Review Article

Antitubercular herbal extracts- A review

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ABSTRACT

Mycobacterium tuberculosis (TB) is a highly infectious pathogen and causative agent for TB. There are many herbal extracts, which have been identified with potential claims of anti TB spectrum. Although established anti TB regimen with drugs are effective, these medications do cause certain adverse effects. The use of herbal extracts in treating TB is becoming more interesting and prevalent due to minimum adverse reactions observed with herbal medications. In this review, the various types, constituents and the antitubercular activity of traditional herbal extracts have been discussed.

KEY WORDS: Antimycobacterial, Drug resistance, Herbal extracts, Treatment, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is caused by an infectious pathogen labeled *Mycobacterium tuberculosis*. It can infect all human tissues with a primary predisposition to affect the lungs and respiratory tract. It is spread usually from person to person through droplet infection during close contact. It is also associated with factors such as low socioeconomic status, poor sanitation, increasing population leading to overcrowding, inhumane living conditions, occupational hazards (health care workers), and immunodeficiency status and malnutrition. Although TB is an ancient disease, a resurgence of the disease was observed in the 1980's leading to a new era of TB. TB can remain in an inactive state for years without causing symptoms or spreading to other people. When the immune system of a patient with dormant TB is weakened, the TB can become active and cause infection in the lungs or other parts of the body. TB bacteria that grows in the lungs may cause mild fever, headache, chills, night sweats, fatigue, loss of appetite, weight loss, cough with or without mucus and pus, coughing up blood, chest pain from inflammation in the lungs, difficulty in breathing, swollen glands, and sore throat.

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The medical tools are making an effort to make TB a disease of the past, yet TB flourishes as the second most deadly infectious disease. A single method of eradication of TB is not possible. In addition, the modern medicines with the development of antibiotic-resistant strains throw interest to find other possible ways to cure TB, one of which is using of herbal extracts. These alternative supplements help to boost the body's immune system to fight the disease.[1,2]

SEARCH METHODOLOGY

Literature search was initiated in PubMed database to identify the plants possessing potential antitubercular activity. The search identified 43 plants are having antitubercular or synergistic antitubercular activity. The identified plants include *Aristolochia taliscana* Hook and Arn. *Aristolochia brevipes* Benth., *Aristolochia elegans*, *Artemisia capillaris*, *Azorella compacta, Azorella madreporica*, *Beilschmiedia tsangii*, *Celastrus vulcanicola*, *Chamaedorea tepejilote*, *Citrullus colocynthis*, *Clavija procera*, *Curcuma longa*, *Euclea natalensis*., *Foeniculum vulgare*, *Justicia adhatoda*, *Kaempferia galangal*, *Lantana hispida*, *Larrea tridentata*, *Plectranthus grandidentatus*, *Plumeria bicolor*, *Tabernaemontana elegans*, and *Diospyros anisandra*.[1]

Few plants are also known to produce synergistic activity with antitubercular drugs, namely, *Galenia*

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africana, *E. natalensis*, *Notopterygium incisum*, *Piper nigrum*, and *Knowltonia vesicatoria*.[1]

DISCUSSION

The antimycobacterial activity of herbal extracts is extensively discussed in the literature. The antitubercular effect has been studied in cell lines, animals and also in human trials. Several primary and secondary plant metabolites were isolated, and their antitubercular properties were evaluated and reported.

Anand *et al.* did a research on antitubercular effects of green tea polyphenol inhibiting the *Mycobacterium* survival within human macrophages. They observed polyphenols from green tea downregulated gene expression of TACO by epigallocatechin-3-gallate, which accompanied the inhibition of the TB bacterial survival within human macrophages.[2] Bai *et al.* showed enhanced human macrophagic control of *Mycobacterium* by Curcumin, a polyphenol present in turmeric. Curcumin is a potent inducer of apoptosis - an effector mechanism used by macrophages to lyse TB pathogens.[3] Changtam *et al*. also evaluated demethoxycurcumin, bisdemethoxy curcumin, and curcuminoid constituents of the medicinal plant *C. longa* against antimycobacterial activity and have observed promising results.[4]

Bapela *et al.* concluded beneficial effects of 7-methyljuglone - a naphthoquinone isolated from roots of *E. natalensis* herb against *M. tuberculosis*.[5] Lall and Meyer isolated binaphthoquinoid, diospyrin from *E. natalensis* that were found to be effective against drug-resistant strains of *M. tuberculosis*.[6] Chen *et al*. observed novel epoxy furanoid lignance, Beilschmin A and Beilschmin B extracted from the leaves of *B. tsangii* exhibiting marked antitubercular activity.[7] Esquivel-Ferriño *et al.* isolated 5-hydroxy furanocoumarin from *F. vulgare*, which exhibited substantial antimycobacterial action.[8]

Favela-Hernández *et al*. demonstrated antimycobacterial in *L. tridentate*.[9] Ge *et al.* showed oleanolic acid extracted from herbs in combination with isoniazid, rifampicin or ethambutol can offer a synergistic effect against proliferation of *Mycobacteria*.[10] Gordien *et al.* showed antimycobacterial activity of *Juniperus communis* that contained a sesquiterpene identified as longifolin initiating the antimycobacterial activity.[11] Gupta *et al.* evaluated the antitubercular activity of *Alpenia galangal* and concluded it to be effective in treating the dormant and non-replicating bacteria of latent TB.[12] Gupta *et al.* used radiometric BACTEC ASSAY to demonstrate antimycobacterial activity by leave extracts from *Mallotus philippensis*.[13] Ignacimuthu *et al*. demonstrated antimycobacterial activity of two natural alkaloids vasicine acetate and 2-acetyl benzylamine from *Adhatoda vasica* Ness. leaves.[14]

Jimenez-Arellanes *et al.* demonstrated antitubercular activity against multidrug-resistant *M. tuberculosis* by micro colorimetric assay and concluded *L. hispida* contains potential compounds that were effective against multidrug-resistant tubercle bacilli.[15] They also observed secondary metabolites from *C. tepejilote* were also effective against multidrug-resistant *Mycobacteria*[16] and antimycobacterial activities in extracts isolated from *A. elegans* rhizomes.[17]

Navarro-García *et al*. isolated a compound aristolactol-1 from *A. brevipes* and showed effective anti TB activity.[18] León-Díaz *et al.* isolated licarin A, licarin B, and eupomatenoid-7-neo lignans from hexanic extract of *Aristalochia teliscana* that showed significant antimycobacterial activity.[19] Jyoti *et al.* demonstrated antimycobacterial activity of methanolic plant extract of *A. capillaris* containing ursolic acid and hydroquinol.[20] Kim *et al*. showed the antimycobacterial effects of *Pelargonium reniforme* and *Pelargonium sidoides* against tubercle bacilli in murine macrophages.[21]

Labuschagné *et al.* isolated two compounds stigmasta-5,23-dien-3-ol (1) and 5 (hydroxymethyl)furan-2(5H)-one(2) from *K. vesicatoria* that showed marked antitubercular activity.[22] Lakshmanan *et al*. isolated an anti TB molecule, ethyl p-methoxycinnamate from *K. galangal,* a traditional antitubercular medicinal herb and observed it to show antimycobacterial activity against multidrug-resistant strains of tubercle bacilli.[23] Luo *et al*. showed benzophenanthridine alkaloid, decarine (1), and an N-isobutylamide, N-isobutyl-(2E,4E)-2,4-tetradecadienamide (15) extracted from *Zanthoxylum capense* showed high activity against *M. tuberculosis* within human macrophages.[24]

Mativandlela *et al.* isolated flavonoids such as (2S)-5,7,2'-trihydroxyflavanone (1), (E)-3,2',4'-trihydroxychalcone (2) and (E)-2',4'-dihydroxychalcone (3), and the new (E)-3,2',4'-trihydroxy-3'-methoxychalcone from the leaves of *G. africana* which produced pronounced activity against *M. tuberculosis*.[25] Mehta *et al.* demonstrated the broad-spectrum antimycobacterial action of *C. colocynthis* that can be used as a natural antitubercular drug for the treatment of drug resistant TB.[26] Rijo *et al*. evaluated antimycobacterial activities of 8 metabolites from *Plectranthus royleanone* derivatives and showed potent antitubercular activity.[27]

Rojas *et al*. isolated Aaegicerin, the first oleanane triterpene with wide-ranging antimycobacterial activity from *C. procera*.[28] Sureram *et al*. isolated

bisbenzylisoquinoline alkaloids, tiliacorinine (1), 2'nortiliacorinine (2), and tiliacorine (3) from the edible plant, *Tiliacora triandra*, as well as a synthetic derivative, 13'-bromo-tiliacorinine (4). These alkaloids have potential to act as new chemical scaffolds for antimycobacterial action.[29] Uc-Cachón *et al*. isolated naphthoquinones from *D. anisandra* and these compounds exhibited potential activity against resistant *M. tuberculosis* strains. Maritinone and 3,3'-bibagam compounds have shown effective antimycobacterial activity.[30]

Despite the extensive research with herbal extracts, the possible side effects, interaction with the medicines, storage, pharmacokinetic, and pharmacodynamic actions of these antitubercular products were not completely reported. The literature also identified lack of highly standardized randomized controlled trials involving human subjects in various clinical settings and the future area of research that can be initiated to help in further understanding and establishing vigorous therapeutic authenticity.

CONCLUSION

There has been an increase in demand for the phytopharmaceuticals all over the world due to the fact that the allopathic drugs have more side effects. This review makes an attempt to compile the herbal extracts with potential anti mycobactericidal properties. Extensive literature is available demonstrating the anti TB efficacy of the plant products. However, more standardized randomized control trials need to be initiated to establish the therapeutic action of these medicinal herbs in clinical practice.

Alkaloids, flavonoids, tannins, xanthones, triterpenes, quinones, etc., were various phytoconstituents involved in activity against tubercle bacilli.

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