



# Ashwagandha: Potential Integrative Management of Tuberculosis

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## Abstract

The World Health Organization TB (Tuberculosis) statistics for India for 2018 give an estimated incidence of 2.69 million cases. TB is being a challenge for India and worldwide developing countries pre and post antitubercular drug era. The major limitations clinicians face in management of TB is its MDR, immunosuppression, bad prognosis during course of treatment and associated side effects of anti-tubercular drugs putting patient in danger for multiple organ failure. The presence of comorbidities, nutritional deficiencies add up toll in the whole clinical presentation of tuberculosis management. There is very systematic pathophysiology and treatment ideology explained in Ayurveda for tuberculosis and related respiratory infections. There is great need to integrate Ayurveda wisdom of understanding tuberculosis and medicinal herbs in protective mode with aggressive targeted anti TB activity of modern medicine. Ashwagandha is strong Rasayana category medicinal plants with ancient references for its beneficial effect in management of tuberculosis also supported by modern day in vitro, in vivo and clinical evidences of effectiveness of Ashwagandha in management of tuberculosis could be ray of hope. There should focused research aimed at unfolding mechanisms and clinical guidelines for the use of Ashwagandha as an adjuvant in the management of tuberculosis.

**Keywords:** Tuberculosis, MDR, isoniazid, Ashwagandha

## Introduction

The World Health Organization (WHO) TB (Tuberculosis) statistics for India for 2018 give an estimated incidence of 2.69 million cases. Though there are measures taken by Government towards TB. It is still prevalent in India. There are many challenges in the way of treatment for TB. The current review addresses the encounters in the clinical management of tuberculosis and emphasizes integrative way of management with Ayurveda. Furthermore the review portrays the references, in vitro, vivo and clinical research with Ashwagandha as a potential agent to be used in the clinical management. The review stresses on the more focused research need with focused research of Ashwagandha in Tuberculosis.

### Post DOTS scenario in India:

Widespread implementation of the DOTS Strategy since the late 1990s has treated millions of patients with TB, and saved many lives<sup>[1]</sup>. The impact of this strategy on reducing transmission and incidence rate is not up to the mark. India could be a good example of this situation. Post National TB Control Program (RNTCP), TB incidence continues to remain high. India contributed for 25% of the 9 million global TB cases in 2013<sup>[2]</sup>. WHO assessments bring about fact that India still has missing TB cases who are either not

diagnosed or not registered. TB is a key cause of death in developing countries and India, and the occurrence of severe forms of drug-resistant TB<sup>[3]</sup>.

There are several reasons to explain the persistent high TB incidence, TB mortality and drug-resistance in India. These includes the social conditions and co-morbidities that work as gasoline for the TB epidemic<sup>[4]</sup>. India is still believed to be holding on malnutrition badly. The association between malnutrition and TB in India is strong<sup>[5]</sup>. Diabetes is another important risk factor for TB, and India is on the verge of getting epicenter of diabetes. Furthermore, tobacco smoking is strongly associated with higher risk of TB mortality<sup>[6]</sup>. The budget sanctioned to the TB program is also an important limitation of the developing countries like India. Lastly, unlike the case of HIV/AIDS, awareness around TB has been weak in India, contributing to limited societal participation to irradiate TB<sup>[7,8]</sup>.

### Challenge with Multi Drug Resistance (MDR):

Multi-drug-resistant tuberculosis (MDR-TB) is caused by bacteria showing resistance to most powerful first-line anti-TB medications and extensively drug-resistant TB is called to the infections resistant to second-line medications as well<sup>[9]</sup>.

Infection of *Mycobacterium tuberculosis* is called as tuberculosis. This infection targets respiratory system and

eventually spreads over vital organs in its aggressive form. In 90% cases there are no symptoms that are very aggressive (latent tuberculosis), in 10% cases the symptoms are so profound and cases advance rapidly making prognosis deadly [10]. TB is contagious disease and air borne. Resistant strains of TB can get transferred in non-infected individual making the newly infected person a primary MDR-TB which counts for 75% cases. Another class is of Acquired MDR-TB which develops when non-resistant strain of TB is not treated properly and results in development of antibiotic resistance. Acquired MRD-TB can affect more people in community. This runs in a vicious cycle [11].

### **Anti-TB drugs and hepatic damage:**

Studied earlier, about 5–20% of individuals, on anti-TB medication reported with hepatic complications [13]. Drug combinations regime in MDR-TB the hepatic damage gets more worsened. Anti-TB drugs are having known side effects as hepatic damage. Clinical symptoms of the hepatotoxicity in TB patients include, jaundice, nausea, vomiting and abdominal pain along with elevated levels of bilirubin and hepatic transaminases. The mortality rate after onset of liver disease in TB patient is 6-12% on continued drug use [14].

### **Need to look back at roots for help:**

In Ayurveda the tuberculosis is being explained since many thousand years together. There were treatments provided in folklore medicine before discovery of anti TB agent in modern science. So its need to look in the Ayurvedic understanding and medicines once again to get help to manage the critical clinical scenario in management of Tuberculosis.

Nature guarantees of plants used to cure illness of mankind. As a solid framework of traditional medical systems, herbs have made an innumerable impact to maintain the human health. Combination of anti-TB agent together with herbs having potential as anti-mycobacterial and hepatoprotective agent could prove the key to the situation. This could lead to amalgamation of targeted therapy of anti-TB drugs with numerous health benefits of medicinal plants to manage health of patient, improve prognosis and avoid hepatotoxicity.

### **Ayurvedic Concept of Pulmonary TB (PTB):**

PTB is suitable to be explained in Ayurvedic pathophysiological aspects as *Rajayakshma*. *Rajayakshma* prominently points out *Dhatukshaya* (tissue damage or loss). This process can initiate inflammation in the PTB pathophysiology. There are obvious metabolic deregulations happening (Dhatwagninasana), which vitiate rasa (tissue fluid), *rakta* (blood), *mamsa* (muscle), *meda* (adipose tissue), and *sukra* (generative tissue). This leads to immune-depression or *ojokshaya*. As per Ayurveda further metabolic destruction leads to depletion of various *dhatu*s (tissue) such as *Ojokshaya*, *sukra*, *medadhatu* to *rasa dhatu* can be termed as *Pratilomakshaya* [12].

### **Ashwagandha: Integrative Management of Tuberculosis:**

*Withaniasomnifera* (Ashwagandha) is much admired herb of the Indian Ayurvedic system of medicine as a Rasayana (tonic). It is very well researched herb for its immunomodulatory, antioxidant, anti-inflammatory, nervine tonic, revitalizing, gastro-protective and

anti-stress properties. It is excellent general tonic and adaptogenic in nature [15].

It is reported from a trusted research that, *Withaniasomnifera* possess activity against *M. tuberculosis*. *Mycobacterium tuberculosis* activity was tested using minimal inhibitory concentration method (MIC). Aqueous extract of *W. somnifera* (0.01-1.0 mg/mL) had significant effect against *M. tuberculosis*. It comprehensively provide evidence of the effective anti-tubercle activity of *W. somnifera* [16].

Debnath et al. assessed the use of Ashwagandha as an adjuvant in the management of PTB. The primary aim of study were to assess toxicity reduction of anti-TB drugs and early repair by adjunct therapy of Ayurvedic drugs improving the bioavailability of anti-TB drugs. There were 99 newly diagnosed PTB patients from both the sexes aged between 10 and 65 years completed the study. Ashwagandha 500 mg 2 caps, twice daily and Chyawanprash (as per Indian Pharmacopeia)-10 g, thrice daily for a period of 28 days was the intervention. The study reported betterment of symptoms, improvement of body weight, reduction in ESR, IgA and IgM patterns, and significant upsurge in bioavailability of isoniazid and pyrazinamide. Bioavailability of isoniazid and pyrazinamide reported 7-10% increase after 28 days of treatment [17].

Vyas et al. carried out a single blind controlled trial to evaluate the adjunct properties of Rasayana compound among 133 TB patients under RNTCP. The Rasayana used in this study were composed of Amalaki (*Emblica officinalis Gaertn.*), Guduchi (*Tinospora cordifolia Willd.*), Ashwagandha (*Withaniasomnifera L.*), Yashtimadhu (*Glycyrrhiza glabra Linn.*), Pippali (*Piper longum Linn*) etc. as a capsule. The study duration was of 60 days. Sputum positive Category I of PTB patients or extra PTB and age group of >13 years were selected for the study. It was reported that the compound is helpful in relieving the symptoms of PTB in the treatment group compared to the control. The Rasayana compound containing Ashwagandha was found to decrease cough (83%), fever (93%), dyspnea (71.3%), hemoptysis (87%), and increase body weight (7.7%) [18].

As per research of Debnath et al. Ashwagandha is in use for respiratory ailments. The potential activity of Ashwagandha on *poshakarasa* level (nutrient supplement) *agni* level (metabolic appreciation) and *srotas* level (tissue nourishment) are well studied [19]. Ashwagandha has shown immunomodulatory activity to boost up or restore immunity as response to defense mechanism [20]. Ashwagandha is reported to possess respiratory system specific immunomodulatory activity leading to role of Ashwagandha in wide range of respiratory diseases [21]. Ashwagandha with building specific immunity works as an anti-stress, inotropic and antioxidant agent protecting vital organs from damage and improving symptoms and quality of life of patients.

As per study reported as a double blind placebo controlled randomized trial, with 60 freshly diagnosed sputum positive PTB patients, Ashwagandha root extract for 12 weeks with anti-tuberculosis treatment proved significant in reducing the symptoms and relieving hepatotoxicity. At the end of 8 weeks, 86% patients recovered on sputum test. There was significant increase in CD4 and CD8 cells in Ashwagandha treated group. There was average gain in body weight in Ashwagandha treated group with improved quality of life. There was significant difference in hepatic enzymes than placebo group with possible hepato-protection [22].

In a clinical study undertaken as an adjuvant to anti TB drugs with Ashwagandha revealed that there was reduction in symptom severity cough (83%), fever (93%), dyspnea (71.3%) with

statistically significant weight gain and quality of life after study [23].

A research was intended to examine combined toxic effects of Isoniazid and Rifampicin (RIF), against effects of Ashwagandha and Vitamin E in animal models of hepatotoxicity. Ashwagandha treated group showed maximum restoration of hepatocellular integrity and improvement in biochemical parameter when compared to negative control group. This suggests potential protective effect of Ashwagandha in Anti-TB drug induced hepatotoxicity [24].

## Conclusion

The Tuberculosis is being a challenge for India and worldwide developing countries pre and post antitubercular drug era. The major limitations clinicians face in management of TB is its MDR, immunosuppression and bad prognosis during course of treatment and associated side effects of anti-tubercular drugs putting patient in danger for multiple organ failure. The presence of comorbidities, nutritional deficiencies add up toll in the whole clinical presentation of tuberculosis management. There is very systematic pathophysiology and treatment ideology explained in Ayurveda for tuberculosis and related respiratory infections. There is great need to integrate Ayurveda wisdom of understanding tuberculosis and medicinal herbs in protective mode with aggressive targeted anti TB activity of modern medicine. Ashwagandha is strong Rasayana category medicinal plants with ancient references for its beneficial effect in management of tuberculosis also supported by modern day in vitro, in vivo and clinical evidences of effectiveness of Ashwagandha in management of tuberculosis could be ray of hope. There should be more research aimed at unfolding mechanisms and clinical guidelines for the use of Ashwagandha as an adjuvant in the management of tuberculosis.

## Ethics approval and consent to participate

Not Applicable

## Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

## Data Availability

Not Applicable

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## Authors' contributions

First Author that is, Dr. Mukund Baburao Bandale did the review and search of literature of Tuberculosis and Ashwagandha and was put up contribution in writing the manuscript and editing of manuscript. Second Author, Dr. Sandipkumar Ramjivan Baheti was also involved in literature search and drafting of manuscript. Both authors review, check, read discussed multiple times and finalized the manuscript.

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