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Anti-viral activity of *Withania somnifera* phytoconstituents against corona virus (SARS-COV-2)

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Introduction: Traditional medicine practitioners use natural active compounds found in medicinal plants to treat a variety of diseases. *Withania somnifera*, also known as Ashwagandha, Winter Cherry, and Indian Ginseng, is one such herb that has been used to cure a variety of ailments since the time of Ayurveda, India's ancient medical system. The Solanaceae family includes *Withania somnifera*.

Method: The exhaustive literature survey has been done via various search engines, review articles, research articles, google scholar, PubMed, internet. According to recent investigations, Withanolides, a bioactive ingredient of *Withania somnifera*, have shown therapeutic efficacy in decreasing the intensity of SARS-CoV-2 and in providing medical care and attention to individuals suffering from COVID-19. Free-radical scavenging is another feature of Ashwagandha. This review article contains information regarding phytochemistry and antiviral activity against coronavirus.

Results: In-silico investigations have revealed that it has a high binding affinity for the ACE2-RBD interface, which could prevent SARS COV 2 from infecting cells. In India, ashwagandha is available as a liquid, tablet, or powder. This review article's aim is to provide all the information and research work that should be done by researchers recently against SARS COVID-19.

Discussion: Due to its immune-modulatory, anti-stress, and antiviral characteristics, Ashwagandha has been chosen. The aim of the review article is to review 'the anti-viral activity of *Withania somnifera* phytoconstituents against coronavirus (SARS-COV-2).

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Introduction

Plants that are used for medicinal purposes can be found all over the world. Many weeds in our surroundings are powerful medicinal plants that can help with a wide range of serious health problems (Parihar and Sharma, 2021; Chaudhary *et al.*, 2021). Among ancient cultures, India has long been renowned as a rich storehouse of natural treatments (Parihar and Sharma, 2021). Traditional medicine practitioners use natural active compounds found in medicinal plants to treat a variety of diseases. *Withania*

somnifera, also known as Ashwagandha, Winter Cherry, and Indian Ginseng, is one such herb that has been used to cure a variety of ailments since the time of Ayurveda, India's ancient medical system. The Solanaceae family includes *Withania somnifera*. According to recent investigations, Withanolides, a bioactive ingredient of *Withania somnifera*, has shown therapeutic efficacy in decreasing the intensity of SARS-CoV-2 and in providing medical care and attention to individuals suffering with COVID-19. Free-radical scavenging is another feature of Ashwagandha. This review article contains information



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regarding phytochemistry and antiviral activity against corona virus.

ACTIVE CHEMICAL COMPOUNDS OR SECONDARY METABOLITES FOUND IN *WITHANIA SOMNIFERA*:

Plants have both primary and secondary metabolites, each of which serves a different purpose. Primary metabolites such as amino acids, simple carbohydrates, proteins, and lipids regulate several aspects of biological processes. Secondary metabolites (also known as natural products) have an impact on other animals. Secondary metabolites are

chemically active chemicals that are generated in response to stress and have a more complex structure and distribution than primary metabolites. Flavonoids, saponins (sitoindoside VII and VIII), phenols, tannins, alkaloids (withanine, isopellertierine, anferine), steroidal lactones (withanolides, withaferins), terpenoids, glycosides, and reducing sugars were found in phytochemical screening of various extractions, which may explain the plant's diverse medicinal properties. Iron is abundant in *Withania somnifera*. **Table 1.** Contain Occurrence of phytomolecules in different parts of *Withania somnifera*

Table 1: Occurrence of phytomolecules in different parts of *Withania somnifera*

Phytomolecules	Molecular formula	Plant part	References
Withaferin A	$C_{28}H_{38}O_6$	Leaves	Tursunova <i>et al.</i> , 1977
Withanone	$C_{28}H_{38}O_6$	Roots, leaves	Chaurasiya <i>et al.</i> , 2007; Chaurasiya <i>et al.</i> , 2009
Ashwagandholide	$C_{56}H_{78}O_{12}S$	Roots	Subbaraju <i>et al.</i> , 2006
Withanamides A-I	$C_{40}H_{62}O_{13}N_2$, $C_{38}H_{62}O_{13}N_2$, $C_{40}H_{66}O_{13}N_2$, $C_{40}H_{66}O_{13}N_2$, $C_{38}H_{60}O_{13}N_2$, $C_{40}H_{58}O_{13}N_2$, $C_{46}H_{72}O_{18}N_2$	Fruits	Jayaprakasam <i>et al.</i> , 2004
Withaferin A, Withanolide A, Withanolide B, Withanolide D	$C_{28}H_{38}O_6$, $C_{28}H_{38}O_6$, $C_{28}H_{38}O_5$, $C_{28}H_{38}O_6$	Roots	Misra <i>et al.</i> , 2008
Withasomnillide, Withasomniferanolide	$C_{28}H_{38}O_6$	Stem	Lal <i>et al.</i> , 2006
Withaferin A, Withanolide D, Withanolide P, Withanolide F, Withanone	$C_{28}H_{38}O_6$, $C_{28}H_{38}O_6$, $C_{28}H_{38}O_5$, $C_{28}H_{38}O_6$, $C_{28}H_{38}O_6$	Leaves, fruits, stem, roots	Misra <i>et al.</i> , 2005
Withanolide A, Withanone, Isowithanone	$C_{28}H_{38}O_6$, $C_{28}H_{38}O_6$	Berries (fruit) and seeds	Lal <i>et al.</i> , 2006
Tropane alkaloids	$C_{17}H_{19}O_3N$	Roots and leaves	Tuli and Sangwan 2010
Flavonoids and Phenolics	$C_{15}H_{10}O_2$, C_6H_6O	Roots	Nur-e-Alam <i>et al.</i> , 2003; Tuli and Sangwan 2010
Terpenoids and Sterols	$(C_5H_8)_n$, $C_{17}H_{28}O$	Fruits	Misra <i>et al.</i> 2005; Misra <i>et al.</i> , 2008

Literature Review On Antiviral Activity Of *Withania Somnifera* Against Corona Virus

Withania somnifera's bioactive components have antiviral properties against a variety of viruses, including SARS-CoV-2 (Kashyap *et al.*, 2020). Withanolides, Withaferin A, Withanone, Withanoside V and X have the potential to treat COVID-19 and lower the incidence of SARS-CoV-2.

SARS-S-Protein CoV-2's (Spike glycoprotein) binds to the ACE2 (angiotensin-converting enzyme 2) receptor on the surface of a variety of human cells, allowing the virus to enter the host cells. The Coronavirus's primary targets include the alveolar, airway, and vascular endothelium, as well as ACE2 receptor-expressing lung macrophages. ACE2 has been found to be more numerous in alveolar cells, giving SARS-CoV-2 a primary entry point into the host cell (Ge *et al.*, 2013; Gheblawi *et al.*, 2020). SARS-

CoV-2 is made up of two subunits: S1 and S2. The S1 subunit's RBD (Receptor-Binding Domain) attaches to the ACE2 receptor on the host cell, while the S2 subunit is in charge of viral membrane fusion (Du *et al.*, 2009).

SARS-CoV-2 activity can be blocked in three methods by natural substances like withanolides, withanone, and withaferin A:

- These phytochemicals bind to the S-glycoprotein of SARS-CoV-2, preventing it from interacting with the host cell receptor ACE2.
- Prevent SARS-CoV-2 from binding to host cells' ACE2 receptor.
- Inhibit SARS-primary CoV-2's viral proteases (Kumar *et al.*, 2020; Aanouz *et al.*, 2020) as well as papain-like proteases. **Table 2** contain Anti-viral activity of different phytoconstituents against SARS-CoV-2

Table 2: Anti-viral activity of different phytoconstituents against SARS-CoV-2

Phytochemical	Anti-viral activity against SARS-CoV-2	References
Withaferin A	Inhibit SARS-CoV-2 main viral proteases (Mpro) Prevent SARS-CoV-2 from attaching to the ACE2 receptor on host cells	Balkrishna <i>et al.</i> , 2020; Kumar <i>et al.</i> , 2020; Pandit and Latha 2020
Withanone	Inhibit SARS-CoV-2 main viral proteases (Mpro) Block ACE2 receptor	Kumar <i>et al.</i> , 2020b; Balkrishna <i>et al.</i> , 2020
Withanoside V	Inhibit SARS-CoV-2 main viral proteases (Mpro) Binding with S-glycoprotein blocks viral entrance	Shree <i>et al.</i> , 2020 Chikhale <i>et al.</i> , 2021
Withanoside X	Binding with S-glycoprotein blocks viral entrance	Chikhale <i>et al.</i> , 2021
Withanolide A	Inhibit SARS-CoV-2 main viral proteases (Mpro)	Pandit and Latha 2020
Withanolide D	Inhibit papain-like proteases (PLpro)	Khanal <i>et al.</i> , 2020
Withanolide G	Inhibit papain-like proteases (PLpro)	Khanal <i>et al.</i> , 2020
Withanolide M	Inhibit SARS-CoV-2 main viral proteases (Mpro) Binding with S-glycoprotein blocks viral entrance	Khanal <i>et al.</i> , 2020
Withanolide Q	Modulation of many important proteins of SARS-CoV-2	Khanal <i>et al.</i> , 2020

3-chymotrypsin-like proteases are another name for main viral proteases (Mpro) (3CLpro).

Cytokine release syndrome and storm are life-threatening immunological reactions caused by the rapid release of a large number of cytokines into the bloodstream caused by the SARS-CoV-2 infection. Dysfunctional and aggressive immune responses that result in cytokine release disorder or storm, which leads to excessive inflammation, can cause a dangerous type of pulmonary and lung pathology.

Furthermore, uncontrolled and excessive cytokine release damages myocardium and causes multiorgan dysfunction

(Ruan *et al.*, 2020). The secretion of cytokines can be inhibited by withanolides and other components. Coronil is a medication that contains withanolides, which can assist to control the cytokine blast during SARS-CoV-2 infection.

Phytochemicals that bind with spike proteins are- Withanolide M, Withanoside V, Withanoside, Withaferin A.

Phytochemicals that block ACE2 receptor: Withanone

Phytochemicals that inhibit proteases:

M^{pro} /3CL^{pro} inhibitors: Withaferin A, Withanone, Withanoside V, Withanolide A, Withanolide M.

PL^{pro} inhibitors: Withanolide D, Withanolide G (Dar et al., 2015; Davis and Kuttan, 2000; Dhawan et al., 2021)

Results and Discussions

Salutogenesis (maintaining optimum health and immunological status) is a fundamental part of the Ayurvedic health system's comprehensive approach to disease management and health preservation. The drug chosen have an immunomodulatory effect, meaning they tend to restore a person's natural immunity. In today's world, where changing lifestyles, diets, and stress are the norm, keeping a natural immune system is extremely rare, making a person vulnerable to infections and diseases. Due to its immune-modulatory, anti-stress, and antiviral characteristics, Ashwagandha has been chosen. In-silico investigations have revealed that it has a high binding affinity for the ACE2–RBD interface, which could prevent SARS COV 2 from infecting cells. In India, ashwagandha is available as a liquid, tablet, or powder. The Indian winter cherry, Ashwagandha (*Withania somnifera*), is well-known for its energy-boosting and stress-relieving qualities. There have been countless studies on Ashwagandha's therapeutic benefits, but this is the first time the ministry has partnered with a foreign institution to look at Ashwagandha's capabilities as they relate to Covid recovery. On the basis of above literature review it is justify that the herbal plant *Withania somnifera* has ability to fight against corona virus.

Conclusion

Numerous investigations on various components of *Withania somnifera* have been undertaken, and this plant has been produced as a medication by pharmaceutical companies. Identification, categorization, and recording of plants required a through and methodical investigation, which could be a useful strategy to promote traditional knowledge of the therapeutic herbal plant.

Conflict of Interest

The author has no conflict of interest

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