



## Systematic review of anti-viral & immunomodulatory potential of *Ashwagandha* (*Withania Somnifera*. Linn) in light of covid-19 pandemic

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### Abstract

**Background:** Traditional medicinal system like the TCM (Traditional Chinese Medicine) has successfully contribution against COVID-19. Now, the ancient science of Ayurveda is being looked upon. Ayurveda holds a treasure of valuable herbs that might help in this situation. *Ashwagandha* (*Withaniasomnifera*.Linn) is one such wonder herb. It holds a prominent place among *Rasayana* herbs of Ayurveda. Many systematic reviews of *Ashwagandha* considering its adaptogen, anti-cancer, cognition enhancer etc. activities are available. However, none could be found to exclusively review its anti-viral and immunomodulator activities.

**Aim:** Hence, these two aspects were chosen especially bearing current COVID-19 situation in mind.

**Conclusion:** The current systematic review study indicates that the use of *Ashwagandha* for immunomodulatory, anti-viral and especially against COVID-19 has a logical and scientific basis.

**Keywords:** Novel coronavirus, *Ashwagandha*, Traditional medicine, *Withaniasomnifera*, Immunity

### Introduction

In December 2019, several patients with pneumonia of unknown cause were identified in Wuhan, China. Coronavirus disease 2019 (COVID-19) is a newly recognized infectious disorder that has to unfold hastily all through Wuhan, Hubei, China, to other provinces in China and numerous countries around the sector. The variety of fatalities day by day due to COVID-19 is escalating <sup>[1]</sup>. The COVID-19 pandemic has changed the world in many ways. Lack of conclusive treatment in modern medicine has been a key feature of this pandemic. Traditional medicinal system like the TCM (Traditional Chinese Medicine) has successfully contribution against COVID-19 <sup>[2]</sup>. According to WHO, management of COVID-19 has mainly focused on infection prevention, case detection and monitoring and supportive care <sup>[3]</sup>.

Now, the ancient science of Ayurveda is being looked upon. Ayurveda holds a treasure of valuable herbs that might help in this situation.

*Ashwagandha* (*Withaniasomnifera*.Linn) is one such wonder herb. It belongs to family Solanaceae and is commonly known as “Indian Winter cherry” or “Indian Ginseng”. A variety of therapeutic uses of *Ashwagandha* have been enlisted in different Ayurveda treatises. It holds a prominent place among *Rasayana* herbs of Ayurveda. It is mentioned as tonic, aphrodisiac, narcotic, diuretic, anthelmintic, and astringent, thermo genic and stimulant <sup>[4-5]</sup>. Many studies have been published regarding its immunomodulatory activity. It has also been studied for its anti-viral potential by many scholars.

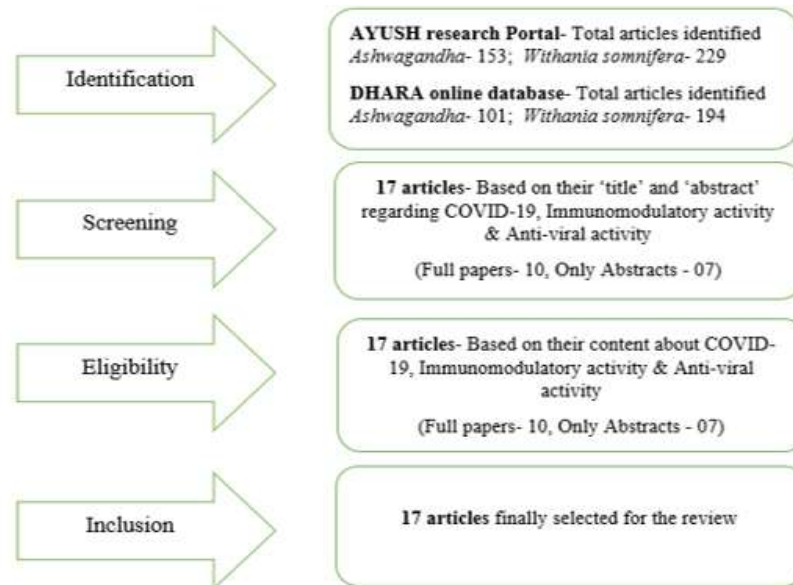
Many systematic reviews of *Ashwagandha* considering its adaptogen, anti-cancer, cognition enhancer etc. activities are available. However, none could be found to exclusively review its anti-viral and immunomodulator activities. These two aspects were chosen especially bearing current COVID-19 situation in mind, where *Ashwagandha* is considered as a potential medicine.

### Materials and Methods

Articles published in AYUSH research portal and DHARA (Digital Helpline for Ayurveda Research Articles) were analyzed for this study. The key words used for the purpose of database search included “*Ashwagandha* and *Withania somnifera*.” The articles published in English language only were included. No other exclusion criteria were applied as regards journal, year, authors etc. A comprehensive list of all articles published until July 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.

The selected articles were screened finally by reading the full-text or abstract as per availability and were analyzed further. This search process for systematic review was done as per Preferred Reporting Items for Systematic review and Meta Analysis (PRISMA) guidelines <sup>[6]</sup>. (Diagram. 1)



**Fig 1:** Flow of information through different phases of systematic review, according to PRISMA guideline

## Results

The ayush research portal search for keyword '*Ashwagandha*' yielded 153 articles; while keyword '*Withania somnifera*' yielded 229 articles. The DHARA online database search for keyword '*Ashwagandha*' yielded 101 articles; while keyword '*Withania somnifera*' yielded 194 articles. However, 17 articles were retrieved on basis of aforementioned inclusion and exclusion parameters. The seventeen articles were further categorized as mentioned in

**Table 1:** Showing categorization of selected articles

Parameter	Full Text	Only Abstract
Immunomodulatory Activity	02	06
Anti-viral Activity	02	01
COVID-19 related studies	06	--
Total	10	07

### 1. Immunomodulatory Activity

Total eight studies were found concerned with immunomodulator activity of *Ashwagandha*. One study was based on review of Ayurveda principles as basis for combating infections through increase in immunity [7]. It enlisted *Ashwagandha* for this purpose based on review of Ayurvedic literature. Rest seven studies included of four pre-clinical studies and three clinical studies.

#### A) Pre-clinical studies

In a pre-clinical study, *Ashwagandha* (*Withania somnifera*) and *Brahmi* (*Bacopa monnieri*) were concentrated to upgrade insusceptible capacity and contrasted their belongings with that of *Echinacea*, noted for its capacity to improve safe function [8]. It was discovered that they could upgrade safe capacity by expanding immunoglobulin creation. It was additionally felt that, these natural medications may manage immunizer creation by expanding both Th1 and Th2 cytokine creation.

In an in-silico study, assessment of the immunomodulatory impact of *Ashwagandha* was clarified utilizing system ethnopharmacology technique [9]. It recognized five bioactive that were equipped for directing fifteen resistant framework pathways through sixteen objective proteins by bioactive-target and protein-protein associations. The

examination additionally uncovered the capability of withanolide-phytosterol mix to accomplish powerful immunomodulation and seven novel bioactive-invulnerable objective mixes.

The immunomodulatory exercises of *Ashwagandha* separates were concentrated in mice model in another study [10]. Immunomodulatory impact was evaluated in If IgE-intervened hypersensitivity in as decrease of ovalbumin-actuated paw oedema, in creatures treated with WS2 at dosages of 150 and 300 mg/kg, and the outcomes were contrasted and the standard medication disodium chromoglycate. A noteworthy increment in white platelet checks and platelet includes was seen in creatures treated with *Ashwagandha* extract. Cyclophosphamide-incited immune suppression was neutralized by treatment with *Ashwagandha* extricates uncovering huge increment in hem agglutinating immunizer reactions and haemolytic counter acting agent reactions towards sheep red platelets.

In a comparative report, the immunomodulatory movement of *Ashwagandha* was concentrated in mice with myelosuppression instigated by at least one of the accompanying three mixes viz, cyclophosphamide, azathioprin, or prednisolone [11]. The evaluation of immunomodulatory movement was completed by hematological and serological tests. A huge regulation of invulnerable reactivity was seen in all the three creature models. It was discovered that, *Ashwagandha* forestalled myelosuppression in mice treated with every one of the three immunosuppressive medications tried.

#### B) Clinical Studies

In a clinical study, a group of 37 underweight patients suffering frequently from seasonal diseases was treated with *Ashwagandha* for one month [12]. It significantly improved the physical strength, functions of the lungs and heart, immediate memory and weight of them. It also significantly increased the immunity of the persons as it increased their serum IgA, IgG and IgM. Immuno enhancing effect of an herbal tea fortified with *Ashwagandha* along with *Glycyrrhizaglabra*, *Zingiberofficinale*, *Ocimumsanctum* and *Elettariacardamomum* was studied on innate immunity of healthy volunteers in another double-blind study [13]. It was

observed that, NK cell activity of the volunteers in study group was significantly improved, which is an important aspect of the early innate immune response to infections.

In a clinical study, assessment of *Rasayana* or immunomodulator activities of wild and cultivated varieties of *Ashwagandha* were studied in healthy volunteers [14]. It was observed that, both varieties brought about significant improvement in various subjective and objective parameters related to immunity as per Ayurveda and modern medicine.

## 2. Anti-viral Activit

Three studies were focused on anti-viral activity of *Ashwagandha* other than COVID-19 infection. There were two pre-clinical studies and one clinical study.

### A) Pre-clinical studies

In -vitro study, *Ashwagandha* and *Ocimum sanctum* Linn, *Tinosporacordifolia* (Willd.) Miers. ex Hook.f. &Thoms, *Avicennia officinalis* Linn. Also, *Rhizophoramucronata* Lam. were screened for against HIV activity [15]. The impacts of various concentrates on gp120/CD4 communication were inspected in the current investigation, utilizing a gp120 catch ELISA unit. It was discovered that, these spices applied their enemy of HIV movement by means of various instruments of activity, viz. impedance with the gp120/CD4 communication and hindrance of viral RT. Consequently, their customary use for the treatment of irresistible infections of viral root was advocated.

As an extension to this study, aqueous extracts of *Ashwagandha* and *Ocimumsanctum* Linn., *Tinosporacordifolia* (Willd.) Miers ex Hook. f. & Thoms, *Avicenniaofficinalis* Linn., *Rhizophoramucronata* Lam. were studied to evaluate inhibitory activity of HIV-protease [16]. Pepsin was used as a substitute for HIV-protease in this study. These extracts showed potent inhibitory activity against pepsin enzyme.

### B) Clinical Study

In a clinical study on patients of acute viral hepatitis, a polyherbal formulation, 'Livwin' containing extracts of seven medicinal plants including *Ashwagandha*, was studied [17]. It was found to be effective in uncomplicated patients of acute viral hepatitis with good biochemical recovery.

## 3. Covid-19 Related Studies

None of the studies related to COVID-19 were of clinical nature. Total six studies were reviewed in this regard. Out of them, one study compiled literary reviews of immunomodulator drugs in Ayurveda and their probable efficacy against COVID-19 [18]. Rests five were laboratory-based studies.

In an in-silico study, the immunomodulatory and hostile to SARS-CoV-2 capability of key phyto constituents from Ayurveda based *Rasayana* drugs, viz., *Ashwagandha*, *Guduchi* and *Shatavari* were investigated utilizing approaches like system pharmacology, and sub-atomic docking [19]. Among these three spices, *Ashwagandha* was seen as the most potent immunomodulator through its capability to adjust T cell separation, NK cell cytotoxicity just as T cell, B cell and NOD like receptor flagging pathways. The investigation gave prompts clinical use of these spices in prophylaxis as a result of their potential in repressing the replication of SARS-CoV-2. In another study with molecular docking approach, exploration of beneficial

roles of phytochemicals and active pharmacological agents present in *Ashwagandha* and *Tulsi*, *Haldi*, *Giloy*, Black pepper, Ginger, Clove, Cardamom, lemon were done [20]. The study revealed their potential to inhibit different stages of SARS-CoV-2 infection as well as other Corona virus target proteins.

Likewise, in another examination screening of photochemical from thirty restorative plants focusing on the proteins of SARS-CoV2 for recognizable proof of antiviral therapeutics was done [21]. Withaferin A from *Ashwagandha* additionally demonstrated noteworthy authoritative to the objective's proteins. This atomic docking study gave a premise to the utilization of traditional therapeutic plants as elective lines of treatment for COVID-19 contamination. In an *in silico* molecular docking procedure, *Ashwagandha* along with *Harsingar* (*Nyctanthesarbor-tristis*), *Giloy* (*Tinosporacordifolia*), *Aloe vera* (*Aloe barbadensis miller*), *Turmeric* (*Curcuma longa*), *Neem* (*Azadirachta indica*), *Ginger* (*Zingiberofficinale*), *Red onion* (*Allium cepa*), *Tulsi* (*Ocimum sanctum*), *Cannabis* (*Cannabis sativa*), *Black pepper* (*Piper nigrum*); was studied [22]. The inhibition potentials of these herbs were assessed by comparing with the binding affinity of hydroxychloroquine. *Ashwagandha* was found to show promising results.

Antiviral capability of *Ashwagandha* against COVID-19 by surveyed methods for computational techniques in another study [23]. The phytochemicals from *Ashwagandha* demonstrated promising activity that could square or hamper viral section into the host cells, by upsetting cooperation's between viral S-protein receptor restricting area and host ACE2 receptor.

## 4. Discussion and Conclusion

The global acceptance of Ayurveda largely depends on evidence-based efforts. Providing backing up of systematic reviews is one such requisite. The ministry of AYUSH has proclaimed *Ashwagandha* as a potential drug against COVID-19 [24]. A number of clinical studies are being conducted due to the proactive measures of Ministry of AYUSH.

The systematic review of articles available from AYUSH research portal and DHARA shows a promising side of situation. Both these databases are credible sources for understanding condition of Ayurveda research. The present review was limited to these two databases and it can be further expanded by taking into account other databases too. Also, only abstracts were available for many articles. A detailed review of their full text may add some more insights in future studies.

*Ashwagandha* is a celebrated herb from science of Ayurveda. Though much deliberation has been done on its adaptogen effects. Still, it holds a lot of potential in terms of immunomodulator activities. Also, its anti-viral activity on viral hepatitis and HIV is promising.

The antiviral therapies like Lopinavir/Ritonavir and Other Antiretrovirals are found to be effective in some cases. Ribavirin is an antiviral inhabits viral RNA-dependent RNA polymerase. Its activity is found beneficial against COVID-19 [25].

It was seen that, numbers of studies for assessing action against COVID-19 were more as compared to other studies. This is a welcome gesture towards government efforts to bring *Ashwagandha* as prophylactic treatment of COVID-19. Though none of the studies were of clinical nature,

laboratory studies show a hopeful scenario. It can be assumed that clinical studies will be carried out and published soon in this regard.

Thus, the above findings clearly indicate that the use of *Ashwagandha* for activities such as immunomodulatory, anti-viral and especially against COVID-19 has a logical and scientific basis.

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