



Role of *Withania somnifera* in combating coronaviruses

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Abstract

Coronavirus disease 2019 (COVID-19) has been increasing and has a widespread prevalence hence it is receiving extensive attention for its incidence. COVID-19 infection is known to affect individuals with weak immunity more severely. Immune functions are requisite for shielding the body against attack by pathogens, and thus play an essential role in the maintenance of health. Therefore, the ingestion of foods with immune-modulating activities is considered an efficient way to prevent immune functions from declining and reduce the risk of infection or cancer. The present review describes Ashwagandha (*W. somnifera*) immunomodulatory effects, activity against microbes and infection, general health benefits.

Keywords: *Withania somnifera*, coronaviruses, COVID-19

Introduction

Coronavirus disease

Coronavirus disease 2019 (COVID-19) has been increasing and has a widespread prevalence hence it is receiving extensive attention for its incidence. (Zhu *et al.*, 2019, Tan *et al.*, 2020) [20]. Currently, this virus causing Coronavirus disease 2019 (COVID-19) is named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (ICTV, 2020) by World Health Organization (WHO, 2020). The main transmission routes of SARS-CoV-2 are Respiratory and contact transmissions. SARS-CoV-2 RNA is also detected in feces of COVID-19 patients, suggesting the possibility of fecal-oral transmission as another potential transmission route. (Zhang *et al.*, 2020) [34, 36]. The incubation period of SARS-CoV-2 is 0 to 24 days where it does not show any symptoms, and average median incubation period is of 3 days (Guan *et al.*, 2020) [1].

Common symptoms reported are fever, cough, dyspnea, muscle soreness and/or fatigue. Sputum production, headache, hemoptysis and/or diarrhea are also reported by few. Mild symptoms include low-grade fevers and mild fatigue. Patients with severe disease experience dyspnea and hypoxemia which can develop into acute respiratory distress syndrome (ARDS), septic shock, and severe metabolic acidosis and coagulation disorders. (Guan *et al.*, 2020 [10]; Zhou *et al.*, 2020 [35]; Huang *et al.*, 2020) [14].

According to Ministry of Health, Govt. of India, tallies of confirmed COVID-19 cases are 59,662 with a death toll of 1,981 as on 09 May 2020. (Government of India, 2020) Confirmed cases worldwide are 3.94M with a death toll of 275K. (Wikipedia, 2020) [13].

Although 12 new drugs are being tried for management of COVID19, currently there are no FDA approved drugs or vaccines to prevent and treat the infection of the SARS-CoV-2. Considering the current state of affairs, there is an urgent unmet medical need to identify novel and effective approaches for prevention and treatment of COVID-19. (Maurya *et al.*, 2020)

Immune functions are requisite for shielding the body against attack by pathogens, and thus play an essential role in the maintenance of health. Therefore, the ingestion of foods with immune-modulating activities is considered an efficient way to prevent immune functions from declining and reduce the risk of infection or cancer. (Kaminogawa *et al.*, 2004)

COVID-19 infection is known to affect individuals with weak immunity more severely. Therefore, enhancing immunity is definitely one of the ways the doctors across the globe have been using for treating COVID-19 cases. In fact, high doses of vitamin C, known to boost immunity, have been administered to the COVID-19 patients in China and elsewhere in the world with promising results. (Saul *et al.*, Feb 2, 2020) [2].

It has been discovered that natural phytochemicals in Ashwagandha, Giloy and Tulsi indeed have potentials to combat COVID-19 and its pathogenicity. Feasible options for controlling COVID-19 entry into host cells. (Balkrishna, 2020) [4, 5] Ashwagandha (*Withania somnifera*) is a well-known herb possessing several health benefits. (Tiwari *et al.*, 2014) [32].

Ashwagandha (*Withania somnifera* [L.] Dunal), also known as Indian Winter Cherry, is broadly used in Ayurveda, the traditional health care system in India. This herb is used as a general tonic and “adaptogen,” helping the body to adapt to stress. (Singh *et al.*, 1982 [26]; Provino, 2010) [22].

The roots of *Withania somnifera* have steroidal lactones (withanolides). It has been implicated in a wide range of therapeutic activities and maintaining general health like immunomodulation, combating infectious agents, anti-cancer, anti-epileptic, memory enhancer, to promote good physical and mental health, mood elevator, diuretic, rejuvenator, stress reliever, cardio-respiratory endurance enhancer, anti-ageing, anti-oxidant, hypoglycemic, hypocholesterolemic and in common an effective adaptogen (Scarfiotti *et al.*, 1997 [24]; Adallu and Radhika, 2000

[1]; Hemalatha *et al.*, 2006 [12]; Naidu *et al.*, 2006 [21]; Mahima *et al.*, 2012; Dhama *et al.*, 2013a) [8].

Withania somnifera has shown rise in the hemoglobin level and red blood cell count, energy levels. It maintains mitochondrial health; has potent antioxidant properties so as to protect cellular damage caused by free radicals and improves the body's resistance against various ailments by improving the cell-mediated immunity (Scarfiotti *et al.*, 1997 [24]; Bhattacharya and Muruganandam, 2003; Arora *et al.*, 2004 [3]; Kuboyama *et al.*, 2005 [17]; Harikrishnan *et al.*, 2008; Sandhu *et al.*, 2010). Ashwagandha is a potent adaptogen

or vitalizer and has powerful antioxidant and detoxifying properties. Multiple actions of this miracle herb include anti-inflammatory, analgesic, anti-stress, immunomodulatory, ant-microbial, cytoprotective, bettering anabolic activities, active against air-pollution and anti-cancer effects (Mishra *et al.*, 2000; Kushwaha *et al.*, 2012; Mahima *et al.*, 2012, 2013a, b; Dhama *et al.*, 2013a) [8]. *Withania somnifera* has also been extensively used to reduce symptoms of anxiety and stress. (Handa, 1995) [11]. A large number of drug formulations in Ayurveda, Unani and Siddha medicines possess its ingredients. (Sangwan, 2004 [23]; Singh, 2010 [25]; Singh, 2001) [27].

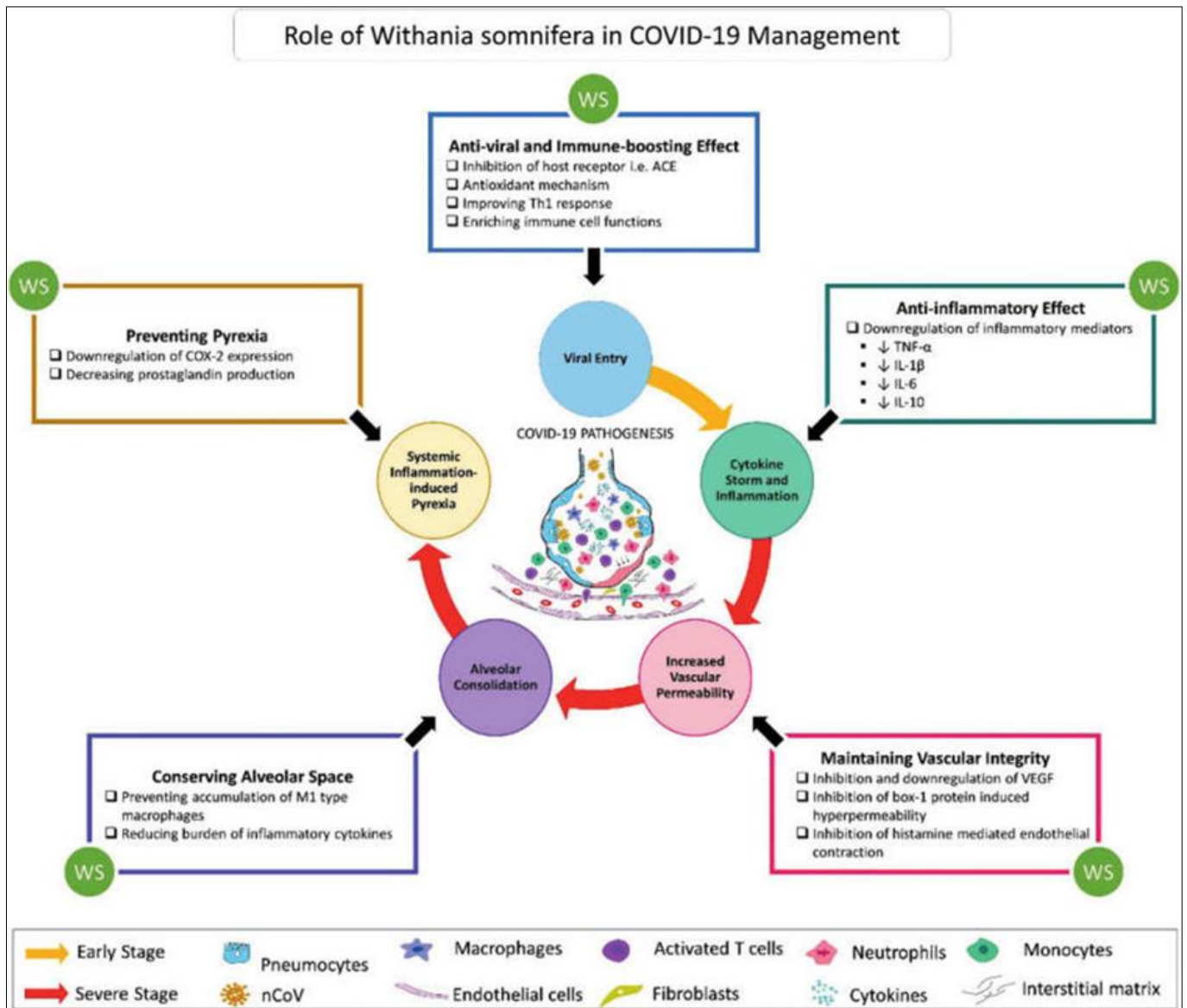


Fig 1: Potential mechanisms of action of *Withania somnifera* in prophylaxis (antiviral, immune boosting, vascular integrity) and management (pyrexia, anti-inflammatory, conserving alveoli) related clinical targets of COVID-19. ACE, angiotensin-converting enzyme; COX 2, cyclooxygenase 2; IL, interleukin; TH1, T helper type 1; TNF a, tumor necrosis factor a; VEGF, vascular endothelial growth factor; WS, *Withania somnifera* (Tillu *et al.*, 2020) [31].

Immunomodulatory Activities

Immunomodulatory potential of Ashwagandha was tested in experimental azoxymethane induced colon cancer in mice. Animals were treated with 400 mg/kg of *W. somnifera* extract once a week for four weeks orally. *W. somnifera* significantly altered the level of leucocytes, lymphocytes, neutrophils, immune complexes and immunoglobulins (Ig A, G and M. (Muralikrishnan, 2010) [19].

Cardiorespiratory endurance

A study done by Choudhary and co researchers demonstrated that using KSM-66 Ashwagandha showed significant improvement in subdomains of QOL Scores of mean VO₂ max as compared to placebo at 12 weeks. The findings suggest that *Ashwagandha* root extract enhances the cardiorespiratory endurance and improves QOL in healthy athletic adults. (Choudhary, 2015) [7].

Antimalarial Potential: Malaria is a serious public health problem and resistance of *Plasmodium falciparum* to chloroquine has been reported in several countries. The cost and side effects of synthetic antimalarial drugs have led to renewed interest in the search of herbal medicines that have the potential to treat malaria with little or no side effects. *In vivo* investigation of antiplasmodial activity of WS extracts by the inoculation of rodent malaria parasite *Plasmodium berghei*, into Swiss albino mice intraperitoneally showed statistically significant percentage inhibition of parasitemia compared to the controls (Dikasso *et al.*, 2006). Interestingly, in combination with chloroquine, the hot water extracts of *W. somnifera* (root bark) extract showed statistically significant and improved suppressions in mice against chloroquine resistant *Plasmodium berghei* NK65 (Muregi *et al.*, 2007) ^[20].

Pulmonary Hypertension (PH): Kaur *et al.*, studied the effect of *W. somnifera* root powder on monocrotaline (MCT)-induced PH in rats. Treatment with 50 and 100 mg/kg *W. somnifera* significantly reduced the RVP and all markers of RVH in MCT-challenged rats. There was an improvement in inflammation, oxidative stress and endothelial dysfunction, and attenuation of proliferative marker and apoptotic resistance in lungs. (Kaur, 2015) ^[16].

Chronic Obstructive Pulmonary Disease: Ashwagandha has been given to patients with COPD due to its rejuvenating and strengthening effects. It has shown to reduce tiredness, frequency of breathing troubles and cough attacks. (Singh, 2015) ^[28]. A molecular docking showed interruption of electrostatic interactions between the RBD and ACE2 which can block or weaken COVID-19 entry and its subsequent infectivity. Hence it shows that natural phytochemicals could well be the viable options for controlling COVID-19 entry into host cells, and *W. somnifera* might curb the COVID-19 infectivity. (Balkrishna, 2020) ^[4, 5]

References

- Andallu B, B Radhika. Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera*, Dunal) root. *Indian J. Exp. Biol.* 2000; 38:607-609.
- Andrew W, Saul Atsuo Yanagisawa. Hospital-based Intravenous Vitamin C Treatment for Coronavirus and Related Illnesses; *Orthomolecular Medicine News Service*, 2020.
- Arora S, Dhillon S, Rani G, Nagpal A. The *in vitro* antibacterial/synergistic activities of *Withania somnifera* extracts. *Fitoterapia.* 2004; 75(3-4):385-388.
- Balkrishna A, Pokhrel S, Singh J, Varshney A. Coronavirus (COVID-19) Entry by Disrupting Interactions between Viral S-Protein Receptor Binding Domain and Host ACE2 Receptor. *BMC Virology*, 2020. DOI:10.21203/rs.3.rs-17806/v1
- Balkrishna Acharya. "Indian Traditional Ayurvedic Treatment Regime For Novel Coronavirus, COVID-19." Patanjali Research Institute
- Bhattacharya Salil K, Raj K. Goel, Ravinder Kaur, and Shibnath Ghosal. "Anti-stress activity of sitoindosides VII and VIII, new acylsterylglucosides from *Withania somnifera*." *Phytotherapy research.* 1987; 1(1):32-37.
- Choudhary B, Shetty A, Langade DG. Efficacy of Ashwagandha (*Withania somnifera* [L.] Dunal) in improving cardiorespiratory endurance in healthy athletic adults. *Ayu.* 2015; 36(1):63-68. doi:10.4103/0974-8520.169002
- Dhama K, Chakraborty S, Tiwari R. Panchgavya therapy (Cowpathy) in safeguarding health of animals and humans: A review. *Res. Opin. Anim. Vet. Sci.* 2013; 3:170-178.
- Dikasso D, Makonnen E, Debella A. Anti-malarial activity of *Withania somnifera* L. Dunal extracts in mice. *Ethiop Med J* 2006; 44(3):279-85.
- Guan WJ, Ni ZY. Clinical characteristics of 2019 novel coronavirus infection in China. medRxiv, 2020.
- Handa SS. *Plants and plant products for mental health. Decade of the brain.* Rockville. MD: US Department of Health and Human Services, 1995, 163-171.
- Hemalatha S, Wahi AK, Singh PN, Chansouria JP. Hypolipidemic activity of aqueous extract of *Withania coagulans* dunal in Albino rats. *Phytother. Res.* 2006; 20:614-617.
- https://en.wikipedia.org/wiki/Template:COVID-19_pandemic_data <https://www.mygov.in/covid-19>
- Huang C, Wang Y, Li X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 2020.
- International Committee on Taxonomy of Viruses (ICTV) Severe acute respiratory syndrome-related coronavirus: the species and its viruses—a statement of the Coronavirus Study Group <https://www.biorxiv.org/content/10.1101/2020.02.07.937862v1>
- Kaur G, Singh N, Samuel SS, Bora HK, Sharma S, Pachauri SD, *et al.* *Withania somnifera* shows a protective effect in monocrotaline-induced pulmonary hypertension. *Pharmaceutical Biology.* 2015; 53(1):147-157.
- Kuboyama Tomoharu, Chihiro Tohda, Katsuko Komatsu. "Withanoside IV and its active metabolite, sominone, attenuate A β (25–35)- induced neurodegeneration." *European Journal of Neuroscience.* 2006; 23(6):1417-1426.
- Mirjalili Mohammad Hossein. "Steroidal lactones from *Withania somnifera*, an ancient plant for novel medicine." *Molecules.* 2009; 14(7):2373-2393.
- Muralikrishnan G, Dinda AK, Shakeel F. Immunomodulatory effects of *Withania somnifera* on azoxymethane induced experimental colon cancer in mice. *Immunological Investigations.* 2010; 39(7):688-698.
- Muregi FW, Ishih A, Miyase T. Antimalarial activity of methanolic extracts from plants used in Kenyan ethnomedicine and their interactions with chloroquine (CQ) against a CQ- tolerant rodent parasite, in mice. *J Ethnopharmacol.* 2007; 111(1):190-195
- Naidu PS, Singh A, Kulkarni SK. Effect of *Withania somnifera* root extract on reserpine induced orofacial dyskinesia and cognitive dysfunction. *Phytotherapy Res.* 2006; 20:140-146.
- Provino R. The role of adaptogens in stress management. *Aust J Med Herbalism.* 2010; 22:41-9.
- Sangwan RS, Chaurasiya ND, Misra LN. Phytochemical variability in commercial herbal products and preparations of *Withania somnifera* (ashwagandha). *Curr Sci.* 2004; 86:461-5.

24. Scarfiotti CF, Fabris B, Cestaro, Giuliani A. Free radicals, atherosclerosis, ageing and related dysmetabolic pathologies: Pathological and clinical aspects. *Eur. J. Cancer Prevention*. 1997; 6:S31-S36.
25. Singh G, Sharma PK, Dudhe R, Singh S. Biological activities of *Withania somnifera*. *Ann Bioll Res*. 2010; 1:56-63.
26. Singh N, Nath R, Lata A, Lata A, Singh SP, Kohli RP, *et al.* *Withania somnifera* (Ashwagandha), a rejuvenating herbal drug which enhances survival during stress (an adaptogen) *Int J Crude Drug Res*. 1982; 20:29-35.
27. Singh S KVS, Singhal S, Singh N. An indian herbal immunomodulator: Highly effective in the treatment of HIV/AIDS. *Proceeding of 6th International Conference AIDS Asian Pacific* October 5-10. Melbourn, Australia, 2001, 5-10.
28. Singh J. Ayurvedic treatment of chronic obstructive pulmonary disease (COPD), 2015. Retrieved from <https://www.ayurtimes.com/ayurvedic-treatment-of-chronic-obstructive-pulmonary-disease-copd/>
29. Subbaraju Gottumukkala V. "Ashwagandhanolide, a bioactive dimeric thiowithanolide isolated from the roots of *Withania somnifera*." *Journal of natural products*. 2006; 69(12):1790-1792.
30. Tan WJ, Zhao X, Ma XJ. A novel coronavirus genome identified in a cluster of pneumonia cases-Wuhan, China 2019–2020. *China CDC*. 2020; 2:61-62. (Chinese)
31. Tillu G, Chaturvedi S, Chopra A, Patwardhan B. Public Health Approach of Surveyed and Yoga for COVID-19 Prophylaxis. *The Journal of Alternative and Complementary Medicine*, 2020.
32. Tiwari, Ruchi. "Ashwagandha (*Withania somnifera*): Role in safeguarding health, immunomodulatory effects, combating infections and therapeutic applications: A review." *J Biol Sci*. 2014; 14(2):77-94.
33. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on, 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020>
34. Zhang H, Kang ZJ, Gong HY. The digestive system is a potential route of 2019-nCoV infection: a bioinformatics analysis based on single-cell transcriptomes. *bioRxiv* 2020, In press.
35. Zhou P, Yang X, Wang X. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, 2020.
36. Zhu N, Zhang D, Wang W. A novel coronavirus from patients with pneumonia in China. *N Engl J Med*. 2019; 382:727-733.