



## Role of *Ashwagandha* (*Withania Somnifera*) as Immunomodulator in Coronavirus in a pandemic – A systemic review

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### ABSTRACT

The novel coronavirus has been transmitted all over the world. Many deaths were occurred due to Coronavirus. The main symptoms are pyrexia, fatigue, and dry cough. Some individual also develops a headache, running nose, congestion, sore throat, shortness of breath. At present, no vaccines or medicines available for the prevention and management of Coronavirus disease. Prevention is better than cure. This verse is famous and all known about it. So now the time has come to used or implement this. Prevention is the only measure to fight against Coronavirus. Ayurveda can offer the best option having preventive as well as curative measures. Many herbs have been mentioned in the Ayurvedic texts, which have immunomodulatory action or works as immunobusting drugs. *Ashwagandha* is well-known or a far old drug which said in Ayurvedic text as a Rasayan and Immunomodulatory activity. *Ashwagandha* can be used for the prevention of Coronavirus due to it has property like promoting betterment for health and longevity by an increase defence mechanism. Many kinds of research are conducted on *Ashwagandha* to prove its immunomodulatory, antioxidant, anti-inflammatory, Neuroprotective. Anti-stress properties. We concluded, in Systemic review to know the role of *Ashwagandha* in the prevention and curing symptoms of Coronavirus its efficacy and mechanism in Coronavirus. Some more research studies should be on COVID -19 for experimental and clinical validation to needed.



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### INTRODUCTION

The novel Coronavirus Disease (nCOVID – 19) is a virus which is spread all over the country through the transmission of human to human. Many populations younger, as well as older, suffered. Many deaths have occurred; many hospitals filled (Wu and McGoogan, 2020; Parwe et al., 2020). It spreads by coughing, sneezing, personal contact, infected material, mass gatherings. It can avoid by regular hand wash and covering of mouth and by maintaining social distance (Nizame et al., 2011). No particular medicine is available for the treatment of COVID -19. So many studies are going on for treatment and prevention. Government has been taking so many

efforts to prevent and control the COVID -19 (Zhang *et al.*, 2020). Traditional herbs are very famous in India and used for COVID -19. The Indian government also published advisory by AYUSH department for COVID -19.

Ayurveda is an ancient science, and so many measures mentioned in Ayurveda for treating and controlling such type of worldwide spreading virus. These measures for improving the good immune system and curative disease.

*Ashwagandha* is very famous herbs in Ayurveda and well-known for its action as Aphrodisiac. *Ashwagandha* is commonly known as his Latin name *Withania Somnifera*, herbs are known as well as Indian ginseng and Winter cherry (Bharti *et al.*, 2016). It is a shrub found in the drier area of India and widely cultivated in different states Gujarat and Haryana, Madhya Pradesh, Punjab and Uttar Pradesh.

In Ayurveda it is mentioned as *Rasayana* (Rejuvenate), used for promoting physical and mental health and providing defence against different disease, slowing the ageing process, revitalizing the body in such severe conditions, it increases the capability of the individual to resist adverse environmental factors and by creating a sense of physical and mental well being (Bhattacharya *et al.*, 2002).

### Botanical Description

*Ashwagandha* is a small shrub being Solanaceae family. It grows up to the two feet height in drier parts of India. Roots are the main which used in therapeutically. The fruit is bright red in colour, seeds are dried for cultivating as a medicinal plant and Table 1 contain Phytochemistry of *Ashwagandha*. All parts of plants used in medicine, each part like roots, leaves, stem, green berries, fruits, seeds, bark have different activity.

This herb was used to treat especially osteoarthritis, rheumatoid arthritis, and gout. *Ashwagandha* has green leaves, branched limbs with seeded yellow flowers. *Ashwagandha* is an essential herb in Ayurvedic context and also used in a variety of infectious diseases and inflammation conditions (Akram *et al.*, 2011).

The pharmacological action of *Ashwagandha* mentioned which used in various disorders of the central nervous system specifically indicated in Neurodegenerative diseases. In Drugs addiction, cerebral ischemia and dyskinesia too (Kulkarni and Dhir, 2008).

The extracted compound of "*W. somnifera* is the phytochemical mixture which has active constitute of phenolic and flavonoid compound. The roots of these compound have a pharmacological effect

of *W. somnifera*, which attributed to withanolides (Dhanani *et al.*, 2017; Chen *et al.*, 1987).

The constituents of withanolides are a sequence of steroids, which is naturally occurring. It contains a lactone with a side chain of nine carbon; in which, richest sources of steroidal lactones. (Srivastava *et al.*, 1992; Ksebati and Schmitz, 1988).

### MATERIALS AND METHODS

The article published in PubMed.gov research online portal were analyzed for this review article. The keywords used for database search which include "*Ashwagandha* and *Withania somnifera*". All articles published in the English language only were included in this review. No other exclusion criteria were applied as regarding journal, years, authors etc. A comprehensive list of all articles published until September 2020 was prepared. In the next stage, all the articles obtained from searching the databases were compiled and screened by reading their "title" and then the "abstract." Studies that satisfied the inclusion criteria, i.e. immunomodulator, anti-viral and COVID-19 studies were only included at this stage and others excluded.

### OBSERVATION

All selected articles were screened finally by reading the full -text or abstract as per availability and were analyzed further. This search process for systemic review was done as per "Preferred Reporting Items for Systemic Review and Meta-Analysis (PRISMA) guidelines" (Moher *et al.*, 2009) , (Figure 1).

### RESULTS AND DISCUSSION

The PubMed research portal search keyword "*Ashwagandha*" and found 1220 articles; while keyword of '*Withania somnifera*' yielded 1161 articles. The PubMed online database search for all articles on the screening regarding anti-viral and immunomodulatory properties. The *Ashwagandha* and its immunomodulatory properties show article were 56 and *Ashwagandha* along with anti-viral properties shows 14 articles. Final inclusion of the articles for a systemic review of Immunomodulatory and anti-viral properties for COVID-19 was 07.

#### Anti-viral effect and Immuno-modulatory effect of *Ashwagandha*

They evaluate in their study by adopting a computational approach, a natural chemical constituent of *Ashwagandha* to explore a possible inhibitor against the main protease of SARS-COV-2. In this article on docking, a study was carried out on four

**Table 1: Phytochemistry of *Ashwagandha***

| Sr. No. | Class               | Chemical constituents   | con- | Activity   |                     |
|---------|---------------------|---|------|--|---------------------|
| 1.      | Alkaloids           | Ashwagandhine, cuscohygrine, anahygrine, tropine                |      | antispasmodic effects<br>anti-microbial activity<br>sedative effects   | Root                |
| 2.      | Steroidal activity  | Ergostane, steroidal lactones, withaferin A, withasomniferin-A. |      | The antioxidant as well as Aphrodisiac reduces cholesterol levels, affects the immune system and tumor cells | Root                |
| 3.      | Saponins            | Sitoindoside IX and X<br><br>Sitoindosides-VII and VIII         |      | Antioxidant<br>Adaptogenic   | Root<br>Root        |
| 4.      | Aqueous Extract     | Withanolides, Glycowithanolides                                 |      | Immunomodulatory   | Root                |
| 5.      | Bioactive compounds | Withanolide sulfoxide   |      | Antimicrobial activity<br>carcinogens tumor promoters, and inflammatory agents                               | Root, Leaf          |
| 6.      | Ethanollic          | Ethanol   |      | anti-proliferative activity against cancer cell, Antibacterial   | leaf, stem and root |
| 7.      | Root Extract        |   |      | Anti-Parkinson's, cardioprotective, neuroprotective,   | Root                |

constituents of *Ashwagandhas* which shows these selected natural constituents have the highest docking energy. In his study they concluded, withanoside V in *Ashwagandha* may serve as potent compound inhibitors of in COVID-19 and may have the effect of anti-viral on nCOVID-19 (Tripathi et al., 2020; Nisargandha and Dadarao Parwe, 2020).

Another study was done on molecular docking analysis data of the cellular receptor Glucose regulated protein (GRP78) with withaferin A from *Withania somnifera* in COVID -19. They reported that the optimal interaction feature of withaferin A with the GRP78 receptor and COVID -19 M<sup>Pro</sup> and mentioned more research required for validating the properties of anti-viral in withaferin A against COVID -19 (Sudeep, 2020).

The study, Chikhle R.V., et al., observed in his work plant *withania somnifera* is well established as anti-viral, immunomodulatory, anti-inflammatory, antioxidant plant using molecular docking and dynamic studies. They mentioned in molecular docking study, pointed out some phytoconstituents properties from *Ashwagandha*. It could be an alternative as an anti-viral agent in the management of coronavirus (Chikhale et al., 2020).

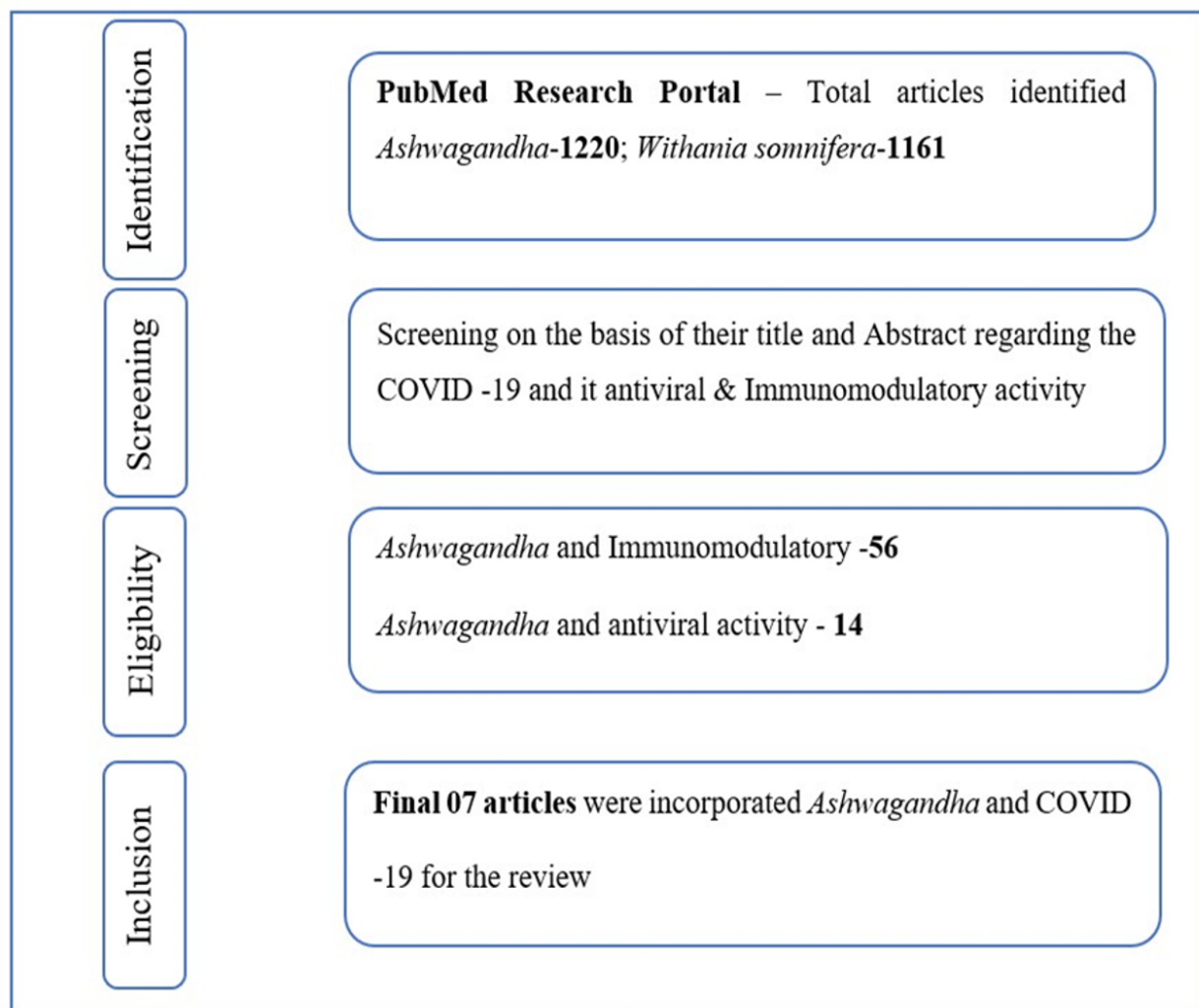
Three ayurvedic medicinal plants used in their

study, in "molecular docking study shows six inhibitors against SARS-CoV-2 M<sup>Pro</sup>. They suggested that active constituents from this medicinal plant could potentially inhibit M<sup>Pro</sup> of SARS-CoV-2" (Shree et al., 2020).

This article is on the withaferin A (WFA) potential therapeutic agent against Coronavirus infection. It suggests that the anti-inflammatory & antitumorogenic "properties may bind the viral spike (S) protein of SARS-CoV-2. WFA does not alter the expression of ACE2 in the lung of tumor bearing female mice" (Straughn and Kakar, 2020; Dhuley, 2001).

It was observed in their study; phytochemicals exhibit remarkable pendency on "various human biological pathways in cancer. They suggest that there should be some clinical and experimental evidence in vitro for observing its potency (Parida et al., 2020).

Two studies carried out by Vipul Kumar et al. In one study they mentioned that binding with an one -N (Wi-N), with none-A (Wi-A) and caffeic acid phenethyl ester (CAPE) highly conserved protein, M<sup>Pro</sup> of COVID -19. They found only WI-N and CAPE bind the substrate-binding pocket of SARS-CoV-2 M<sup>Pro</sup> with efficacy, not the Wi-A. Data presented in his study these are the natural compound



**Figure 1: Flow chart of all articles Identified, Screen, Included for review, according to PRISMA guidelines**

for actively inhibit the functional activity of SARS - CoV-2 protease (Kumar *et al.*, 2020b). In his other study Wi-A and Wi -N could bind and stably interact with the catalytic site of trans membrane protease serine 2 (TMPRSS2). They observe the effect of Wi-N on TMPRSS2 expression in MCF7 cell and found remarkable reduce into the host cell. They may offer therapeutic and preventive value in the management of nCOVID-19. They also make attention to the alert about the use of different parts of *Ashwagandha*. (Kumar *et al.*, 2020a)

## CONCLUSION

In the Indian system of Ayurveda, *Withania somnifera*, also known as *Ashwagandha*. The roots of *W. somnifera* have been extensively used as a valuable drug in Ayurveda. However, its therapeutic potential as immunomodulatory, apoptogenic, antioxidant, hypoglycemic and anti-cancer activities have been reported. The systemic review of the articles

available from the PubMed database shows confirming to the current situation of COVID -19 and role of *Ashwagandha* as immunomodulatory and anti-viral activity articles. The seven full articles are available on SARS- CoV-2 and *Ashwagandha* emphasis mainly on their therapeutic use as an anti-viral and immunomodulatory activity. Out of seven articles, five articles mentioned anti-viral, and two reported as immunomodulatory action. We conclude, there needs some experimental and clinical validation to know the reliability and preventive measurement in COVID-19.

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**Conflict of Interest**

The authors declare that they have no conflict of interest for this study.

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