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Review Article

A review on plants possesses anti tubercular activity

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ABSTRACT

Introduction: Tuberculosis is an infectious disease condition that mainly affects the lungs, and the responsible bacteria is *Mycobacterium tuberculosis*. Over 4,000 people each day die from this disease, which also claims 1.2–1.5 million lives annually and has infected 1.7–2 billion individuals globally.

Materials and Methods: The literature review was conducted by studying the research papers and review articles concentrating on the traditional plants having “Antituberculosis activity or anti-mycobacterial activity”, in electronic databases like PubMed, Science Direct, Scopus, and Google Scholar.

Results: The available synthetic therapy for tuberculosis treatment includes first-line treatment of five drugs namely “Isoniazid, Rifampicin, Ethambutol, Pyrazinamide, and Streptomycin. The synthetic drugs used in the treatment of tuberculosis result in hepatotoxicity and also cause resistance against *mycobacterium tuberculosis* bacteria, resulting in MDR TB and XDR TB. Plant-derived drugs have potent activity against tuberculosis bacteria also they give hepatoprotective activity, unlike the synthetic drugs with no resistance against the bacteria.

Conclusion: Medicinal plant products are good alternatives to allopathic medicine with fewer side effects and with less chances of resistance. Because polyherbal formulation act by different mechanisms to inhibit the growth of bacteria. More research is required to explore the plant-based treatment of TB.

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1. Introduction

Plants have been used for human and animal welfare since the beginning of time and according to several scientists, there are over 25,000 biologically active chemicals. The plant itself is an entire bioagent for treatment. Tuberculosis is the second most prevalent bacterial infection. It is a communicable disease caused by the organism *Mycobacterium tuberculosis*. This bacterium is stained by Ziehl–Neelsen dye. *M. tuberculosis* is an internal pathogenic bacterium that divides its cells only occasionally, has a mycolic acid coating and is non-motile. Tuberculosis

(TB) is brought on by microbes that travel from person to person through the air. Although TB most frequently affects the lungs, it can also harm the brain, kidneys, lymph nodes, bones, spine, and skin. TB bacteria move from the lungs through the blood or lymphatic system to different parts of the body (Cobat et al., 2013; Walker & Whittlesea, 2012; World Health Organization, n.d.). The World Health Organization (WHO) declared tuberculosis (TB) a worldwide emergency in 1993 as a result of an upsurge in cases of TB being recorded in nations on all continents (World Health Organization, n.d.). Over 4,000 people each day die from this disease, which also claims 1.2–1.5 million lives annually and has infected 1.7–2 billion individuals globally. With as many as 13 million latent tuberculosis

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infections in the United States (LTBI) (World Health Organization, n.d.). 5–10% of these LTBI patients will evolve to active tuberculosis. There are roughly 15 million active tuberculosis occurrences each year, with India, Indonesia, South Africa, Nigeria, the Philippines, Pakistan, Bangladesh, and China suffering the heaviest burden. Multidrug-resistant tuberculosis (MDR-TB) epidemics in several parts of the world have raised further concerns. A bacterium that is resistant to at least isoniazid and rifampin, the two most effective TB medications, it causes multidrug-resistant tuberculosis (MDR TB). A minimum of four second-line anti-TB medications should be used in the MDR regimen. All regimens should contain a second-line injectable medication, other second-line oral medications, and a later-generation fluoroquinolone such as levofloxacin or moxifloxacin (Seung et al., 2015). An uncommon form of multidrug-resistant tuberculosis (MDR TB) known as extensively drug-resistant TB (XDR TB) is resistant to isoniazid, rifampin, a fluoroquinolone, and at least one of three injectable second-line medications (i.e., amikacin, kanamycin, or capreomycin). Seung et al., 2015; Drug-resistant TB requires a more complicated, expensive, and prolonged course of therapy than drug-susceptible infections (Iseman, 2002; World Health Organization, n.d.). In this review, we discuss the biological source, geographical source, chemical constituents, extraction method, and type of plant extract with anti-tubercular activity. And also, the reported activity of different plants. (Abdulhamid et al. 2021, Almeida et al. 2019).¹⁻³

2. Materials and Methods

The study of the literature review was conducted by studying the research papers and review articles concentrating on the traditional plants having “Antituberculosis activity or anti-mycobacterial activity”, in electronic databases like PubMed, Science Direct, Scopus, and Google Scholar.⁴⁻¹⁰

3. Introduction of Traditional Plant

Traditional plant having an anti-TB activity: (Mentioned in Table)

Brief introduction of the herbal plant having anti-TB activity.

3.1. *Saussurea lappa*

Biological source: It consists of dried root and bark of *Saussurea lappa* belonging to the family Asteraceae. (Zahara et al., 2014b)

Synonym/Common name (Góis et al., 2017; Zahara et al., 2014b)

1. Hindi: - Kuth,
2. Sanskrit: - Kushta

Geographical source: (Amara et al., 2017; Singh et al., 2017)

The regions of the Himalayas, Kashmir-Jammu, Kishenganga valley, Panjab, Himachal Pradesh, Western Ghats, Tamil Nadu, and Uttar Pradesh. It is a native of the cool temperate and arctic regions of Asia, Europe, North America, the Himalayas, and Central Asia.

Taxonomy: (Singh et al., 2017)

1. Kingdom - Plantae
2. Subkingdom – Viridiplantae
3. Division - Tracheophyta
4. Subdivision – Spermatophytina
5. Class - Magnoliopsida
6. Family - Asteraceae
7. Species - *S. lappa* C.B. Clarke

Morphological description: (Amara et al., 2017; Singh et al., 2017)

1. Height - 1-2 meters
2. Stem - Upright, stout, and fibrous
3. Root - Long stout of approximately 60 cm with a characteristic odour
4. Leaves - Lobate, stalked, membranous, irregularly toothed
5. Upper leaves – Small while basal leaves are large with long lobately winged stalks.
6. Flowers - Stalkless, dark purple to black in color and are arranged in terminal and axillary heads
7. Fruit - Cupped, Curved, Compressed Hairy

Chemical constituents: Amara et al., 2017; Singh et al., 2017

The roots mainly contain Monoterpenes, Sesquiterpenoids, Flavonoids, Lignans, Triterpenes, Steroids, Glycosides, etc. The roots are a rich source of sesquiterpenoids especially sesquiterpene lactones. The principal compounds are Dehydrocostus lactone and Costunolide.

Pharmacological activity: (Amara et al., 2017; Singh et al., 2017; Zahara et al., 2014b)

Anti-tubercular activity: Using a fluorometric Alamar Blue microassay (FMABA), the in-vitro antimycobacterial activity of *S. lappa* was examined. The results showed that costunolide and dehydrocostuslactone, with MICs of 6.25 and 12.5 mg/L, respectively, were primarily responsible for the antimycobacterial activity against *Mycobacterium TB H37Rv*. It was discovered that the combination's antimycobacterial activity was superior to that of the individual compounds, and as a result, both lactones displayed synergistic action, with an X/Y value of 0.5 at a concentration of 1/8 of the MIC for each component.¹¹⁻¹⁶

Other reported activity

1. Antiulcer activity

2. Antitumor activity
3. Anti-inflammatory activity
4. Immunomodulatory effect
5. Hepatoprotective effect
6. Cardioprotective effect
7. Anticonvulsant activity
8. Larvicidal activity
9. Antiangiogenic effect
10. Antidiarrheal activity
11. Anti-epileptic

3.2. *Bauhinia purpurea*

Biological source:(Rashed et al., n.d.)

It consists of dried roots of *Bauhinia purpurea* belonging to the family Fabaceae. *Synonym/Common name*:(Rashed et al., n.d.; Sumit K Arora et al., 2020a)

English: -Purple Bauhinia, Orchid Tree, Camel's Foot Tree, Butterfly Tree, Geranium Tree

Hindi: -Kaniar

Geographical source:(Boonphong et al., 2007; Kittakoop et al., n.d.)

Native: Bangladesh, Bhutan, China, India, Indonesia, Japan, Malaysia, Myanmar, Pakistan, Sri Lanka, Taiwan, Province of China, Thailand

Exotic: Australia, Egypt, Kenya, Mauritius, Philippines, Puerto Rico, Sierra Leone, Uganda, United States

Miscellaneous: Pacific Islands, United States of America

Taxonomy: (Sumit K Arora et al., 2020a)^{17–20}

1. Kingdom-Plantae
2. Class-Dicotyledonae
3. Order-Fabales
4. Family-Fabaceae
5. Subfamily -Caesalpinaceae
6. Species-Bauhinia purpurea

Morphological description:(Sumit K Arora et al., 2020a)

1. Height: -10 M. Tall
2. Bark: - Smooth and Fibrous
3. Leaves: - Deeply Divided, Similar to A Cow's Foot
4. Flowers: -Pink, Fragrant
5. Fruit: -Flat Bean Like, Woody, Coils After Splitting Open

1. *Chemical constituents*: (Boonphong et al., 2007; Rashed et al., n.d.) The plant mainly contains secondary compounds like Glycosides, Flavonoids, Saponins, Triterpenoids, Phenolic Compounds, Oxepins, Fatty Acids and Phytosterols. The principal constituents are Bauhinioxepin, Dihydrodibenoxepins and dihydrobenzofuran.

2. *Pharmacological activity*: (Apisantiyakom et al., n.d.; *Bauhinia purpurea*, n.d.; Boonphong et al., 2007; Góis et al., 2017; Kittakoop et al., n.d.; Rashed et al., n.d.; Sumit K Arora et al., 2020a, 2020b)

3. *Antimycobacterial activity*: Antimycobacterial activity of *B. purpurea* root extract was examined against *Mycobacterium tuberculosis* H37Ra using the microplate Alamar Blue assay. The properties in comparison with those of the kanamycin sulfate and isoniazid standard drugs. The extract and its separated bioactive components had strong antimycobacterial activity.

3.3. *Acorus calamus*

Biological source: It consists of dried rhizomes of *Acorus calamus* belonging to family Acoraceae.(Rajput et al., 2014)

Synonym/Common name: (Rajput et al., 2014)

English-Sweet Flag

Hindi-Bajai,Gora-bach,

Geographical source: Rajput et al., 2014; Yende et al., n.d.

It is native of central Asia and eastern Europe, and is indigenous to the mountains of India. It is cultivated throughout India at an altitude of about 2200m mainly at Jammu-Kashmir, Himachal Pradesh, Manipur, Nagaland, Uttarakhand, Uttar Pradesh, Tamil Nādu, Andhra Pradesh, Maharashtra and Karnataka.^{21–23}

Taxonomy: Rajput et al., 2014; Yende et al., n.d.

1. Kingdom: - Plantae
2. Subkingdom: -Tracheobionta (Vascular plant)
3. Super division: -Spermatophyta (Seed plants)
4. Division: -Magnoliophyta (Flowering plants)
5. Class: -Liliopsida (Monocotyledons)
6. Subclass: -Arecidae
7. Order: -Arales
8. Family: -Acoraceae
9. Species: -calamus

Morphological description:

1. Height - 1-2 m
2. Rhizomes - brown in colour, twisted, cylindrical, curved, and shortly noded
3. Leaves - radiant green, with a sword like structure, thicker in the middle and has curvy margins

Chemical constituents: Sharma et al., 2020

Rhizomes and leaves of *Acorus calamus* contain compounds like Phenylpropanoids, Sterols, Triterpene Glycosides, Triterpenoid Saponins, Sesquiterpenoids, Monoterpenes and Alkaloids. The principal constituents are α and β -asarone.

Table 1: Tabular presentation of the plant having anti-TB activity

| Sr. No. | Plant Name | Biological Source | Solvent & Type of extraction | Active constituents | |
|---------|----------------------------|---|---|---|---|
| 1. | <i>Saussurea lappa</i> | It consists of dried root and bark of <i>Saussurea lappa</i> Family: Asteraceae | Ethanol (Soxhlet extraction) | Dehydrocostuslactone, Costunolide α -hydroxydehydrocostus lactone, β -hydroxydehydrocostus lactone, lappadilactone | (Ambavade et al., 2009; Singh et al., 2017; Zahara et al., 2014a) |
| 2. | <i>Bauhinia purpurea</i> | It consists of Dried roots of <i>Bauhinia purpurea</i> Family: Fabaceae | Dichloro methane (Maceration) | Bauhinoxepin, Dihydrodibenoxepins and dihydrobenzofuran | (Boonphong et al., 2007; Rashed et al., n.d.; SumitKArora et al., 2020a) |
| 3. | <i>Acorus calamus</i> | It consists of dried rhizomes of <i>Acorus calamus</i> Family: Acoraceae | Water (Maceration and Soxhlet extraction) | α and β -asarone, | (Sharma et al., 2020; Webster et al., 2010) |
| 4. | <i>Morinda citrifolia</i> | It consists of leaves and fruits of <i>Morinda citrifolia</i> . Family: Rubiaceae | Ethanol (Soxhlet extraction) | Lucidin, Rubiadin, Rutin, Narcissoside Quercetin, Scopolectin. | (Almeida et al., 2019; Mohamad Shalan et al., 2016; Sudha et al., 2019) |
| 5. | <i>Alpinia galanga</i> | It consists of roots and rhizomes of <i>Alpinia galanga</i> Family: Zingiberaacee | Dichlorom ethane and Ethanol (Soxhlet extraction) | 1'-acetoxychavicol acetate | (Alajmi et al., 2018; Chouni Anirban., 2017a, 2017b; Gupta et al., 2014; Trimanto et al., 2021; Verma et al., n.d.) |
| 6. | <i>Acacia nilotica</i> | It consists of the dried fruits of <i>Acacia nilotica</i> Family: Fabaceae | aqueous methanolic extract (Soxhlet) | D-Pinitol | (Abdulhamid et al., 2021; Foyzun et al., 2022; Samuel, n.d.) |
| 7. | <i>Aegle marmelos</i> | It consists of Unripened pulp of Fruit of <i>Aegle marmelos</i> Family: Rutaceae | Aqueous extract (Maceration) | Coumarins and marmelosin | (Chinchansure et al., n.d.; Suja et al., 2017) |
| 8. | <i>Micromelum hirsutum</i> | It consists of stem bark of <i>Micromelum hirsutum</i> Family: Rutaceae | Dichloromethan Extract (Maceration) | Carbazole | (Ma et al., 2005) |
| 9. | <i>Acalypha indica</i> | It consists of leaves of <i>Acalypha indica</i> Family: Euphorbiaceae | Aqueous extract (Maceration) | Cyanogenic Glucoside Acalyphin | (Ramalingam Govt & Manickan, 2016) |
| 10. | <i>Juniperus procera</i> | It consists of leaves and bark of <i>Juniperus procera</i> Family: Cupressaceae | Ethanolic extract (Soxhlet) | Diterpenes 1–3 | (Ghany & Hakamy, 2012; Mossa et al., 2004a, 2004b) |
| 11. | <i>Plumbago zeylanica</i> | It consists of aerial parts of <i>Plumbago zeylanica</i> Family: Plumbaginaceae | Ethanolic extract (Soxhlet) | Plumbagin | (Mossa et al., 2004a; Nayak et al., 2014) |
| 12. | <i>Ocotea notata</i> | It consists of Wood, leaf of <i>Ocotea notate</i> Family: Lauraceae | Ethanolic extract (Maceration) | Apomorphine | (Costa et al., 2015) |

Table 2: Other reported activity

| | |
|--------------------------------|---|
| Anti-diabetic activity | Anti-Depressant activity |
| Cytotoxic activity | Anti-inflammatory and Anti-arthritis activity |
| Antimalarial | Antinoceptive |
| Antifungal activity | Anti-Inflammatory |
| Hyperthyroidism | Antipyretic activity |
| Anti-diarrheal potential | Nephroprotective activity |
| Antimicrobial activity | Wound Healing activity |
| Fibrolytic Effect | Antioxidant activity |
| Antiepileptic (Anticonvulsant) | Anti-hyperlipidemic activity |
| Hepatoprotective activity | Anti-cancer activity |
| | Anti-Obesity activity |

Pharmacological activity: Rajput et al., 2014; Yende et al., n.d.

Antimycobacterial activity: Using the micro plate Alamar Blue assay technique, the anti-mycobacterial activity of *Acorus calamus* was examined. The result showed that the constituents namely α and β -asarone were responsible for the antimycobacterial activity against *Mycobacterium* bacteria.^{24–29}

Table 3: Other reported activity

| | |
|---------------------------|--------------------------|
| Anti-inflammatory | Anticancer Activity |
| Immunomodulatory activity | Antimicrobial Activity |
| Anti-oxidant | Pesticidal properties |
| Anticonvulsant | Antihypertensive Effect |
| Anti-spasmodic activity | Antidepressant effects |
| Hypolipidemic activity | Neuroprotective effects |
| Anti-diabetic activity | Cardioprotective effects |

3.4. *Morinda citrifolia*

Biological source: Mohamad Shalan et al., 2016; Sudha et al., 2019

It consists of leaves and fruits of *Morinda citrifolia* belonging to family Rubiaceae.

Synonym/Common name: Mohamad Shalan et al., 2016; Sudha et al., 2019

1. English: - Indian Mulberry, great morinda
2. Hindi: - Bartundi
3. Telugu: - Mogali

Geographical source: BS Thorat, 2017

It is native to Southeast Asia and Australia. In India it is cultivated at Tamil Nadu, Kerala Maharashtra, Karnataka, Andhra Pradesh and Odisha.

Taxonomy: Sudha et al., 2019

1. Kingdom: -Plantae
2. Class: -Magnoliopsida (dicot)

3. Order: -Rubiales

4. Family: -Rubiaceae (coffee family)

5. Genus: -Morinda

6. Species: -citrifolia

Morphological description: Mauliku et al., 2017; Sudha et al., 2019^{30–33}

1. Height: - 3 to 10 m
2. Leaves: - Opposite, pinnately veined and glossy, blades membranous, elliptic to elliptic-ovate, 20 to 45 cm long, 7 to 25 cm wide,
3. Flowers: -White in color
4. Fruit: - Yellowish white; fleshy, 5 to 10 cm long, about 3 to 4 cm in diameter, soft and fetid when ripe
5. Seed: - It has a distinct air chamber, and can retain viability even after floating in water for a month.

1. **Chemical constituents:** (BS Thorat, 2017; Mauliku et al, 2017 The fruits of *Morinda citrifolia* contain flavonoids, coumarins, anthraquinone, alkaloids and terpenoids. The responsible constituents for anti-tuberculosis activity are lucidin, rubiadin, Rutin, Narcissoside, Quercetin, and scopoletin.

2. **Pharmacological activity:** (Almeida et al., 2019; BS Thorat, 2017; Maulikku et al., 2017; Mohamad Shalan et al., 2016; Sudha et al., 2019)

3. **Anti-TB activity:** At different concentrations, noni fruit's active ingredients, including flavonoids, scopoletin, anthraquinone, and alkaloids, greatly inhibit the growth of *Mycobacterium tuberculosis* strain H37Rv. In comparison to scopoletin, the crude extract containing alkaloids, anthraquinones, and flavonoids had the strongest anti-tubercular activity in preventing the growth of the *Mycobacterium tuberculosis* strain H37Rv. At a dosage of 40 mg/ml, the lowest inhibitory concentration was discovered.

3.5. *Alpinia galangal*

Biological source: (Alajmi et al., 2018; Ghosh & Rangan, 2013)

Table 4: Other reported activity

| | |
|--------------------------------------|---------------------------|
| Anti-tumour and anti-cancer activity | Hypoglycemic activity |
| Bactericidal activity | Anthelmintic activity |
| Antifungal activity | Bone protective effect |
| Antiviral activity | Antidepressant/sedative |
| Antioxidant activity | Analgesic |
| Hypotensive activity | Skincare/hair |
| Immunostimulant activity | Wound healing activity |
| Anti-obesity activity | Hepatoprotective activity |

It consists of roots and rhizomes of *Alpinia galanga* belonging to the family Zingiberaceae.

Synonym/Common name: (Gupta et al., 2014; Verma et al., n.d.)

1. Hindi - Kulanjan
2. Gujarati – Kulinjan

Geographical source: Ghosh & Rangan, 2013; Verma et al., n.d.

It is native to Thailand, Malaysia, and China. In India it is cultivated in the Himalayas, the Southern region of the western ghats in India.

Morphology

1. Height: - 2 to 3 m
2. Root: - Tuberos and slightly aromatic
3. Leaves: - Oblong-lanceolate, acute, glabrous, green above, paler beneath, with slightly callus-white margins
4. Flowers: - Greenish white, in dense flowered, 30 cm Panicles Fruit: - Small cherry size, orange red colour

Chemical constituents: Chouni Anirban., 2017a; Ghosh & Rangan, 2013; Verma et al., n.d.

The roots and rhizomes of *Alpinia galanga* contain essential oils, flavonoids, Phenolic compounds (phenylpropanoids), and terpenoids.

The rhizome of *Alpinia galanga* contains 5,7 Dihydroxyflavone, 1'acetoxy eugenol acetate, 1 acetoxyl chavicol acetate, Trans – cinnamic acid, etc.

The principal constituent for the anti-tuberculosis activity is 1 acetoxyl chavicol acetate.

1. Pharmacological activity: Alajmi et al., 2018; Chouni Anirban., 2017a; Ghosh & Rangan, 2013; Gupta et al., 2014; Trimanto et al., 2021; Verma et al., n.d.
2. Anti-tubercular activity: The active ingredient of the roots and rhizomes of *Alpinia galanga* namely 1 acetoxyl chavicol acetate has shown inhibitory activity

against the growth of *M. tuberculosis* bacteria strain H37Rv.

Table 5: Otherreported activity of *Alpinia galangal*

| | |
|--------------------------|----------------------------|
| Carminative | As Stomachic and stimulant |
| Digestive tonic | Improve appetite |
| Anti-emetic | Expectorant |
| Anti-fungal | Chest pain |
| Anti-tumour | Diabetes |
| Anti-helminthic | Burning of liver |
| Anti-diuretic | Kidney disease |
| Anti-ulcerative | Anti-bacterial |
| Anti-dementia | Anti-inflammatory |
| Bronchial catarrh | Flavoring agent |
| Used in Disease of heart | Anti-asthma |
| | Anti-rheumatoid |

4. Discussion

The rapid growth of drug resistance to the currently available medications makes the development of new, efficient, and cost-effective anti-TB treatments necessary (Gupta et al., 2014). Terpenoids, alkaloids, peptides, phenolics, and coumarins are only a few of the groups of plant-derived anti-mycobacterial chemicals (BS Thorat, 2017). As a result, medicinal plants continue to be a valuable source for discovering new therapeutic compounds. Less negative side effects, higher patient acceptance due to long-standing use, lower costs, and cultivability make employing antimicrobial chemicals from medicinal plants advantageous. These compounds are renewable in nature and have fewer adverse effects (Gupta et al., 2014). This review provides a thorough analysis of 12 plants namely *Saussurea lappa*, *Bauhinia purpurea*, *Acorus calamus*, *Morinda citrifolia*, *Alpinia galanga*, *Acacia nilotica*, *Micromelum hirsutum*, *Aegle marmelos*, *Acalypha indica*, *Juniperus procera*, *Plumbago zeylanica*, *Ocotea notata* those have anti-tuberculosis activity. All 12 plants have different principal chemical constituents that are responsible for the anti-mycobacterial activity. The phytochemical constituents of all plants are active against the mycobacterium bacteria with characteristic mechanisms of action that can't cause resistance against bacteria, which is the markable property of the plant's chemical constituent. Further studies are required for the preparation of an effective herbal formulation for tuberculosis treatment that also provides the hepatoprotective effect unlike the synthetic drugs available for tuberculosis treatment.

5. Conclusion

We conclude that Medicinal plant products are good alternatives to allopathic medicine with fewer side effects

and with less chances of resistance. Because polyherbal formulations act by different mechanisms to inhibit the growth of bacteria. More research is required to explore the plant-based treatment of TB.

6. Source of Funding

None.

7. Conflict of Interest

None.

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