudates, heartwood, bark, leaves and fruit. Scientific research reported the type and concentration of phytochemicals obtained from medicinal plants depend on the specific plant part used (10). Common phytochemicals extracted from plants, which contain medicinal properties include alkaloids, essential oils, phenols, terpenoids, carotenoids, xanthophyll and flavonoids (11). Additionally, some plants contain unique species-specific compounds including andrographolides, amaranthine, allicin and other distinctive therapeutic components. The demand for effective and affordable antibiotics and antimicrobials has driven the search for new sources, including medicinal plants, fungi, archaea, etc. Traditional herbal remedies, also known as phytomedicine, are derived from plants and contain individual compounds or synergistic combinations that aid in disease treatment (12). The rise of antibiotic resistance has created an urgent need for the discovery and development of new classes of antibacterial drugs (13). Extensive research has been conducted on the pharmacological properties of medicinal plants, as they are a potential source for developing novel medications and may enhance the efficacy of conventional antimicrobials, reducing costs and improving treatment outcomes. However, some plants may also have adverse interactions when used alongside antibiotics (7).

Herbal therapy is increasingly utilizing medicinal plants as a less toxic alternative for treating various diseases (14). Compared to synthetic and chemical drugs, plant-derived medicines exhibit better bioactivity and have demonstrated curative potential against a wide range of illnesses. Consequently, pharmaceuticals derived from medicinal plants may offer greater effectiveness than conventional medications (10). Phytocompounds used in pharmaceutical formulations provide therapeutic benefits against numerous microbiological infections and illnesses. The effectiveness of specific phytocompounds is initially evaluated through *in-vitro* or *in-silico* methodologies before advancing to *in-vivo* models, clinical trials and eventual human use. Infectious diseases caused by bacterial pathogens pose a significant global public health threat. While antibiotics remain a primary treatment for bacterial infections, issues related to toxicity and the growing problem of antimicrobial resistance have significantly reduced their efficacy (8).

Medicinal plants contain various bioactive metabolites, including alkaloids, flavonoids, terpenoids and phenolic compounds, which contribute to their therapeutic features. These bioactive compounds have been widely studied for their mode of action against microbial growth and their potential applications in treating human diseases.

Alkaloids

Alkaloids are nitrogen-containing compounds found in various medicinal plants. They often exhibit antibacterial properties by disrupting microbial enzymes, cellular structure, or metabolic processes. For instance, alkaloids such as berberine and quinine can inhibit bacterial protein synthesis and interfere with DNA replication (12) (Table 3).

Flavonoids

A class of polyphenolic compounds, that exhibit diverse biological activities. They possess antibacterial properties by disrupting microbial membranes, inhibiting microbial enzymes and interfering with DNA replication. Notable flavonoids with antibacterial, antiviral and antifungal properties include quercetin and apigenin (13).

Table 2. Active plant anti-tuberculosis molecules of Indian origin

Family	Botanical name	Plant part used	Extract type	References
Amaranthaceae	*Chenopodium ambrosioides*	Whole plant	Hydroethanolic crude extracts	Nguta et al. (1)
Apocynaceae	*Alstonia scholaris (L.) R. Br.*	Bark	Ethanol extract	Gupta et al. (2)
	Holarrhena antidysenterica (Roth) Wall. ex A.DC.	Seeds	Ethanol extract	Gupta et al (2)
	Tabernaemontana coronaria	Leaf	n-hexane	Mohamad et al. (3)
Asphodelaceae	*Aloe vera var. barbadensis*	Whole plant	Hydroethanolic crude extracts	Nguta et al. (1)
Asteraceae	*Artemisia abyssinica*	leaves	Methanolic crude extract	Gemechu et al. (4)
	Sphaeranthus indicus L	floral head	Ethanol extract	Gupta et al. (2)
Boraginaceae	*Cordia dichotoma Forst.*	Root.	Methanolic extract	Jamkhande et al. (5)
Cannabaceae	*Cannabis*	Root (Friedelin)	Whole plant	Russo et al. (6)
Costaceae	*Costus speciosus*	Stem-flower	n-hexane partition	Mohamad et al. (3)
Cyperaceae	*Cyperus rotundus L*	Roots	Ethanol extract	Gupta et al. (2)
Euphorbiaceae	*Croton macrostachyus*	Leaves	Methanolic crude extract	Gemechu et al. (4)
	Mallotus philippensis (Lam.) Müll.Arg.	Fruits	Ethanol extract	Gupta et al. (2)
Fabaceae	*Cassia sophera*	(Alkaloids Saponins Flavonoids Terpenoids Anthraquinones Cardiac glycosides)	Methanol extract	Singh et al. (7)
	Glycyrrhiza glabra L.	Roots	Ethanol extract	Gupta et al. (2)
	Pueraria tuberosa (Willd.) DC.	Tubers	Ethanol extract	Gupta et al. (2)
Graminae	*Cymbopogon citratus*	Stem-rhizome	n-hexane	Mohamad et al. (3)
Justiciaadhatoda	*Adhatoda vasica*	Leaves	_____	Sharma et al. (8)
Lamiaceae	*Ocimum basilicum*	Seeds	Methanolic crude extract	Gemechu et al. (4)
Leguminosae	*Calpurnia aurea*	Roots	Methanolic crude extract	Gemechu et al. (4)
Melastomataceae	*Dissotis rotundifolia*	Whole plant	Hydroethanolic crude extracts	Nguta et al. (1)
Menispermaceae	*Cocculus hirsutus (L.) Diels*	Leaves	Ethanol extract	Gupta et al. (2)
Mimosaceae	*Acacia Senegal*	Leaves	_____	Nguta et al. (10)
Myrtaceae	*Eucalyptus camaldulensi*	Leaves	Methanolic crude extract	Gemechu et al. (4)
Orchidaceae	*Eulophia nuda Lindl.*	Tubers	Ethanol extract	Gupta et al. (2)
Piperaceae	*Piper corcovadensis*	Roots	Dichloromethane extract	Fernandez et al. (9)
Rubiaceae	*Morinda citrifolia*	Leaves	_____	Sharma et al. (8)
Solanaceae	*Solanum torvum*	Whole plant	Hydroethanolic crude extracts	Nguta et al. (1)
Urticaceae	*Urtica dioica*	(Tannins Terpenoids Anthraquinones)	Hexane extract	Singh et al. (7)
Verbenaceae	*Lantana camara*	Leaves	-	Sharma et al. (8)
Zingiberaceae	*Curcuma caesia Ro xb.*	Rhizome	Ethanol extract	Gupta et al. (2)
	Zingiber officinale	Whole plant	Hydroethanolic crude extracts	Nguta et al. (1)

Table 3. Active anti-Bovis molecules of plant origin

Family	Botanical name/ Common name	Plant parts	Plant derivatives	References
Eucalyptus camaldulensis	Myrtaceae/ red gum	Leaves	Methanolic crude extract	Gemechu et al. (4)
Ocimum basilicum	Lamiaceae/Basil	Seeds	Methanolic crude extract	Gemechu et al. (4)
Croton macrostachyus	Euphorbiaceae/croton	Leaves	Methanolic crude extract	Gemechu et al. (4)
Calpurnia aurea	Leguminosae/ Cape laburnum	Roots	Methanolic crude extract	Gemechu et al. (4)
Artemisia abyssinica	Asteraceae	Leaves	Methanolic crude extract	Gemechu et al. (4)
Solanum torvum (unripe fruit)	Solanaceae/ Turkey Berry	Unripe fruits	Microplate alamar blue assay (MABA)	Nguta et al. (10)
Pterodon emarginatus	Fabaceae/ Sucupira-branca	Fruits, which contained seeds	Hexane extract	Nguta et al. (10)

Terpenoids

Terpenoids form a large and structurally varied category of compounds found in medicinal plants. They exhibit antimicrobial activity by disrupting microbial membranes, inhibiting microbial enzymes and interfering with cellular functions. Known for their strong antibacterial properties, terpenoids are often used as natural preservatives. Notable examples include thymol and carvacrol (14).

Phenolic compounds

Phenolic compounds, such as tannins and phenolic acids, are widely distributed in medicinal plants. They exhibit antimicrobial activity by disrupting microbial membranes, inhibiting microbial enzymes and interfering with microbial metabolism. For instance, tannins can precipitate microbial proteins and enzymes, rendering them inactive (15). The mechanisms of action of these bioactive metabolites vary depending on the target microorganism and the specific compound involved. They can compromise microbial cell membranes, inhibit essential enzymes required for microbial growth and metabolism, obstruct protein synthesis and DNA replication and induce oxidative stress in microbes. It is significant to note that the effectiveness of medicinal plants and their active metabolites can be influenced by factors such as plant species, plant parts used, extraction methods and formulations. Further, research is needed to fully understand the mechanisms of these active metabolites and their potential applications in treating specific diseases.

Humans have long used medicinal plants in various forms to cure tuberculosis. In Ethiopia, traditional medicinal plants such as *Croton macrostachyus, Allium sativum* and *Myrsine africana* are commonly utilized for tuberculosis treatment, often administered orally using preparations made from fresh plant materials. However, the effectiveness of many of these plants lacks scientific validation, emphasizing the need for further research and clinical testing (28). Similarly, in South Africa's Limpopo Province, traditional healers use plants such as *Artemisia afra* and *Eucomis pallidiflora* to treat tuberculosis. These remedies are primarily derived from leaves and roots, with their therapeutic potential supported by antimicrobial properties or ethnomedicinal evidence from other regions (29). Studies indicate the plant families like Leguminosae (Fabaceae) and Compositae (Asteraceae) include numerous species traditionally used for tuberculosis treatment, summarized in Table 2.

Challenges in the development and utilization of medicinal plants as anti-mycobacterial agents

The development and utilization of medicinal plants as anti-mycobacterial agents encounter several challenges, as outlined by various studies. One major challenge is establishing standardized extraction protocols to ensure consistent quality and concentration of bioactive components (30). Another key issue is identifying the specific bioactive components responsible for anti-mycobacterial activity within the complex plant extract mixtures (31). Ensuring the safety of these medicinal plants is also crucial, as they must exhibit minimal toxicity and side effects (32). The emergence of drug-resistant *Mycobacterium tuberculosis* strains further complicates treatment, necessitating an evaluation of whether plant-derived compounds remain effective against these resistant variants (31). Moreover, investigating the potential synergy between plant-derived compounds and conventional antibiotics is essential, as these interactions may enhance treatment efficacy while minimizing adverse effects (30). To validate the safety and therapeutic potential of plant-derived compounds in humans, well-structured randomized controlled trials are necessary (31). Regulatory approval processes for such plant-derived products pose other challenges, such as their complexity (31). Protecting Further, safeguarding intellectual property rights for plant-derived compounds is vital to encourage investment in research and development (31). Another critical consideration is the sustainable and scalable sourcing of medicinal plants, ensuring that ecosystems and local ecosystems and local communities are not negatively impacted (33). Finally, increasing awareness and education among healthcare professionals and the public about the benefits and limitations of medicinal plants as anti-mycobacterial agents is vital for successful integration into modern medicine (33).

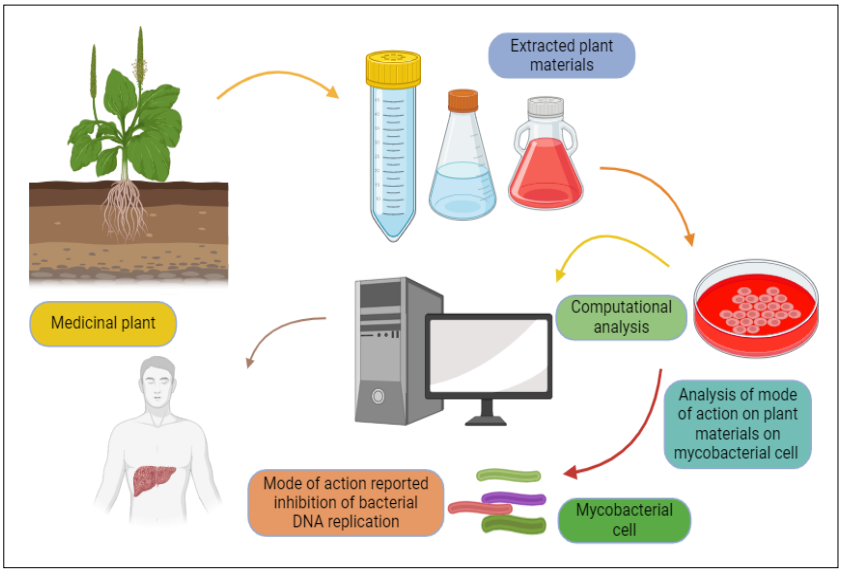

Fig. 3. Medicinal plant of anti-mycobacterial activity against *Mycobacterium tuberculosis.*

Conclusion

Researcher indicates that plants serve as a valuable source of anti-mycobacterial agents, with plant-derived drugs playing a crucial role in combating drug resistance. Major studies focus on identifying plant metabolites with bioactive properties and exploring crude plant extracts with anti-mycobacterial potential. There is an urgent requirement for renewed interest from both academia and indigenous pharmaceutical industries in plant-derived drug development. Furthermore, studies on efficacy, toxicity and safety should be initiated to accelerate the discovery of new anti-TB treatments. This could potentially lead to the development of more effective plant-based medications. In India and other countries, several laboratories are actively engaged in identifying bioactive compounds from natural plant-based anti-tuberculosis products, with early findings showing promising results.

Acknowledgements

The corresponding author is thankful to Sanskriti University, Mathura 281 401 for providing the necessary facilities and support for writing this review.

Authors' contributions

UG, MK, DD and NJ drafted this manuscript. KKC did the conception and design of this manuscript. KKC, SS and KDR performed the literature search and synthesis. DS, KKC, ST, SYM, NK, AKS and ANY helped in the revision of this manuscript. UG, AKP and MK created figures and tables. DD and DS participated in referencing. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None

References

1. Nguta JM, Appiah-Opong R, Nyarko AK, Yeboah-Manu D, Addo PGA, Otchere ID, et al. In-vitro antimycobacterial and cytotoxic data on medicinal plants used to treat tuberculosis. Data Brief. 2016;7:1124–30. https://doi.org/10.1016/j.dib.2016.03.088
2. Gupta VK, Kaushik A, Chauhan DS, Ahirwar RK, Sharma S, Bisht D. Anti-mycobacterial activity of some medicinal plants used traditionally by tribes from Madhya Pradesh, India for treating tuberculosis related symptoms. J Ethnopharmacol. 2018;227:113–20. https://doi.org/10.1016/j.jep.2018.08.031
3. Mohamad S, Ismail NN, Parumasivam T, Ibrahim P, Osman HA, Wahab H. Antituberculosis activity, phytochemical identification of *Costus speciosus* (J. Koenig) Sm., *Cymbopogon citratus* (DC. Ex Nees) stapf. and *Tabernaemontana coronaria* (L.) wild. and their effects on the growth kinetics and cellular integrity of mycobacteria. BMC Complement Altern Med. 2018;18:5. https://doi.org/10.1186/s12906-017-2077-5
4. Gemechu A, Giday M, Worku A, Ameni G. *In-vitro* anti-mycobacterial activity of selected medicinal plants against Mycobacterium tuberculosis and Mycobacterium bovis strains. BMC Complement Altern Med. 2013;13:291. https://doi.org/10.1186/1472-6882-13-291
5. Jamkhande PG, Ghante MH, Barde SR, Ajgunde BR. Antimycobacterial, antimicrobial, antioxidant activities and in-silico pass investigations of root fractions and extract of *Cordia dichotoma* Forst. Orient Pharm Exp Med. 2019;19:485–96. https://doi.org/10.1007/s13596-019-00399-5
6. Russo EB, Marcu J. Chapter Three - Cannabis pharmacology: the usual suspects and a few promising leads. Vol. 80: Adv Pharmacol Academic Press Inc; 2017. p. 67–134. https://doi.org/10.1016/bs.apha.2017.03.004
7. Singh R, Hussain S, Verma R, Sharma P. Anti-mycobacterial screening of five Indian medicinal plants and partial purification of active extracts of Cassia sophera and Urtica dioica. Asian Pac J Trop Med. 2013;6:366–71. https://doi.org/10.1016/S1995-7645(13)60040-1
8. Sharma P, Goyal RK, Nandave M. A review: prevention, treatment and management of tuberculosis through combinational approaches of different Indian systems of medicine. Drug Res (Stuttg). 2020;70:65–70. https://doi.org/10.1055/a-1078-1087
9. Fernandez CMM, Baldin VP, Ieque AL, Bernuci KZ, Almeida RT, Valone LM, et al. Anti-mycobacterium tuberculosis activity of dichloromethane extract of Piper corcovadensis (Miq.) C. DC. roots and isolated compounds. Ind Crops Prod. 2019;131:341–47. https://doi.org/10.1016/j.indcrop.2019.01.064
10. Nguta JM, Appiah-Opong R, Nyarko AK, Yeboah-Manu D, Addo PGA, Otchere ID, et al. In-vitro antimycobacterial activity and toxicity of eight medicinal plants against pathogenic and nonpathogenic mycobacterial strains. Vol. 5: In: Proceedings of the Int J Mycobacteriology; Elsevier Ltd, December; 2016. p. S106–07. https://doi.org/10.1016/j.ijmyco.2016.05.004
11. Dey P, Kundu A, Kumar A, Gupta M, Lee BM, Bhakta T, et al. Analysis of alkaloids (indole alkaloids, isoquinoline alkaloids, tropane alkaloids). In: Recent Adv Nat Prod Anal; 2020. p. 505–67. https://doi.org/10.1016/b978-0-12-816455-6.00015-9
12. Cushnie TP, Lamb AJ. Antimicrobial activity of flavonoids. Int J Antimicrob Agents. 2005;26(5):343–56. https://doi.org/10.1016/j.ijantimicag.2005.09.002
13. Masyita A, Mustika SR, DwiAstuti A, Yasir B, RahmaRumata N, Emran Tb, et al. Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. Food Chem. 2022;13:100217. https://doi.org/10.1016/j.fochx.2022.100217
14. Miklasińska-Majdanik M, Kępa M, Wojtyczka RD, Idzik D, Wąsik TJ. Phenolic compounds diminish antibiotic resistance of Staphylococcus aureus clinical strains. IJERPH. 2018;15(10):2321. https://doi.org/10.3390/ijerph15102321
15. Quémard A, Lacave C, Lanéelle G. Isoniazid inhibition of mycolic acid synthesis by cell extracts of sensitive and resistant strains of *Mycobacterium aurum*. Antimicrob Agents Chemother. 1991;35(6):1035–39. https://doi.org/10.1128/AAC.35.6.1035
16. Campbell EA, Korzheva N, Mustaev A, Murakami K, Nair S, Goldfarb A, et al. Structural mechanism for rifampicin inhibition of bacterial RNA polymerase. Cell. 2001;104(6):901–12. https://doi.org/10.1016/s0092-8674(01)00286-0
17. Goude R, Amin AG, Chatterjee D, Parish T. The arabinosyltransferase EmbC is inhibited by ethambutol in Mycobacterium tuberculosis. Antimicrob Agents Chemother. 2009;53(10):4138–46. https://doi.org/10.1128/AAC.00162-09
18. Garvin RT, Biswas DK, Gorini L. The effects of streptomycin or dihydrostreptomycin binding to 16S RNA or to 30S ribosomal subunits. Proc Natl Acad Sci USA. 1974;71(10):3814–18. https://doi.org/10.1073/pnas.71.10.3814
19. Zhang Y, Shi W, Zhang W, Mitchison D. Mechanisms of

pyrazinamide action and resistance. Microbiol Spectr. 2014;2(4):1–12. https://doi.org/10.1128/microbiolspec.MGM2-0023-2013

20. Lin Y, Li Y, Zhu N, Han Y, Jiang W, Wang Y, et al. The antituberculosis antibiotic capreomycin inhibits protein synthesis by disrupting the interaction between ribosomal proteins L12 and L10. Antimicrob Agents Chemother. 2014;58(4):2038–44. https://doi.org/10.1128/AAC.02394-13
21. Sagbo IJ, Hussein AA. Are plants used as a combating strategy against tuberculosis in the Mpumalanga province, South Africa? Appl Sci. 2023;13(8):5008. https://doi.org/10.3390/app13085008
22. Zheng J, Rubin EJ, Bifani P, Mathys V, Lim V, Au M, et al. para-Aminosalicylic acid is a prodrug targeting dihydrofolate reductase in Mycobacterium tuberculosis. J Biol Chem. 2013;288(32):23447–56. https://doi.org/10.1074/jbc.M113.475798
23. De Chiara C, Homšak M, Prosser GA, Douglas HL, Garza-Garcia A, Kelly G, et al. D-cycloserine destruction by alanine racemase and the limit of irreversible inhibition. Nat Chem Biol. 2020;16(6):686–94. https://doi.org/10.1038/s41589-020-0498-9
24. North E J, Jackson M, Lee RE. New approaches to target the mycolic acid biosynthesis pathway for the development of tuberculosis therapeutics. Curr Pharm Des. 2021;20(27):4357–78. https://doi.org/10.2174/1381612819666131118203641
25. Shams WE, Evans ME. Guide to selection of fluoroquinolones in patients with lower respiratory tract infections. Drugs. 2005;65(7):949–91. https://doi.org/10.2165/00003495-200565070-00004
26. Field SK. Bedaquiline for the treatment of multidrug-resistant tuberculosis: great promise or disappointment? Ther Adv Chronic Dis. 2015;6(4):170–84. https://doi.org/10.1177/2040622315582325
27. Khoshnood S, Taki E, Sadeghifard N, Kaviar VH, Haddadi MH, Farshadzadeh Z, et al. Mechanism of action, resistance, synergism and clinical implications of delamanid against multidrug-resistant Mycobacterium tuberculosis. Front Microbiol. 2021;12:717045. https://doi.org/10.3389/fmicb.2021.717045
28. Getachew S, Medhin G, Asres A, Abebe G, Ameni G. Traditional medicinal plants used in the treatment of tuberculosis in Ethiopia: A systematic review. Heliyon. 2022;8(5):e09478. https://doi.org/10.1016/j.heliyon.2022.e09478
29. Semenya SS, Maroyi A. Medicinal plants used for the treatment of tuberculosis by Bapedi traditional healers in three districts of the Limpopo Province, South Africa. Afr J Tradit Complement Altern Med. 2012;10(2):316–23. https://doi.org/10.4314/ajtcam.v10i2.17
30. Gupta VK, Kumar MM, Bisht D, Kaushik A. Plants in our combating strategies against Mycobacterium tuberculosis: progress made and obstacles met. Pharm Biol. 2017;55(1):1536–44. https://doi.org/10.1080/13880209.2017.1309440
31. Gautam S, Qureshi KA, Jameel PSB, Dhanasekaran S, Aspatwar A, Parkkila S, et al. Medicinal plants as therapeutic alternatives to combat Mycobacterium tuberculosis: A Comprehensive Review. Antibiotics. 2023;12(3):541. https://doi.org/10.3390/antibiotics12030541
32. Dzoyem JP, Aro AO, McGaw LJ, Eloff JN. Antimycobacterial activity against different pathogens and selectivity index of fourteen medicinal plants used in southern Africa to treat tuberculosis and respiratory ailments. S Afr J Bot. 2016;102:70-74. ISSN 0254-6299. https://doi.org/10.1016/j.sajb.2015.08.002
33. Xu Y, Liang B, Kong C, Sun Z. Traditional medicinal plants as a source of antituberculosis drugs: A system review. BioMed Res Int. 2021;9910365. https://doi.org/10.1155/2021/9910365

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

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

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc
See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

Publisher information: Plant Science Today is published by HORIZON e-Publishing Group with support from Empirion Publishers Private Limited, Thiruvananthapuram, India.