



## Current and Future Prospective in Management of Tuberculosis

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### ABSTRACT:

One of the main causes of death worldwide, TB is a chronic, airborne bacterial infection brought on by the bacterium *Mycobacterium tuberculosis*. Symptoms include respiratory sickness and immune system impairment. The development of cross- or multidrug resistance, which makes therapy more difficult, as well as the major negative side effects of traditional synthetic therapeutic techniques have a negative influence on people's health. The Short Course (DOTS) programme, multidrug-resistant tuberculosis (MDRTB), unrestricted private health care resulting in widespread irrational use of first- and second-line anti-TB drugs, HIV coinfection, and unsatisfactory diagnostics and treatment are some of the main causes of the ongoing challenges in TB control. Natural goods have been and will continue to be a major source of cutting-edge treatments for a variety of diseases. It is possible to find novel molecules to prevent infection thanks to the revolutionary clinical care offered by antituberculous medicinal plants. Growing interest in natural products in the search for new antitubercular leads is a result of the predominance of multidrug-resistant MTB strains and the negative effects of first- and second-line antitubercular drugs. Ayurvedic therapies drastically reduce TB patients' fatality rates, according to prior study. Due to its low toxicity and safety as compared to allopathic therapies, ayurvedic medicine is become most popular.

Numerous medicinal plants have showed promise as drug-hit candidates, while numerous other medications are currently undergoing various stages of clinical studies. In order to deliver medications to the intended site with greater effectiveness and less risk of toxicity, researchers are actively looking into new drug delivery systems. The current review offers detailed information on antituberculosis plants, chemical components, antitubercular traits, and their potential to influence the early stages of drug discovery and serve as novel therapy options for TB.

**Keywords-**Tuberculosis, management of TB, natural products, recent approved anti-tubercular agents, novel treatment for TB, Ayurveda in TB.

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### INTRODUCTION

**Global TB Burden:** For many years, tuberculosis has been the most common infectious disease and an essential global health issue. Although the World Health Organization (WHO) has been striving towards its elimination, progress has been difficult, particularly in places with significant workloads like India.

**fatalities from TB:** The number of TB-related fatalities in 2021 serves as a sobering reminder of the disease's effects. It is particularly disturbing because drug-resistant TB strains, poor access to healthcare, and other factors contribute to these accidental deaths despite the fact that TB is a treatable and curable illness.

**TB Cases to Rise in 2021:** The disruptions brought on by the COVID-19 pandemic may be one of numerous causes for the rise in infections caused by TB from 2020 to 2021. Healthcare systems have been impacted by this pandemic. The kind of bacteria that causes TB is called *Mycobacterium tuberculosis* (Mtb). If untreated, it mainly affects the lungs but has the potential for spread to other bodily organs.

**Respiratory Illness and Immune System Impairment:** The respiratory system is the system that is usually affected by TB, which can result in symptoms such a chronic cough, chest discomfort, and trouble breathing. Additionally, it may cause nonspecific symptoms including fever, weakness, and weight loss. Active TB illness is prone to develop in those with weakened immune systems, especially people with HIV/AIDS.

Global Efforts to Fight TB: The WHO and other international organizations are trying to fight TB by enhancing diagnostic procedures, treatment plans, and preventative methods. The goal is to drastically lower TB incidence and death.

(Tufariello *et al.*, 2003. Mtb transmission: The primary manner in which that Mtb is spread is through absorbing respiratory droplets that translate the bacteria. These contagious droplets are released into the air when a person with active TB infection wheezes, coughs, or even speaks. These droplets, particular those with a diameter of 1 to 5 microns (referred to as droplet nuclei), may carry infection to those who inhale them.

The innate immune system of the host, which includes a number of immune cells such as alveolar macrophages, dendritic cells, monocytes, and neutrophils, acts to Mtb when it is swallowed. To get rid of the infection, these cells try to eliminate (engulf) the bacteria. Granulomas form: Despite the immunological the interaction of the host, Mtb can survive and elude therapy. Granulomas, which are arranged formations where immune cells surround and hinder the microbes, often arise as a result of this. Granulomas are the body's effort to wall off the infection, so to speak.

therapeutic Obstacles: The strange cell wall of Mtb, made up of mycolic acids, presents a considerable therapeutic obstacle. The bacterium's resistance to several antimicrobial medications is facilitated by mycolic acids. Due of this, treating TB is exceedingly difficult and requires using multi-drug regimens for a long time to ensure total eradication of the infection. Immune Evasion: The mycolic acid-rich cell wall of *M. tuberculosis* helps it bypass the immune system and flourish inside the host. Additionally, the bacterium uses a number of plans, such as repressing immune cell activation and interfering with the antigen-presenting process, to impede the host's immune response.

Determination of Outcome: The very first interactions between Mtb and the host following infection are crucial to determining how TB diseases will develop. Latent TB infection results when the infection is successfully controlled by the host's immune system and the bacteria stays dormant. If the immune response is poor in certain individuals, active TB illness might appear. (Maurya *et al.*, 2015) . Although extrapulmonary tuberculosis (EPTB) is more generally thought as a lung ailment, tuberculosis (TB) can also affect a number of tissues and organs that lie outside the lungs. The lymph nodes, stomach, genitourinary system, skin, bones, and meninges are only a few of the organs that EPTB can impact. Clinical signals, imaging, and organ-specific microbiological investigations serve to make the diagnosis of EPTB. According to the symptoms you presented, if a patient with EPTB also has a tubercular lesion in their pulmonary parenchyma, they may be diagnosed with pulmonary TB (more precisely, military TB). The categorization aids in choosing the best management and treatment options for the patient.

Definition of EPTB: EPTB can be defined as the presence of intrathoracic mediastinal and/or hilar lymph node TB, TB pleural effusion, or both in spite of radiographic lung abnormalities. With the typical location of infection being the lungs, pulmonary TB may be identified as EPTB using this criterion. EPTB can develop into several results. It may turn into pulmonary or extrapulmonary active TB, when the infection develops clinically and circulates easily. It may also develop into latent tuberculosis, in which the bacteria are to sleep in the body and do not cause symptoms but may awaken later if the person's immune system deteriorates. Some EPTB instances may clear up on their own without developing into active diseases, which is another kind of self-clearance. A key challenge in the fight against TB is the rise of *Mycobacterium tuberculosis* (the germs that causes TB) strains that are extensively drug-resistant (XDR) and multidrug-resistant (MDR). In comparison to XDR-TB, MDR-TB is resistant to at least two of the most powerful first-line TB therapeutics. (Magiorakos *et al.*, 2012).

**Tuberculosis in India :** High TB Burden: The TB burden in India is among the highest in the world. Based on forecasts, India is home to roughly 30 percent of the world's TB sufferers, as you indicated. A number of factors, such as population density, socioeconomic events, and healthcare issues, relate to this tendency.

Government Statistics: The Indian government continually monitors and updates the nation's TB condition. From knowledge you stated from the Ministry of Health and Family Welfare, India gets millions of new TB cases each year. This information is necessary in tracking the disease's progression and putting in place successful treatment options

India's TB plague has an extensive impact on the TB landscape worldwide. The nation causes a significant proportion of all TB cases globally, making it one of the top contributors to the global TB burden. Given that TB is an international outbreak, this emphasizes the necessity of broad strategies to combat it.

Deaths From TB: It's shocking to learn that a sizable fraction of TB-related deaths happens at India, particularly for those who were do not have HIV. The elevated rate of mortality in India emphasizes the significance of early identification and efficient treatment for TB, a disease that can be severe if left untreated or if treatment is not complete.

Efforts to combat TB in India include various strategies such as expanding access to healthcare, improving diagnostic capabilities, ensuring the availability of TB medications, and raising awareness about TB prevention and treatment. Additionally, India has made efforts to align with global initiatives, such as the End TB Strategy set by the World Health Organization (WHO), to reduce TB incidence and mortality. Addressing TB in India and globally remains a complex challenge that requires ongoing commitment and collaboration among governments, healthcare providers, international organizations, and communities to achieve the goal of eliminating TB as a public health threat. (Bagecchi, 2022). Isoniazid (INH): Isoniazid is in particular efficient in eradicating strains of TB into sizeable lung cavities. But the caseous lesions (regions of tissue injury) and TB bacteria in macrophages (immune cells that may hold TB germs) are effectively treated by it. Despite these drawbacks, INH is an important aspect of TB therapy, particularly for incidents of active pulmonary TB.

Rifampin is a solid anti-TB antibiotic that's effective well against TB viruses, especially in caseous lesions where the bacterial population might fluctuate. Being able to target TB bacteria in various groups thanks to its broad-spectrum steps rifampin is a vital aspect of the TB treatments.

Streptomycin: Streptomycin largely combats the extracellular TB bacterial population. Streptomycin is less often utilized during modern TB treatment regimens due to its poor effectiveness and the availability of pharmaceuticals that have improved activity.

Pyrazinamide (PZA): In an acidic location, such as the cytoplasm of macrophages, pyrazinamide can work against TB bacteria. It targets the TB bacteria that are found in macrophages. PZA is frequently used in the first portion of TB treatment in order to isolate TB germs in various environments. PZA is crucial during the initial phases of therapy since clinical research has found that it has the greatest effect within the first few months of medication. (Addington, 1979; Laurenzi *et al.*, 2008).

he Revised National TB Control Program (RNTCP) in India is a comprehensive government-sponsored initiative aimed at combating tuberculosis (TB) in the country. It has undergone various transformations and is now known as the National Tuberculosis Elimination Program (NTEP), but the core goal remains the same: to reduce the burden of TB and ultimately eliminate the disease.

Here are some key points about the RNTCP/NTEP:

1. **Government-Sponsored Program:** The RNTCP/NTEP is fully supported and funded by the Indian government. It plays a critical role in TB control efforts by providing free TB diagnosis and treatment services to patients across the country.
2. **TB Control at the Neighborhood Level:** The program operates at the grassroots level, aiming to control TB in local communities. It involves setting up TB diagnostic and treatment centers in various regions, including rural areas, to ensure that TB services are easily accessible to people.
3. **Free Treatment and Diagnostic Services:** One of the significant advantages of the RNTCP/NTEP is that it offers free TB diagnosis and treatment to patients. This is essential in a country like India, where affordability and access to healthcare can be significant challenges.
4. **Private Clinics and TB Management:** Despite the availability of government-sponsored TB services, many people in India still seek care at private clinics when they experience TB symptoms. There are several reasons for this, including a preference for private healthcare, perceived quality of care, and a desire for more personalized services. Some individuals may not be aware of the free TB services offered by the government.
5. **Challenges and Collaboration:** Addressing TB in India is a complex challenge due to the country's size and population. The government recognizes the importance of collaboration with the private healthcare sector to reach and treat all TB cases effectively. Efforts are being made to engage with private healthcare providers and encourage them to adhere to national TB treatment guidelines.
6. **Awareness and Education:** Increasing awareness about TB, its symptoms, and the availability of free treatment under the government program is crucial. Public education campaigns are conducted to inform people about the importance of seeking timely diagnosis and treatment. (Narayan and Walt 1998).

It's true that a significant percentage of tuberculosis (TB) patients in India seek treatment from private practitioners, including general practitioners and chest specialists. Additionally, some private practitioners may incorporate traditional and alternative forms of medicine, such as Ayurveda, into their approach to TB care. Here are some key points to consider:

1. **Private Sector Engagement:** It is widely accepted that one of India's challenges in the battle towards TB is the significant proportion of TB patients to seek care from private doctors. In India, there is a strong private healthcare enterprise that is essential to the delivery of health care, particularly TB treatment.

2. **Integration of Ayurveda:** One of India's ancient medical traditions, Bactrim has an extensive past. Even while Ayurveda has unique methods to enhance well-being and good health, it generally not covered by the RNTCP or approved allopathic (current Western medicine) TB treatment process.
3. **Use of Ayurvedic Remedies:** Ayurvedic medicines or other conventional therapies may be included into the behaviors of some private practitioners. This could be nutrition proposals, alternative remedies, or behavioral changes. It's key to remember that these methods might not be coherent with the evidence-based TB medications advised by the World Health Organization (WHO).
4. **Challenges and Concerns** Concerns relating to the successful outcome of the therapy, possible medication interactions, and the threat of delayed diagnosis and adequate therapy could come up when common TB treatment is combined by alternative or traditional medicine. There hasn't been extensive study on or clinical trial support of Ayurvedic TB treatment options. (McDowell and Pai 2015)

**Current therapeutic strategies and limitations :** The success rates of tuberculosis (TB) treatment can vary significantly depending on several factors, including the type of TB (regular TB vs. drug-resistant TB), the specific drugs used, treatment adherence, and the individual patient's response to treatment. The information you provided suggests that first-line anti-TB medications, such as isoniazid, rifampicin, ethambutol, and pyrazinamide (PZA), have a higher success rate in regular TB compared to multidrug-resistant TB (MDR-TB) or rifampicin-resistant TB.

Here's a breakdown of the information:

1. **Regular TB:** Regular TB, also known as drug-susceptible TB, is caused by *Mycobacterium tuberculosis* strains that are sensitive to the standard first-line TB drugs like isoniazid, rifampicin, ethambutol, and PZA. When these drugs are used in combination as part of a well-structured treatment regimen and the patient adheres to the treatment plan, the success rate can be quite high. The reported 86% success rate likely reflects the overall effectiveness of first-line TB treatment in cases of regular TB.
2. **MDR-TB and Rifampicin-Resistant TB:** MDR-TB refers to TB strains that are resistant to at least isoniazid and rifampicin, which are the two most potent first-line drugs. Rifampicin resistance is often used as a marker for MDR-TB because it is a key drug in TB treatment. Treating MDR-TB and rifampicin-resistant TB is more challenging and requires a more complex and longer treatment regimen. The reported 59% success rate in these cases suggests that treatment outcomes for drug-resistant TB are generally less favorable than for regular TB.

It's important to note that drug-resistant TB cases often require second-line drugs, which are less effective and may have more side effects than first-line drugs. Additionally, the duration of treatment for drug-resistant TB is typically longer, often extending to 18 to 24 months or more.

Treatment success rates can also be influenced by factors such as healthcare infrastructure, access to quality care, patient adherence to treatment, and the presence of additional medical conditions. Efforts to improve the management of drug-resistant TB, including the development of new drugs and treatment regimens, are ongoing to enhance treatment success rates in these more challenging cases. (Mirzayev *et al.*, 2021). While rifampicin is one of the most potent first-line medications used to treat TB, rifampicin resistance is a major convey for multidrug-resistant TB (MDR-TB). MDR-TB results from the TB bacteria becoming resilient to rifampicin as well as to other important first-line drugs like isoniazid.

This report highlights how crucial it is to combat drug-resistant TB as a significant public health issue. Treatment for MDR-TB involves longer, more involved regimens which usually involve second-line medications that are less efficient and have more possible adverse effects than first-line medications. In order to improve the impact of drug-resistant TB on the public health, more efforts to detect, eradicate, and prevent it are needed in light of an increasing number of RR-TB cases in 2020. (Shah *et al.*, 2022).

1. **Challenges in MDR/XDR-TB Treatment:** MDR-TB and XDR-TB are types of TB that are resistant to several second-line cures as well as the strongest first-line drugs such as isoniazid and rifampicin in the case of XDR-TB. Due to the requirement for intricate and extensive treatment regimens, sometimes including toxic and poorly tolerated drugs, treating certain types of TB has historically been tricky.
2. **FDA Approval of Second-Line Anti-TB Medications:** Over the past decade, the U.S. Food and Drug Administration (FDA) approved three important second-line anti-TB medications: bedaquiline (Bdq), delamanid (Dlm), and pteromalid (Ptm). These medications have provided new hope for the treatment of MDR/XDR-TB.
3. **Potential for Shorter and Easier Regimens:** The introduction of these second-line drugs has the potential to significantly improve the treatment of MDR/XDR-TB. They offer the possibility of shorter and all-oral treatment regimens, which can be more tolerable for patients and may improve treatment outcomes.
4. **Global Use of Bedaquiline:** Bedaquiline (Bdq) has been particularly notable in the treatment of DR-TB. By the end of 2020, it had been included in the treatment regimen for DR-TB in 109 countries, indicating its widespread adoption as a critical tool in TB control efforts.
5. **All-Oral Regimens:** The use of all-oral extended and shorter regimens in several countries for the treatment of MDR/RR-TB is a significant advancement. These regimens offer the potential to simplify treatment, reduce the burden of injectable drugs, and improve patient adherence.

6. **Global Efforts:** These developments align with global efforts to combat drug-resistant TB and achieve the goal of ending TB as a public health threat, as outlined in the World Health Organization's End TB Strategy. (Black and Buchwald 2021; Dookie *et al.*, 2022; Ignatius and Dooley 2019).

Groups	Drugs	ADR
First-line oral	Isoniazid (INH)	GI upset, epigastric pain, hepatotoxic, psychosis, convulsive seizures, mental confusion, and coma etc.
	Rifampin	hepatotoxicity, immunological reactions, dizziness, headache, dyspnoea, and ataxia etc.
	PZA	Severe exanthema, pruritus, rhabdomyolysis with myoglobinuria, kidney failure, acute arthritis in gouty individuals and hepatotoxicity.
	Ethambutol	Retrobulbar neuritis, hepatotoxicity, hematological symptoms, hematological symptoms and hypersensitivity etc.
Second-line drugs/ Oral bacteriostatic	Aminoglycosides	Ototoxic, neurotoxic, nephrotoxic, neuromuscular blockage and hypersensitivity.
	Fluoroquinolones	Adversely impact gastrointestinal, central nervous system, cardiovascular system, urinary tract, endocrine system, also cause skin reactions and allergies.
	second-line anti-TB drugs	Neurological and psychic alterations

**Table 1: Common ADR of anti-tubercular medications.**

### Importance of Herbal medicine.

**Ayurveda** : Nearly 5,000 years ago, in India, the Ayurvedic medical system was born. It places a high value on a multifaceted approach to wellness and physical health that unites the body, mind, and spirit. Herbal therapies, dietary adjustments, and modifications to one's lifestyle can be part of ayurvedic treatments.

**Herbal remedies** : Herbal treatments play a crucial part in Ayurvedic medicine. Numerous health issues are dealt with by Ayurveda through thousands of different medicinal plants and herbs. These herbs are utilized in plenty of ways, like as powder , oils

**Traditional Healers:** There are a lot of traditional healers and practitioners in India who have been brought down their knowledge of and competency in herbal medicine for many centuries. These professionals play an essential part in rural healthcare and often become well-liked in their communities.

**Religious and Cultural Significance** : In India, there are several natural therapies that have an enduring religious and cultural foundation. The information about those therapies is passed down through scripture and oral traditions, and they frequently appear in rites and partying.

**Medicinal Plant Diversity** : India's amazing biodiversity, which include a large array of medicinal plants, is influenced by its unique terrain and weather. The availability of a wide variety of herbal substances utilized in traditional therapy is made achievable by this diversity.

**Preventive and Therapeutic Use:** Herbal remedies in India are used not only for therapeutic purposes but also for preventive healthcare and wellness. Ayurveda, in particular, emphasizes the importance of maintaining balance in the body to prevent illness. (Mangwani *et al.*, 2020).

Botanical Name Common Name	Possible Mechanism	Therapeutic Applications	Reference
<i>Justicia vasica</i> Adulsa	<ul style="list-style-type: none"> <li>Inhibitory activity against initial step of fatty acid biosynthesis.</li> </ul>	<ul style="list-style-type: none"> <li>Coughs</li> <li>Chronic Bronchitis</li> <li>Asthma</li> <li>Colds</li> <li>Antispasmodic</li> </ul>	(Jha <i>et al.</i> , 2012; Kumar <i>et al.</i> , 2016)
<i>Withania somnifera</i> Ashwagandha	<ul style="list-style-type: none"> <li>Immunomodulation by acting on the nervous and respiratory systems</li> <li>Anti-inflammatory and rejuvenating</li> <li>Down regulate TB symptoms such as cough, cold, and bronchitis</li> </ul>	<ul style="list-style-type: none"> <li>Arthritic</li> <li>Asthma</li> <li>Cancer</li> <li>Diabetes</li> <li>Hypertension</li> <li>Stress</li> </ul>	(Dar <i>et al.</i> , 2015; Singh <i>et al.</i> , 2022)
<i>Bacopa monnieri</i> Brahmi	<ul style="list-style-type: none"> <li>Significantly reduces hepatotoxicity of INH and Rifampicin when administered in combination</li> </ul>	<ul style="list-style-type: none"> <li>Alzheimer's disease</li> <li>Dementia</li> <li>Anxiety</li> </ul>	(Prince <i>et al.</i> , 2016; Rai <i>et al.</i> , 2017)
<i>Ocimum tenuiflorum</i> Tulsi	<ul style="list-style-type: none"> <li>Activates hypoxia-inducible factor which enhanced the autophagy in TB infected cells and production of IL-6 and TNF-<math>\alpha</math> that control the Mtb infection.</li> <li>Up-regulates the T cell receptor which results to enhances the immunity</li> </ul>	<ul style="list-style-type: none"> <li>Bronchitis</li> <li>Asthma</li> <li>Malaria</li> <li>Dysentery</li> <li>Skin Diseases</li> <li>Arthritis</li> </ul>	(Mahajan <i>et al.</i> , 2013; Tabassum <i>et al.</i> , 2022)

<i>Aloe barbadensis</i> Alovera	<ul style="list-style-type: none"> <li>• It can inhibit the production of TNF-alpha and the proportion of Th17 cells.</li> <li>• Strong antioxidant and antibacterial properties.</li> </ul>	<ul style="list-style-type: none"> <li>• Anti-tubercular</li> <li>• Skin Diseases</li> </ul>	(Arjomandzadegan <i>et al.</i> , 2016; Mawarti <i>et al.</i> , 2017)
<i>Allium sativum</i> Garlic	<ul style="list-style-type: none"> <li>• Prevents sulfhydryl metabolic enzymes to exert its antibiotic action.</li> <li>• Modulate the production of ROS and autophagy in Mtb.</li> <li>• Strong Antioxidant properties</li> <li>• Immunomodulatory</li> </ul>	<ul style="list-style-type: none"> <li>• Immuno-modulatory</li> <li>• Hypolipidemic</li> <li>• Stomach disorders</li> </ul>	(Bhatwalkar <i>et al.</i> , 2021; Muniyan and Jayaraman, 2016)
<i>Cryptolepis sanguinolenta</i> Karond orondo	<ul style="list-style-type: none"> <li>• Antimicrobial</li> <li>• Fungicidal</li> <li>• Antibacterial</li> <li>• Strong antioxidant properties.</li> </ul>	<ul style="list-style-type: none"> <li>• Anticancer</li> <li>• Antidiarrheal</li> <li>• Antifertility</li> </ul>	(Tuyiringire <i>et al.</i> , 2020, 2022)
<i>Zanthoxylum lepreurii</i>	<ul style="list-style-type: none"> <li>• Antimicrobial</li> <li>• fungicidal</li> <li>• Insecticidal</li> <li>• Strong Antioxidant properties.</li> </ul>	<ul style="list-style-type: none"> <li>• HIV/Aids</li> <li>• Malaria</li> <li>• Urinary infections</li> <li>• Rheumatic Pain</li> </ul>	(Tuyiringire <i>et al.</i> , 2020, 2022)
<i>Lantana camara</i>	<ul style="list-style-type: none"> <li>• Antimicrobial</li> <li>• Fungicidal</li> <li>• Antibacterial</li> <li>• Strong antioxidant properties</li> </ul>	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• Skin Itches</li> <li>• Leprosy</li> <li>• Chicken Pox</li> <li>• Asthma</li> <li>• Ulcers</li> </ul>	(Tuyiringire <i>et al.</i> , 2020, 2022)

**New drug delivery system.** The medications used to treat TB have a number of serious adverse effects, such as hepatotoxicity, which could lead to patients becoming discontinuing using prescription drugs, which has the effect of resistance to anti-TB drugs (Yee *et al.*, 2003). Sub-therapeutic drug concentrations are another element that contributes to the emergence of resistance. The only thing that has to be done to stop all of this is to give the medication to the macrophages where Mtb thrives. The right concentration and non-systemic treatment would stop the emergence of resistance. A nano-delivery technology is used to deliver the medication selectively to the macrophages of infected organs such as the lungs, liver, and spleen. Additionally, it will shield the medication from metabolism before it is given to the tissues that are Mtb-infected. Nanoparticles, a cutting-edge technology that has been extensively researched in the realm of healthcare, have shown positive results in the detection and management of TB healthcare (Rossi *et al.*, 2021; Xu *et al.*, 2018). Recent research has shown that using carbon nanotubes, also known as CNTs, as nanoparticle suspensions or nanofluids could be useful for both TB diagnosis and therapy (Sheikhpour *et al.*, 2022). Mycobacterium cell walls can be destroyed and MDR can be blocked by employing targeted medicine administration. It has been found that fluoxetine and isoniazid given jointly in CNT inhibit Mtb development. Fluoxetine causes the Mtb-infected macrophages to secrete more TNF- $\alpha$  and to undergo autophagy. For the administration of anti-Mtb drugs, silver nanoparticles trapped in biopolymers have a synergistic effect that induces cytotoxicity. Another example of these functionalized biodegradable polymers is their use in conjunction with Curdlan nanoparticles and cyclodextrin. Curdlan is recognized by the macrophage dectin-1 receptor. It has anti-infective and immunomodulatory effects as a result, and it also releases medications into macrophages. Similar to this, isoniazid-loaded nanostructured lipid carriers have the ability to target infected macrophages precisely and increase the intracellular effectiveness of anti-TB medications. An intriguing nano-delivery method was the subject of another recent investigation. It is an inorganic nanolayer made of magnesium layered hydroxide (MgLH). Because they are biodegradable and may transport a medicine and release it gradually at the desired spot, inorganic nanolayers are biocompatible. The study results for the second-line anti-TB drug MgLH with intercalated PAS were extremely encouraging. These results highlight the remarkable potential of nanostructures for extending shelf lives, enhancing medication absorption, enhancing safety profiles, and enhancing therapeutic outcomes (Ibarra-Sánchez *et al.*, 2022; Saifullah *et al.*, 2021).

## CONCLUSIONS

The World Health Organization (WHO) has implemented all-oral regimens for more efficacy and safety, but there are still issues that must be effectively addressed, necessitating the creation of novel medications and a lot of effort in this area. There are many plants found in nature that can be used to heal human ailments. Herbs are a fundamental and crucial component of traditional medical systems and have a wide range of impacts on human health. The effectiveness of chemically diverse substances and plants as potential hepatoprotective and antimycobacterial medicines may serve as a sign of progress in the search for exceptional remedies. Thus, combining the multiple health benefits of medicinal plants with the receptor-specific properties of anti-TB drugs may be a useful strategy to control TB and its negative consequences (Swain and Hussain 2022). Numerous medicinal plants have showed promise as drug-hit possibilities,

while numerous additional medications are now through various stages of clinical studies (Tuyiringire *et al.*, 2020). As medications are delivered to the intended place, new drug delivery methods are being researched to improve efficacy and decrease the likelihood of toxicity (Dua *et al.*, 2018). Many people in developing countries combine the use of prescription drugs with natural supplements. Therefore, appropriate study is required to combat this common occurrence. Therefore, appropriate study is required to combat this pervasive frequency. Little research has been done on the mechanism through which herbal components interact with anti-TB medications. Between attending doctors and the therapeutic use of herbal adjuvants, there is a substantial knowledge gap. Plants with anti-tubercular and anti-oxidant properties may be researched for their potent compounds and used in the creation of novel formulations that are well-liked by a wider variety of medical professionals. Numerous different substances shown anti-TB action in the current review. These provide novel potential for the development of novel anti-TB medications. Some of the compounds could be applied in the medical field to treat fatal illnesses. Therefore, to ensure the safety and efficacy of such combinations before widespread human use, thorough research of herb-drug interactions in several traditional experimental settings are necessary.

## FUTURE SCOPE

Traditional pharmaceutical treatments have several unanticipated side effects in addition to not offering enough relief from TB-related issues. For the management of TB, employing alternative pharmaceuticals such as modern agents and plant-based therapies may be a feasible therapeutic option. Further research is necessary to provide a more targeted method for treating TB patients.

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