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A review on immunomodulatory traditional siddha herbs prescribed for the prevention of COVID 19

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Abstract
The worldwide pandemic SARS – COVID – 2 has created a panic situation in human beings. Covid-19 viruses spread is very faster and its replication inside the human body is also speedy. When any infection enters into the body it is destroyed by the antibodies present in our body. Many research works are going to find the exact vaccine to control the spread of this virus. Many vaccines were discovered and used across the world. Still new variants of SARS COVID virus were discovered and spreads in different parts of the world and it is big headache to solve this serious situation. At this pandemic period, boosting of the immune system is the only way to fight against this virus. From ancient times, Siddha medicines is well known for its immune boosting herbs and medicines. This review is based on a brief discussion of the pharmacological actions, active ingredients, and potential therapeutic properties of some of the Siddha medicinal plants such as Tinospora cordifolia, Withania somnifera, Nigella sativa, Cinnamon cassia, Justicia adhatoda Citrus limonum and Ocimum sanctum which are widely advertised to boost immunity and reduce the risk of developing COVID-19.

Keywords: SARS–Covid 19, siddha medicines, withania somnifera, immunity

Introduction

The siddha system of medicine is one of the most ancient system of medicine. It has a basic rule as 'Prevention is better than cure'. The siddha system uses the herbs which rejuvenates the body system. The natural immune modulators greatly play a role in our immune system. In the COVID-19 pandemic, the immune modulators play a great role. In this, we have explained some of the herbs which act as immune modulators, antioxidants, anti-microbial, anti-fungal which is very useful for peoples in this pandemic.

The Coronavirus disease 2019 called as COVID -19, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a newly developed respiratory disease The coronavirus outbreak came to bright on 2019 December when China informed the World Health Organization of a cluster of cases of pneumonia of an unknown cause in Wuhan City. Consequently the disease spread to many Places in China, and to the rest of the world. The WHO has then declared it a pandemic The World Health Organization has then declared it a pandemic on March 2020. Nearly 1 million people were infected and 50,000 died in the first three months after COVID-19 outbreak.

SARS-CoV-2 is single-stranded ribonucleic acid - RNA virus, enveloped in a lipid bilayer, belongs to the genus Beta coronavirus and family Coronaviridae. Zoonotic originated and transmitted to humans. The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, breathlessness, sore throat, fatigue, malaise among others. SARS-CoV-2 affects the human respiratory tract's epithelial cells, leading to a proinflammatory cytokine storm and chronic lung inflammation Most patients with COVID-19 exhibit mild to moderate symptoms it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction(1). Most of the people are asymptomatic. In this situation improving our immunity through healthy food habits and taking certain Indian medicinal herbs in siddha system like *Tinospora cordifolia*, *Withania somnifera*, *Nigella sativa*, *Cinnamon cassia*, *Justicia adhatoda*, *Citrus limonum* and *Ocimum sanctum* etc.., are being widely propagated to boost immunity and reduce the risk of developing COVID-19.

Tinospora cordifolia

Tinospora cordifolia is a climber which belongs to family Menispermaceae. is a large, glabrous, deciduous climbing shrub. It is distributed throughout the tropical Indian subcontinent and ascending to an altitude of 300m [2, 3, 4]. The plant mainly contains alkaloids, glycosides, steroids, sesquiterpenoid, aliphatic compound, essential oils, mixture of fatty acids and polysaccharides, Aporphine alkaloids, clerodane diterpenes, berberine, palmatine, tembertarine, magniflorine, choline, and Tinosporin etc. It also contains the Alkaloids like Berberine, Palmatine, Tembetarine, Magnoflorine Choline, Tinosporin. They have immunomodulatory, antioxidant, antidiabetic and cytotoxic effects. The phytoconstituents which are responsible for immunomodulatory effects are Tinocordioside, Cordifolioside A, and Magnoflorine. An active phytoconstituent of Tinospora cordifolia is a glycoside called Tinocordioside which acts as a potential inhibitor for

SARS-CoV-2 Mpro. Mainly the aqueous extract of the plant have the immunological activity. They influence cytokine production and mitogenicity. They help in B cell differentiation by regulating the IL-6 cytokine [5].

Fig 1

Withania somnifera

Withania somnifera is an herb which belongs to family Solanaceae. They have immune boosting, hepatoprotective, anxiolytic, antidepressant, nootropic, anti-inflammatory, antioxidant, anti-stress, anticonvulsant, antitumor, anti-genotoxic, and immunomodulatory activities.

Priya shree *et al* Studied the Targeting COVID-19 (SARS-CoV-2) main protease through active phytochemicals of ayurvedic medicinal plants – *Withania somnifera* (Ashwagandha), *Tinospora cordifolia* (Giloy) and *Ocimum sanctum* (Tulsi) – a molecular docking study. In COVID-19 it has the potential to inhibit the SARS COV-2 entry and replication. An active phytoconstituent of Withania somnifera is withanoside and somniferine which acts as a potential inhibitor for SARS-CoV-2 Mpro. The aqueous extracts of Withania somniferine along with fatty acids they inhibit IL-6 and IL-6β released by the monocytes and macrophages. The root powder of the Withania somniferine inhibit the IL-6 secretion [6, 7, 8].

Fig 2

Nigella sativa

Nigella sativa is an herb which belongs to family Ranunculaceae. They have a good immunodulatory effects in COVID-19. The phytoconstituents present in the seeds of Nigella sativa are thymoquinone, nigellone, and thymohydroquinone. The interferon regulatory factor 3 (IRF-3) activation is inhibited by the thymoquinone which plays an important role in innate immunity

during virus entry. The seeds of Nigella sativa has stimulatory and suppressive effect on lymphocytes [9].

Fig 3

Cinnamon cassia

Cinnamon cassia is a tree which belongs to family Lauraceae. They have anti-inflammatory and immunomodulatory effects. Kurt Lucas *et al* studied the Extracts of cinnamon as Potential Immunomodulators for Severe COVID-19 Cases. The bark of cinnamon contains cinnamaldehyde, benzhaldehyde, cuminaldehyde and terpenes. They increases the cell mediated and humoral immunity.They also inhibit the INF-ϒ levels in the body without changing the IL-2 and IL-4. Cinnamaldehyde is a strong regulator in macrophage related immune responses [10].

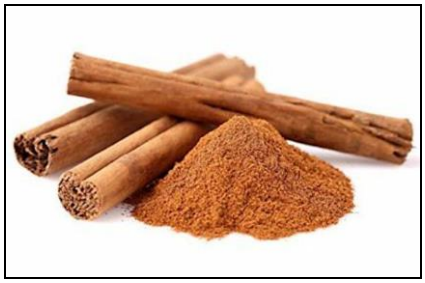

Fig 4

Justicia adhatoda

Justicia adhatoda is a shrub which belongs to the family Acanthaceae. They have antiviral, antibacterial, immunomodulatory and bronchodilatory action. The leaves, roots and flowers of Adathoda vasica contain an alkaloid called vasicine. The aqueous extracts of adathoda vasica inhibit the viral attachment, replication and release.

Vasicine with ACE 2 Receptor shown higher docking affinity score -7.1 K/cal respectively when compared to other virus proteins. AutoDoc 1.5.6 screening study report showed that vasicine promotes good inhibitory constant 486.54 mM on 3CL protease more than others. Results reveal that the vasicine could be a potential target for the treatment of COVID 19 (11). that the vasicicould be a potential targ.

Fig 5

Citrus limonum

Citrus limonum belongs to the family Rutaceae is small, straggling tree reaches upto 11 feet height, irregularly branched. The leaves are ovate-oval about two inches long. The flower is solitary with 5 petals white inside and tinged with deep pink outside. The well-known fruit is an ovoid berry which is 3 inches long with bright yellow colour indended over the oil glands having an acid pale yellow. They have stimulant and carminative activity due to the presence of active constituents Limonene (90%), Citral (4%), Hesperidine, Neohesperidine, Rutin, Pectin, Vitamin C and Calcium oxalate crystals.

Manuel Viuda-Martos *et al* studied the antifungal activity of Essential oil obtained from lemon. The essential oil obtained from the Citrus limon is mainly constituted by monoterpene hydrocarbons that showed a significant antifungal activity against Aspergillus flavus, Penicillium chrysogenum and Aspergillus niger and is widely used in food and pharmaceutical industries for its antifungal property [12].

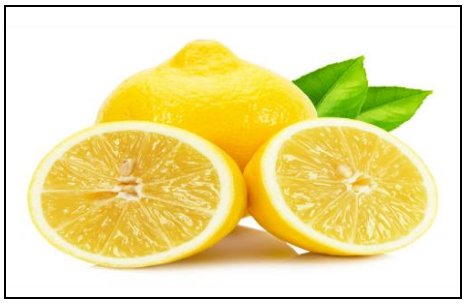

Fig 6

P. Verlekar and N. Chandak *et al* studied the antibacterial potential effect of lemon juice, citric acid and lemon peel extract was screened against resistant MRSA and *P. aeruginosa* by using agar well diffusion method and the shows significant anti-bacterial effect. All the above three samples were diluted to certain concentration with antibiotics which resulted in the inhibition of drug resistant bacteria and it is used as a liquid sanitizer [13].

Dr. Maruti J. Dhanavade *et al*. studied the antimicrobial activity of lemon peel against bacteria. Flavanones and many polymethoxylated flavones are rich in lemon peel. The citrus peel oils show strong antimicrobial activity against microorganisms like Pseudomonas aeruginosa in presence of methanol, Salmonella typhimurium in presence of acetone and Micrococcus aureus in presence of ethanol [14]. Lemon peel possessed the strongest antioxidant activity, the lowest effective concentration 50% (EC50= 42.97 mg extract/ mL), and the highest Trolox equivalent antioxidant capacity (TEAC=0.157) against DPPH radical scavenging. In addition to that citrus peels possessed immuno stimulatory activity via augmentation of proliferation of splenocytes in mouse). Citrus extracts exhibited noncytotoxic, and antigenotoxic activities through remarkable reduction of CAs induced by cisplatin in mouse splenocytes for 24 h [15].

Ocimum sanctum

Tulsi is also known as holy basil, which belongs to the family Lamiaceae. It is an aromatic plant. It contains Eugenol, α – Farnesene, 1, 2 dimethoxy - 4 – (2- propenyl), cyclohexane, Benzene, 1, 2, 4 triethenyl.

Fig 7

These phytochemicals are meant for the Analgesic, Anti-inflammatory, Immunomodulatory, Anti stress, Anti-microbial and antiseptic properties. It is used as one of the ingredient of Ayush kwath for controlling viral infections like COVID 19 [16].

Five clinical studies were done with Ocimum sanctum, all these 5 shows immunomodulatory effect [17-21].

A small randomized double blind and placebo controlled study was done in healthy volunteers compared with placebo volunteers. In this study 300 mg of ethanolic extract of Tulsi leaves were given for 3 weeks. The results showed the increase in immune response with increased natural killer cells and T helper cells [22].

A further study was done with dried leaves of Tulsi in asthmatic patients. In this study 500 mg of dried Tulsi leaves given to the asthmatic patients and from the results it was found that after 3 days of this treatment the vital capacity of the lungs is increased in those patients [19].

Conclusion

From this review the Immunomodulatory action of some selected traditional Siddha herbs have been evaluated and discussed. These herbs can be used as preventive medicine to the COVID affected patients to boost their immunity and a few of them also possess anti-oxidant, anti-fungal and antioxidant activity besides having immunomodulatory action.

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