



REVIEW

Herbal Medicines in management and prevention of COVID-19

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Abstract

Traditional herbal medicines are widely accepted in the world. Certain countries and WHO have research investment in traditional herbal medicines. COVID-19 came as a major Health care challenge for human in 2019. 480 deaths have been recorded till 18th of April 2020 in India. No pharmaceutical products have yet been shown to be safe and effective for the treatment of COVID-19. Major 3 types of targets of COVID-19 were identified by researches, which are as follow – 1) Inhibit coronavirus at structural level, 2) Inhibit coronavirus RNA synthesis and replication and 3) Inhibit virulence factor of Coronavirus. Certain Herbal medicines like *Tribulus terrestris*, *Withania somnifera*, *Curcuma longa*, *Ocimum sanctum*, and *Phyllanthus emblica* have potent Anti-COVID properties, which is indicating new sunrise in the direction of Herbal medicine.

Keywords: Traditional Herbal Medicine; COVID19; Structural levels; RNA synthesis; *Tribulus terrestris*; *Withania somnifera*; *Curcuma longa*; *Ocimum sanctum*; *Phyllanthus emblica*

Introduction

Traditional herbal medicines are getting significant attention in global health debates. India, The United States of America (USA), China, Nigeria and World Health Organization - WHO have all made substantial research investments in traditional herbal medicines [1]. Herbal medicine finds itself in a race to develop new medicines, with fewer or no adverse effects, for therapeutic and preventive application in illnesses [2].

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As per the Ministry of Health and Family welfare, Government of India, there are 11, 906 Active Cases of COVID-19. 480 deaths has been reported, 1991 patients were discharged till 18th April 2020 [3].

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But Still, No pharmaceutical products have yet been shown to be safe and effective for the treatment of COVID-19. However, a number of medicines have been suggested as potential investigational therapies, many of which are now being or will soon be studied in clinical trials, including the SOLIDARITY trial co-sponsored by WHO and participating countries [4].

Targets of COVID-19

Major 3 types of targets of COVID-19 are (i) Inhibit coronavirus at structural level (ii) Inhibit coronavirus RNA synthesis and replication (iii) Inhibit virulence factor of Coronavirus [5].

Effective Herbal Plants in COVID-19

Certain natural products from Indian natural medicines, bind to the active sites of COVID-19 proteases, hence are likely to hinder viral replication [6].

Tribulus terrestris

Tribulus terrestris fruits are well known for their usage in pharmaceutical preparations and food supplements. The methanol

Table 1 Targets of COVID-19

Sr No. #	Major Targets of COVID-19		
	Inhibit SARS-CoV-2 RNA synthesis and replication	Inhibit SARS-CoV-2 at structural level	Inhibit virulence factor of SARS-CoV-2
1	Papain-like proteinase (PLpro)	Spike Protein	Nsp1
2	3C-like main protease (3CLpro)	E protein Or N protein	Nsp3c
3	RNA-dependent RNA polymerase (RdRp)		ORF7
4	Helicase		

extract of *T. terrestris* fruits showed potent inhibition against the papain-like protease (PLpro), an essential proteolytic enzyme for protection to pathogenic virus and bacteria. Major bioactive compounds, are six cinnamic amides and ferulic acid, were showing inhibition of Papain-like proteinase (PLpro), which is major protein target of COVID-19 [7].

Withania somnifera

Withania somnifera contains variety of phytoconstituents like Withanolide A & B, Withaferin A, Withanone, Withanoids [8].

WSG (*Withania somnifera* glycoprotein) isolated from *Withania somnifera* root tubers revealed (protease inhibitor) antimicrobial activity against few bacterial and phytopathogenic virus [9].

W. somnifera would be an effective agent in the management of COVID-19 through modulation of host Th-1/Th-2 immunity. WS may be beneficial in inducing anti-viral immunity (owing to increased IFN-gamma responses) and optimum anti-inflammatory activities (down-regulation of IL-1, IL-6, TNF-alpha and other inflammatory mediators), which are the key targets relevant to COVID-19 [10].

As per the recent Molecular Docking Studies, Withanolide D, Withaferin A, as most appropriate inhibitors against 3C-like main protease (3CLpro), which can be further explored to test against Coronavirus (COVID-19) in pre-clinical and clinical settings [11].

Withanolide-B, Withanone and Withaferin-A, major phytochemicals of *W. somnifera* have predicted binding energy lower than the pharmacological inhibitor, N3. The binding of these phytochemicals with main protease may slow down the cleavage of PPs to releases NSPs and decrease the process of viral replication and transcription [12].

Curcuma longa

Curcuma longa contain demethoxycurcumin, curcumin, Diacetylcurcumin [13], as a major phytoconstituents, which are the most recommended compounds found in medicinal plants

that may act as potential inhibitors of COVID-19 Main Protein (Mpro) [14].

Curcumin is strongly bind to 3CL-protease of COVID-19 in comparison to the antimalaric drugs and promote important structural changes in this viral protease, inducing folding of the enzyme [15].

Diacetylcurcumin present in *Curcuma longa* have been found as more effective on COVID-19 (Mpro) than Nelfinavir [16].

From the recent Docking studies, it can be concluded that Binding energy of Curcumin (-38.84 kcal/mol) had greater than hydroxychloroquine (HCQ) (-35.87 kcal/mol) in case of S1 receptor binding domain. Therefore, Curcumin could be used as combination therapy along with hydroxychloroquine for disrupting the stability of SARS-CoV2 receptor proteins [17]. Curcumin and HCQ interact with the C-terminal of S1 domain with binding energies of -7.1 and -5.6 Kcal/mol [18].

Ocimum sanctum

Ocimum sanctum extract can be included as a preventive measure against COVID-19 due to its potential to inhibit replication of COVID-19 supported with its immune-modulatory feature and ACE II blocking properties. *Ocimum sanctum* containing, Tulsinol (A, B, C, D, E, F, G) and dihydrodieuginol-B inhibit SARS Coronavirus Main Protease and Papain-like Protease [19].

O. sanctum is being used in the management of pain, diarrhea, cough and fever, which are the common symptoms of COVID-19 [20]. *O. sanctum* boosts the immunity of the body and helps to defense the threatening virus and bacteria [21].

Phyllanthus emblica

Phyllanthus emblica also have immunomodulatory properties, and may have the potential to bolster health and immunity of the community in the fight against SARS-CoV-2 infection [10].

Phyllaemblicin-B and phyllaemblinol from *P. emblica* showed high binding affinity to helicase protein, which is one of the major targets of COVID-19. Phyllaemblicin G7 from *Phyllanthus emblica* exhibited high binding affinity to the Spike Protein of COVID-19 [5].

The antioxidative and anti-inflammatory properties of *Phyllanthus emblica* are the key to its therapeutic effect.

Table 2 Herbal medicines and its effective targets against COVID-19

Sr. no	Herbal Medicines	Effective Targets of COVID-19	Ref.
1	<i>Tribulus terrestris</i>	Papain-like protease (PLpro)	(7)
2	<i>Withania somnifera</i>	3C-like Main protease (3CLpro)	(11)
3	<i>Curcuma longa</i>	3C-like Main protease (3CLpro)	(15)
4	<i>Ocimum sanctum</i>	Main Protease and Papain-like Protease.	(19)
5	<i>Phyllanthus emblica</i>	Helicase protein and Spike Protein	(5)

Conclusion

Novel evidence based approach of Herbal medicine plays preventive role in the COVID-19 pandemic. Naturally occurring plants are source of wide variety of Phytoconstituents. *Tribulus terrestris*, *Withania somnifera*, *Curcuma longa*, *Ocimum sanctum*, *Phyllanthus emblica* are primarily observed as effective against COVID-19. Moreover, In-vitro and In-vivo studies require to identify efficacy of Herbal medicine. However, Combination therapies of Allopathy and Herbal medicines lead towards the Best treatment options. Still, many unknown Herbals medicines are waiting for their Identification and Purification and pharmaceutical evaluation.

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