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Herbal Medicines in the Management of Tuberculosis: Ethnobotanical Insights and Pharmacological Perspectives

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Abstract

Background: Tuberculosis (TB) remains a major global public health challenge, further aggravated by the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Mycobacterium tuberculosis* strains. The limitations of conventional anti-TB therapy, including prolonged treatment duration, adverse drug reactions, and increasing antimicrobial resistance, have prompted interest in alternative therapeutic approaches, particularly plant-derived medicines. **Aim:** This review critically evaluates ethnomedicinal plants used in tuberculosis management, their phytochemical constituents, antimycobacterial mechanisms, pharmacological evidence, and their potential role in combating MDR/XDR-TB. **Methods:** A comprehensive literature review was conducted using published articles retrieved from electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar. Relevant studies on medicinal plants, phytochemicals, antimycobacterial activity, ethnomedicine, and tuberculosis published in peer-reviewed journals were critically analysed. **Results:** Numerous medicinal plants possess diverse bioactive phytochemicals, including alkaloids, flavonoids, terpenoids, phenolics, and glycosides, which exhibit significant antimycobacterial, immunomodulatory, antioxidant, and anti-inflammatory activities. Several plant-derived compounds have demonstrated promising inhibitory effects against drug-sensitive as well as MDR/XDR *M. tuberculosis* strains, highlighting their potential as complementary therapeutic agents. **Conclusion:** Ethnomedicinal plants represent a valuable source of novel bioactive compounds for tuberculosis management. Integrating phytopharmacological evidence with modern drug discovery approaches may facilitate the development of safer and more effective adjunctive therapies against drug-resistant tuberculosis. However, further preclinical, clinical, and translational studies are required to validate their efficacy and safety.

Major Findings: Medicinal plants rich in bioactive phytochemicals exhibit promising antimycobacterial activity against MDR/XDR *M. tuberculosis*. This review highlights their therapeutic potential and emphasises the need for further translational research to support their integration into tuberculosis management.

Keywords: Antimycobacterial Activity, Drug-resistant Tuberculosis, Ethnobotanical Knowledge, Herbal Medicine, *Mycobacterium tuberculosis,* Phytochemicals, Tuberculosis

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1. Introduction

1.1 Historical Perspectives

Tuberculosis (TB) is among the ancient recognised contagious diseases, with its origins traceable to ancient civilisations. Paleopathological examinations have identified characteristic tuberculous lesions in Egyptian mummies dating back to approximately 2400 BCE, providing some of the earliest physical evidence of the disease[1]. Comparable skeletal findings from

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prehistoric populations in Europe, South America and Asia further demonstrate that TB has coexisted and evolved alongside humans across millennia[2]. Early descriptions of illnesses resembling TB appear in classical medical literature from India, China and Greece - including the *Charaka Samhita, Huangdi Neijing* and the writings of Hippocrates - who used the term phthisis or "consumption" to describe the progressive wasting characteristic of the condition[3]. In ancient Indian medical tradition, the disease was referred to as "*Rajayakshma*" or "King's Evil", and *Ayurvedic* practitioners documented herbal formulations containing plants such as *Withania somnifera*, *Curcuma longa* and *Piper longum* for symptom management[4]. Conventional medical systems, including Traditional Chinese Medicine (TCM), *Siddha, Ayurveda* and *Unani,* have long used plant-based therapies for respiratory and pulmonary illnesses, including conditions resembling TB[5].

A primary shift in the scientific understanding of TB occurred in the late 19th century, when Robert Koch identified *M. tuberculosis* in 1882, conclusively establishing its bacterial aetiology and laying the foundation for modern diagnostic and therapeutic approaches[6]. The subsequent development of key anti-tubercular drugs - including streptomycin, isoniazid and rifampicin - revolutionised TB treatment and dramatically reduced mortality during the 20th century[7]. Despite these advances, the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains in recent decades has renewed global concern. As a result, interest has intensified in exploring traditional medicinal knowledge and ethnobotanical resources as complementary or alternative avenues for TB drug discovery[8,9].

1.2 Limitations of Current Anti-tuberculosis Therapy

Tuberculosis (TB) is the foremost annihilating transmissible disease globally. It is caused by *M. tuberculosis*, a creeping intracellular pathogen that predominantly targets the lungs but is capable of infecting multiple organs and remains one of the leading infectious causes of morbidity and mortality worldwide. Although effective chemotherapeutic options have been available for decades, it continues to be a major public health issue. According to the WHO Global Tuberculosis Report 2024, an estimated 1.06 crore new TB cases and 13 lakh deaths happened world-wide in 2023, making it the primary cause of mortality from a single infective pathogen after COVID-19. The rise of multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains has further complicated disease management and negatively impacted treatment outcomes[8].

Despite the availability of standardised chemotherapy for decades, the effective management of TB continues to be hindered by several major limitations associated with current anti-tuberculosis therapy. The standard first-line anti-TB regimen for drug-susceptible tuberculosis consists of isoniazid, rifampicin, pyrazinamide and ethambutol, requiring treatment durations of 6–9 months, which frequently contribute to poor patient compliance, treatment interruption and therapeutic failure[10]. Non-adherence significantly contributes to disease relapse, continued transmission and the emergence of drug-resistant strains.

Another major concern associated with conventional anti-TB therapy is the occurrence of adverse drug reactions. Hepatotoxicity, peripheral neuropathy, gastrointestinal disturbances, hypersensitivity reactions and optic neuritis are commonly reported complications, particularly with prolonged use of first-line agents such as isoniazid and rifampicin[11]. These adverse effects often necessitate treatment modification or discontinuation, further compromising clinical outcomes and increasing healthcare burden. The emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) has further complicated global TB control efforts. MDR-TB is defined as resistance to at least isoniazid and rifampicin, whereas XDR-TB includes additional resistance to fluoroquinolones and second-line injectable agents or other key reserve drugs. These resistant forms require longer, more expensive, and more toxic treatment regimens with comparatively lower success rates[4]. Although newer regimens such as BPaLM (bedaquiline, pretomanid, linezolid and moxifloxacin) have improved therapeutic outcomes, accessibility and affordability remain major challenges, particularly in low- and middle-income countries[8,12].

Furthermore, the current drug discovery pipeline for tuberculosis remains slow and limited. The development

of new synthetic anti-TB agents is associated with high cost, long timelines and frequent clinical failures. In addition, many existing drugs primarily target bacterial elimination without adequately addressing host immune dysfunction, inflammation and oxidative stress that contribute significantly to TB pathogenesis and disease progression[13]. This has prompted growing interest in host-directed therapies and adjunctive treatment strategies. These limitations highlight the urgent need for safer, more effective, affordable and multi-targeted therapeutic alternatives. In this context, medicinal plants and herbal medicines have gained considerable attention due to their rich phytochemical diversity and demonstrated antimycobacterial, immunomodulatory, antioxidant and anti-inflammatory properties. Integrating ethnobotanical knowledge with modern pharmacological research may provide promising avenues for the development of novel adjunctive or alternative therapies for tuberculosis management[13,14].

Ethnobotanical investigations from TB-endemic regions have identified a wide range of medicinal plants with worthy antimycobacterial, anti-inflammatory, antioxidant and immunomodulatory activities[15]. These therapeutic effects are largely associated with alkaloids, flavonoids, terpenoids, phenolics and tannins that can disrupt mycobacterial cell wall biosynthesis, modulate host immune responses and mitigate oxidative stress[16]. Several plant-derived compounds, such as curcumin, piperine, berberine and quercetin, have shown significant inhibitory effects towards both drug-susceptible and drug-resistant *M. tuberculosis* strains, underscoring their potential as lead candidates for anti-Tubercular drug development[7]. In parallel, advances in molecular docking, *in silico* ADMET analysis, and pharmacokinetic modelling have improved understanding of how these phytoconstituents interact with key *M. tuberculosis* targets, including InhA, DprE1 and RNA polymerase[17].

The combination of traditional ethnobotanical expertise with contemporary pharmacological and computational methodologies offers a promising framework for identifying and developing novel plant-based anti-TB therapeutics. Accordingly, this review synthesises information on medicinal plants traditionally employed in TB management, highlights their bioactive constituents and pharmacological profiles and outlines mechanistic pathways that may contribute to their antimycobacterial effects. The review also discusses the opportunities and challenges associated with incorporating herbal medicines as adjunctive or alternative options in TB therapy[10,18].

1.3 Types of Tuberculosis

Tuberculosis, inception by *M. tuberculosis*, dispense in diverse clinical and pathological forms that are shaped by host immune status, the site of infection and pathogen virulence. Clinically, TB is generally categorised into pulmonary and extrapulmonary, with further sub-classifications based on disease activity and patterns of drug resistance[19,20]. Tuberculosis can be classified into pulmonary, extrapulmonary, latent, miliary and drug-resistant forms, as shown in Figure 1.

1.3.1 Pulmonary Tuberculosis (PTB)

Pulmonary tuberculosis (PTB) is the most common clinical form, representing approximately 70–80% of all TB cases worldwide. It affects the lungs and is transmitted through infectious aerosolised droplets. Clinical manifestations include persistent cough, sputum production, haemoptysis, chest discomfort and unintentional weight loss. Confirmation is by phlegm smear microscopy, radiological assessment, GeneXpert MTB/RIF testing and mycobacterial culture[1]. Pulmonary tuberculosis (PTB), the most common and infectious form of tuberculosis, primarily affects the lungs and is characterised by chronic cough, sputum production, hemoptysis, chest pain, and progressive pulmonary tissue damage, as illustrated in Figure 2[19,21].

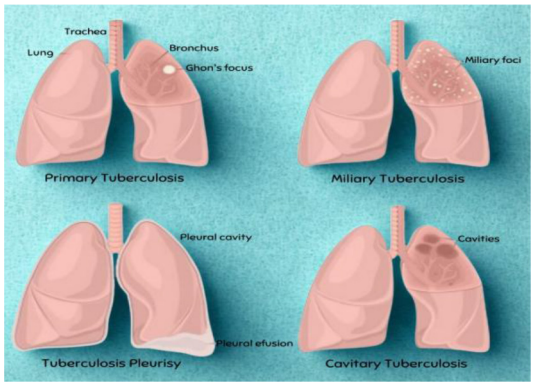


Figure 1. Clinical classification of tuberculosis based on site of infection, disease progression, and drug resistance patterns.

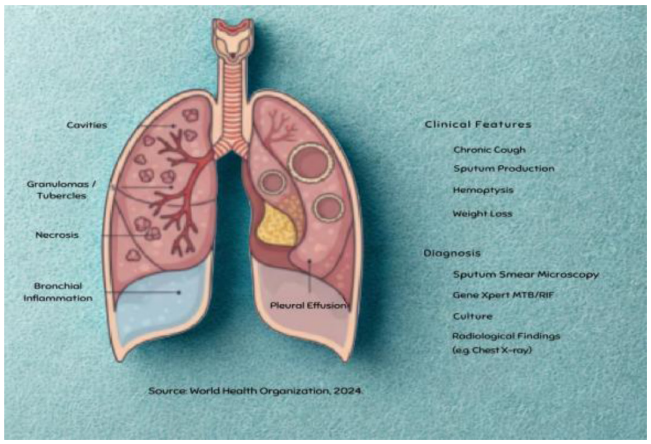


Figure 2. Clinical presentation and pathological features of Pulmonary Tuberculosis (PTB) showing lung involvement, chronic cough, sputum production, hemoptysis, and progressive pulmonary tissue damage caused by *M. tuberculosis*.

1.3.2 Extrapulmonary Tuberculosis (EPTB)

Extrapulmonary tuberculosis (EPTB) refers to infection involving sites outside the lungs. It typically arises from hematogenous or lymphatic spread of *M. tuberculosis*. Most common forms include tuberculous lymphadenitis, pleural TB, tuberculous meningitis, skeletal TB (such as Pott's disease) and genitourinary TB. Although it is generally less infectious than PTB, it contributes substantially to overall morbidity and mortality, particularly among immunocompromised individuals, including those living with HIV[11]. Extrapulmonary tuberculosis (EPTB) refers to the spread of *M. tuberculosis* beyond the lungs to other organs such as lymph nodes, pleura, meninges, bones, genitourinary tract and abdominal organs, leading to diverse clinical manifestations depending on the site involved, as shown in Figure 3[19,21].

1.3.3 Miliary Tuberculosis

Miliary tuberculosis is a disseminated form of TB resulting from extensive hematogenous spread of *M. tuberculosis*, leading to numerous tiny, millet seed–like lesions across multiple organs, including the lungs, liver and spleen. Clinically, associated with severe general symptoms such as persistent fever, respiratory distress and hepatosplenomegaly. This occurs more frequently in individuals who are immunocompromised or malnourished[19].

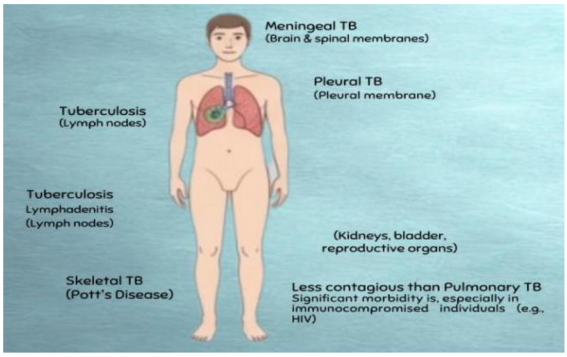


Figure 3. Clinical manifestations and common anatomical sites of Extrapulmonary Tuberculosis (EPTB), illustrating the spread of *M. tuberculosis* beyond the lungs to lymph nodes, pleura, meninges, bones, genitourinary system and abdominal organs.

1.3.4 Latent Tuberculosis Infection (LTBI)

Latent tuberculosis infection (LTBI) is characterised by a continuous immune reaction to *M. tuberculosis* antigens without clinical manifestations of progressive disease. Roughly one-quarter of the world's population carries LTBI, with a lifetime risk of reactivation ranging from 5–10%, particularly in individuals with compromised immunity and may progress to secondary or post-primary TB. Diagnosis is primarily based on the Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (IGRAs)[22].

1.3.5 Drug-resistant Tuberculosis

The rise of drug-resistant forms of tuberculosis projects an crucial global health challenge. These include:

- Multidrug-resistant TB (MDR-TB): Defined by resistance to at least isoniazid and rifampicin, the two most effective induction therapy anti-TB drugs.
- Pre-extensively drug-resistant TB (pre-XDR-TB): Characterised by rifampicin resistance accompanied by resistance to any fluoroquinolone.
- Extensively drug-resistant TB (XDR-TB): Pronounced by resistance to isoniazid, rifampicin, a fluoroquinolone and at the minimun of one second-line injectable agent like amikacin or capreomycin.
- Totally drug-resistant TB (TDR-TB): Documented in a limited number of cases and defined by resistance to all currently available anti-TB medications[23].

These increasingly resistant phenotypes significantly hinder treatment success and underscore the need to

explore plant-derived antimycobacterial compounds as potential adjunctive or alternative therapeutic options.

1.3.6 Primary and Secondary Tuberculosis

- Primary TB occurs upon the first exposure to the pathogen, often asymptomatic or manifests as a self-limiting illness in individuals with competent immune systems.
- Secondary (Post-primary) TB arises from reactivation of latent infection or reinfection, typically localised in the upper lung lobes with pronounced tissue damage and cavitation.
- In contrast, secondary or post-primary tuberculosis results either from the reactivation of a latent focus or from a new exposure to *M. tuberculosis*. This form typically affects the lung's upper lobes and is characterised by more extensive tissue destruction and cavitary lesions[19].

1.3.7 MDR/XDR-TB Crisis

The global rise of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) has become one of the most serious obstacles to effective tuberculosis control. Drug-resistant TB develops primarily due to spontaneous genetic mutations in *M. tuberculosis*, which are further amplified by inappropriate antibiotic use, poor treatment adherence, incomplete therapeutic regimens, delayed diagnosis and inadequate public health infrastructure[24]. These resistant strains significantly reduce treatment success rates and increase both morbidity and mortality worldwide.

Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to at least rifampicin and isoniazid, the two most potent first-line anti-tubercular drugs. Extensively drug-resistant tuberculosis (XDR-TB) represents a more severe form, characterised by MDR-TB with additional resistance to fluoroquinolones and at least one second-line priority drug, making therapeutic management highly complex[25]. The increasing prevalence of these resistant forms threatens decades of progress achieved in global TB control programs.

According to the World Health Organisation Global Tuberculosis Report 2024, nearly 410,000 new cases of rifampicin-resistant TB (RR-TB) were reported globally in 2023, with a substantial proportion progressing to MDR-TB. Countries with high TB burden continue to face major challenges in early detection, access to rapid molecular diagnostics and implementation of effective treatment strategies[8]. Delayed diagnosis and inappropriate therapy allow continued transmission of resistant strains within communities, particularly in resource-limited settings.

The treatment of MDR/XDR-TB is substantially more difficult than drug-susceptible TB. Conventional second-line regimens often require 18–24 months of therapy and are associated with severe adverse effects such as nephrotoxicity, ototoxicity, myelosuppression and psychiatric disturbances[25]. These prolonged regimens impose a significant financial burden on healthcare systems and reduce patient adherence, thereby further increasing the risk of treatment failure and additional resistance development.

Recent therapeutic advances, including the WHO-recommended BPaLM regimen comprising bedaquiline, pretomanid, linezolid and moxifloxacin, have shown improved treatment outcomes with shorter duration and reduced toxicity. However, limited affordability, restricted availability, and concerns regarding emerging resistance to newer agents remain significant barriers to widespread implementation[8,26]. Moreover, the scarcity of novel anti-TB drugs in the development pipeline emphasises the urgent need for alternative therapeutic approaches.

In this context, plant-derived bioactive compounds have gained increasing scientific attention as potential adjunctive or alternative therapies against MDR/XDR-TB. Several phytochemicals, including curcumin, piperine, berberine, quercetin and flavonoid-rich extracts, have demonstrated inhibitory activity against drug-resistant *M. tuberculosis* strains through mechanisms such as disruption of mycolic acid synthesis, inhibition of efflux pumps, immune modulation and oxidative stress reduction[14]. These findings suggest that medicinal plants may serve both as direct antimycobacterial agents and as supportive host-directed therapies in combating resistant tuberculosis.

Thus, addressing the MDR/XDR-TB crisis requires a multidimensional strategy that integrates improved diagnostics, shorter and safer drug regimens, host-directed therapies and the exploration of ethnobotanically validated medicinal plants for next-generation anti-tubercular drug discovery.

2. Pathogenesis of Tuberculosis

Tuberculosis (TB) is caused principally by *M. tuberculosis*, an intracellular, acid-fast bacillus associated with the *M. tuberculosis* complex (MTBC). The pathogen primarily targets the lungs but can disseminate to other organs, leading to extrapulmonary manifestations. The hallmark of TB pathogenesis is the complex interplay between the host immune response and bacterial survival mechanisms, facilitating *M. tuberculosis* to persist in a latent or active form within the host[27-29].

Recent progress in tuberculosis diagnostics has shifted toward the development of biosensor technologies, nanomaterial-assisted platforms and metabolomics-based detection strategies. These next-generation tools aim to provide higher sensitivity, faster results and improved applicability in point-of-care settings. In parallel, growing interest has been directed toward phytochemical-based biosensors and herbal-derived immunodiagnostic systems, which offer low-cost and environmentally sustainable options for TB detection[20]. The pathogenesis of tuberculosis involves inhalation of *M. tuberculosis*, infection of alveolar macrophages, granuloma formation, immune evasion, latent persistence and eventual progression to active pulmonary or extrapulmonary disease, as illustrated in Figure 4[27-29].

2.1 Infection and Initial Immune Response

Transmission of *M. tuberculosis* happens principally through inhalation of aerosolised droplets coughed out by individuals with active pulmonary TB. After reaching the alveoli, the bacilli are engulfed by alveolar macrophages, which paradoxically act as both host cells and sites for bacterial replication. *M. tuberculosis* employs multiple immune-evasion mechanisms, including resisting reactive oxygen and nitrogen species, blocking phagosome–lysosome fusion and altering host cytokine signalling to promote its survival and persistence[28]. The early stage of tuberculosis begins with inhalation of *M. tuberculosis*, followed by alveolar deposition, phagocytosis by alveolar macrophages, intracellular survival of bacilli and activation of the innate immune response, as illustrated in Figure 5[27,28].

2.2 Granuloma Formation

A main attribute of tuberculosis pathogenesis is the development of granulomas - highly organised immune aggregates consisting primarily of macrophages, T lymphocytes and fibroblasts. These structures function to confine the infection, yet they also create a specialised niche that supports long-term bacterial survival[29]. *M. tuberculosis* actively modulates host immune pathways to maintain this milieu, enabling the pathogen to persist in a latent state and establishing a delicate equilibrium between bacterial dormancy and immune containment.

2.3 Latent and Active Tuberculosis

Nearly 90% of individuals with *M. tuberculosis* infection progress to a latent tuberculosis infection

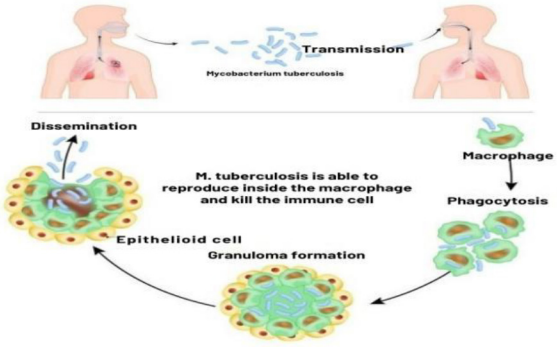


Figure 4. Schematic representation of the pathogenesis of tuberculosis showing inhalation of *M. tuberculosis*, alveolar macrophage infection, granuloma formation, latent persistence, immune evasion and progression to active pulmonary or extrapulmonary disease.

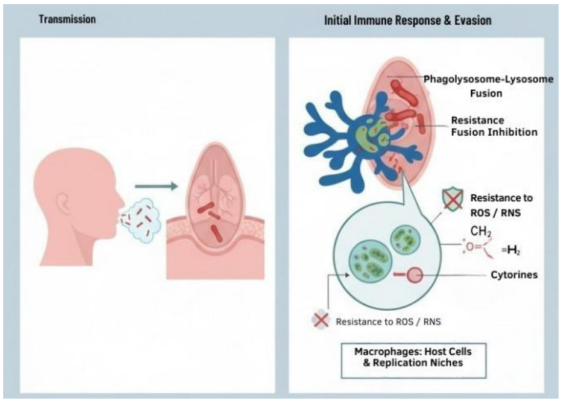


Figure 5. Early infection and initial immune response in tuberculosis showing inhalation of *M. tuberculosis*, alveolar deposition, phagocytosis by alveolar macrophages, intracellular survival, and activation of the host innate immune response.

(LTBI), in which the bacilli persist in a non-replicating or slow-growing state without producing clinical symptoms. This equilibrium can be disrupted when host immunity is compromised - for example, due to HIV co-infection, diabetes or malnutrition—allowing latent organisms to reactivate and cause active disease characterised by pulmonary tissue damage and increased transmissibility[30]. Latent tuberculosis is characterised by the dormant persistence of *M. tuberculosis* without clinical symptoms, whereas active tuberculosis results from reactivation of the infection, leading to symptomatic disease, pulmonary tissue damage and increased transmissibility, as shown in Figure 6[29,30].

2.4 Mechanisms of Drug Resistance

The rise of multidrug-resistant (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) poses a significant obstacle to effective TB control. Resistance typically develops directly from spontaneous chromosomal mutations in genes related to key drug targets, including katG for isoniazid resistance and rpoB for rifampicin resistance. Factors such as poor treatment adherence, incomplete therapeutic courses and suboptimal drug quality further promote the selection and amplification of resistant strains[30]. Drug resistance in tuberculosis develops through genetic mutations in *M. tuberculosis* that alter drug targets, reduce drug permeability, activate efflux pumps and promote the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis, as illustrated in Figure 7[29,30].

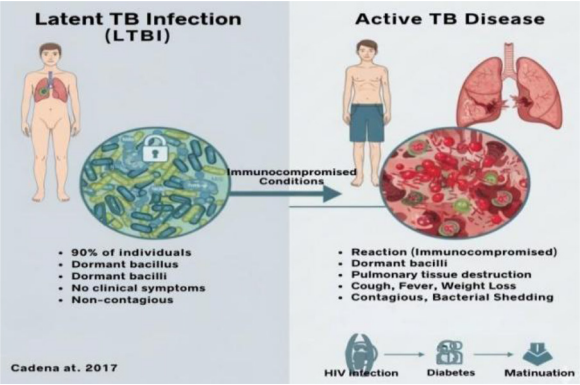


Figure 6. Comparison between latent and active tuberculosis showing dormant persistence of *M. tuberculosis* in latent infection and reactivation leading to symptomatic, transmissible active disease with pulmonary tissue damage.

2.5 Host-pathogen Interaction and Immunomodulation

Mycobacterium tuberculosis strategically modulates host immunity by interfering with toll-like receptor (TLR) signalling, suppressing autophagic pathways, and reshaping cytokine responses—most notably through the downregulation of key pro-inflammatory mediators such as TNF-α and IFN-γ. This ability to evade immune clearance has stimulated growing interest in plant-derived immunomodulators, including *W. somnifera*, *C. longa*, and *T. cordifolia*, which have been shown to enhance macrophage activity and strengthen host defensive responses[7]. *M. tuberculosis* modulates host immunity by suppressing macrophage function, interfering with cytokine signalling and evading immune clearance, while plant-derived immunomodulators may help enhance host defence mechanisms, as illustrated in Figure 8[28,30,31].

3. Current Treatments of Tuberculosis

Despite significant advancements in tuberculosis (TB) diagnosis and prevention, chemotherapy remains the foundation of TB management. The primary goal of current treatment regimens is to eliminate *M. tuberculosis* effectively, prevent relapse and curb the outgrowth of drug-resistant strains. Treatment protocols are stratified based on drug-susceptible TB

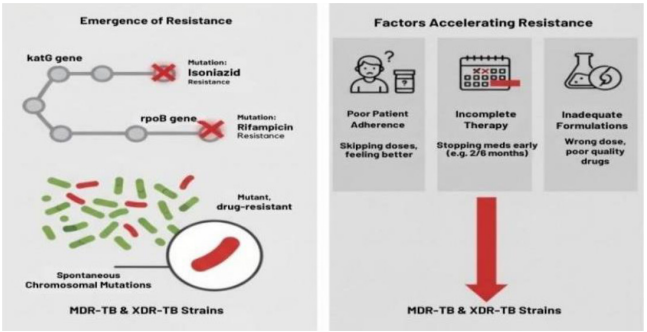


Figure 7. Molecular mechanisms of drug resistance in tuberculosis illustrating genetic mutations in *M. tuberculosis,* altered drug targets, reduced drug permeability, efflux pump activation, and the development of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis.

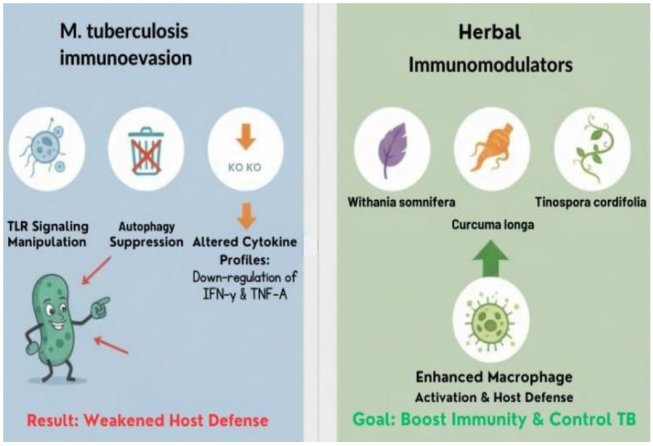


Figure 8. Host–pathogen interaction and immunomodulation in tuberculosis showing immune evasion by *M. tuberculosis*, suppression of macrophage function, altered cytokine responses, and the role of plant-derived immunomodulators in enhancing host defence mechanisms.

(DS-TB) and drug-resistant TB (DR-TB), particularly multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) forms[8].

3.1 First-line Anti-tuberculosis Drugs

The accepted regimen for treating drug-sensitive tuberculosis consists of a six-month treatment incorporating four key first-line drugs such as rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB), collectively referred to as HRZE[24].

- Intensive phase (first 2 months): INH, RIF, PZA and EMB are administered concurrently.
- Continuation phase (subsequent 4 months): Therapy is maintained with INH and RIF.

These agents act on distinct bacterial pathways: isoniazid suppresses mycolic acid synthesis, rifampicin targets RNA polymerase, pyrazinamide disrupts membrane transport and energy production, and ethambutol impedes arabinogalactan formation in the mycobacterial cell wall. The combination regimen minimises the risk of drug resistance and enhances overall treatment efficacy[18].

3.2 Treatment of Drug-resistant Tuberculosis

Drug-resistant tuberculosis remains a significant global health challenge. Multidrug-resistant TB (MDR-TB) is defined by resistance to both rifampicin and isoniazid, whereas extensively drug-resistant TB (XDR-TB) involves additional resistance to fluoroquinolones and at least one second-line injectable drug such as amikacin, kanamycin or capreomycin. Managing MDR/XDR-TB is considerably more challenging, requiring lengthy, expensive and often highly toxic treatment regimens that may extend for 18–24 months.

Updated WHO guidelines advocate for shorter, fully oral regimens built around linezolid, bedaquiline, pretomanid and moxifloxacin (the BPaLM regimen) for eligible MDR and XDR-TB patients. These newer therapeutic combinations have markedly improved clinical outcomes by shortening therapy duration and reducing treatment-related toxicity[8,11].

3.3 Adjunct Therapies and Supportive Approaches

Adjunctive strategies, particularly host-directed therapies (HDTs) and immune-modulating agents, are gaining attention for their potential to enhance mycobacterial clearance and regulate inflammatory responses. Compounds such as N-acetylcysteine, vitamin D and omega-3 fatty acids have demonstrated the ability to strengthen host immunity. In addition, plant-based immunomodulators including *T. cordifolia*, *C. longa* and *W. somnifera* have shown encouraging results in preclinical models, where they appear to augment antimicrobial defences and attenuate oxidative stress[9].

3.4 Challenges in Current TB Therapy

Although current chemotherapeutic regimens have markedly improved TB outcomes, several challenges remain. The prolonged duration of therapy often contributes to suboptimal adherence, while adverse drug effects, including hepatotoxicity and gastrointestinal disturbances, further complicate management. Incomplete or inconsistent treatment fosters the outgrowth of drug-resistant strains, and existing programs show limited effectiveness against Latent Tuberculosis Infection (LTBI). These constraints highlight the need for innovative therapeutic options, particularly plant-derived bioactive molecules that may enhance the activity of standard drugs or provide scaffolds for developing new antitubercular agents[26].

Increasingly, the convergence of conventional ethnomedicinal knowledge with contemporary

pharmacological research is opening new avenues for identifying compounds with antimycobacterial and immunomodulatory properties. This progression—from long-standing herbal practices to contemporary drug development—underscores the sustained relevance of plant-based interventions in advancing tuberculosis treatment.

4. Need for Plant-based Alternatives

The growing limitations of conventional anti-tuberculosis therapy, together with the increasing burden of multidrug-resistant and extensively drug-resistant tuberculosis (MDR/XDR-TB), have intensified the search for safer, more effective and affordable therapeutic alternatives. Although existing anti-TB regimens remain the cornerstone of treatment, their prolonged duration, serious adverse effects, high treatment costs and declining efficacy against resistant strains highlight the urgent need for novel therapeutic strategies[18,25]. In many low- and middle-income countries where tuberculosis remains highly prevalent, access to advanced treatment regimens is often restricted, further emphasising the importance of accessible and sustainable interventions.

Medicinal plants have served as an essential component of healthcare systems for centuries and continue to play a major role in disease management across Asia, Africa and South America. Traditional systems of medicine such as *Ayurveda, Siddha, Unani*, Traditional Chinese Medicine (TCM) and African ethnomedicine have long employed plant-based remedies for respiratory disorders and chronic infections resembling tuberculosis[14]. These remedies are often used not only for symptom relief but also for strengthening host immunity, improving nutritional status and supporting recovery from prolonged illness.

Plant-based medicines are particularly attractive because they contain a wide variety of bioactive phytochemicals such as alkaloids, flavonoids, terpenoids, phenolics, tannins, saponins and glycosides that possess multiple pharmacological activities relevant to tuberculosis management. Several of these compounds exhibit direct antimycobacterial effects by inhibiting mycolic acid synthesis, disrupting bacterial cell wall integrity, interfering with nucleic acid replication and suppressing essential metabolic pathways in *M. tuberculosis*[13]. In addition, many phytoconstituents demonstrate immunomodulatory, antioxidant and anti-inflammatory properties that may help reduce tissue damage and improve host defence mechanisms during infection.

Several medicinal plants, including *C. longa*, *A. sativum*, *T. cordifolia*, *W. somnifera*, *O. sanctum* and *A. vasica*, have shown promising *in vitro* and *in vivo* anti-tubercular activity. Curcumin, piperine, berberine, quercetin and allicin are among the most extensively studied phytochemicals demonstrating inhibitory effects against both drug-sensitive and drug-resistant strains of *M. tuberculosis*[34]. Some plant-derived compounds also enhance the efficacy of standard anti-TB drugs through synergistic interactions, improved drug bioavailability and efflux pump inhibition, thereby offering potential as adjunctive therapies[9].

Another major advantage of herbal medicines lies in their potential for multi-targeted therapeutic action. Unlike many synthetic drugs that act on a single molecular target, phytochemicals often influence multiple biological pathways simultaneously, which may reduce the likelihood of resistance development and improve overall therapeutic outcomes[33]. This multi-mechanistic approach is particularly valuable in complex diseases such as tuberculosis, where both pathogen eradication and host immune regulation are critical.

Recent advances in molecular docking, network pharmacology, metabolomics and *in silico* ADMET analysis have further strengthened the scientific basis for plant-based anti-TB drug discovery. These modern tools enable the identification of active phytoconstituents and their interactions with key mycobacterial targets such as InhA, DprE1, KatG and RNA polymerase, thereby bridging traditional ethnobotanical knowledge with contemporary pharmacological validation[34].

Therefore, plant-based alternatives represent a promising and scientifically relevant approach for the development of novel anti-tubercular therapies. Integrating ethnobotanical evidence with modern pharmacological and clinical research may contribute significantly to overcoming current therapeutic limitations and addressing the global challenge of tuberculosis.

5. Ethnobotanical Importance

Ethnobotany plays a crucial role in the discovery and development of plant-based therapeutics for tuberculosis (TB), particularly in regions where traditional medicine remains an integral part of primary healthcare. Ethnobotanical knowledge refers to the systematic understanding of how indigenous communities use plants for the prevention, treatment and management of diseases. In the context of TB, this knowledge provides valuable leads for identifying medicinal plants with potential antimycobacterial, immunomodulatory and symptom-relieving properties[15].

Tuberculosis has been recognised since ancient times, and long before the advent of modern chemotherapy, various traditional medical systems employed herbal remedies for conditions resembling pulmonary consumption or chronic respiratory infections. Classical systems such as *Ayurveda, Siddha, Unani*, Traditional Chinese Medicine (TCM) and African indigenous medicine have documented the use of numerous medicinal plants for chronic cough, fever, hemoptysis, weight loss, fatigue and respiratory weakness—symptoms commonly associated with TB[37]. In *Ayurveda*, the condition resembling tuberculosis was described as "*Rajayakshma*" and herbal formulations containing *W. somnifera*, *C. longa*, *P. longum* and *T. cordifolia* were widely recommended for strengthening vitality and restoring immune balance[35].

Ethnobotanical investigations conducted in TB-endemic regions of Asia, Africa and South America have identified more than 200 plant species traditionally used in tuberculosis management. Commonly reported plants include *A. vasica*, *A. sativum*, *O. sanctum*, *Glycyrrhiza glabra*, *Warburgia salutaris*, *Sutherlandia frutescens*, *Nigella sativa* and *Eucalyptus globulus*[36].

These plants are often administered as decoctions, infusions, powders, tinctures or inhalational preparations, depending on regional practices and cultural beliefs. The importance of ethnobotanical documentation lies not only in preserving indigenous medical knowledge but also in guiding scientific validation and drug discovery. Many modern drugs have originated from traditional medicinal knowledge, and ethnobotanical leads significantly improve the probability of identifying pharmacologically active compounds compared to random screening approaches[37].

For TB, plants selected through ethnobotanical surveys have shown higher rates of antimycobacterial activity against *M. tuberculosis*, supporting the reliability of traditional knowledge as a starting point for pharmacological research. In addition to direct antimicrobial effects, ethnomedicinal plants often provide supportive therapeutic benefits by reducing inflammation, enhancing appetite, improving nutritional status, alleviating chronic cough, and strengthening host immunity. This holistic therapeutic approach is particularly important in tuberculosis, where both pathogen eradication and restoration of host health are essential for successful recovery[14].

Furthermore, in rural and resource-limited communities with restricted access to modern healthcare facilities, medicinal plants continue to serve as affordable and culturally acceptable treatment options. Recent scientific investigations have increasingly focused on validating ethnobotanically important plants using phytochemical analysis, *in vitro* antimycobacterial assays, *in vivo* studies, and molecular docking approaches. Several traditionally used plants have demonstrated significant activity against both drug-sensitive and drug-resistant strains of *M. tuberculosis*, confirming the relevance of ethnobotanical knowledge in contemporary TB drug development[38]. This integration of traditional wisdom with modern scientific methods offers a promising strategy for discovering safer and more effective anti-tubercular agents.

Therefore, ethnobotanical research serves as a bridge between indigenous healing practices and modern pharmacological innovation. Preserving and scientifically validating this traditional knowledge can contribute substantially to the development of next-generation plant-based therapies for tuberculosis and support global efforts to combat drug-resistant TB.

6. Pharmacological Perspectives

6.1 Antimycobacterial Activity

In vitro investigations have revealed that various plant extracts and bioactive compounds exhibit inhibitory

action against some drug-sensitive and drug-resistant strains of *M. tuberculosis*. For instance;

- Ethanolic extracts of *A. sativum* and *C. longa* demonstrated minimum inhibitory concentrations (MICs) between 25 - 100 µg/mL against the *M. tuberculosis* H37Rv strain.
- Similarly, alkaloids from *A. vasica*, including vasicine and vasicinone, were found to suppress bacterial respiration by targeting NADH dehydrogenase.

6. Immunomodulatory Effects

Several herbal agents are known to modulate both innate and adaptive immune mechanisms, which are essential for tuberculosis (TB) control. *T. cordifolia* and *W. somnifera* have been reported to enhance macrophage activation, whereas *O. sanctum* stimulates the production of interferon-γ and interleukin-2, thereby reinforcing host immune defences.

6.3 Antioxidant and Anti-inflammatory Actions

Oxidative stress and inflammation are key contributors to the pathogenesis of tuberculosis (TB). Extracts rich in flavonoids and phenolic compounds from *C. longa*, *A. indica* and *P. emblica* have been shown to alleviate oxidative damage and tissue injury, thereby supporting pulmonary healing and minimising secondary complications.

7. Phytochemical Constituents with Antitubercular Potential

Phytochemical analyses have revealed multiple classes of bioactive compounds exhibiting antimycobacterial activity:

- Alkaloids: Molecules such as berberine, piperine and harmine inhibit *M. tuberculosis* growth by interrupting cell wall biosynthesis and energy metabolism.
- Flavonoids: Quercetin, kaempferol and luteolin display inhibitory effects against the *M. tuberculosis* H37Rv strain through interference with key enzymatic pathways and modulation of oxidative stress.
- Terpenoids: Compounds including lupeol, betulinic acid and ursolic acid suppress mycolic acid biosynthesis, impairing bacterial cell wall integrity.
- Phenolics and Tannins: These constituents exhibit potent antioxidant and protein-binding activities that contribute to bacterial enzyme inhibition.
- Curcuminoids and Essential Oils: These agents enhance macrophage activation and modulate immune function, thereby promoting more efficient bacterial clearance.

8. Ethnobotanical Overview of Anti-tuberculosis (Anti-TB) Plants

Ethnobotanical investigations serve as a critical link between conventional healing practices and contemporary scientific research. In many cultural and geographic contexts, a wide range of medicinal plants has been utilised historically to manage respiratory disorders, including tuberculosis (TB). Documentation of these practices has helped identify species with potential antimycobacterial activity and has guided the search for novel therapeutic candidates. Such plants are commonly prepared as decoctions, infusions, powders or extracts and administered orally or through inhalation to relieve hallmark TB-related symptoms, including chronic cough, fever, weight loss and chest discomfort.

9. Novelty of Integrating Ethnobotany, Phytopharmacology and Molecular Targets

The discovery of new therapeutic agents for tuberculosis (TB) requires a multidisciplinary approach that extends beyond conventional antimicrobial drug development. Although numerous medicinal plants have traditionally been used for respiratory illnesses and tuberculosis-like conditions, many earlier reviews have discussed these plants only from a general ethnobotanical perspective without systematically correlating traditional use with pharmacological mechanisms and molecular target validation. The present review addresses this gap by integrating ethnobotanical knowledge, phytopharmacological evidence, and modern molecular target analysis to provide a more comprehensive understanding of plant-based anti-tubercular therapy[14,15]. Ethnobotanical studies offer the primary foundation for identifying medicinal plants with therapeutic relevance in TB management.

Indigenous knowledge systems such as *Ayurveda, Siddha, Unani*, Traditional Chinese Medicine (TCM) and African traditional medicine have documented the use of numerous plant species for chronic cough, fever, hemoptysis, fatigue and pulmonary weakness associated with tuberculosis[35]. However, traditional use alone is insufficient for scientific acceptance unless supported by pharmacological validation and mechanistic evidence.

Phytopharmacological investigations provide this essential scientific validation by identifying the active phytoconstituents responsible for therapeutic effects and evaluating their antimycobacterial, immunomodulatory, antioxidant and anti-inflammatory activities. Several plants such as *C. longa*, *T. cordifolia*, *W. somnifera*, *A. sativum* and *P. longum* have demonstrated significant activity against both drug-sensitive and drug-resistant strains of *M. tuberculosis* through *in vitro* and *in vivo* studies[13,32]. These findings strengthen the translational potential of ethnobotanical remedies and support their development as evidence-based therapeutic agents.

Recent advances in molecular pharmacology and computational biology have further enhanced this research field by enabling the identification of specific mycobacterial molecular targets for plant-derived compounds. Phytochemicals such as curcumin, berberine, quercetin, piperine and ursolic acid have shown strong interactions with key TB drug targets including InhA (enoyl-acyl carrier protein reductase), DprE1 (decaprenylphosphoryl-β-D-ribose oxidase), KatG (catalase-peroxidase), RNA polymerase, DNA gyrase and ATP synthase[9]. These targets are critical for mycobacterial cell wall biosynthesis, replication, energy metabolism and persistence, making them highly relevant for anti-TB drug development.

Molecular docking, ADMET prediction, network pharmacology and metabolomics-based approaches now allow rapid screening of phytochemicals for efficacy, selectivity, pharmacokinetic behaviour, and toxicity profiles before extensive laboratory validation. This significantly accelerates the drug discovery process and reduces the cost and time associated with synthetic drug development[34]. Such computational strategies also help identify synergistic interactions between phytoconstituents and standard anti-TB drugs, which may improve treatment outcomes and reduce resistance development.

The novelty of this review lies in its integrated perspective that connects traditional medicinal knowledge with experimental pharmacology and molecular target-based validation. Rather than presenting medicinal plants merely as folklore-based remedies, this review critically evaluates their therapeutic relevance through mechanistic evidence and target-specific pharmacological insights. This approach strengthens the scientific rationale for plant-based interventions and highlights their role not only as complementary therapies but also as potential sources of lead compounds for future anti-tubercular drug discovery.

Furthermore, special emphasis is placed on the application of this integrated strategy in addressing multidrug-resistant and extensively drug-resistant tuberculosis (MDR/XDR-TB), where conventional therapies are increasingly limited. By combining ethnobotanical wisdom with modern phytopharmacology and computational drug discovery, the development of safer, affordable and multi-targeted anti-TB therapies becomes more feasible and clinically relevant[33].

Thus, the integration of ethnobotany, phyto pharmacology and molecular target analysis represents a novel and promising framework for advancing tuberculosis therapeutics and overcoming current challenges in global TB management.

10. Global Ethnobotanical Practices and Regional Diversity

Ethnomedicinal traditions across the globe provide a diverse repertoire of plant-based remedies relevant to tuberculosis management:

- Asia (India, China, Nepal, Thailand): Traditional practices such as *Ayurveda, Siddha, Unani* and Chinese Medicine employ a variety of botanicals, including *A. vasica* (*Vasaka*), *O. sanctum* (*Tulsi*), *C. longa* (Turmeric), *P. longum* (Long pepper), *T. cordifolia* (*Guduchi*) and *G. glabra* (Liquorice), to treat chronic respiratory ailments and TB-associated symptoms. These plants are well recognised for their antimycobacterial, anti-inflammatory and immunomodulatory properties.
- Africa (South Africa, Ethiopia, Nigeria, Kenya): African traditional healers rely on species such as

Table 1. Ethnobotanically documented medicinal plants with reported anti-tubercular activity, major phytoconstituents, traditional uses and pharmacological relevance

Sr. No.	Botanical Name	Common Name	Family	Part Used	Major Phytoconstituents	Traditional Use	Reported Anti-TB/ Pharmacological Activity	References
1	*Adhatoda vasica* Nees	Malabar Nut/*Vasaka*	*Acanthaceae*	Leaves	Vasicine, vasicinone, flavonoids	Used for cough, asthma, bronchitis and TB	Inhibits *M. tuberculosis* H37Rv; bronchodilator and expectorant.	14, 32
2	*Curcuma longa* L.	Turmeric	*Zingiberaceae*	Rhizome	Curcumin, demethoxycurcumin	Used for respiratory and inflammatory disorders	Curcumin has demonstrated inhibitory effects against *M. tuberculosis* through suppression of DNA gyrase and modulation of oxidative stress pathways.	33, 42
3	*Allium sativum* L.	Garlic	*Amaryllidaceae*	Bulb	Allicin, ajoene, diallyl sulfide	Used as an antimicrobial and immune tonic	Allicin suppresses *M. tuberculosis* growth and enhances macrophage activity.	32, 39
4	*Ocimum sanctum* L.	Holy Basil/ *Tulsi*	*Lamiaceae*	Leaves	Eugenol, ursolic acid, rosmarinic acid	Used in chronic cough, fever, and chest congestion	Methanolic extract shows antimycobacterial and antioxidant activity	14, 15
5	*Tinospora cordifolia* (Willd.) Hook. f. and Thomson	Guduchi	*Menispermaceae*	Stem	Tinosporin, berberine, tinosporide	Used for fever, cough, and immunity	Immunostimulant; inhibits *M. tuberculosis* H37Rv strain.	15, 38
6	*Phyllanthus emblica L.*	Indian Gooseberry/ *Amla*	*Phyllanthaceae*	Fruit	Ascorbic acid, gallic acid, ellagic acid	Used for fever, lung and immune disorders	Antioxidant and adjunct in TB therapy.	32, 41
7	*Sutherlandia frutescens* (L.) R. Br.	Cancer Bush	*Fabaceae*	Leaves	L-canavanine, pinitol, GABA	Used for pulmonary infection, fatigue	Ethanolic extract active against *M. tuberculosis* H37Rv.	14, 36
8	*Warburgia salutaris* (Bertol. f.) Chiov.	Pepper-Bark Tree	*Canellaceae*	Bark	Warburganal, polygodial	Used for TB, cough, and fever	Drimane sesquiterpenes are active against MDR-TB isolates.	37, 42
9	*Terminalia chebula* Retz.	*Haritaki*	*Combretaceae*	Fruit	Chebulagic acid, gallic acid, ellagic acid	Used for cough, asthma, digestive ailments	Ethanolic extract inhibits *M. tuberculosis* H37Rv.	32, 43
10	*Eucalyptus globulus* Labill.	Eucalyptus	*Myrtaceae*	Leaves	Eucalyptol (1,8-cineole), flavonoids	Used for chest congestion and respiratory infections	Essential oil inhibits *M. tuberculosis* and MDR strains.	14, 43

Table 1. Continued...

Sr. No.	Botanical Name	Common Name	Family	Part Used	Major Phytoconstituents	Traditional Use	Reported Anti-TB/ Pharmacological Activity	References
11	*Nigella sativa* L.	Black Cumin	*Ranunculaceae*	Seeds	Thymoquinone, nigellone	Used for chronic cough, fever	Thymoquinone enhances immune function and inhibits *M. tuberculosis*	38, 44
12	*Piper longum* L.	Long Pepper	*Piperaceae*	Fruit	Piperine, piperlongumine	Used in *Ayurveda* for cough, asthma, TB	Synergistic with isoniazid; increases drug uptake.	32, 41
13	*Zingiber officinale* Roscoe	Ginger	*Zingiberaceae*	Rhizome	Gingerols, shogaols	Used for cough, cold, and bronchitis	Extracts inhibit *M. tuberculosis*; antioxidant and anti-inflammatory.	14, 33
14	*Calotropis procera* (Aiton) Dryand	Sodom Apple	*Apocynaceae*	Leaves, latex	Calotropin, uscharin, flavonoids	Used in folk medicine for TB and fever	Leaf extract shows antimycobacterial effect	14, 45
15	*Withania somnifera* (L.) Dunal	Ashwa gandha	*Solanaceae*	Roots	Withanolides, sitoindosides	Used for chronic illness, fatigue, and cough	Immunomodulatory; improves TB recovery	32, 38
16	*Glycyrrhiza glabra* L.	Licorice	*Fabaceae*	Root	Glycyrrhizin, liquiritin, flavonoids	Used for cough, sore throat, and TB	Inhibits bacterial growth; anti-inflammatory.	32, 41
17	*Justicia adhatoda* L.	*Vasaka*/ Malabar Nut	*Acanthaceae*	Leaves	Vasicine, vasicinol	Used for asthma, TB, cough	Bronchodilator and antimycobacterial.	14, 33
18	*Uncaria tomentosa* (Willd. ex Schult.) DC.	Cat's Claw	*Rubiaceae*	Bark	Oxindole alkaloids, tannins	Used by Amazon tribes for respiratory infections	Extracts show anti-TB and immune-enhancing effects.	32, 40
19	*Azadirachta indica* A. Juss.	Neem	*Meliaceae*	Leaves, bark	Azadirachtin, nimbin, quercetin	Used for fever, infections, TB	Methanolic extract active against *M. tuberculosis*.	38, 46
20	*Artemisia afra* Jacq. ex Willd.	African Wormwood	*Asteraceae*	Leaves	Artemisinin, flavonoids, terpenes	Used for cough, fever, and chest pain	Ethanolic extract inhibits *M. tuberculosis* H37Rv.	36, 37

W. salutaris, *S. frutescens*, *C. molle*, *T. sericea* and *A. afra* for managing pulmonary and respiratory disorders. Experimental studies have validated the inhibitory activity of several of these plants against *M. tuberculosis*.

- South America (Peru, Brazil, Colombia): Indigenous communities throughout the Amazon region use *Uncaria tomentosa* (Cat's Claw), *E. globulus* and *B. dracunculifolia* to treat respiratory infections, including TB. These species contain diverse phytochemicals such as terpenoids, alkaloids and polyphenols with demonstrated antimicrobial and antioxidant activities.
- Middle East and North Africa: Herbal medicines including *N. sativa* (Black cumin), *Z. officinale* (Ginger) and *B. serrata* (Frankincense) have historically been utilised for their expectorant, antibacterial and immune-enhancing effects, contributing to symptomatic relief in TB-affected individuals.

10.1 Ethnobotanical Documentation and Indigenous Knowledge

Ethnobotanical investigations in tuberculosis (TB)-endemic regions have documented over 200 plant species traditionally employed in TB management. The selection of these plants is primarily based on indigenous knowledge, empirical evidence and longstanding therapeutic practices. Commonly utilised plant parts include leaves, roots, bark, and rhizomes, with aqueous and ethanolic extracts being the most frequent preparation methods. The continued reliance on these herbal remedies underscores both the conservation of cultural inheritance and the limited availability of modern healthcare services in rural and indigenous communities. Table 1 presents selected ethnobotanical plants with documented anti-TB potential.

11. Pharmacological Relevance of Phytoconstituents

The therapeutic potential of medicinal plants in tuberculosis (TB) management is largely attributed to the presence of diverse bioactive phytoconstituents with significant antimycobacterial and host-protective properties. These phytochemicals, including alkaloids, flavonoids, terpenoids, phenolics, tannins, glycosides, saponins and essential oils, exhibit multiple pharmacological activities that can directly or indirectly contribute to the control of *M. tuberculosis* infection[16]. Their broad-spectrum biological actions make them valuable candidates for adjunctive therapy as well as lead molecules for the development of novel anti-tubercular drugs.

Alkaloids represent one of the most extensively studied groups of phytoconstituents with anti-TB potential. Compounds such as berberine, piperine, vasicine and harmine have demonstrated inhibitory effects against *M. tuberculosis* by interfering with cell wall biosynthesis, disrupting membrane integrity and suppressing essential metabolic enzymes involved in bacterial survival[13]. Piperine, isolated from *P. longum*, has also been shown to enhance the bioavailability of rifampicin and isoniazid, thereby improving therapeutic efficacy and reducing the risk of resistance development[44].

Flavonoids such as quercetin, kaempferol, luteolin and catechins possess strong antimycobacterial, antioxidant and anti-inflammatory activities. These compounds inhibit bacterial growth by targeting enzymes involved in DNA replication, fatty acid synthesis and energy metabolism while simultaneously reducing oxidative stress-induced tissue damage in the host[33]. Quercetin, for instance, has shown promising inhibitory activity against the H37Rv strain of *M. tuberculosis* and may also contribute to immune modulation by regulating cytokine production.

Terpenoids and triterpenes, including lupeol, betulinic acid, ursolic acid and artemisinin derivatives, are also important contributors to anti-tubercular pharmacology. These compounds primarily act by disrupting mycolic acid synthesis and impairing the structural integrity of the mycobacterial cell wall, thereby enhancing bacterial susceptibility to immune clearance and standard anti-TB drugs[40]. Several essential oils rich in terpenoid constituents, such as eucalyptol from *E. globulus*, have demonstrated inhibitory activity against both drug-sensitive and MDR strains of *M. tuberculosis*.

Phenolic compounds and tannins contribute significantly through their antioxidant and enzyme-inhibitory properties. Curcumin from *C. longa* is one of the most extensively investigated phenolic compounds with proven anti-TB relevance. It exhibits

antimycobacterial activity through inhibition of DNA gyrase, suppression of inflammatory cytokines and modulation of oxidative stress pathways[9]. Curcumin has also shown synergistic effects with isoniazid and rifampicin, suggesting its potential role as an adjunctive therapeutic agent.

In addition to direct antimicrobial effects, many phytoconstituents function as host-directed therapeutic agents by enhancing macrophage activation, stimulating phagolysosome fusion, promoting autophagy and regulating immune mediators such as TNF-α, IFN-γ, IL-2 and IL-12. Immunomodulatory plants such as *T. cordifolia*, *W. somnifera* and *O. sanctum* have demonstrated the ability to strengthen host defence mechanisms and improve resistance against persistent TB infection[32]. This is particularly important in latent TB and drug-resistant cases where immune dysfunction plays a major role in disease progression.

The multi-targeted action of phytoconstituents provides a major pharmacological advantage over conventional single-target synthetic drugs. By simultaneously affecting bacterial survival pathways and host immune responses, these compounds may reduce the likelihood of resistance development while improving therapeutic outcomes[34]. Such pharmacological versatility supports their growing relevance in contemporary anti-tubercular research.

Therefore, the pharmacological significance of phytoconstituents extends beyond their traditional use and establishes them as scientifically validated candidates for future anti-TB drug discovery. Continued investigation into their mechanisms of action, synergistic potential and clinical applicability may significantly contribute to the development of safer and more effective tuberculosis therapies.

12. Future Perspectives

Although considerable progress has been made in identifying medicinal plants with promising antimycobacterial activity, the translation of ethnobotanical insights into clinically validated treatments remains limited. Future investigations should emphasise detailed phytochemical profiling, elucidation of molecular mechanisms and the use of molecular docking and omics-driven approaches to identify the specific targets of plant-derived bioactives against *M. tuberculosis*. Advanced methodologies—including metabolomics, network pharmacology and *in silico* modelling—can accelerate the discovery of novel compounds and synergistic phytochemical interactions. Furthermore, nanotechnology-enabled delivery platforms offer potential advantages by improving the bioavailability, stability and targeted delivery of herbal constituents, thereby enhancing therapeutic efficacy while minimising toxicity. Strengthening collaboration among ethnobotanists, microbiologists, pharmacologists and clinical researchers will be crucial for developing standardised formulations and rigorously assessing their safety and efficacy through comprehensive preclinical and clinical evaluations. Integrating these multidisciplinary strategies can bridge traditional medicinal knowledge with modern scientific validation and support the development of next-generation phytotherapeutics for improved tuberculosis management and global health outcomes.

13. Conclusion

The global impact of tuberculosis, intensified by the increasing prevalence of multidrug-resistant and extensively drug-resistant strains, highlights the pressing need for new, safe and effective therapeutic options. Herbal medicines, long embedded in ethnobotanical practices, have emerged as promising complementary or foundational sources for anti-tubercular drug development. Many medicinal plants contain bioactive constituents, including alkaloids, flavonoids, terpenoids, phenolics and saponins, that exhibit notable antimycobacterial, immunomodulatory and antioxidant activities. Integrating traditional medicinal knowledge with contemporary pharmacological approaches not only strengthens the scientific rationale for their therapeutic use but also supports the discovery of phytochemicals with potential for detailed mechanistic, preclinical and clinical investigations. Future research should prioritise bioassay-guided fractionation, elucidation of molecular targets and assessment of synergistic effects with existing anti-TB drugs. Collectively, the ethnobotanical and pharmacological insights summarised in this review underscore the significant promise of herbal medicines as valuable contributors in the fight against

tuberculosis and the escalating challenge of drug resistance.

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Author Contribution

S. A. Vadivel: Conceptualised and designed the review framework, performed literature collection and critical analysis of ethnobotanical data, and drafted the original manuscript. Dr. Agilandeswari Devarajan: Contributed to the pharmacological interpretation of anti-tubercular herbal medicines, supervised the scientific content, and critically revised the manuscript for intellectual quality. Dawn V Tomy: Assisted in systematic literature search, data organisation, and compilation of traditional medicinal practices related to tuberculosis management. Hoor-Ul-Aeen: Contributed to data validation, reference formatting and manuscript editing. All authors have read and agreed to the published version of the manuscript.