INTRODUCTION

Tuberculosis (TB) is an infectious disease of worldwide occurrence.1 Each year approximately 2 million persons worldwide die of tuberculosis and 9 million become infected.2 In the United States, approximately 14,000 cases of tuberculosis were reported in 2006, a 3.2% decline from the previous year; however 20 states and the district of Columbia had higher rates.3 India is the highest TB burden country in the world. In 2008, nearly 2 million cases were reported in India, and 276,000 persons die of this disease.4 The prevalence of tuberculosis is continuing to increase because of patients infected with human immunodeficiency virus (HIV),5 bacterial resistance to medications.6 Manifestation of TB often includes progressive fatigue, malaise, weight loss, and a low grade fever accompanied by chills and night sweats.6 Although the pulmonary system is the common location for TB, extrapulmonary disease occurs in more than 20% of immune-competent patients, and risk for extrapulmonary disease increases with immunosuppression.7 Lymphatic TB is the most common extrapulmonary tuberculosis, and cervical adenopathy occurs most often occurs most often and other possible location includes bones, joints, pleura, and genitourinary system.8 Another fatal form of extrapulmonary tuberculosis is infection of blood-stream by mycobacteria; this form of disease is called disseminated or miliary tuberculosis, progresses rapidly and can be difficult to diagnose because of its systemic and non-specific sign and symptoms.9 Also patient with latent tuberculosis have no sign and symptoms of the disease, do not feel sick and are not infectious.10 Although co-infection with human immunodeficiency virus is the most notable cause for progression to active disease, other factors, such as uncontrolled diabetes mellitus, sepsis, renal failure, malnutrition, smoking, chemotherapy, organ transplantation, and long-term corticosteroids usage, that can trigger reactivation of remote infection are more common in critical care setting.11

The drugs currently used to treat the TB infections are mainly rifampicin, ethambutol, isoniazid and pyrazinamide but the emergence of multiple drug resistant (MDR) strains of M. tuberculosis (defined resistance against isoniazid and rifampin) is now common in number of patients because of uncontrolled application of these anti-tuberculosis drugs (Gupta et al 2010).12 At present, the more drug resistant form of tuberculosis XDR-TB (extensively drug resistant tuberculosis) has been reported such as current front-line drugs (isoniazid and rifampin) in addition to any fluoroquinolone and at least of the three injectable second-line drugs (capreomycin, kanamycin, and amikacin).13 The medicinal properties of plants have been well known from ancient times and plants offer a new source of potent anti-microbial agents in the form of secondary metabolites.14 Anti-tuberculosis activity has been reported in number of higher plants.15 In Ayurveda tuberculosis is known as Rajayaksha, Yakshma, Shosha, Kshaya.16 Tuberculosis is an infection caused by the rod-shaped non–spore-forming, aerobic bacterium Mycobacterium tuberculosis and is 0.5 μm to 3 μm long, are classified as acid-fast bacilli and have a unique cell wall structure crucial to their survival.17 The composition and quantity of the cell wall components affect the bacteria’s virulence and growth rate.18 The peptidoglycan polymer confers cell wall rigidity and is just external to the bacterial cell membrane, another contributor to the permeability barrier of mycobacteria.19 Another important component of the cell wall is liposarabonominan, a carbohydrate structural antigen on the outside of the organism that is immunogenic and facilitates the survival of mycobacteria within macrophages.20

TRANSMISSION

Mycobacterium tuberculosis is spread by small airborne droplets called droplet nuclei, generated by the coughing, sneezing, talking, or singing of a person with pulmonary or laryngeal tuberculosis ie. Transmission mode can be Inhalation, Ingestion, Inoculation, and Transplacental route .These minuscule droplets can remain air-borne for minutes to hours after expecoration.21 Introduction of M tuberculosis into the lungs leads to infection of the respiratory system; however, the organisms can spread to other organs, such as the lymphatics, pleura, bones/joints, or meninges, and cause extrapulmonary tuberculosis.22

PATHOPHYSIOLOGY (figure 1)

After transmission into immune system, mycobacteria interfere with different immunological mediators. The interaction of T cells with infected macrophages is central to protective immunity against M tuberculosis and depends on the interplay of cytokines produced by each cell.21 TNF-α, IL-12, and IFN-γ are central cytokines in the regulatory and effector phases of the immune response to M tuberculosis. TH1 cells and natural killer (NK) cells secrete IFN-γ, which activates alveolar macrophages to produce a variety of...
substances involved in growth inhibition and killing of mycobacteria. Macrophages also secrete IL-12, amplifying this pathway in a positive feedback loop. IL-12 has been implicated in the pathogenesis of T-cell-mediated pathology because it drives antigen-naive TH cells towards development into TH1 cells. \(^{25}\) TNF-α is believed to play multiple roles in the immune and pathological responses in tuberculosis. M tuberculosis induces TNF-α secretion by macrophages, dendritic cells, and T cells. The production of anti-inflammatory cytokines such as IL-4, IL-10 and TGF-β in response to M tuberculosis may down-regulate the immune response and limit tissue injury, but excessive production of these cytokines may result in failure to control the infection. \(^{26}\) Macrophages are the part of the innate immune system and provide an opportunity for the body to destroy the invading mycobacteria and prevent infection. The complement system also plays a role in the phagocytosis of the bacteria. The complement protein C3 binds to the cell wall and enhances recognition of the mycobacteria by macrophages. The subsequent phagocytosis by macrophages initiates a cascade of events that results in either successful control of the infection, followed by latent tuberculosis, or progression to active disease called primary progressive tuberculosis. \(^{27}\) After being ingested by macrophages, the mycobacteria continue to multiply slowly, with bacterial cell division occurring every 25 to 32 hours. Initial development of TB involves production of proteolytic enzymes and cytokines by macrophages in an attempt to degrade the bacteria. Released cytokines attract T lymphocytes to the site, the cells that constitute cell-mediated immunity. In fact, M tuberculosis organisms can change their phenotypic expression, such as protein regulation, to enhance survival. Lesions in persons with less effective immune systems progress to primary progressive tuberculosis. \(^{28}\) In patients infected with M tuberculosis, droplets can be coughed up from the bronchus and infect other persons. Bacilli can also drain into the lymphatic system and collect in the trachea-bronchial lymph nodes of the affected lung, where the organisms can form new caseous granulomas. \(^{29}\) 

### TREATMENT

#### Anti-Tubercular Drugs

Anti-TB allopathic drugs have been prescribed to control symptoms of this disease but they result into side effects like hepatitis, hypersensitivity reactions, nausea, vomiting etc. This problem has become more serious as Mycobacterium tuberculosis developed resistance against both the first line (Essential) and second line (Reserve) anti-TB drugs. \(^{30}\) Essential anti-TB drugs are usually used for the treatment of TB patients with susceptible Mycobacterium Tuberculosis and Reserve anti-TB drugs used for the treatment of multidrug-resistant TB (MDR). Various anti-TB drugs with their side effects and resistance are given below in the table1.

### HERBAL PLANTS USEFUL IN TUBERCULOSIS TREATMENT

#### Brief Description Of Plants Having Anti-Tubercular Activity

**Lantana camara l**

**Botanical name:** Lantana camara L  
**Synonyms:** Camara vulgaris, Lantana scabrida  
**Family:** Verbenaceae.  
*Lantana camara* is a low, subscandent, vigorous shrub which can grow to 2 - 4 meters in height. Leaves are bright green, rough, finely hairy and emits a pungent odor when crushed. \(^{32}\) Reports indicates that Leaf extracts of Lantana exhibit anti-microbial, fungicidal, insecticidal and nematicidal properties. Lantana oil is sometimes used for the treatment of skin itches, as an antiseptic for wounds and externally for leprosy and scabies. The leaves are used in the treatment of tumors, tetanus, rheumatism, and reported to possess diaphoretic, carminative, anti-septic properties, and are main source of phosphorous and potassium. \(^{33}\) Chloroform and methanol extracts of lantana camara. This plant is claimed for antimicrobial activity. The leaf extract of lantana camara. L was screened against three strains of mycobacterium tuberculosis using agar–well diffusion method. Methanolic extract of lantana camara showed highest antimicrobial activity but it was much less activity then Rifampicin whereas chloroform extract of lantana camara. L showed activity against all three strains of mycobacterium tuberculosis but it was less active than Methanolic extract. \(^{34}\)  

**Morinda citrifolia l**

**Botanical name:** Morinda citrifolia  
**Family:** Rubiaceae (coffee family), rubioideae (subfamily).  
**Common name:** Canary wood (Australia), Fromager, Murier indien (French).  

Noni is the common name for Morinda citrifolia L. It has been reported to have a broad range of health benefits for cancer, infection, arthritis, diabetes, asthma, hypertension, and pain. A number of major components have been identified in the Noni plant such as scopoletin, octanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones (such as nardsmannanthal, morindone, rubiadin, and rubiadin-1-methyl ether, anthraquinone glycoside), β-sitosterol, cardotene, vitamin A, flavone glycosides, linoleic acid. \(^{35}\) A concentration of extracts from Noni leaves killed 89 percent of the bacteria in a test tube, almost as effective as a leading anti-TB drug, Rifampicin, which has an inhibition rate of 97 percent at the same concentration. Although there had been anecdotal reports of the native use of Noni in Polynesia as a medicine against tuberculosis, this is the first report demonstrating the antimycobacterial potential of compounds obtained from the Noni leaf. \(^{36}\) Recently, Duncan demonstrated that scopoletin, a health promoter in Noni, inhibits the activity of E coli, commonly associated with recent outbreaks resulting in hundreds of serious infections and even death. Noni also helps stomach ulcer through inhibition of the bacteria H pylori. \(^{37}\)  

**Acacia senegal l**

**Synonyms** - A. verek Guillem  
**Family**- Mimosaceae.  
**Ayurvedic** - Shveta Babbuul

Acacia Senegal belongs to the family Fabaceae (mimosaceae). The leaves of the plant is used in traditional medicine to treat illness such as Dysentery, diarrhoea, gonorrhoea, cough, gastric disorder and Nodular leprosy. The stem bark extract is commonly used as remedy for respiratory tract infections. \(^{38}\) It is reportedly used as for its astrangent properties, to treat bleeding, bronchitis, diarrhoea, gonorrhoea, leprosy, typhoid fever and upper respiratory tract infections. \(^{39}\)  

**Acacia senegal** produces the only acacia gum evaluated toxicologically as a safe food additive. Nowadays the gum is present in a wide range of everyday products. 60-75% of the world production of gum arabic is used in the food industry and in human and animal medicine. Acacia Senegal have been reported various activities like anti-bacterial, anti-microbial, spomogenic, immunomodulator and anti-oxidant. \(^{40}\)
Adhatoda vasica I
Botanical Name: Adhatoda vasica linn.
Synonym: Justicia adhatoda Linn.
Family: Acanthaceae.
It is bronchodilatory, expectorant (Indian Herbal Pharmacopoeia.) The Ayurvedic Pharmacopoeia of India indicates its use in dyspnoea. Adhatoda vasica (Acanthaceae) commonly known as vasaka distributed throughout India up to an altitude of 1300m. The leaves, flowers, fruit, and roots are extensively used for treating cold cough, whooping cough, chronic bronchitis and asthma as sedative, expectorant and antispasmodic. Leaves are anti-inflammatory, analgesic effective in skin disorders, cardioactive. Leaves are anti-inflammatory, analgesic effective in skin dis orders, cardioactive. The Adhatoda vasica was considered so useful in tuberculosis that it was said that no man suffering from this disease need despair as long a vasika plant exists in this world. The juice of the leaves is used in diarrhoea and dysentery and powdered leaves in malaria in southern India. The oil obtained from leaves flowers and roots of vasika plant possesses significantly high activity against tubercle bacilli. The growth of M.tuberculosis B 19-4 (human) is inhibited in a concentration of 2 µg. An important chemical constituent of leaf includes pyrroloquinazoline alkaloids, viscine, vasicine, adhatone, vasicinine, vasicolin and vasicinoline. Vascine has been considered as active principle of A. vasica which shows numerous pharmacological activities such as anti-malarial, anti-inflammatory, antioxidant, antidiabetic, Antibacterial etc.

CONCLUSION
The above review has been concluded for natural herbal remedies that have been updated with its pharmacological and therapeutic role in treatment of tuberculosis as the synthetic drugs commonly used has many side effects and also causes resistance.

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REFERENCES
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Table 1: Drugs used in treatment of Tuberculosis with their adverse effects and gene responsible for mutation in mycobacterium tuberculosis to specific drugs.31-37

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>ADR’s</th>
<th>RESISTANCE</th>
</tr>
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<tbody>
<tr>
<td>Rifampicin (RMP)</td>
<td>Hepatitis &amp; Flu like Syndrome</td>
<td>Point mutation in rpoB gene.</td>
</tr>
<tr>
<td>Ethambutol (EMB)</td>
<td>Gouty Arthritis &amp; Colour Blindness</td>
<td>Point mutation in embB gene.</td>
</tr>
<tr>
<td>Pyrazinamide (PZA)</td>
<td>Hepatotoxicity &amp; Hyperuricaemia</td>
<td>Mutation in pcnA gene.</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>Gastro irritation, Neurological toxicity, hepatotoxicity</td>
<td>Mutation in inhA gene.</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Nephrotoxicity &amp; Ototoxicity</td>
<td>Point mutation in rpsL and rrs genes.</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>Nephrotoxicity &amp; Ototoxicity</td>
<td>Mutation in tlyA gene.</td>
</tr>
</tbody>
</table>

Figure 1  Pathophysiology of tuberculosis: Inhalation of bacilli, containment in a granuloma, and breakdown of the granuloma in less immunocompetent individuals.31