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Review Article

EXPLORATION OF AYURVEDA POTENTIAL IN TUBERCULOSIS: CURRENT SCENARIO AND FUTURE PROSPECT

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ABSTRACT

Tuberculosis remains the world's deadliest infectious killer despite the availability of highly efficacious treatment for decades and one of the top 10 causes of death worldwide. As per WHO, global report 2019 Eight countries accounted for 66% of the new cases with India (27%) at top. Anti-TB drugs are one of the commonest group underlying idiosyncratic hepatotoxicity worldwide. Ayurveda is living science which is helpful to each individual to be a healthy by advocacy of lifestyle and treatment by universal principle. In present scenario the role of Ayurveda in the management of TB is very scanty and mostly limited to adjunct or supportive therapy which cannot be simply neglected. In this review an attempt is made to throw a light on history of tuberculosis, it's related literature in Ayurveda classics, different *Kalpas* and drugs which may useful, and their anti-tubercular potential and current trend of practice and research on tuberculosis. The main objective is to make familiar the researchers and readers to take further initiative in future to conduct more research on this contagious killer disease.

KEYWORDS: Ayurveda, Antitubercular activity, Clinical research, Rajyakshma, Tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a communicable disease caused by bacteria (Mycobacterium tuberculosis) that most often affect the lungs but can also affect other sites (extra-pulmonary TB). Tuberculosis is curable and preventable[1]. TB is transmitted from person to person through coughing and breathing in airborne droplets that contain bacteria. As one of the most common infections in the world, TB remains a foremost problem in many countries and among vulnerable populations[2]. The theme of World TB Day 2019 - 'Its time' – puts the accent on the urgency to act on the commitments made by global leaders, World Health Organization (WHO) has launched a joint initiative "Find. Treat. All. #End TB[3]"

People infected with Mycobacterium tuberculosis bacteria have a 5–15% lifetime threat of falling ill with TB. Persons with compromised immune systems, such as known cases of HIV, malnutrition or diabetes, or people, who addicted for tobacco, have a higher risk of falling ill. When a person develops active TB disease, the symptoms (such as cough, fever, night sweats, or weight loss) may be mild for many months. This may lead to delays in seeking care, and results in transmission of the bacteria to others. People with active TB can infect 5–15 other people through close contact over the course of a year. Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die[4]. India contributes to one-fourth of the global burden of multidrug-resistant tuberculosis (MDR-TB) with inadequate diagnostic infrastructure for drug susceptibility testing (DST)[5].

According to an estimate of World Health Organization (WHO), an approximately 85–90% of the world's population consumes traditional medicines due to better tolerance and fewer adverse drug reactions. Indeed, both general practitioners and specialists use various types of traditional medicines to support Tuberculosis management. Ayurveda have some solutions to these problems.

Different names used for TB[6]

Tuberculosis, Phthisis, Tabes, Schachepheth, "The white plague", Consumption, Captain of all these men of death, Scrofula.

Today, we classified TB from where it is located (pulmonary, extrapulmonary) and the way to treat (drug- susceptible, drug- resistant, multidrug resistant, and extensively drug-resistant[6].

History of Tuberculosis in Global and Indian Scenario

It has been hypothesized that the genus Mycobacterium originated more than 150 million years ago. In the Middle Age, Scrofula, a disease affecting cervical lymph nodes, was described as a new clinical form of TB. The illness was known in England and France as "king's evil", and it was widely believed that persons affected could heal after a royal touch. In 1720, for the first time, the infectious origin of TB was conjectured by the English physician Benjamin Marten, while the first successful remedy against TB was the introduction of the sanatorium cure. The famous scientist Robert Koch was able to isolate the tubercle bacillus and presented this extraordinary result to the society of Physiology in Berlin on 24 March 1882. In the decades following this discovery, the Pirquet and Mantoux tuberculin skin tests, Albert Calmette and Camille Guérin BCG vaccine, Selman Waksman streptomycin and other anti-tuberculous drugs were developed[7].

TB has been part of the human experience for a long time, in humans can be traced back to 9,000 years ago in Atlit Yam, a city now under the Mediterranean Sea, off the coast of Israel. Archeologists found TB in the remains of a mother and child buried together. The earliest written mentions of TB were in India (3,300 years ago) and China (2,300 years ago)[6].

TB in India is an ancient disease. In Indian literature there are passages from around 1500 BCE in which consumption is mentioned, and the disease is attributed to excessive fatigue, worries, hunger, pregnancy and chest wounds. Sanskrit manuscripts around 500 BCE which are the texts from which the Ayurveda system of general Indian medical practice is derivedthere is a group of diseases referred to as *Shosha* with a prominent feature of wasting, and there are other symptoms such as "cough and blood-spitting". It is also said that the Moon-god, the king of the *Brahmanas* was the first to become a victim of this disease, which is as a result also known as *Rajayakshma*, or king's disease.

In *Madhukosha*, one of the commentaries of *Madhavnidana* describes the disease referred to in a number of different texts as *Yakshma*, consumption or *Rajyakshma* (kingly consumption) and it also refers to how it has been identified by many as being what is in the twenty first century called Tuberculosis. However, the commentary also said that ancient disease *Yakshma* had a much wider range than TB and covers a number of conditions between physical exhaustion through to cachexia or physical wasting[8].

TB disease burden

A total of 1.5 million people died from TB in 2018 (including 251000 people with HIV). Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). In 2018, the 30 high TB burden countries accounted for 87% of new TB cases. Eight countries account for two thirds of the total, with India (27%), leading the count, followed by, China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%)[9].

Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. WHO estimates that there were 484000 new cases with resistance to rifampicin – the most effective first-line drug, of which 78% had MDR-TB[4]. In 2018, India was able to achieve a Total Notification of 21.5 LakhTB cases[10]. It is estimated that about 40% of the Indian population is infected with TB bacteria, the vast majority of whom have latent TB rather than TB disease[11].

Role of Immunity in Tuberculosis and HIV:

The risk of developing TB is estimated to be between 16-27 times greater in people living with HIV than among those without HIV infection. In 2015, there were an estimated 10.4 million cases of tuberculosis disease globally, including 1.2 million [11%] among popilation living with HIV. Almost 60% [57%] of tuberculosis cases among people living with HIV were not diagnosed or treated, resulting in 390 000 tuberculosis-related deaths among people living with HIV in2015[12].

An article lead to, M. tuberculosis and HIV act in synergy, accelerating the decline of immunological functions and leading to subsequent death if untreated. An author gave some evidences about mechanisms behind the breakdown of the immune defense of the co-infected individual to highlight immunological events that may accelerate the development of one of the two diseases in the presence of the coinfecting organism.

Cell-mediated immunity play an important role for control of *M. tuberculosis* infection; activation of both $CD4^+$ and $CD8^+$ T cells is seen in active TB in humans as well as in mice after experimental infection.

Programmed- Death 1 (PD-1) and T cell immunoglobulin and mucin domain 3 (Tim-3) are two examples of markers of T cell exhaustion in HIV-1^+ patients caused by constant antigenic stimulation. The publication reports that Tim-3 was up-regulated on antigen-specific $CD8^+$ T cells in patients with active TB, indicating that similar inhibitory receptor/ ligand interactions play a role in modulating host

immunity to both HIV and *M. tuberculosis* infections in humans[13].

Antitubercular Drugs and Hepatotoxicity

Omaima El Bouazzi et al. stated that Hepatotoxicity is the most common adverse reaction of anti-TB treatment that leads to interruption of therapy. The exact mechanism of Antitubercular drug induced hepatotoxicity (ATDH) is not well defined but is due to toxic metabolites. Studies reported in several countries are shown in the Orientals are reported to have the highest rates, especially Iran (27.7%) and Pakistan (19.7%). However other studies reported in developed countries showed low incidences (USA, Spain and Dutch). The incidence of ATDH is much higher in studies from developing countries compared with developed countries. Several factors can be at the origin of this difference as: Malnutrition, chronic co-infections, ethnic factors or genetic predisposition[14].

The liver has a central role in drug metabolism and detoxification; and is consequently vulnerable to injury. The pathogenesis and types of drug induced liver injury (DILI) are presented, ranging from hepatic adaptation to hepatocellular injury[15].

Chart 1: Showing Diagnostic protocol as per modern system of medicine[16]

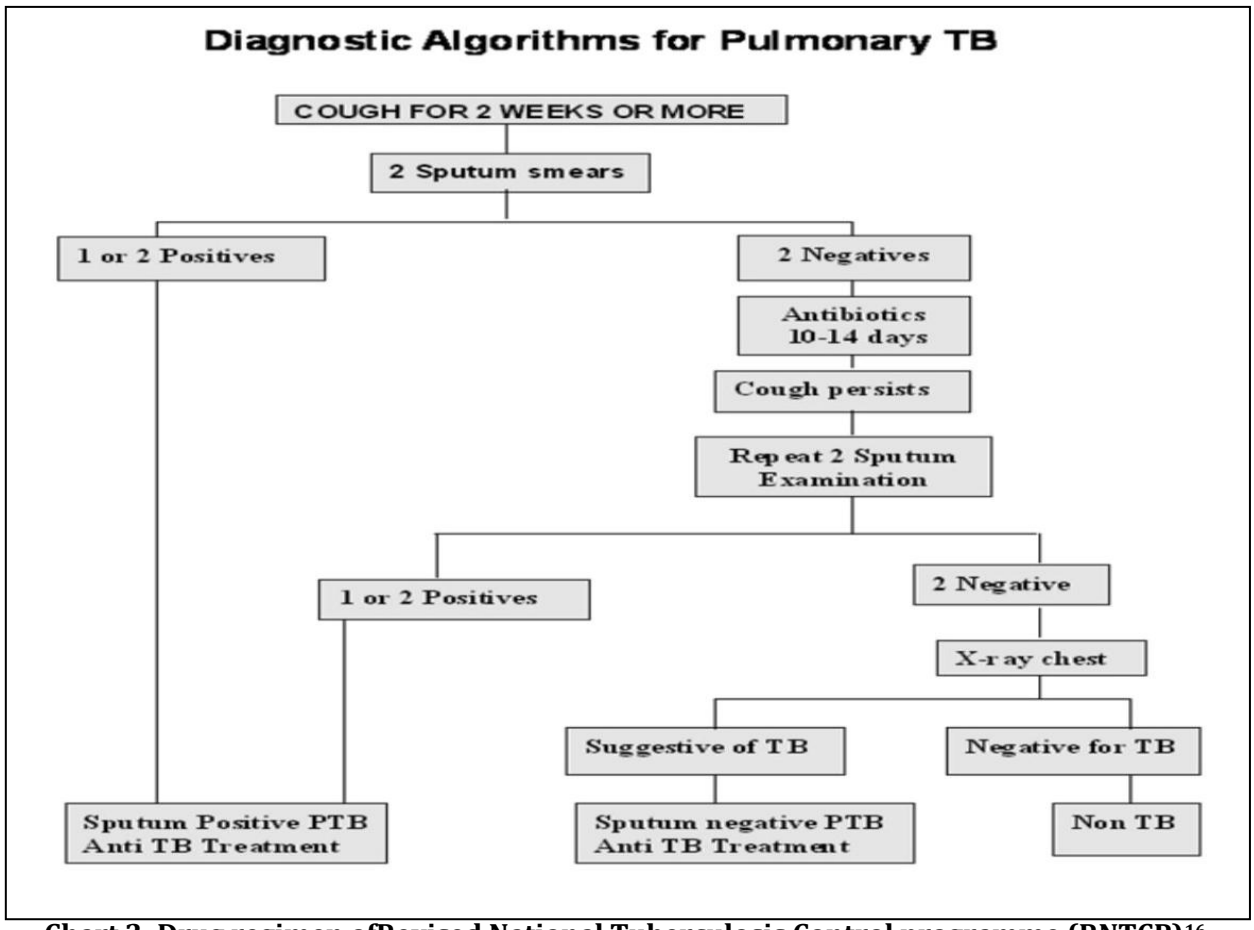


Chart 2: Drug regimen ofRevised National Tuberculosis Control programme (RNTCP)[16]

Treatment Groups	Type of Patient	Regimen	
		Intensive Phase	Continuation phase
New (Cat I)	New sputum smear positive New sputum smear negative New extra-pulmonary New others	2H3R3Z3E3	4H3R3
Previously Treated (Cat II)	Smear positive relapse Smear positive failure Smear positive treatment after default Others	2H3R3Z3E3S3 1H3R3Z3E3	5H3R3E3

Tuberculosisin Ayurveda perspectives[17,18,19]

Ayurveda is a whole medical system that is based on various theories about health and illness and on ways to prevent, manage, or treat health problems. Tuberculosis is not a modern disease; in fact, it is mentioned in the Rigveda, which was written over 3500 years ago. Tuberculosis is compared to *Rajyakshma* mentioned in Ayurvedic treatises. *Rajayakshma* is primarily attributable to *Dhatukshaya* (tissue emaciation or loss), also termed as *Shosha*. In Charak Samhita *Krodha, Yakshma, Jvara, Roga* and *Dukha* are used as synonyms to each other.

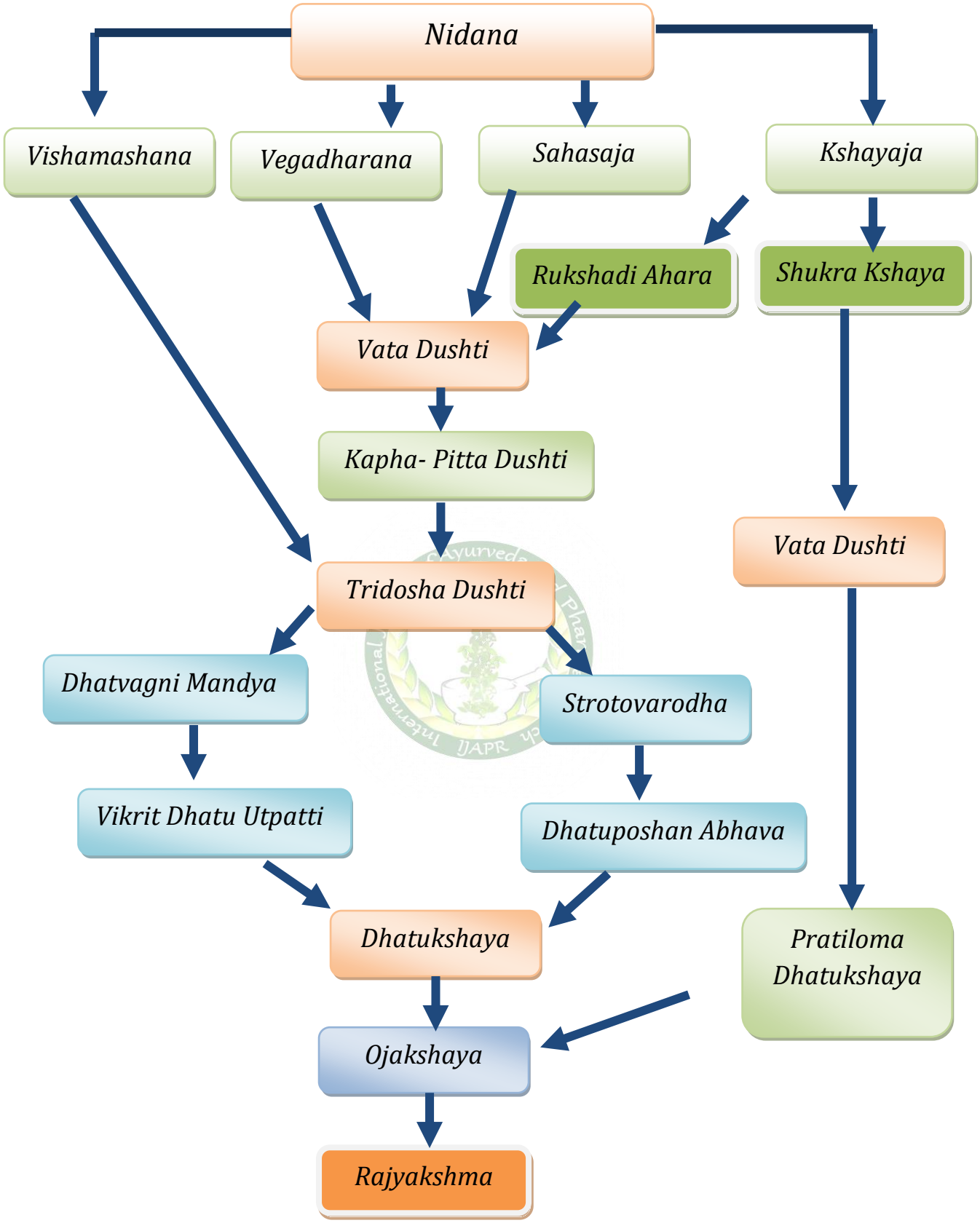
In Ayurveda four types of pathophysiological factors considered for *Yakshma* i.e., *Ayathabalamarambham* or *Sahas* ((physical exertion disproportionate to strength), *Vegasandharanam* (suppression of natural urges), *Kshayam* (wasting) & *Vishamashanam* (improper diet). According to the pathophysiological factor different types of sign and symptoms are observed in the patient. This process universally initiates the process of pathogenesis in *Rajayakshma* patients. In the Ayurveda *Yaksma* has been classified on the basis of cluster of symptoms observed in *Yakshma* patients like *Trirupa Yakshma, Shadrupa Yaksma* and *Ekadashrupa Yakshma*. As per Ayurvedic concepts *Yaksma* is considered as *Tridoshja Vyadhi*, there is inevitable metabolic dysfunction (*Dhatwagninasana*), in which *Rasa* (tissue fluid), *Rakta* (blood), *Mamsa* (muscle), *Meda* (adipose tissue), and *Shukra* (generative tissue) are lost. This leads to ultimate deterioration of immunity or *Ojokshaya*. As per the pathophysiological process involved in the body the *Yaksma* has been classified as *Anuloma* or *Pratiloma Yakshma*.

An observational study suggests that unwholesome diet and irregular dieting, exertion, suppressing of the natural urges and stressful lifestyle play an important role in the manifestation of tuberculosis disease. *Trirupa* (3 symptoms) and *Shad Rupa* (6 symptoms) are found in earlier stage of the tuberculosis and *Ekadasharupa* (11 symptoms) in chronic condition of tuberculosis[20].

Chart 3: Showing sign and symptoms in patient of *Rajyakshma* as per *Charak Samhita*.

Early stages clinical features of *Rajyakshma* (Tuberculosis)		**Clinical features of Chronic condition of *Rajyakshma* (Tuberculosis)**
Trirupa Yakshma	***Shadrupa Yakshma***	***Ekadashrupa Yakshma***
1. *Amsa –Parshvaabhitapa* (Distress in shoulder and Chest) 2. *Kara-Pada samtap* (Burning sensation in hands and feet) 3. *Jwara* (Fever)	1. *Parshvashoola* (Pain in sides) 2. *Kasa* (cough) 3. *Jwara* (Fever) 4. *Swarabheda* (Hoarseness of voice) 5. *Atisaara* (Diarrhoea) 6. *Aruchi* (Anorexia)	1. *Parshvashoola* (Chest pain) 2. *Kasa* (Cough) 3. *Jvara* (Fever) 4. *Swarabheda* (Hoarseness of voice 5. *Atisaara* (Diarrhoea) 6. *Aruchi* (Anorexia) 7. *Amsashoola* (Shoulder pain) 8. *Shirshoola* (Headache) 9. *Raktachardi* (Haemoptysis) 10. *Shthivan/ Kapha Sraava* (Excretion of sputum) 11. *Shvasa* (Dyspnoea)

Chart 4: Probable mode of *Samprapti* in *Rajyakshma* disease



Clinical Management of *Rajyakshma* in Ayurveda Literature[17,18,19]

It is advised to avoid purgation in *Yakshma* patients i.e. *"Purisham Sanrakshyam"*. Goat Milk, meat and soup of *Jangal* category animals, *Yusha* of grams & Green grams, Wheat, *Seedhu, Arishta, Sura, Asava* are advised as a *Pathya* (advocacy) in *Yakshma. Rakayakshma* disease is caused by *Tridosha*, so *Vaidya* should consider the state of *Dosha* and treat Tuberculosis according to the severity of the symptoms and patient's condition. Most of the *Yogas* (formulations) mentioned in *Jwara* (Fever) treatment can be used along with *Ghrita* in the *Yakshma* for the symptoms like *Jwara* and *Daha* (burning sensation). *Ghrita* consumption after food is advised for *Shirashoola* (Headache), *Parshvashoola*, *Ansashoola*, *Kasa* and *Shwasa*.

Panchakoladi Ghrita, Dashamooladya Ghrita, Kharjuradi Ghrita, Vasa Ghrita, Shatavari Ghrita, Duralabhadya Ghrita, Jeevantyadi Ghrita, Sitopaladi Churna, Talishadi Churna, are advised by Acharya Charaka for the treatment of *Yakshma*[17].

Brihan Chikitsa, Snigdha food and drink and *Vatanashak* medicines, food and drink are beneficial. *Ashwagandhadi Churna, Ashwagandha Ksheera, Ashwagandha Utsadan, Vasaghrita, Eladi Ghrita, Rasona Yogas* are advised by Acharya Sushruta.

Dashamoola Ghrita, Jeevantyadi Ghria, Kharjura Shatpal Ghrita, Ashwagandha siddha milk and ghee extracted from that milk, *Guda-Sarpi yoga* are advised in *Ashtang Hridya*.

The overall approach of the treatment is *Deepan-Pachan, Laghu Santarpan and Brihan* of weakened *Dhatu* (body tissues) and to boost the immunity of the patient by use of *Rasayana* (Immunomodulator) drugs.

Ayurveda Products/Herbs for Tuberculosis Disorder

Chart 5: Showing Formulations mentioned in AFI which can be useful in *Rajyakshma* (TB) / *Yakshma* (TB) / *Kshaya* (Pthisis)[21]

Dosage Form	AFI	Name of the Formulations
Churna /Kwatha Churna	AFI Part I	*Vidaryadi Kwatha Churna, Karpuradi Churna, Yavandyadi Churna, Drakshadi Churna, Narsimha Churna, Bhaskarlavan Churna, Sitopaladi Churna*
	AFI Part II	*Agnimukha Churna, Ashwagandhadi Churna, Mahatalisadi Churna, Madhyamanayika Churna, Badaradya Churna,*
	AFI Part III	*Lavangadi Curna, Yogaraja Rasayana*
Vati /Tablet /Guggulu	AFI Part I	*Mahayogaraj Guggulu, Saptavimshatik Guggulu, Dhanvantar Gutika, Shiva Gutika, Shankhavati, Suvarna Vatak*
	AFI Part II	**Sanshamani Vati*
Asava /Arishta	AFI Part I	*Kanakasava Kumaryasava-A, Kumaryasava-B, Dantadyarishta, Dashmoolarishta, Draksharishta, Pippalyadyasava, Vasakarishta*
	AFI Part II	*Babbularishta*
Avleha /Paka /Khanda	AFI Part I	*Agastyaharitaki Rasayana, Kushmandaka Rasayana, Guduchyadi Modaka, ChitrakHaritaki, *Chyavanprasha, Narikela Khanda, Guduchyadi Modaka, Pugakhsnda, *Vasavleha, Shatavari Guda*
	AFI Part II	*Ardrakakhanda Avleha, Vyaghri Haritaki*
	AFI Part III	*Methi Modaka, Abhayadi Modaka, Brihat Vasavaleha,*
Sneha /Taila /Ghrita	AFI Part I	*Indukanata Ghrita, Eladi Ghrita, Chagaladya Ghrita, Nirgundi Ghrita, Panchatiktaguggulu Ghrita, Pippalyadi Ghrita, Vidaryadi Ghrita, Chandanadi Taila, Chandanbalalakshadi Taila, Bala Taila, Balashwagandhalakshadi Taila, Vasachandanadi Taila*
	AFI Part II	*Madhyam Narayan Taila, Visnu Taila, Brihat Ashwagandha Ghrita*
	AFI Part I	*Guduchi Sattva*
Parpati /Rasayoga /Bhasma	AFI Part I	*Kantavallabha Rasa, Rasasindura, Panchamrita Parpati, Svarna Parpati, Manikya Pishti, Kapardika Bhasma, Tamra Bhasma, Pravala Bhasma, Mukta Bhasma, YashadaBhasma, Vanga Bhasma, Vajra Bhasma, Vaikranta Bhasma, Svarna Bhasma, Svarnamakshika Bhasma, Haratala Bhasma, Chaturbhuja*

		*Rasa, Chaturmukha Rasa, Navaratnarajmriganka Rasa, Nagavallabha Rasa, *Mahalaxmivilas Rasa, Muktapanchamrita Rasa, Yogendra Rasa, Rajmriganka Rasa, Laghumalinivasant Rasa, Laxmivilas Rasa, Vasantkusumakar Rasa, Svarnabhupati Rasa, Sutshekhar Rasa*
	AFI Part II	*Akika Pishti, Akika Bhasma, Varatika Bhasma, Kanchanabhra Rasa, Kantavallabha Rasa, Grahanikapat Rasa, Vasantatilaka Rasa, Hemanath Rasa, Kanchanabhra Rasa, Brihachhanagarabhra Rasa, Shringabhra Rasa, Sutshekhar Rasa, Yogaraj, Shilajatvadi Lauha*
	AFI Part III	*Vidyadharabhra Rasa, Kancanabhra Rasa, Brhat Sarvalokasraya Rasa, Mahasvasari Lauha, Svasakalesvara Rasa Sutasekhara Rasa (Svaranarupyarahita)*

Antitubercular Potential of some traditional herbs/Products

MR Hema et al. in the bio-activity study of the methanol extract of *Artocarpus integrifolia* exhibited anti-tuberculosis activity, even at very low concentration (less than 1mg) which led to the isolation of two known compounds homopterocarpin and cycloheterophyllin[22].

Mahesh AR et al. found that water soluble portion of the methanolic extract of the dried peels of *Citrus sinensis* shows better antitubercular activity at 50µg/ml[23].

Shivakumar BS et al. in his study observed that ethanol extract of the stem and leaves of *Barlaria Buxifolia* Linn Using Microplate Almar Blue Assay (MABA) was found to be active at minimum inhibitory concentrations (MIC) of 25 and 50µg/ml and provides potential for the development of urgently needed novel antituberculous therapeutics[24].

Ehsanifar et al. in his study, by using proportional method on 7 clinical samples and one reference sample with its six concentrations in addition to the effects of plant extracts in combination with rifampicin the Methanolic extract of *Capparis spinosa* plant revealed anti-mycobacterial effect[25].

Rahna K. Rathnan et al. in his study screened the antituberculosis properties of leaf and callus extracts of *Ipomea turpethum* by broth dilution method. Among the extract tested, they observed significant inhibitory activity in ethanol extract of leaf callus and the aqueous extract did not show any significant activity[26].

Villaflores, et al. studied on *Alpinia purpurata* or red ginger for its phytochemical constituents on Philippine Zingiberaceae plants that may exhibit antimycobacterial activity. This study demonstrates the promise of this plant as a source of phytomedicinals that can fight TB[27].

Kumar JK et al. conducted study on crude extracts of legume leaves of five medicinal plant i.e *Kingiodendron pinnatum, Humboldtia brunonis, Derris scandens, Ceasalpinia mimosoides* and *Indigoferra cassiodes*. In the result they showed that leaf extracts of these medicinal legumes possess anti-tubercular activity and offers the scope for the development of potential anti-tubercular crude drugs[28].

Sharma VK found in his study that aqueous extract of *Henna* has strong *in vitro* and *in vivo* tuberculostatic acitivity[29]. Subsequently Bina Shaheen Siddiqui et al. investigated the antituberculosis activity of six constituents including three triterpenoids, lawsowaseem, lawsonic acid, lawsonin; a dihydrobenzofuran derivative, lawsonicin; a naphthoquinone derivative, lawsonadeem, and vomifoliol isolated from the aerial parts of *Lawsonia alba* and validate the earlier findings of Sharma VK[30].

Archana Mehta, et al. showed that three isolated compounds from fruit of *Citrullus colocynthis* (ursolic acid, cucurbitacin, E 2-0-β-D-glucopyranoside and cucurbitacin E 2-0-β-Dglucopyranoside) having good anti-tubercular activity by inhibiting 7 non-MDR, 8 MDR and 1 XDR M. tuberculosis and 2 MOTT clinical isolates. The bioactive fractions as a whole showed better antitubercular activity than the isolated compounds against the drug resistant and MOTT clinical isolates may be due to synergistic effect of other compounds[31].

B.S. Siddiqui et al. stated in his study that inhibition of M. tuberculosis by pure compounds from *Ocimumbasilicum* supports the use of this plant in ethno medicine as a remedy for symptoms of tuberculosis. They also suggested that the activity of the plant may be due to a synergistic effect of active compounds including those investigated in the present studies, and hence this plant is a potential candidate for obtaining further new antituberculosis natural products[32].

Shashikant Vaidya et al. in their study showed that aqueous & methanolic extracts of *Cinnamomum* prepared by soxhet extraction and their phytochemical analysis showed flavanoids, tannins, steroids & essential oils in both extracts. Study

demonstrated antituberculosis activity of plants, though antagonistic activity with INH[33].

Dini et al; in their review article mentioned studies carried out about antitubercular properties of *Allium sativum* both in vitro and in vivo is provided. The researches about the garlic extracts effectiveness against clinical isolates of MDR-TB are of scientific importance. Allium sativum offers a hope for developing alternative drugs. The involvement of traditional healers (TH) in the TB health management could facilitate the administration of garlic extracts to the infected patients[34].

Alka Sharma and Ashwani Kumar in their review article given various references for antitubercular activity of *Justicaadhatoda* plant[35].

Hepatoprotective activity of some traditional herbs/Products againstantitubercular drugs

Geetha KM et al. found that aqueous alcoholic (70%) extract of *Rhodomyrtus tomentosa* exhibit hepatoprotective activity against antitubercular drug induced hepatotoxicity through a free radical scavenging effect and reduces oxidative damage caused by antitubercular drugs[36].

Chandane RD et al. in his study reveals that honey significantly prevent as well as reverse hepatotoxicity induced by antitubercular drugs in rats. Study concluded that honey by way of inhibiting lipid peroxidation and by increasing antioxidant defence mechanism has a significant hepatoprotective action[37].

B.P. KALE et al. stated that aqueous leaf extract *Azadirachta indica* significantly prevents and reverses the hepatotoxic damage induced by antitubercular drugs in rats[38].

Shoba Rani et al. found that methanolic pericarp extract of *Sapindusemarginatus* possess hepatoprotective activity against anti tubercular drugs induced liver damage in rats[39].

T.S.Panchabhai et al. seen the Hepatoprotective effect of two Indian medicinal plants *Tinospora cordifolia* (Tc), *Phyllanthus emblica* (Pe), and their combination, in a rat model of isoniazid, rifampicin and pyrazinamide induced hepatic damage[40].

S.A.Tasduq et al. showed that, 50% Hydroalcoholic Fruit Extract of Emblica officinalis have the hepatoprotective property against antituberculosis (anti-TB) drugs-induced hepatic injury in rats[41].

Current Practices & Researches in Tuberculosis:

Ayurvedic treatment of tuberculosis was initiated in 1933, by the establishment of Patipukur Tuberculosis Hospital, Kolkata. Later, a full-fledged research unit was commissioned with exclusive budget. Treatment guidelines were adopted on Ayurvedic principles for therapeutic management which was a unique effort of its kind in Pre-Independence India. This regimen was discontinued from 1st November 1947 on the introduction of synthetic ATDs. Drugs containing mercury, gold, calcium was prepared at the in-house pharmacy and was administered to the patients with fresh juice of herbs cultivated in the hospital garden. Formulations like *Vasantamalati, Kanchanabhra rasa, Rajamrigankarasa* were under use including *Bhallataka (Semicarpusanacardium) Rasayan, Mallasindura*, *Vasa (Adatodavasica)* etc. The statistics on the treatment of Tuberculosis using Ayurvedic medicine over a period of 13 years is of immense value[42].

The Renowned practitioner from Maharashtra Vaidya P T Joshi in his Post graduation thesis compilation 'Role of *Panchakarma* in Acute stages of Disease' mentioned a case study of 42 year male patient diagnosed as pulmonary Tuberculosis having symptoms of Haemopthasis, loss of weight & appetite, low grade fever and coughing for 3 years and treated by *Shodhana* (*Vasa Ghrita-Swedana-Vamana*), and then *Shamana* (*Draksharishta*, *Shringa Bhasma*, *Pipplai Rasayan*)

Ayurvedic treatment of Tuberculosis was common practice right until 1947, when modern anti-Tuberculosis drugs became available. Antibiotic Tuberculosis medications are very effective but eventually they are rendered ineffectual when drug resistant strains emerge. However, recent research proves that Ayurvedic treatments may hold the key to fighting this growing problem[43].

Chart 6: Showing details of Clinical Evidences conducted on Ayurveda Formulations.

Study Type & Intervention	Treatment Outcome	Ref.
Subhash Singh et al; Case Report 36 year old female known case of drug resistant pulmonary TB **Purification of body (*Samsodhan*):** *Snehapan* uncted with Ghrit of goat and sheep processed with decoction of *Laghu Panchmool* for three days. On fourth day in the morning *Piper longum* (*Pippali*) powder 2g for mild emesis and *Terminalia chebula* (*Haritaki*) powder 6g for laxation	*Mahalaxmi Vilas Rasa* is found useful for the treatment of TB. Drug is as effective as R H E & Z, available in conventional medicine for treatment of TB.	44

Oral treatment: After *Samshodhana* regular therapy with *Mahalaxmi Vilas Ras* 250 mg per day empty stomach in the morning **Duration:** for five years		
Deshpande Vaishali et. al.Case Study Female patient of 58 year along with ATT given **Oral treatment:** *Kaishora Guggulu* 500mg TDS AF with warm water, *Samshamani Vati* 1gm TDS AF with warm water. Combination (*Swarna Malini Vasanta* 60mg + *Abhrak Bhasma* 120mg + *Chausasti Pippali* 250 mg) BD with honey ***Panchakarma* treatment:** Gentle application of sesame oil on both lower extremities and *Matra Basti* of *Guduchi Siddha Yamaka Sneha*. **Duration:** 85 days	After completing 55 *Basti* and 85 days of oral treatment complete remission seen in low back pain, tingling, numbness, body ache, loss of appetite. Improvement in Muscle power and weight gain.	45
Singhal Pragya, Case Study 50 year old male patient with past history of pulmonary TB **Oral treatment:** *Vasa avhleha,*1 tsf BD *Talishadichoorna* 3gm BD *Godantibhasma* 500mg BD *Madhuyasthichoorna* 3gm BD with milk **Duration:** 08 months	Improvement in declining sputum production and cough relief, blood tinged sputum. Having no episode of chest infection during treatment and chest X-ray found normal after treatment.	46
Dr. A. P. Rana et al; Case Study 14 years old female patient known case of MDR TB **Oral treatment:***Jaimangal Rasa, Rajmrugank Rasa, Swarnasutshekhar Rasa, Shwas Kas Chintamani Rasa, Shwas Kuthar Rasa, Nagarjunabhra Rasa* ***Panchakarma* treatment:** *Bahya Abhyanga: KsheerBalaTaila* *Uro Abhyanga: BrihatShatavariTaila*	Significant relief in symptoms as compared to earlier severity. Improvement in appetite, weight gain, and help the patient to get back to his routine life after one year of regular treatment.	47
Sathya N. Dornalaet al; Clinical Trial Group of 60 patients of PTB divided into two equal groups. **Control group:** DOTS therapy **Test group:** DOTS for 6 or 8 months + *Bhringarajasava* (30 ml thrice a day AF) for 2 or 3 months i.e., during the intensive phase. **Follow-up:** 6-8 months based on treatment category.	The purpose is to improve the resistance of the patient to damage caused by the tubercle bacilli, and to create an environment in the body unsuitable for proliferation of the bacilli. Improvement in weight gain was also observed.	48
Purvi Vyas et al; **Single Blind Controlled Trial** 133 patients of TB (Category-I) randomly divided into two groups **Control group:**Standard regime of RNTCP **Study group:** *Rasayana* compound (aqueous extract of *Amalaki +Ashwagandha +Guduchi +Yashtimadhu +Sariva + Haridra +Pippali +Kushtha +Kulinjana*) daily Three capsules morning and two capsules evening with milk along with the standard regimen of AKT **Duration: 02 months**	Improvement in symptoms of *Kasa* (cough), *Raktanisthivana*, *Shwasa*, *Parshwashoola*, appetite, fatigue, *Ratriprasweda*, Body weight. Adjunct therapy of *Rasayana* drugs with AKT provides better physical and mental wellbeing to patient and also counteracting the unwanted effects caused by AKT.	49
Ranjeet Kumar et al; Randomized, Double-Blind Placebo-Control Study	*Withaniasomnifera* has shown better relief of symptoms andsignificantly	50

60 newly diagnosed sputum smear positive cases of pulmonary TB on Directly Observed Treatment – short course (DOTS) regime divided in two groups. **Study group:** *W.somnifera* root extract capsule 500mg BD with water with DOTS **Control group:** placebo capsules containing dextrose powder along with DOTS **Duration: 12 weeks**	favourable effects on liver transaminase levels and serum uric acid levels. It has also improved Health Related Quality of Life (HRQoL) scores in pulmonary TB patients.	
Sanjay Chhajed et al; Clinical Study 23 patients of tuberculosis were randomly divided into three groups **Standard Group** (7 patients): DOTS regime ***Ashvagandha* Group** (8 patients): *Ashvagandgā Kshirapaka* in the dose of 300 mg/kg/day with DOTS ***Pippali* Group** (8 patients): *Pippali Kshirapaka* in the dose of 150 mg/kg/day with DOTS	Addition of *Pippali* and *Ashvagandha* as adjuvant to the modern anti Koch's treatment (AKT) helps in providing better and faster relief as well as in preventing their side effects. The effect of *Pippali* seems to better in respect to *Ashvagandha*.	51
Debnath et al; **Pilot study and an** **open labelled trial with therapeutic control add on therapy** 99 newly diagnosed pulmonary tuberculosis patients randomly divided into different groups *Aswagandha* (*Withania somnifera*) capsule 500mg - 2 caps twice daily for 28 days *Chyawanprash* - 10 g thrice daily for 28 days	The symptoms subsided, body weight showed improvement, ESR values were normal, there was an appreciable change in IgA and IgM patterns and significantly increased the bioavailability of isoniazid and pyrazinamide were recorded.	42
Sharma et al; Clinical Trial Known cases of TB put on the antitubercular treatment were taken in study. 40 patients registered out of 10 patients in each group completed trial **Group A:** Liv-600 Capsule (200mg each Hydroalcoholic extract of *Daruharidra*, *Kakamachi*, *Ghritkumari*) TDS **Group B:** Decoction of 10gm of *Bhumyamalaki* (Phyllanthus fraternus) OD **Group C:** Placebo 600mg Capsule **Duration:** 90 days	Both of these preparationsexhibited hepato- protective properties compared to the placebo treatment on periodic liverfunctions evaluations	52
Narayana, D.B.A., et al; Randomized controlled Trial 90 patients of pulmonary tuberculosis taking ATD are divided in three groups **Group I:** 10 g of *Chyavanprash* (CP) twice a day as an adjuvant therapy, in addition to ATD **Group II (Combine therapy):** Combination of anabolic steroid (25mg once a week IM), protein supplement (2 tea spoonful or 4g thrice a day) and vitamins (one cap/day) along with ATD **Group-III:** only ATDs without an adjuvant Therapy	Symptoms like Cough, expectoration, weakness, loss of appetite, loss of weight, fever, oedema aches and haemoptysis almost disappeared in CP and combine therapy group completely as compare to group III. Mean of weight gain and serum protein was better in CP group compared to other group. Improvement in the Hb levels was seen in CP and combine therapy group. Comparison of X-ray chest before and after treatment showed Effective healing in CP and combine therapy group compared to the observations in group-III.	53

Kurane SB et al; **Randomized control trial** Group Sixty patients who had completed treatment for pulmonary tuberculosis were divided into two groups of thirty each. **Group A:** *Kharjuradi* G*hrita* 20ml R*asayankale* **Group B:** *Kharjuradi Ghrita* 20ml *Rasayankale* and *Pranayama* exercise daily once. **Duration:** 3months	The *Kharjuradighrita* gives significant results in the period of post tuberculous treatment to increase appetite, to strengthen body and to tackle different diseases like *Kasa*, *Jwara* etc. *Pranayam* is a body and mind strengthening exercise and helps to recover the damage that took place due to pulmonary tuberculosis	54
Kale NB,**Case Study** 30 year old female patienttreated with Anti- Tubercular drugs i.e. DOTS (Directly observed treatment shortchemotherapy) of category – I along with *Jivantyadi Ghrita* 10ml BD with milk for six months.	*Jivantyadi Ghrit* of *Rajyakshma Rogadhikar* along with DOTS (CAT–I) helpful in improving the appetite, reduces the local inflammation & improve the function of genital organ which initiates the regular & adequate menses. It also reduces the side effects of anti – tubercular drugs and ultimately responsible for improvement in general metabolism & condition of the patient.	55

DISCUSSION:

Tuberculosis being the world's deadliest infectious killer despite the availability of highly efficacious treatment, it is a serious health threat, especially for people living with HIV. People living with HIV are more likely than others to become sick with TB. Worldwide, TB is one of the leading causes of death among people living with HIV. Without treatment, as with other opportunistic infections, HIV and TB can work together to shorten life span. Drug-induced hepatotoxicity (DIH) is the most common adverse drug reaction leading to interruption of antituberculosis treatment. Worldwide, different reintroduction regimens have been advocated, but no consensus guidelines are available. Reintroduction of antitubercular drugs in patients with DIH has never been studied systematically.

Ayurveda is living science which helpful to everyone to be a healthy by advocacy of lifestyle and treatment by universal principle. As per Ayurveda, classification of Tuberculosis as a *Trirupa, Shadrupa, Ekadashrupa* may be for the assessment of the severity and prognosis of the disease. It is time to conduct more systematic research on this aspect *Trirupa, Shadrupa, Ekadashrupa Rajyakshma* which can be beneficial in the management of TB to improve quality of life.

As mentioned, HIV and Tuberculosis are work together to shorten lifespan and, risk of TB infection and mortality is much higher in patients infected with HIV; in both conditions, Ayurveda considered *Dhatvagnimandya* and *Oja Dushti* as a main pathological events or clinical feature in Tuberculosis and *Dhatvagnivardhak* (metabolism enhancer) and *Ojovardhak Rasayana* (immune modulators) treatment can be helpful to improve their lifespan.

In present scenario the role of Ayurveda in the management of TB is very scanty and mostly limited to adjunct or supportive therapy which cannot be simply neglected. The supportive or adjunct therapy of Ayurveda intervention can be helpful to improve quality of life of the patient, to avoid hepatotoxic effect of the drug, to increase the bioavailability of the drug as well as to reduce the treatment duration.

Most of the physicians are currently using Ayurveda preparations having *Tikta* (Bitter) *Rasa* dominant ingredients and used in *Ghrita* and *Kshirapaka* dosage as an adjunct to tuberculosis treatment. Some of the clinical evidences are also generated for herbs like *Ashwagandha, Pippali, Garlic, Guduchi, Amalaki* and preparations like *Vasa Ghita, Jeevantyadi Ghrita, Kharjuradi Ghrita, Chyavanprash, Bhringarajasava, Mahalaxmivilas Rasa* which are proven beneficial in the management of tuberculosis.

The accountability and reproducibility of the evidences presented in this review are again a debatable issue. More scientific evidences of Ayurvedic principle and their treatment modalities on tuberculosis are need to be published in highly reputed journal in future, and for that purpose collaborative approach is needed from modern as well as Ayurveda fraternity.

CONCLUSION

Need of collaborative approach from modern as well as traditional system of medicine, to conduct a more research on Ayurveda formulations and single herbs having *Rasayana* properties; which will generate the evidence base medicine. While conducting a research on Ayurveda preparations it is essential to find out any kind of drug interactions with standard antitubercular drugs to establish the safety of adjunct medicine. Scientific Collaborative approach will be benefited to the society to improve the quality of life of the patient, to reduce the hepatotoxicity, incidence of MDR Tuberculosis and to extend the life span of the patients.

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