1. Introduction

1.1. Tuberculosis : An overview

Tuberculosis (TB) is a major global health problem. It causes poor health among millions of people each year and is close to the human immunodeficiency virus (HIV) as one of the leading cause of death worldwide. In 2014, it is estimated that there were 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. There were also 1.5 million deaths from tuberculosis (1.1 million HIV-negative people and 0.4 million HIV-positive people), of whom around 890 000 were men, 480 000 were women and 140 000 were children. (Global Tuberculosis Report 2015, WHO)

It is estimated that the prevalence of HIV in adults in India is 0.27%, which translates into 2.1 million people living with HIV / AIDS (PLHIV) in 2011. This is the third highest burden in the world. On the other hand, India is the country with the highest tuberculosis burden (TB) in the world with about 2.2 million new cases of tuberculosis occurring each year. Although TB is the most common opportunistic infection (OI) in people with HIV infection, HIV infection is an important risk factor for the acquisition of tuberculosis infection and its progression to active tuberculosis. HIV / TB as a whole is a fatal combination with extremely high mortality rates (15 to 18%) reported among HIV-infected tuberculosis cases reported in the National Tuberculosis Control Program (RNTCP). In general, TB is estimated to account for about 25% of all deaths among PLHIV in India.(National Framework for Joint HIV/TB Collaborative Activities, Government of India, November 2013).

Tuberculosis is most common opportunistic infection (OI) in people infected with Human Immuno-deficiency Virus (HIV) . M. tuberculosis, M. avium and M. kansasii which have recently emerged as important opportunistic infections among patients with Acquired Immuno Deficiency Syndrome (AIDS). (Rastogi N et al., 1998)
1.2. Drug Resistant Tuberculosis

Tuberculosis becomes a more serious problem as, *Mycobacterium* developed resistance against both the first line and the second line drugs. Because of this, there is emergence of multi-drug resistant (MDR) and extensively-drug resistant (XDR) strains of *M. tuberculosis* worldwide, including India. Globally, an estimated 3.3% of new TB cases and 20% of previously treated cases have MDR- TB. By 2015, 105 countries had reported drug-resistant tuberculosis (XDR-TB). It is estimated that 9.7% of people with MDR-TB have XDR-TB. (WHO Global Tuberculosis Report 2015).

In 2005, extensively drug-resistant (XDR) cases of TB were detected and were identified as cases of patients who do not respond to any of the antitubercular drugs used, are resistant to at least Isoniazid (INH), Rifampicin (RIF), one fluoroquinolone and any of the second-line injectable drugs (amikacin, kanamycin, or capreomicin).

The presence of XDR-TB is due to poor diagnosis, inadequate treatment and the abandonment of the patient’s treatment. Side effects also appear because the second-line drugs are more toxic and the treatment must be undergone for a longer duration period (up to 36 months), complex regime, ineffective, poorly tolerated and expensive (Brigden G et al., 2014)

**Multidrug-Resistant TB (MDR TB)**

MDR TB case: A presumptive Drug resistant TB case, whose biological specimen resistant to both isoniazid and rifampicin with or without resistance to other first line drugs, based on the results from a quality assured laboratory.

**Extensively Drug-resistant TB (XDR TB)**

XDR TB Case is an MDR TB case, whose recovered *M. tuberculosis* isolate is resistant to at least isoniazid, rifampicin, a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and also a second-line injectable anti-TB drug (kanamycin, amikacin, or capreomycin) at a quality assured Laboratory.
Because XDR TB is resistant to the most powerful TB drugs, patients are left with much less effective treatment options.

XDR TB is a special concern for people with HIV or other conditions that can weaken the immune system. These people are more likely to develop tuberculosis disease once they have been infected and also have an increased risk of death once they have developed tuberculosis.

In addition to resistance development, Anti-TB drug induced hepatotoxicity, which is a serious adverse reaction common to the drug, is one of the most difficult clinical problems and the root cause of treatment interruption during treatment of tuberculosis that causes hospitalization and potentially fatal event. Among the first-line anti-TB drugs, pyrazinamide, isoniazid and rifampicin have been associated with hepatotoxicity and the risk increases when these drugs are used in combination. (Hasan Ali A et al., 2013 and Singla R et al., 2010)

Several studies have reported that between 1% and 31% of patients with tuberculosis experienced drug-related hepatotoxicity after tuberculosis treatment. (Van der Walt M et al., 2013)

Rifampicin is an important drug for the treatment of tuberculosis. However, the administration of rifampicin in combination with antiretroviral therapy, particularly protease inhibitors, is difficult due to drug interactions. (Mallolas J et al., 2007)

### 1.3. Medicinal Plants : A Great Hope

The World Health Organization (WHO) reported that 80% of the world's population depends mainly on traditional medicine and most traditional therapies, which implies the use of plant extracts or active components (Ahmad, Mehmood and Mohammad, 1998)
Medicinal plants offer great hope to meet these needs and have been used to treat diseases of many centuries. These have been widely used as pure or as a raw material. India is one of the few countries in the world that has a unique wealth of medicinal plants and extensive traditional knowledge on the use of herbal medicine to treat various diseases. Therefore, it has an immense sense to explore the empirical wisdom of the old with modern research technology.

The variety and the high number of plants with therapeutic properties are quite surprising. It is estimated that about 70,000 species of plants, from lichens to imposing trees, have been used at one time or another for medicinal purposes. Herbs provide the starting material for the isolation or synthesis of conventional drugs. In Ayurveda, around 2000, it is believed that plant species have a medicinal value, while the Chinese pharmacopoeia lists more than 5,700 traditional medicines, most of them of plant origin. About 500 herbs are still used in conventional medicine, although whole plants are rarely used.

In India, medicinal plants have made a good contribution to the development of the ancient Indian medical material. One of the first treatises on Indian medicine, Charak Samhita (1000 B.C) records the use of over 340 drugs of plant origin. Most of these continue to be harvested from wild plants to meet the demand of the medical profession. Therefore, despite the rich heritage of knowledge on the use of plant drugs, little attention was paid to their cultivation as field crops in the country until the second part of the 19th century.

In India, the Vedas are the epic poems written c. 1500 BC. These volumes contain abundant material on herbal knowledge of that time. The Vedas were followed around 700 BC by the Charak Samhita, written by the physician Charaka. He is known as the father of medicine in India. This medical treatise includes details of around 350 medicinal herbs. Among these are visnaga (Ammi visnaga), an herb of Middle Eastern origin that has recently proved effective in the treatment of asthma, and the gotu kola (Centella asiatica), which has long been used to treat leprosy.

Ayurvedic treatment differs from modern medicines in the way the disease is seen. In general, Ayurvedic doctors say that antibiotics can have their applications, especially in surgery, but that antibiotics attack fundamentally and are considered to cause disease. Ayurvedic doctors prefer to restore the balance of the body. The causative factors, which allow the germs to grow, must be
Drugs in Ayurveda
The drugs used in Ayurveda are made from various processes of vegetables and mineral raw materials. It seems that plant alkaloids are mainly active ingredients. Obviously, with the exception of some chemical changes, they are mainly chemical derivatives (even modern drugs are based on these, but the proportion of synthetic derivatives is higher). However, plants that grow on particular soils, with weather patterns, sunlight, harvest time, and method of drug preparation are all very important. Identical species of plants that grow in the rainforest and in the courtyard of the city may not have the same medicinal value. Herbal medicines have the ability to influence the body's system. Those selected depend on the chemical constituents present in the plant used. Scientists began to extract and isolate plant chemicals in the 18th century, and since then we have become accustomed to observing herbs and their effects in terms of the active components they contain. This encyclopedia is not an exception, as it provides details on all the main active components of the medicinal herbs that appear explaining their actions. (A manual of medicinal plants: a complete book of sources, N. D. Prajapati, 2010)

The constituents of pure and isolated plants are of great importance because they have given the worlds the most useful drugs. For example, tubocurarine, the most potent muscle relaxant that comes from curare (Chondrodendron tomentosum), and the strongest painkiller of all, morphine comes from the opium poppy (Papaver sominifarum). Many anesthetics are also derived from plants, for example, cocaine, coming from coca (Coca erythroxylem). It is difficult to think of a private world of the antimalarial properties of quinine; or heart medicine digoxin (Digitalis) or cough relieving ephedrine, which is present in many recipes and home remedies for the cold. These and many other conventional drugs derive from isolated plant constituents. These are the most effective of all conventional drugs. They have tested a hundred species of plants and have been shown to have anti-mycobacterial activities. (Gautam R et al., 2007)
Various plants extracts have been used as traditional medicines against disease including tuberculosis and *Lantana camara*, *Acacia Senegal*, *Aloe vera* and *Ocimum sanctum* have been reported which have anti-mycobacterial activity. (Gautam AH et al. 2012, Nandagopal B et al.,2011, Santhosh RS et al. 2014 Sharma P et al.,2013, Jethva K et al. 2016).

Herbal Plants are Useful in Tuberculosis Treatment. Brief descriptions of plants that have anti-tuberculosis activity and used in this study are:-

**Lantana camara L.**

Botanical Name : *Lantana camara L*

Synonyms : Camara vulgaris, Lantana scarbida

Family : Verbenaceae

A large scrambling evergreen, strong smelling shrub with stout recurved prickles; leaves opposite often rugose, scabrid on both sides; flowers small, normally orange but often white to dark red in heads which are prominently capitates; bracts conspicuous, persistent; fruits fleshy drupes, 5 mm in diameter; endocarp hard green when young and blue or black on ripening.

Chemical constituents: catalase, amylase, invertase, lipase, tannase and glucosidase. Appreciable amount of tennis and sugar, crystalline glucoside has been separated from the resin by ether extraction.

Uses: The plant is vulnerary, diaphoretic, carminative, antispasmodic, and tonic. It is useful in tetanus, vitiated conditions of vata malaria, epilepsy and gastropathy. A decoction fresh root is a good gargle odontalgia and this is used hills tribes for all types of dysentery. Powdered leaves are used for cuts, wounds, ulcers and swellings. An infusion of leaves is used for bilious fever, vitiated conditions of eczema and eruptions, vata and kapha. The fruits reported to be useful in fistula, pustules and tumors of rheumatism.

*Lantana camara* is a low subcandent, vigorous shrub which can grow to 2-4 meters in height. Leaves are bright green, rough finally hairy and emits a pungent odour when crushed. Reports indicate that leaves extract of lantana
exhibit anti microbial, fungicidal insecticidal and nematocidal properties. Lantana oil is sometimes used for the treatment of skin itches as an antiseptic for wounds and externally for leprosy and scabies. In various studies methanolic extract of Lantana camara showed highest anti microbial activity but it was much less activity than rifampicin whereas chloroform extract of Lantana camara showed activity against all three strains of mycobacterium tuberculosis but it was less active than methenolic extract. (Kirimuhuzya C et al., 2009)

Fig 1: Lantana camara leaves
Acacia Senegal L

Synonyms : A verekguillem
Family : Mimosaceae
Ayurvedic Name : Shwet Babuul

Acacia Senegal belongs to the family fabaceae. The leaves of the plant are used in traditional medicine to treat illness such as dysentery, diarrhea, gonorrhea, cough, gastric disorder and nodular leprosy. Acacia Senegal have been reported various activities like antibacterial, anti tubercular, immunomodulator, and anti oxidant.

Fig 2: Acacia senegal leaves
*Aloe vera* L

Family : Xanthorrhoeaceae  
Sub family : Asphodeloideae  
Genus : Aloe  
Species : A. vera

*Aloe vera* is frequently cited for being used in herbal medicine since the beginning of the first century AD. Extracts from *A vera* are widely used in the cosmetics and alternative medicine practitioners, being marketed as having rejuvenating, healing, or soothing properties. There is, however, little scientific evidence of the effectiveness or safety of *Aloe vera* extracts for either cosmetic or medicinal purposes, and what positive evidence is available is frequently contradicted by other studies.

Fig 3 : *Aloe vera* leaves
*Ocimum sanctum*

Family : Lamiaceae  
Genus : Ocimum  
Species : O. tenuiflorum

*Ocimum sanctum* is commonly known as Tulasi (Sanskrit: Surasa) has been used for thousands of years in Ayurveda for its immense medicinal properties. Charaka Samhita, an ancient Ayurvedic text also mentioned the medicinal properties of this plant.

![Ocimum sanctum leaves](image)

**Fig 4 : Ocimum sanctum leaves**