

## Herbal approach for tuberculosis management: A systematic review

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### Abstract

**Background:** Tuberculosis is an airborne infection that causes lung damage, and it is particularly harmful to patients with weakened immune systems or other health problems. Allopathic medications are associated with development of cross resistance or multidrug resistance in diseases such as TB, making treatment more difficult. In this case, Herbal remedies are the most effective in treating this disease. Medicinal plants with antituberculous qualities provide pharmacists with a new supply of medicine, allowing them to create novel drugs depending on their active constituents or intermediate metabolites.

**Objective:** Many recent studies have shown that ayurvedic medicines can reduce mortality dramatically when administered in such situations because they interact with the body's natural environment. Ayurvedic medicine is growing in popularity due to its low toxicity study and lack of side effects when compared to allopathic treatments.

**Conclusion:** Considering botanical categorization and anti-tubercular action, Anti-tubercular medicinal herbs have been chosen from scientific literature for this review. A primary objective of this study is to highlight antituberculosis plants, their chemical compounds, and their anti-tubercular properties.

**Keywords:** Tuberculosis; Herbal Medicine; Chemotherapy; Adjuvant

### 1. Introduction

As an endemic ailment of the urban poor in the 19th and early 20th centuries, tuberculosis sparked great public concern (13). As per the World Health Organization (WHO) (1), tuberculosis (TB) (1) is a bacterial infection produced by Mycobacterium tuberculosis (13) that very usually attacks the lungs. The infection is conveyed through people to people by wet particles from both lungs and throats of persons who have prevalent respiratory diseases (20).

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## 2. Epidemiology

TB spread from Eastern Africa to the entire world when Homo sapiens migrated from Eastern Africa to the world, especially over open supply routes with greater population mixing and overcrowding (19). Every year, nearly ten million new instances of active disease are identified, with over 1.3 million fatalities. Over the lengthy period of combating this ancient plague, several nations created their own traditional anti-TB medicines in accordance with its spreading route. Many of the TM medical system's ancient documents, including TCM, Ayurveda, and TAM, have TB data (19). This is owing to the TM clinical system's lengthy history of coexisting with humans for over 70,000 years. According to studies on TM formulations, the active molecules or semi-metabolites provide a plentiful basis of innovative medications (19).

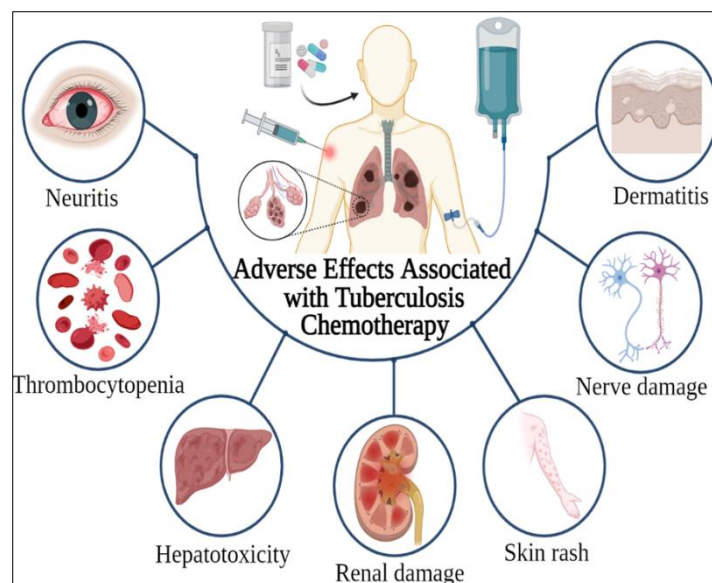
### 2.1. Tuberculosis in India

The Indian government now claims that the overall number of persons infected with tuberculosis has increased from 2.2 million to 2.6 million, based on examinations of medicine sales. India's Ministry of Health and Family Welfare said on World TB Day, March 24, 2019, that 2.15 million new tuberculosis cases were diagnosed in 2018. Current TB treatment, Program support the particular effects of each bactericidal agent govern the rational usage of antituberculosis treatments. Isoniazid is particularly effective against big cavities, although it also has limited efficacy in caseous lesions and macrophages (2). Rifampin is effective against the intermittently increasing population in caseous lesions and is active in all populations. 86 Streptomycin is only effective against the extracellular population, but PZA is only active in an acidic environment and has a particular effect on macrophages (2). PZA produces its maximal impact only within the first few months of medication, according to clinical trials (2).

In India, the Revised National TB Control Programme (RNTCP) is an officially backed TB management programme that controls TB in the community (12). Despite the fact that it is a government-sponsored programme with treatment and diagnostic services for free, many still flock to private physicians when they have a symptom. According to investigations (19), 50-80 percent of TB patients seek treatment from private practitioners. Ayurvedic medications are currently not included in the RNTCP (3). Private practitioners, including general practitioners and chest specialists, employ a variety of Ayurvedic remedies to help in TB care.

### 2.2. Severe side effects of exiting anti-TB medicines

Antituberculosis drugs can cause hematological reactions, gastrointestinal intolerance, hepatitis, renal failure, and dermatological reactions. These unfavorable repercussions should be discovered soon in order to decrease linked illness and death (1).



**Figure 1** The severe adverse effects of Tuberculosis Chemotherapy drugs

Rifampin has following few of the most dangerous adverse effects include hemolysis, thrombocytopenia, and kidney failure (Fig. 1) (2). Anti-rifampin antibodies are absorbed by platelets, causing thrombocytopenia, which leads to platelet loss after complement fixing. PAS has so many gastrointestinal side effects that it is no longer prescribed to adults as a primary medicine (2). The liver damage caused by isoniazid and rifampin seems to be supplementary (Fig. 1). Because they are not synergistic, neither one nor the other should be given to individuals even without liver disease who are alcoholics. Retrobulbar neuritis is the most serious adverse effect of ethambutol (Fig. 1). Patients taking Dilantin and isoniazid must be advised regarding the danger of Dilantin over dosage since isoniazid is seen to hamper the metabolism of diphenylhydantoin (4).

**Table 1** A possible adverse effect associated with anti-TB Chemotherapy

Chemotherapeutic agents	Adverse Effects
Streptomycin	Renal damage, Vestibular and Auditory nerve damage,
Isoniazid	Hepatitis
Rifampicin	Thrombocytopenia, Pain, Vomiting, Nausea, Hepatitis
Pyrazinamide	Arthralgia, Hepatitis
Ethambutol	Neuritis, Color blindness
Cycloserine	Convulsions, Dizziness, Depression, Psychotic Reactions
Ethionamide	Diarrhoea, Abdominal pain, Hepatotoxicity
Kanamycin	Vertigo, Auditory nerve damage, Nephrotoxicity
Thioacetazone	Skin rash, Exfoliative dermatitis

### 2.3. Cost of existing modern medicine

Rifampin every day for 4 months (4R) is much cheaper and much better efficient as compared to other therapies (QALY) excluding for isoniazid plus rifapentine once a week for 3 months (3HP) (19), which is active at a price of \$ 49,000 per year (Holland et al., 2009). 3HP is additional rate effective than 9H at \$20,207 per QALY. 4R and 3HP are the most popular alternatives, with 3HP being more active than 4R at a price of \$20,000 per QALY (19). 4R and 3HP are at the same price, however 3HP is more effective. 3HP has complete control over all strategies (5).

### 2.4. Guidelines of WHO

Traditional medicine will be integrated into National Health Systems (NHS) across the world, according to the WHO (6). This is a unique chance to create a safe, inexpensive, and effective NHS, particularly for Third World nations with abundant medicinal plant resources and traditional medical expertise. Instead of wasting further billions on 'health genomics,' which will increase intervention and iatrogenic harm to health, it is time for governments to fund research into holistic health models (6).

## 3. Ayurvedic approach in tuberculosis

In Ayurveda PTB is similar to Rajayakshma. Rajayakshma is firstly the responsibility of Dhatushaya (19). This stage always initiates the pathogenesis process in Rajayakshma patients (12). Furthermore, with the loss of rasa (tissue fluid), mamsa (muscle), rakta (blood), sukra (skin) and meda (adipose tissue), metabolic dysfunction (Dhatwagninasana) is unavoidable (generative tissue). As a result, immunity, or ojakshaya, deteriorates with time (12). Pratilomakshaya happens when a unique metabolic shift occurs, resulting in the harm of many dhatus (tissue) including sukra, Ojakshaya, and meda dhatus to rasa dhatu foregoing each other, according to Ayurvedic principles (3).

Bioactivity-guided fractionation was largely used to identify bioactive chemicals in medicinal plants rather than traditional drug development, which involves screening huge molecular libraries and in silico data withdrawal created on cheminformatics modelling (19). The structural data was collected by isolating them from the essential plant parts, then fractionating and characterizing them with infrared spectroscopy, NMR spectroscopy, and mass spectrometry (19). Finally, the bioactivities of the microorganisms were investigated in a range of mycobacteria. Many research groups compiled a list of anti-TB natural compounds through various organs. In early 2007, Copp and Pearce collected a list of natural chemicals (19) (secondary metabolites) from terrestrial and marine sources, animals, and microbes that have been shown to impede the development of TB or comparable organisms.

(23) highlighted herbal antimycobacterial peptides obtained from plants, fungi, bacteria, and animals. Chinsebu mentioned herbal antimycobacterial substances obtained from medicinal plants and endophytes throughout South America, Europe, Africa, Asia, and Canada (7). There were 156 species, 123 genera, and 64 families represented in this review, with the Fabaceae (10 genera, 13 species), Rutaceae (7 genera, 10 species), and Lamiaceae (7 genera, 9 species) being the leading families, with higher genera belonging to the above-mentioned families showing antitubercular action (19).

There were various anti-TB components in many plants, and this assessment only covers the active compounds that have been identified. (Table 1) shows the examples of drugs that were examined for anti-TB activity. The drugs tested included terpenes, ketones, acids, alcohols, esters, hydrocarbons, quinones, furan, phenols, and quinolones (19). The compounds typical structures are as follows (21) and (22) examined the analogues of terpenoids, flavones, and phytol for their pharmacological activity in various illnesses out of every anti-TB natural substance (19). The substances in this study were all natural products or secondary metabolites, with just a limited synthetic altered versions indicated (7). “Many semisynthetic derivatives were found to be more active than the parent compounds; for example, methylation of natural mulinenic acid and 13-hydroxy-mulin-11-en-20-oic acid methyl ester decreased the minimum inhibitory concentration (MIC) by 8 times; n-propyl ester and n-butyl ester of isomulinic acid reduced the MIC by 4 times. Because acetylation improved the lipophilic character of methyl gallate, the MIC of triacetylated methyl gallate was reduced by 2-4 times” (19). Herbs and trees accounted for 38 percent of all growth types in a study of therapeutic class used of Bapedi traditional therapists to treat TB, followed by shrubs with 19 percent (8). *Pellaea calomelanos*, a lone fern species, represented Pteridophytes. Plant parts used in herbal medicines included bark, tubers, roots, fruits, bulbs, leaves, and seeds. “The leaves (34%) were the most commonly used, followed by roots (21%), whole plant (11%), bulbs and tubers (9% each), fruits (7%), bark (4.5%), and seeds (4.5%). The complete plant was provided to herbaceous plant species” (8). A single species produced a total of 28 tuberculosis therapies (96.6%) (8). Crushed *Artemisia afra* leaves and roots were combined with crushed *Mentha* spp. leaves and smoked three times a day. Oral, smoking, and inhalation were all methods of herbal delivery. Using a metal cup, extracts or decoctions were administered orally (250 ml). *Salix mucronata* fruits were consumed uncooked three times a day.

“Traditional healers burnt leaves of *Artemisia afra*, *Myrothamnus flabellifolius* (whole plant), *Carica papaya* (leaves), roots of *Zanthoxylum capense*, and *Combretum hereroense* (seeds) thrice to four times a day in the consultation tent, inhaling the smoke twice to four times a day” (14). Patients inhaled steam made by placing *Artemisia afra* (19) and *Lippia javanica* (19) leaves into hot water sink and a blanket was wrapped over their heads (14). Crushed Citrus lemon, *Artemisia afra*, and *Mentha* sp. leaves are to be burned in a paper wrapper 2 or 3 times a day. Every ayurvedic formulations are consumed about 2 weeks upto a month, based on the individual reaction to medicine and the patient's ability with tubercular therapy as well as administration (8).

### 3.1. Herbal medicine

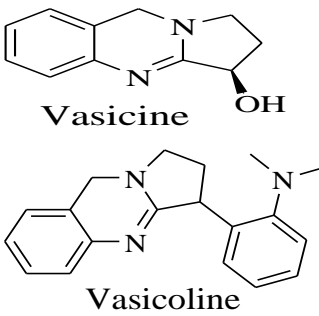
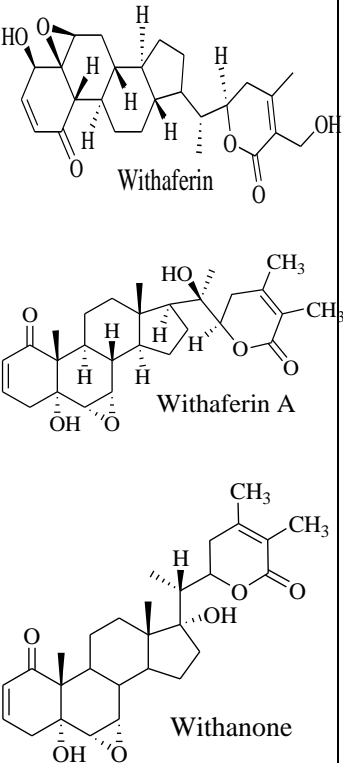
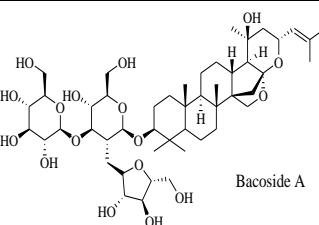
India has one of the world's most extensive plant-based medicinal traditions. In India, there are an predictable 25,000 efficient herbal-centre medicines that are utilised in religious remedy and are known to rural populations (9).

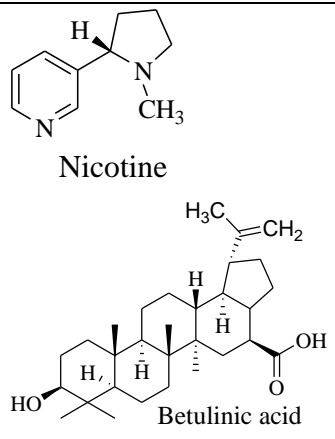
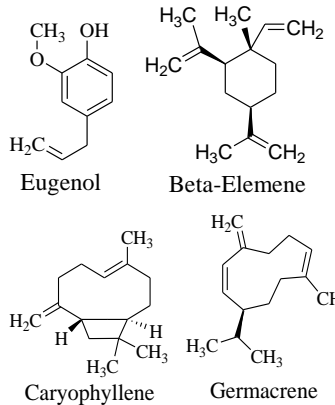
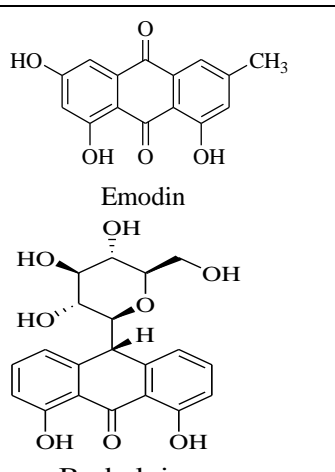
Over 1.5 million people practise traditional medicine, which uses medicinal herbs for preventative, promotional, and curative purposes. India is expected to have about 7800 medical medicine production plants, which utilise over 2000 tonnes of herbs each year (9). The creation of effective therapeutic medicines relies heavily on medicinal plants. Approximately 100 novel herbal-based medications were released into the American drug market between 1950 and 1970, deserpidine, reserpine, vinblastine, vincristine and reseinnamine are only a few examples of compounds originating from higher plants (18). Between 1971 and 1990, novel medications such as ectoposide, artemisinin, teniposide, eguggulsterone, plaunotol, lectinan, nabilone and ginkgolides were established over the universe. Pacitaxel, toptecan, gomishin, irinotecan, and other drugs were introduced between 1991 and 1995, accounting for 2% of all prescriptions. Serpentine, for example, was found in 1953 in the root of the plant *Rauwolfia serpentina* and was found to be a game-changer in therapy of high blood pressure. Vinblastine (9) is a drug that comes from the *Catharanthus roseus* plant that is used to treat Hodgkins lymphoma, non-Hodgkins lymphomas, paediatric leukaemia, testicular cancer, choriocarcinoma and neck melanoma as vincristine is a kind of vitamin C (9).

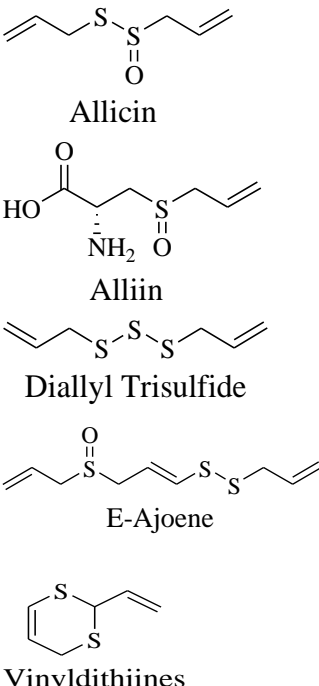
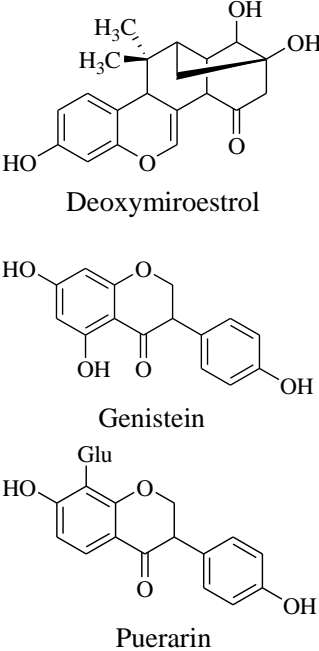
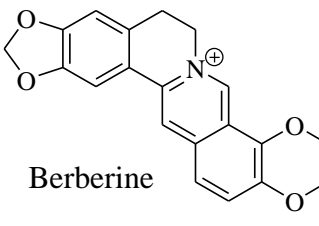
Acute lymphocytic leukaemia in children, advanced Hodgkins's disease, lymphosarcoma, cervical cancer, and breast cancer are all possible causes (18). Phophyllotoxin is a substance found in the *Phodophyllum emodi* plant that is currently used to treat testicular cancer, minor lung tumor, and lymphomas. Herbal derivative drugs are used to treat skin diseases, jaundice, psychological illness, high blood pressure, tuberculosis, malignance and diabetes. The creation of effective therapeutic medicines relies heavily on medicinal plants. Plant-derived medications emerged in

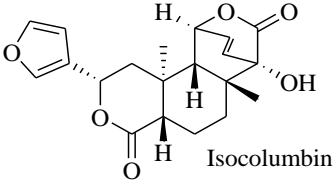
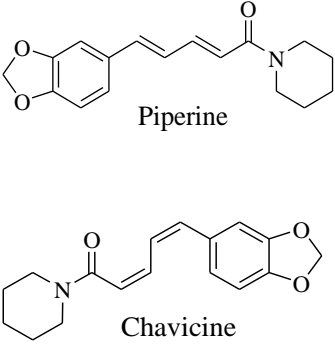
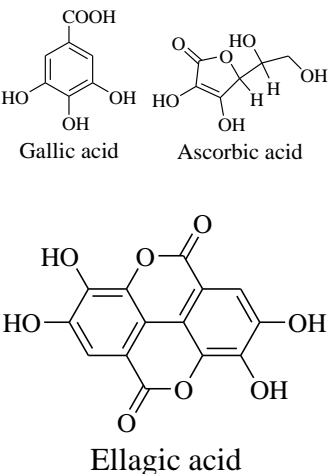
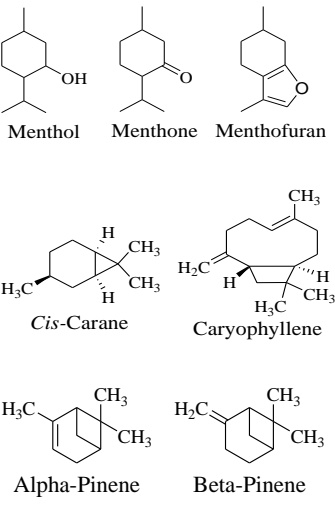
contemporary medicine as a result of folklore or traditional medicine's utilisation of plant material as an indigenous treatment.

**Table 2** Ayurvedic approach for treating tuberculosis and its symptoms with herbal medicines

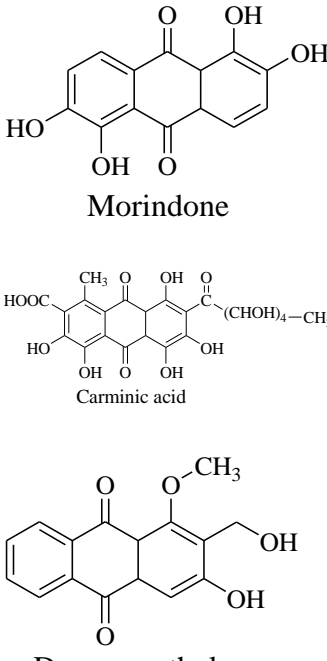
Common Name Botanical Name [Family]	Chemical Constituents	Chemical Structure	Category of Activity	Medicinal Uses
Adulsa (Vasaka) <i>Justicia vasica</i> [Acanthaceae]	Adhatodine, Anisotine, Sicinolone, Vasicine, Vasicinone, Vasicoline, Vasicolinone.	 <p>Vasicine</p> <p>Vasicoline</p>	Antibiotic Antibacterial Antisclerostin Anticoagulant (10)	Coughs, chronic bronchitis, asthma, colds, antispasmodic, and bronchitis disorders are all treated.
Ashwagandha (Indian ginseng) <i>Withania somnifera</i> [Solanaceae] (11)	Alkaloids, Saponins, Steroidal lactones, Withaferin A, Withanone.	 <p>Withaferin</p> <p>Withaferin A</p> <p>Withanone</p>	Arthritic diseases Asthma Cancer Diabetes Hypertension Stress (10)	Herb that boosts immunity by acting on the nervous and respiratory systems. It has wonderful wound healing effects, as well as anti-inflammatory and rejuvenating characteristics. It treats tuberculosis symptoms such as cough, cold, and bronchitis.
Brahmi (Indravalli) <i>Bacopa monnieri</i> [Plantaginaceae] (10)	Brahmine, Herpestine, Nicotine, D-Mannitol, Hersaponin, Monnierin, Bacosides A, Bacosides B,	 <p>Bacoside A</p>	Alzheimer's disease, Antibacterial, Antifungal, Improving memory, Anxiety, Attention Deficit-	Acts on the respiratory, neurological, digestive, circulatory, and excretory systems. It has a number of therapeutic properties, including rejuvenating properties, and can be used to treat colds and coughs, as well as other common symptoms.

	Saponins A, Saponins B, Saponins C, Betulinic acid, Stigmasterol.	 <p>Nicotine</p> <p>Betulinic acid</p>	Hyperactivity Disorder (ADHD), Allergic conditions (10)	
Tulsi (Holy basil) <i>Ocimum tenuiflorum</i> [Lamiaceae] (10)	Essential oil consists mostly: Eugenol (~70%) $\beta$ -elemene, Caryophyllene, Germacrene, Isothymusine, $\beta$ -bisabolene (13- 20%), 1,8-cineole (9-33%), Methyl chavicol (2-12%).	 <p>Eugenol</p> <p>Beta-Elementene</p> <p>Caryophyllene</p> <p>Germacrene</p>	Adaptogenic Analgesic Antiasthmatic Anticancer Antidiabetic Antiemetic Antifertility Antifungal Antimicrobial Antispasmodic Cardioprotective Hepatoprotective	Treatment of bronchitis, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bite etc. (10)
Alovera (Ghritkumaari ka) <i>Aloe barbadensis</i> [Liliaceae] (12)	Anthraquinone glycosides: Emodin, Barbaloin; Galacturonic acid, Vitamins, Enzymes, Minerals, Sugars, Lignin, Saponins, Salicylic Acids (12)	 <p>Emodin</p> <p>Barbaloin</p>	Antibacterial, Antiviral, Antiseptic, Anti-inflammatory, Laxative, Antitumor, Purgative, Anti-oxidative.	Active components in anthraquinone glycosides have anti-tubercular properties. It can inhibit the production of TNF- $\alpha$ and the proportion of Th17 cells.

<p>Garlic (Lahsun) <i>Allium sativum</i> [Amaryllidaceae]</p>	<p>Aliin, Allicin, E-Ajoene, Allylpropyl Disulfide, Diallyl Trisulfide, Sallylcysteine, Vinylidithiines, Allylmercaptocystein, Several enzymes (Allinase, Peroxidases, Myrosinase) (10)</p>	 <p>Allicin</p> <p>Alliin</p> <p>Diallyl Trisulfide</p> <p>E-Ajoene</p> <p>Vinylidithiines</p>	<p>Antioxidant, Antithrombotic, Antihypertensive, Antimutagenic, Anticarcinogenic, Antiviral, Antifungal, Antiparasitic, Antidiabetic, Immunomodulatory, Hypolipidemic.</p>	<p>Garlic has incredible antioxidant, bacteriostatic, and antifungal capabilities, as well as the ability to treat stomach disorders. It is essential in the treatment of several common Tuberculosis symptoms, such as cough, cold &amp; others (10)</p>
<p>Vidirakand (Bhukushmandi) <i>Pueraria tuberosa</i> [Fabaceae] (12)</p>	<p>B-Sitosterol, Stigmasterol, Deoxymiroestrol, Puerarin, Isoflavone, Puerarin, Daidzein, Tuberosi, Genistein, Quercetin, Irisolidone, Biochanin A, Biochanin B, Isoorientin, and Mangiferin (12)</p>	 <p>Deoxymiroestrol</p> <p>Genistein</p> <p>Puerarin</p>	<p>Hepatic Diseases, Fever, Antiaging, Spermatogenic, Boost-Immune, Restorative Tonic (13)</p>	<p>Vidirakand is a nutrient-dense plant that primarily benefits the digestive, respiratory, and circulatory systems. It assists ill individuals in gaining weight, as weight loss is a common sign of Tuberculosis.</p>
<p>Guduchi (Giloy) <i>Tinospora cordifolia</i> [Menispermaceae] (10)</p>	<p>Berberine, Isocolumbin, Chasmanthin, Palmarin, Tinosporon, Tinosporoside, Tinosporic acid and Tinosporol. (10)</p>	 <p>Berberine</p>	<p>Antidiabetic, Immunomodulation, Antioxidant, Anticancer, Hypoglycaemic, Hepatoprotective</p>	<p>Related antimicrobial qualities aid in the treatment of tuberculosis and its symptoms. Powders and extracts are commonly used (10)</p>

		 <p style="text-align: center;">Isocolumbin</p>		
Black Pepper (Peppercorn) <i>Piper nigrum</i> [Piperaceae] (14)	Aristolactams, Dioxoaporphin, Isobutyl amide, Lignin, Piperine, Longamide, Pluviatilol, Chavicine, Fargesin, Asarinine.	 <p style="text-align: center;">Piperine</p> <p style="text-align: center;">Chavicine</p>	Antioxidant, Anti-inflammatory, Anticancer, Anti-obesity, Antidepressant, Antidiabetic, Antimicrobial, Gastroprotective (15)	Piperine has anticongestion properties and clears clogged passages, and it helps TB patients breathe better by acting as a bronchodilator
Amla (Amalaki) <i>Phyllanthus emblica</i> [Phyllanthaceae] (16)	Ascorbic acid Ellagic acid, Chebulinic acid, Gallic acid, Chebulagic acid, Apeigenin, Quercetin (16)	 <p style="text-align: center;">Gallic acid      Ascorbic acid</p> <p style="text-align: center;">Ellagic acid</p>	Antioxidant, Hepatoprotective Cardioprotective Immuno-modulatory, Hypolipemic, Anticancer, Antidiabetic, Antidepressant, Antiulcerogenic, Insecticidal, Larvicidal.	Patients' immunity is boosted, and their digestion is improved; they also have a strong antibacterial activity. It's available as syrups, amla juice, chewing tablets.
Mint (Peppermint, Pudina) <i>Mentha piperita</i> [Lamiaceae] (17)	Essential oils: Menthol (29.38%), Menthone (16.88%), Menthofuran (11.38%), Cis-carane (14.39%), 1,8-cineole (9.45%), Caryophyllene (2.76%), β-Pinene (2.26%), α-Pinene (1.55%) (17)	 <p style="text-align: center;">Menthol      Menthone      Menthofuran</p> <p style="text-align: center;">Cis-Carane      Caryophyllene</p> <p style="text-align: center;">Alpha-Pinene      Beta-Pinene</p>	Astringent, Antiseptic, Antipruritic, Antispasmodic, Antiemetic, Carminative, Diaphoretic, Mild Bitter, Analgesic, Anticatarrhal, Antimicrobial, Rubefacient, Stimulant, Emmenagogue. (17)	Mint leaves can improve gastrointestinal issues, as well as relieve the symptoms of a common cold, cough, and congestion. They're also antibacterial and anti-inflammatory.



<p>Noni or Ashoka (Indian mulberry) <i>Morinda citrifolia</i> [Rubiaceae] (15)</p>	<p>Anthraquinones: Morindone Glycosides: Flavanol &amp; Iridoid, Triterpenoids, Ursolic acid, <math>\beta</math>-sitosterol, Asperuloside, Carminic acid, Damnacanthol.</p>	 <p>Morindone</p> <p>Carminic acid</p> <p>Damnacanthol</p>	<p>Antileucorrhoeic Antidysenteric, Emmenagogue, Antibacterial, Antiviral, Antifungal, Antihelminthic, Antitumor, Analgesic, Hypotensive, Anti-inflammatory, and Immune enhancing effect.</p>	<p>Morinda contains antibacterial properties that are effective against TB bacteria. The phytochemical derived from medicinal plants can destroy the tuberculosis causative agent (<i>M. tuberculosis</i>).</p>
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More than 64 plants have been shown to have antibacterial qualities, while over 24 plants have been discovered to have anti-diabetic effects (9). *Naja kaouthia* and *Daboia russellii* are antidotes. Venom is neutralized by lupeol acetate, which is obtained from the Indian sarsaparilla *Hemidesmus indicus*'s root extract. The current work aims to isolate and purify other active component via the root of *Hemidesmus indicus* (12), which is capable for neutralizing snake venom. Both cobra venom and viper antagonism, antioxidant potential and antiserum activity potentiation of the active component are examined in experimental animals (18). An active component derivative from extract of seed of *Strychnos nux vomica* decreased lipid peroxidation of viper venom in experimental mice. In order to develop a plant-derived therapeutic antagonist for snakebite, more research into the pharmacological of action of plant-obtained micro molecules that cause venom neutralization is needed (9).

### 3.2. Adjuvant treatment

By restoring oxidoreduction homeostasis, generating a cytokine equilibrium, and increasing redox homeostasis, liposomal GSH supplementation improved immune responses against *M. tuberculosis* infection (3). When compared to antibiotics alone, *Mtb* intracellular survival was significantly reduced when inadequate dosages to macrophages of any of the first-line antibiotics were combined with a precursor of GSH known as N-acetyl cysteine (NAC) (11). When NAC was coupled with antibiotics, macrophages produced less TNF-, "an inflammatory cytokine highly expressed in *Mtb* infection, and IL-10, an immunosuppressive cytokine" (11). These studies imply that to treat *Mtb* infection GSH may be used in addition to first-line antibiotics. T cells originate in variability in shapes and sizes as section of adaptive immune response to protect the human body (18). T helper cells are amongst the most frequent kinds of T cells, and they help mediate immune responses by producing cytokines. Controlling *Mtb* intracellular infections requires Th1 cells in particular. 1,25 (OH)<sub>2</sub>D and Vitamin D inhibit Th17 and Th1 cell proliferation and the production of pro-inflammatory chemokines including IFN- $\alpha$ , IL-2, and IL-17, while also triggering T regulatory responses. Vitamin D makes *Mtb* less viable (19). Due to their significant anti-inflammatory properties, synthetic steroids (Corticosteroids) like prednisone and dexamethasone have been commonly active in the action of several autoimmune and viral disorders (18). According to a 2017 study, glucocorticoids help mycobacteria survive by blocking TBK1 Kinase, a moderator of nitric oxide production and autophagosome maturation, as well as down regulating autophagy helping genes. Glucocorticoids stimulate Akt/mTOR pathway, that suppresses cell death (19). These approaches demonstrate how glucocorticoids may compromise TB therapy by suppressing the immune system, allowing mycobacteria to thrive and latent TB to reawaken (18).

### 3.3. Nutritional value (patients need nutrition)

Nutritional supplements might help people with tuberculosis have a better prognosis (11). According to a study, dietary guidance to increase energy intake combined with supplements caused in a significant rise in body weight, and physical

role after 6 weeks when begun during the preliminary stage of TB therapy (11). Vitamins and minerals have been demonstrated to aid in the treatment of tuberculosis. Participants in a research with 110 new cases of active TB were given either tuberculosis chemotherapy alone, or tuberculosis chemotherapy with preantrol thiamine, vitamin B6, and oral multivitamin supplement or vitamin C (19). The vitamin supplemented groups all had significantly higher lymphocyte proliferation responses than the control group. Another study indicated that adding vitamins C and E to multidrug TB treatment boosted tuberculosis immune responses. Vitamin A and zinc supplementation enhance the efficacy of antitubercular drugs in the first two months (11). A better follow-up was predicted by the higher quantity of patients with bacilli-free sputum and a substantially lesser mean lesion size in the lungs.

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#### 4. Conclusion

Nature provides a plentiful supply of plants that can be utilized to treat human illnesses. Herbs have had a wide range of effects on human health as a foundational and important structure of traditional medicinal systems. Progress in the quest for exemplary treatments may be shown in the potency of chemically different compounds and herbs as prospective hepatoprotective and antimycobacterial agents. Combining the receptor specific characteristics of anti-TB medications with the many health advantages of medicinal plants might thus be a beneficial method to control tuberculosis and its adverse effects. Many people in poor nations use both prescription medications and herbal supplements at the same time. As a result, suitable research is needed to counteract this prevalent frequency. The mechanism behind the engagement of anti-TB drugs with herbal constituents has received little attention. There is a significant knowledge gap between attending physicians and the medicinal usage of herbal adjuvants. Plants having anti-tubercular and anti-oxidant capabilities might be investigated for their effective molecules and utilized in the development of new formulations that are acceptable to a larger range of doctors. Thus, before large-scale human usage, detailed studies of herb–drug interactions in many conventional experimental setups are required to assure the safety and effectiveness of such combos.

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#### Compliance with ethical standards

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##### *Disclosure of conflict of interest*

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work.

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#### References

- [1] Sudre P, ten Dam G, Kochi A. Tuberculosis: a global overview of the situation today. *Bull World Health Organ.* 1992;70(2):149-159.
- [2] Addington WW. The side effects and interactions of antituberculosis drugs. *Chest.* 1979; 76(6), 782–784.
- [3] Amin A, Vartanian A, Yegiazaryan A, Al-Kassir AL, Venketaraman V. Review of the effectiveness of various adjuvant therapies in treating mycobacterium tuberculosis. *Infectious Disease Reports.* 2021; 13(3): 821.
- [4] Debnath PK, Chattopadhyay, et.al. Adjunct therapy of Ayurvedic medicine with anti-tubercular drugs on the therapeutic management of pulmonary tuberculosis. *Journal of Ayurveda and Integrative Medicine.* 2012; 3(3): 141–149.
- [5] Devade O, Londhe R, Rathod N, Kupate J, Meshram N. Ayurvedic Remedies of Covid-19. *International Journal of Pharmaceutical Sciences Review and Research.* 2021; 70(2): 280–290.
- [6] Forget EJ, Menzies D. Adverse reactions to first-time antituberculosis drugs. *Expert Opinion on Drug Safety.* 2006; 5(2): 231–249.
- [7] Holland DP, Sanders GD, Hamilton CD, Stout JE. Costs and cost-effectiveness of four treatment regimens for latent tuberculosis infection. *American Journal of Respiratory and Critical Care Medicine.* 2009; 179(11): 1055–1060.
- [8] Khan KH. Roles of *Emblca Officinalis* (Amla) in Medicine. 2014; 3(6): 604–615.

- [9] Khusro A, Aarti C, Barbabosa-Pliego A, Salem AZM. Neoteric advancement in TB drugs and an overview on the anti-tubercular role of peptides through computational approaches. *Microbial Pathogenesis*. 2018; 114: 80–89.
- [10] Kurane SB, Singh VB, Waghmare SD. Rehabilitation of pulmonary tuberculosis patient with Kharjuradi Ghrita and Pranayama: A study. *International Journal of Research in Health Sciences*. 2014; 2(3): 755–760.
- [11] Mueller-Wieland K. Tuberculosis and nutrition. *Deutsches Medizinisches Journal*. 1961; 12: 145–149.
- [12] Samal J. Ayurvedic management of pulmonary tuberculosis: A systematic review. *Journal of Intercultural Ethnopharmacology*. 2016; 5(1): 86–91.
- [13] Saroya AS. Herbal drugs as therapeutic agents. *Herbal Drugs as Therapeutic Agents*. August 2014; 1–214.
- [14] Semanya SS, Maroyi A. Medicinal plants used for the treatment of tuberculosis by Bapedi traditional healers in three districts of the Limpopo Province, South Africa. *African Journal of Traditional, Complementary, and Alternative Medicines: AJTCAM / African Networks on Ethnomedicines*. 2013; 10(2): 316–323.
- [15] Shingate PN DP, KD. New Method Development for Extraction and Isolation of Piperine from Black Pepper | *International Journal of Pharmaceutical Sciences and Research*. *International Journal of Pharmaceutical Sciences and Research*. 2013; 4(8): 3165–3170.
- [16] Starke JR. Modern approach to the diagnosis and treatment of tuberculosis in children. *Pediatric Clinics of North America*. 1988; 35(3): 441–464.
- [17] Tandon N, Yadav SS. Contributions of Indian Council of Medical Research (ICMR) in the area of Medicinal plants/Traditional medicine. *Journal of Ethnopharmacology*. 2017; 197: 39–45.
- [18] Verma S, Singh SP. Current and future status of herbal medicines. *Veterinary World*. 2008; 1(11): 347–350.
- [19] Xu Y, Liang B, Kong C, Sun Z. Traditional Medicinal Plants as a Source of Antituberculosis Drugs: A System Review. *BioMed Research International*. 2021.
- [20] Mathew TS. Performance of the Alcohol Use Disorders Identification Test among Tuberculosis Patients in Russia. *Substance Use & Misuse*. 2010; 45(4): 598–612.
- [21] Singh M, Kaur M, Silakari O. Flavones: an important scaffold for medicinal chemistry. *European Journal of Medicinal Chemistry*. 2014; 84: 206–239.
- [22] Cantrell CL, Franzblau S, Fischer N. Antimycobacterial plant terpenoids. *Planta Medica*. 2001; 67(8): 685–694.
- [23] Abedinzadeh M, Gaeini M, Sardari S. Natural antimicrobial peptides against *Mycobacterium tuberculosis*. *Journal of Antimicrobial Chemotherapy*. 2015; 70(5): 1285–1289.