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# Herbal Medicines in Management and Prevention of Coronavirus Disease 2019 (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. Coronavirus Disease 2019 (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 coronavirus 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-viral (AntiCOV-19) properties against novel coronavirus, which is indicating new sunrise in the direction of Herbal medicine.

Keywords: Traditional herbal medicine; COVID-19; AntiCOV-19; 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].

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].

But still, no pharmaceutical products have yet been shown to be safe and effective for the treatment of coronavirus (COV-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]. Major targets of COV-19 are Enlist the major targets of COVID-19 [5] (Table 1).

S. 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 protease (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	-	-		

Table 1: Enlist the major targets of COVID-19.

Major 3 types of targets of COVID-19 are:

- Inhibit coronavirus at structural level
- Inhibit coronavirus RNA synthesis and replication
- Inhibit virulence factor of Coronavirus.

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# **Effective Herbal Plants against COV-19**

Certain natural products from Indian natural medicines, bind to the active sites of COV-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 extract of *T. terrestris* fruits showed potent inhibition against the papain-like protease (PLpro), an essential proteolylic enzyme for protection to pathogenic virus and bacteria.

Major bioactive compounds, are six cinnamic amides and ferulic acid, were showing inhibition of Papain-like protease (PLpro), which is major protein target of COV-19 [7].

### Withania somnifera

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

*W. somnifera* glycoprotein (WSG) isolated from *W. 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 COV-19 through modulation of host Th-1/Th-2 immunity. *W. somnifera* 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 COV-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 (COV-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 pseudo-particles (PPs) to releases non-structural proteins (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 potential compounds that may act as potential inhibitors of COV-19 Main Protein (Mpro) [14].

Curcumin is strongly bind to 3CL-protease of COV-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 *C. longa* have been found as more effective on COV-19 (Mpro) than Nelfinavir [16].

Docking studies suggesting 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 [17]. As, Curcumin and HCQ interact with the C-terminal of S1 domain with different binding energies [18]. Therefore, Curcumin could be used as combination therapy along with hydroxychloroquine for disrupting the stability of SARS-CoV2 receptor proteins.

#### Ocimum sanctum

*Ocimum sanctum* extract can be included as a preventive measure against COVID-19 due to its potential to inhibit replication of COV-19 supported with its immune-modulatory feature and ACE II blocking properties. *O. sanctum* containing Tulsinol (A, B, C, D, E, F, G) and dihydrodieuginol-B inhibit COV-19 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 COV-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 COV-19 infection [10].

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

The antioxidative and anti-inflammatory properties of *P. emblica* are the key to its therapeutic effect **(Table 2).** 

**Table 2:** Herbal medicines and its effective targets againstCOV-19.

S r. n	Herbal		
0	Medicines	Effective Targets of COV-19	Ref.
1	T. terrestris	Papain-like protease (PLpro)	-7
2	W. somnifera	3C-like Main protease (3CLpro)	-11
3	C. longa	3C-like Main protease (3CLpro)	-15
4	O. sanctum	Main Protease and Papain-like Protease.	-19
5	P. emblica	Helicase protein and Spike Protein	-5

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# **Discussion and 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 COV-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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