Review Article

Comparative Analysis of the Therapeutic and Pharmacological Effectiveness of Indian Medicinal Plants as an Alternative to Allopathic of Tuberculosis

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ABSTRACT

The main ingredients of the many oriental formulas used in various traditional medical systems across the world are medicinal plants. Pharmacists are motivated to create novel medications based on the active ingredients or semi-metabolites of medicinal plants that have antituberculosis (TB) capabilities because these plants are a burgeoning supply of medicine. The scientific literature was used to choose the anti-TB medicinal plants that are included in this review, using both the botanical categorization and the anti-TB activity as criteria. The gathered anti-TB medicinal plants were split into three categories: 159 plants that underwent extensive investigation and yielded 335 isolated chemicals; 131 plants whose crude extracts shown anti-TB action; and 27 plants that were discovered in published studies and contained the traditional healers' recommended formula. Our thorough analysis of the medicinal plants can aid in the creation of fresh, more effective anti-tuberculosis drugs.

Keywords: Mycobacterium tuberculosis, in vitro activity polyherbal medicine Allopathic medicine.

INTRODUCTION

The face of tuberculosis (TB) has changed over time, going from an incurable illness to one that is treatable[1]. Mycobacterium tuberculosis is an infectious bacterium that is the cause of it. The growth of drug-resistant bacteria is the reason behind the global increase in tuberculosis incidence. Mycobacterium TB is developing resistance to the first and second-line medications used in treatment[2].

TB is a disease that majorly affects the lungs but can also affect other parts of the body and even lead to death of the individual if treatment gets neglected[3].

One significant development in the fight against tuberculosis (TB) was the development of antibiotics for its treatment. When the anti-tuberculosis medication schedule is adhered to precisely and thoroughly, medication treatment plays a critical role in managing tuberculosis, encouraging patient recovery, and severing the chain of transmission[4].

It is imperative to find and develop novel anti-TB medications with distinct pharmacological targets.

For millennia, people have used medicinal plants to treat a variety of illnesses, including tuberculosis. Native Americans around the world have been using infusions, macerations, tinctures, and decoctions of medicinal plant parts, including as leaves, roots, stem bark, stem, flowers, and fruits, as traditional therapies for tuberculosis (TB) for generations[5].

One test used to determine tuberculin infection is the Mantoux tuberculin skin test (TST). The test, which involves injecting pure protein derivative (PPD) of tuberculin intradermally, is based on the patient's cell-mediated immune system's delayed responsiveness to tuberculin antigens[6].

Numerous diagnostic procedures are frequently used, such as bacterial culture, immunological, radiography, microscopy, and clinical approaches[7].

The earliest experimental proof of the possible effectiveness of novel antituberculosis medications was gained in 1940 when a group of guinea pigs were given a chemical called promin, which is a derivative of dapsone. But that sulfonamide was never administered to anybody[8].

A new chapter in the history of tuberculosis control was written. For every afflicted person on the planet, seeking treatment to cure became their ultimate objective[9].

Throughout human history, the control and avoidance of tuberculosis (TB) have presented ongoing difficulties because of the disease's contagious nature, intricate immune response, long-term progression, and requirement for long-term treatment. In recent times, the rise of drug-resistant strains of tuberculosis and the ongoing HIV epidemic, together with their detrimental effects on society, have elevated tuberculosis to a significant health hazard. [10]

This paper aims to provide the comparative study of allopathy and herbal medicine in the treatment of tuberculosis.

Discovery of Mycobacterium tuberculosis (first TB drug)

The German physician Robert Koch's announcement on March 24, 1882, regarding his discovery of the tuberculosis cause, marked a turning point in the development of a therapy for the disease. In little than a year, when working alone, Koch achieved one of the most profound medical and scientific feats in human history[11]. Mycobacterium tuberculosis was identified as the causative bacillus. Details of Koch's discovery was published in a significant scientific journal seventeen days later—a very quick turnaround when compared to modern publishing standards[12]. Several promises of healing tuberculosis were made every year, but even many of the skeptics of the time were persuaded by Koch's presentation, which acted as a preamble to the formation of Koch's postulates. The news quickly reached to the world's major cities, inspiring triumphant acknowledgment and warm welcome. For this accomplishment, Koch received the 1905 Nobel Prize in Physiology or Medicine.

Guidelines of WHO:

The creation of evidence particular to IPC procedures in tuberculosis has not advanced much, and as of now, no data are available to assess the advancement of IPC measures' implementation worldwide, even in settings with high tuberculosis burdens. The guidelines and evidence for tuberculosis infection control in homes, healthcare facilities, and congregate settings were published by the World Health Organization in 2009. It has been expected that these documents will require updating. The updated guidelines also incorporate current World Health Organization (WHO) recommendations within the broader framework of IPC initiatives.[13]

We anticipate that Member States will develop national and subnational policies based on these guidelines. By lowering the number of TB cases and deaths in the upcoming years, the successful implementation of these recommendations will help achieve the "End TB Strategy."[14]

Guidelines are as follows;

1. Preventive Therapy: For those who are at a high risk of contracting tuberculosis (TB), such as those who are HIV-positive and have close contacts with TB patients, the WHO advises preventative medication. This entails giving medicine to stop a tuberculosis infection from becoming an active illness[15].

2. Diagnostic Algorithms: WHO has developed diagnostic algorithms to increase the precision and efficacy of tuberculosis (TB) diagnosis. These algorithms include recommendations for the quick identification of tuberculosis and drug resistance utilizing molecular techniques such as GeneXpert MTB/RIF. [16]

3. Treatment Regimens: For both drug-susceptible and drug-resistant tuberculosis, the World Health Organization (WHO) advises particular treatment plans, highlighting the significance of finishing the entire course of treatment to avoid the emergence of drug resistance.[17]

4. Infection Control Measures: The World Health Organization prioritizes the adoption of infection control strategies in hospital environments to impede tuberculosis (TB) transmission. These strategies include appropriate ventilation, donning personal protective equipment, and promptly identifying and isolating patients who are infected. [18]

5. Collaborative TB/HIV Activities: In order to address the dual burden of TB and HIV, WHO encourages cooperation between TB and HIV programs. Examples of such cooperation include integrated service delivery, TB screening for HIV-positive individuals, and antiretroviral medication for TB patients who are also co-infected with HIV. [19]

To effectively prevent, diagnose, and treat tuberculosis (TB), healthcare professionals and policymakers must adhere to these principles, which will also support international efforts to control and eradicate the illness.

Epidemiology:

When Homo sapiens left Eastern Africa for the rest of the world, TB expanded throughout, particularly along open supply routes where there was more population mixing and overcrowding. Over 1.3 million people die from active disease each year, out of approximately ten million new cases that are discovered. Several countries developed their own traditional anti-TB medications in accordance with the old plaque's spreading route during the protracted battle against it. There is TB data in numerous old texts from the traditional medicine system, such as TCM, Ayurveda, and TAM. This is because humans and the TM therapeutic system have coexisted for over 70,000 years. Studies on TM formulations indicate that the semi-metabolites or active compounds offer a rich foundation for novel drugs[20].

Improved access to healthcare and the introduction of immunization programs are to blame for the drop in the incidence of tuberculosis.8 In addition, the Saudi government increased the scope of the national tuberculosis control program (NTCP) in response to a call from the WHO in order to bring it into line with the objectives and benchmarks of the end-TB plan[21].

Pathogenesis:

Only a small number of MTB-containing droplet nuclei from infectious people reach alveoli; the majority are retained in the upper respiratory tract and ejected by ciliated mucosal cells. The mycobacteria then bind to the complement, mannose receptors, or type A skimmer on the cell surface of the alveolar macrophages. After phagocytosis, mycobacteria reduce the phagosome's acidity, and lipoarabinomannan, a component of the cell wall, influences the Caþ/calmodulin pathway to stop the phagosome from fusing with the lysosome. The bacilli proliferate and the macrophage ultimately bursts to

release its bacilli, which are subsequently picked up by macrophages and go on the infection cycle, further spreading the infection, once the phagosome's development is successfully terminated. MTB bacilli increased both lymphatically and hematogenously during the initial. Eventually, microbes enter the circulation of blood and go to other organs. This lympho-hematogenous dispersion, which can happen during a primary infection or later in life after a disease reactivation, results in extrapulmonary tuberculosis. While any area of the body could be impacted by EPTB, lymph nodes are most commonly suffering. However, there have been cases of involvement in the pleura, brain, synovium, pericardium, abdomen, and genitourinary system[1].

a. Tubercular Lymphadenitis

b. Pleural TB

c. Abdominal TB

d. Central Nervous System (CNS) tuberculosis

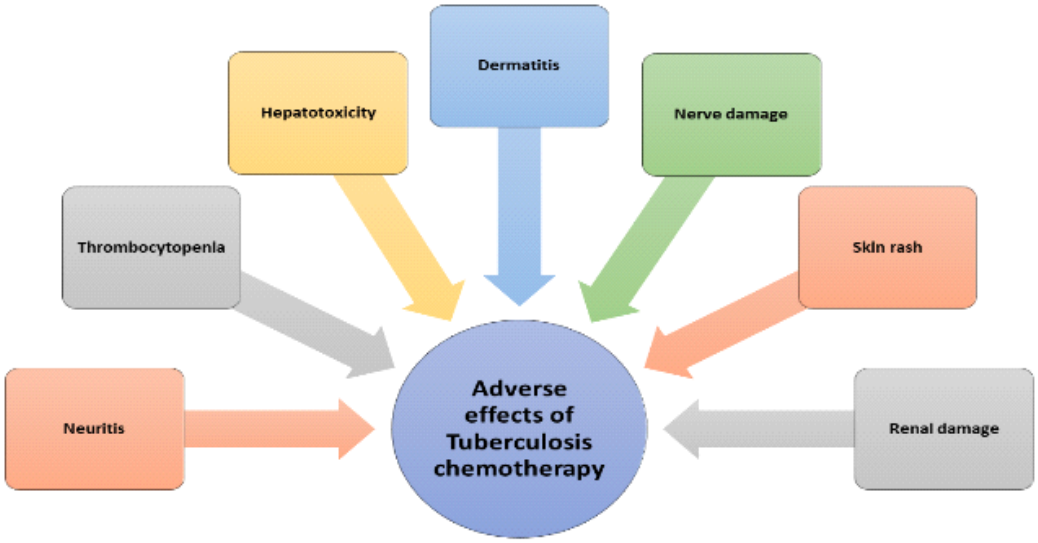
e. Bone and Joint TB

f. Genito-urinary TB (GUTB)

g. miliary TB

Clinical features:

Haematological reactions, gastrointestinal intolerance, hepatitis, renal failure, and dermatological reactions are all possible side effects of antituberculosis medications. Early detection of these detrimental effects is necessary to reduce associated disease and mortality[20].



Lab diagnosis table:

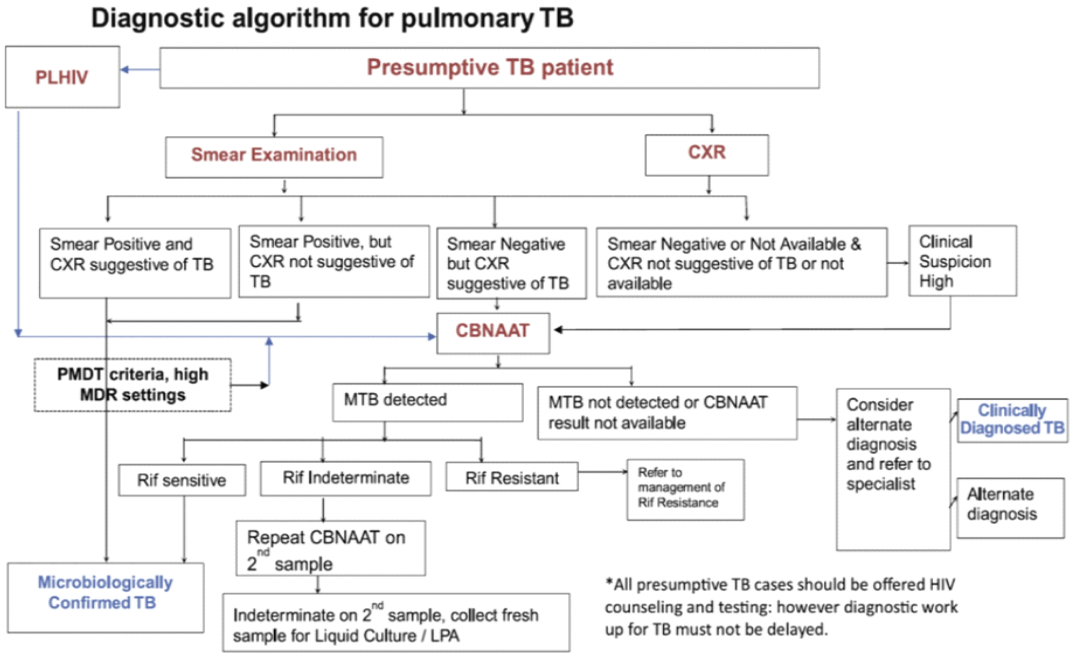


Figure 1: Diagnostic formula for tuberculosis in the lungs. Chest X-rays (CXRs), People Living with HIV (PLHIVs

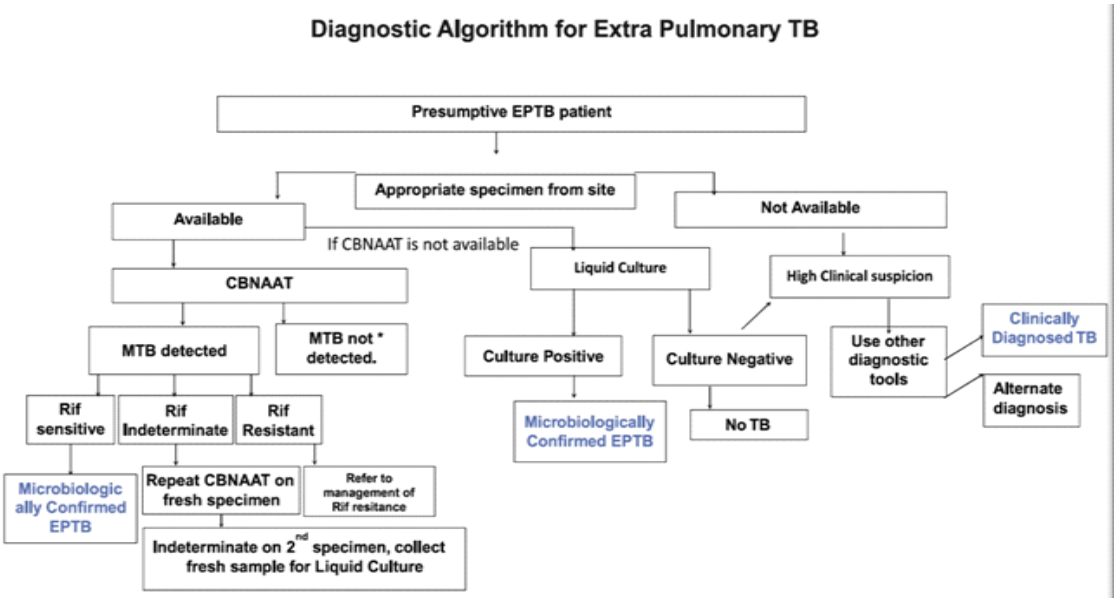
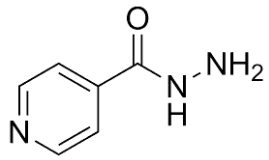
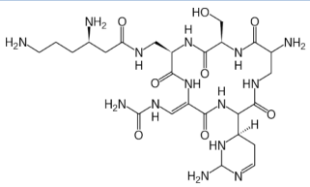
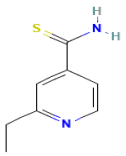
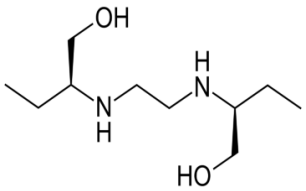
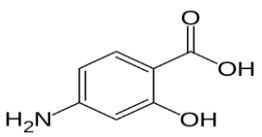
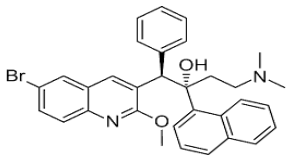
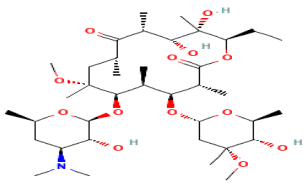
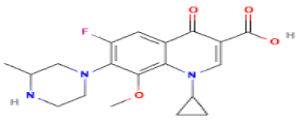
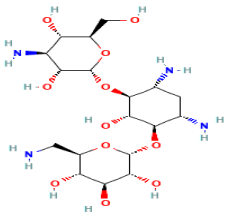
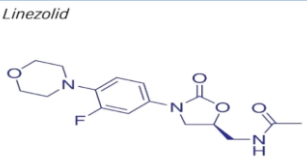
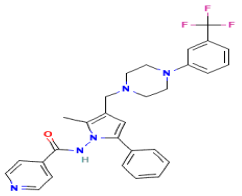
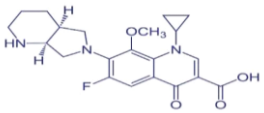
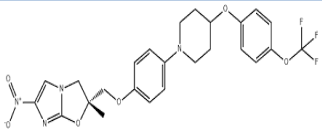
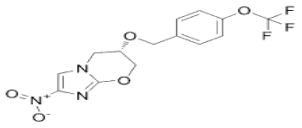
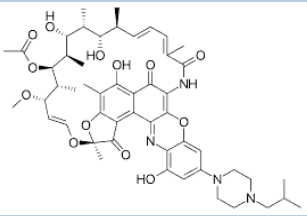


Figure 2: Formulary for diagnosing extrapulmonary tuberculosis[1]

TREATMENT

Use of allopathic medicines for the treatment of tuberculosis;

Name of drug	MOA	Side effects	Structure	Molecular formula	Ref
Isoniazid	Prevent the development of bacterial cell walls in Mycobacterium tuberculosis (Mtb) bacteria once they have been activated by the bacterial catalase–peroxidase enzyme KatG.	Neuropathy, Uncommonly hepatitis, Hypersensitivity			[22]
Capreomycin	Inhibit protein synthesis by binding to the 70S ribosomal unit.	derange renal function tests, Hearing damage, vestibular disturbance,		$C_{25}H_{44}N_{14}O_8$	[2]
Ethionamide	Inhibit peptide synthesis in susceptible organisms.	blue-yellow colour blindness, blurred vision or loss of vision, with or without eye pain,		$C_8H_{10}N_2S$	[2]
Ethambutol	Ethambutol inhibits arabinosyl transferases involved in cell-wall biosynthesis	Optic neuropathy /optic neuritis/ retrobulbar neuritis, Decreased visual acuity. Scotoma. Colour blindness, Peripheral neuropathy, Hepatotoxicity.		$C_{10}H_{24}N_2O_2$	[2]
Para- amino salicylic acid	Amino salicylic acid inhibits folic acid synth	anorexia, diarrhoea, nausea, and vomiting		$C_7H_7NO_3$	[2]

TMC-207	directed at ATP Synthase's C subunit	Acne and noncardiac chest pain, bilateral hearing impairment		$CH_{31}BrN_2O_2$	[2]
Clarithromycin	It binds to 50s ribosomal subunit and inhibit bacterial protein synthesis	Dryness, nausea, Excitement		$C_{38}H_{69}NO_{13}$	[2]
Gatifloxacin	Make an impact by entangling a DNA drug-enzyme complex and selectively blocking topoiso merase II (DNA gyrase) and topoisomerase IV, two ATP-dependent enzymes	Difficulty with swallowing, Dizziness, fast heartbeat, hives or welts, or skin rash		$C_{19}H_{22}FN_3O_4$	[2]
Kanamycin	It binds to conserved site of 16s rRNA in 30s ribosomal subunit and inhibits protein synthesis	Vestibular disturbance, Deranged renal function tests, Hearing damage,		$C_{18}H_{36}N_4O_{11}$	[2]
Linezolid	Inhibit translation in early phase preventing proper binding of formyl-methionine tRNA By binding to 23s rRNA	Headache, Diarrhoea, Dyspepsia	*Linezolid* 	$C_{16}H_{20}FN_3O_4$	[2]
LL-3858	Undefined mechanism				[2]
Moxifloxacin	Use a DNA drug enzyme complex to enact their actions, notably blocking the ATP-dependent enzymes	Insomnia, CNS dysfunction and Cardiotoxicity, Thrush, Gastrointestinal reactions,	*Moxifloxacin* 	$C_{21}H_{24}FN_3O_4$	[2]
OPC-67683	Inhibits the formation of mycolic acid, namely the inclusion of fatty acid and 14C-acetate.	Not defined		$C_{25}H_{25}F_3N_4O_6$	[2]
PA-824	Inhibit both protein and lipid synthesis	Headache, Stomach discomfort, Elevated serum creatinine level,		$C_{14}H_{12}F_3N_3O_5$	[2]
Rifalazil	Acts early in transcription to inhibit the crucial rpo B gene product b-subunit of DNA dependent RNA polymerase activity.	White cells and absolute neutrophil numbers, Decrease in blood counts including platelets		$C_{51}H_{64}N_4O_{13}$	[2]

Herbal medicines used in the treatment

Historically, a number of diseases, including tuberculosis, have been ameliorated by medicinal herbs. It is estimated that between 70% and 80% of people worldwide rely on the traditional medical system, which mostly uses herbal remedies. While some research has been done to employ medicinal plants as pure compounds, most applications of these plants are for their medical qualities when they are used as raw materials. One of the very few nations in the world having an important grasp of employing herbal medicine to treat a wide range of disorders and an abundance of medicinal plants is India. India is one of the world's top growers of medicinal plants and is referred to as the "Botanical Garden of the World".[2]

Some of the medicinal plants used are given below:

Sr. No.	Plant Name	Common Name	Plant Part	Family	Chemical constituent	References
1	*Acalypha indica L*	Acalypha	Leaf	Euphorbiaceae	Flindersin, acalyphamide, acalyphal acetate, succinimide and acalyphin	[23, 24]
2	*Adhatoda vasica Nees.*	Vasaka	Leaf	Acanthaceae	Volatile oil, quinazoline derivatives, turgorins, adhatodic acid, vasakin, betalin	[23, 24]
3	*Allium cepa L.*	Onion	Bulb	Alliaceae	Resins, cardiac glycosides alkaloids, flavonoids, terpenes and steroids	[23, 25]
4	*Allium sativum L.*	Garlic	Clove	Alliaceae	Disulfides and trisulfides,	[23, 26]
5	*Aloe vera L.*	*Aloe vera*	Leaf	Aloaceae	Lsobarbaloin, Anthrone-C-glycosides, chromones, aloe-emodin-9-anthrone, and barbaloin	[23, 27]
6	*Ocimum sanctum Linn.*	Holy Basil (Tulsi)	Leaves	Lamiaceae	orientin luteolin, luteolin-7-Oglucuronide, Ursolic acid, apigenin-7-Oglucuronide	[28, 27]
7	*Piper nigrum Linn.*	Black pepper (Kali Mirch)	Seeds	Piperaceae	pellitorine, pipnoohine, piperonal, guineensine	[20, 21]
8	*Trichosanthes dioica*	Patola	Leaves	Cucurbitaceae	Cucurbitacins, Tetra & pentacyclic triterpenes,	[22,23]
9	*Vitex negundo*	Nirgundi	Leaves, Seeds	Verbenaceae	7-diene, valencene, caryophyllene epoxide, guaia-3 (E)-nerolidol and p -cymene	[23,24]
10	*Aegle marmelos Corr.*	Rutaceae	Leaf	Bel	Cuminaldehyde, Eegelin, Cineol, Citral, Citronellal, Eugenol, Lupeol	[25,26]

Newer drugs[27]

1.Bedaquiline (PHASE II)

2.Pretomanid

3.Linezolid (PHASE II)

4.PA-824 (PHASE II)

5.Sutezolid (PHASE II)

6.AZD-5847 (PHASE II)

7.SQ-109 (PHASE II)

8.Delamanid (PHASE III)

9.Rifapentine (PHASE III)

10. Moxifloxacin (PHASE III)

Future prospective Management;

A new and effective vaccination by 2015, a new and effective TB medicine by 2010 (the first in 40 years), and a treatment regimen lasting 1-2 months shortly after are all notable turning points. However, achieving these will come at a hefty price: US$56 billion, which is US$31 billion more than the monies that have been identified thus far. Nevertheless, there are finally indications that business, academia, and philanthropy are collaborating—to differing degrees—through organizations such as, the Global Alliance for TB Drug Development (the TB Alliance), and the Aeras Global TB Vaccine Foundation. Unlike HIV/AIDS, TB now fills that function, and its victims are too few, strong, and well-spoken to change public opinion. Not just scientific but also social and political reforms are required if we hope to outperform our previous 25 years in the coming[27-28].

MARKETED PRODUCT OF TB (ALLOPATHIC)

MARKETED PRODUCT OF TB (HERBAL)

CONCLUSION

In conclusion, our review underscores the symbiotic relationship between herbal and allopathic treatments for Tuberculosis. While allopathic medications offer standardized protocols and proven efficacy, herbal therapies provide complementary approaches rooted in tradition and validated by modern research.

By leveraging the strengths of both modalities, we can enhance treatment outcomes, particularly in addressing challenges like drug resistance and adverse effects. This side effects associated with the allopathic drugs have remarkedly necessitate the need of herbal drugs. In this review have tried to make a complete description of all the antitubercular drugs around the globe. The various constitution present in plant make them as an antitubercular drugs.

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