

Ashwagandha (*Withania somnifera* Linn): Therapeutic and Preventive Value, Immunomodulatory Effects And Battling Infections

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Abstract :

Since ancient times, natural products have been used for the treatment of different type of diseases in several ways. The plant contains different type of phytoconstituents which showed different pharmacological activities. Ashwagandha (*Withania somnifera* (WS), a shrub known for its numerous therapeutic properties is also used as a antiviral herb for the treatment of several viral diseases. The major biochemical constituents of Ashwagandha root are alkaloids (isopellertierine, anferine), steroidal lactones (withanolides, withaferins), saponins containing an additional acyl group (sitoindoside VII and VIII), and withanolides with a glucose at carbon 27 (sitonidoside XI and X). The steroidal lactones (withanolides) obtained from its roots have been implicated in a wide range of therapeutic activities. It can reduce anxiety and stress, help fight depression, boost fertility and testosterone in men, and a memory enhancer. It helps in immunomodulation, anti-cancerous and anti-epileptic, diuretic, antiageing, anti-oxidant, hypoglycemic and rejuvenator. Ashwagandha enhances nitric oxide synthetase activity of the macrophages, which in turn increases the killing power of these immune cells thereby enhancing the Cell Mediated Immune response. Thus this plant is an important ingredient in many polyherbal preparations. Researchers from leading institutes in India are exploring the properties of the Ashwagandha on "therapeutic and preventive value" against COVID-19 infections.

Keywords : COVID-19, Withanolides, Cell mediated immunity, Withaferins.

Introduction :

Ayurveda is a Sanskrit word, which means "the scripture for longevity". It represents an ancient system of traditional medicine prevalent in India and in several other south Asian countries. It is based on a holistic view of treatment which is believed to cure human diseases through establishment of equilibrium in the different elements of human life, the body, the mind, the intellect and the soul. Ashwagandha (*Withania somnifera*) is a well known herb possessing several health benefits and is an important 'Rasayana' as "Sattvic

"Kapha Rasayana" in Indian Ayurveda, used since centuries for its marvelous advantages (Mahima et al., 2012). Ashwagandha (*Withania somnifera*) is a traditional medicine with growing needs due to its remedial potentials. Chinese, Unani, Ayurveda and Siddha literatures admire the therapeutic merits of plant-derived medicines against almost all ailments. An esteemed Rishi (sage) Punarvasu Atriya was the first person who gave the teaching regarding the use of Ashwagandha that extends back over 3000 to 4000 years ago wherein its use is widely extolled as a tonic particularly for emaciation in all age group of people. This causes enhancement of the reproductive function of both men as well as women (Mathur and Velpandian, 2009; Verma and Kumar, 2011; Mahima et al., 2012; Dhama et al., 2013a). Ancient ayurvedic scriptures named this plant Ashwagandha which means 'odour of the horse' as its roots smell like horse's urine. It is also known as Ashwakandika, Ashgandh, Gandhapatri and Palashparni.

The present evaluation describes Ashwagandha (*W. somnifera*) and its active compounds, mechanism of action and biological activity and classical beneficial applications of Ashwagandha in biomedicine and veterinary sciences viz., immunomodulatory effects, activity against microbes and infection and usefulness as an alternative, chemotherapeutic agent, promoting vigour and vitality, strain reliever, antidepressant, anti-inflammatory and adaptogenic property, cardioprotectant, role in treating sexual disability, potent anti-cancer effects, anti-aging activities, memory enhancer, treating neurodegenerative disorders, anti-viral properties.

Classification and Characteristics of Plant

1. Ashwagandha (*Withania somnifera* Linn)

2. Family-solanaceae/apocynaceae

3. Popular/common name: Indian ginseng/winter cherry: Ashwagandha is an exceptionally important medicinal plant with valuable and wide therapeutic benefits in the alternative system of medicine. The plant grows in form of shrub with branching, height reaches to around 150 cm, leaves are up to 10 cm long; flowers present greenish or lurid yellow color, fruits/berries when mature are orange colored and its seeds are sown mostly during month of June or July (Khanna et al., 2006a; Dasgupta et al., 2008). Roots are 20-30 cm long and 6-12 mm in diameter, with few (2-3) lateral roots of slightly smaller size, straight and are unbranched. Outer surface is buff to grayish-yellow with longitudinal wrinkles and in the center soft, solid mass with scattered pores. It has a characteristic odor, taste bitter and is acrid. Whole plant, leaves, roots, stem, green berries, fruits, seeds and bark are used for therapeutic purpose, while roots are mostly utilized (Kirtikar et al 1991).

Active constituents/compound/principle: Withania somnifera has more than 50 active chemical constituents. Steroidal alkaloids and lactones (Withanolides, Withaferins): Anaferine alkaloid, anahygrine, isopelletierine, cuseohygrine, Ashwagandhanolide (dimeric thiowithanolide), chlorogenic acid, beta-Sisterol, fruit cysteine, iron, scopoletin, somniferinine, somniferiene, tropanol, withananine, withanoside IV, withanolides A-Y (Steroidal lactones) and saponins sitoindosides and acylsterylglucosides. The sitoindosides VII-X and withaferin-A are anti-stress agents which support immunomodulatory actions and have antifungal properties also (Abraham et al., 1975; Choudhary et al., 1995; Singh et al., 2006). Most of the pharmacological activities of Ashwaganda have been attributed to two main withanolides, withaferin A and withanolide D (Singh et al., 2010).

Ethnopharmacological aspects : The pharmacological as well as metabolic effects of ashwagandha reveal that it can be used both as herbal tonic as well as health supplements. In rats the swimming time is increased by Ashwagandha as determined by physical working capacity test (swimming endurance test). By performing such test it has been found that the weight of the heart increases relatively and the content of glycogen in myocardium increased significantly (Dhuley, 2000).

Two major classes of compounds viz., steroidal lactones and steroidal alkaloids are accountable for the wide range of useful effects of Ashwagandha. Withanolides are a class of compound included in the group of steroidal lactones and are responsible for antioxidant properties as well as free radical scavenging activities. Till date several alkaloids, withanosides and withanolides have been studied. Several studies have also revealed the antimicrobial properties of ashwagandha along with antibacterial activity against potentially dangerous like Salmonella (food poisoning causing organism). The ability of macrophage and immune cells to eat pathogens is enhanced by the root extract of Ashwagandha in comparison to macrophages (in control group) that have not received ashwagandha (Davis and Kuttan, 2000b; Govindarajan et al., 2005; Owais et al., 2005).

Mode of action : Due to the property of helping in regulation of important physiologic processes Ashwagandha is assumed to be amphoteric. Withanolides act as important hormone precursor that has got the capability to convert into human physiologic hormones. According to some hypothesis, the plant-based hormone precursor occupies the receptor sites in the cell membrane thereby preventing the attachment and subsequent exertion of the effect of actual hormone. Some effect is exerted by the plant-based hormone if the level of native hormone is low (Misra, 2004). The anti-stress effect of ashwagandha was due to stimulation of respiratory function causing relaxation of smooth muscle along with stimulation of thyroid synthesis and secretion. Increase in dopamine receptors in the

corpus callosum of brain induced by stress is suppressed by ashwagandha. Stress-induced increase in corticosterone in plasma along with blood urea nitrogen as well as blood nitric acid is also reduced.

Bio-chemistry of *Withania somnifera* : Withanolide obtained from the roots of *W. somnifera* possess anti-inflammatory and analgesic activity due to its cyclooxygenase-2 inhibition property (Nair and Jayaprakasam, 2007). Peroxidases enzyme have been purified from this herb. Withanolides I-III and IV-V isolated from *W. somnifera* inhibited cholinesterase, acetylcholinesterase and butyrylcholinesterase, toxic phospholipase enzymes and therefore, are under consideration to be among the potent therapeutic candidate for treatment of Alzheimer's disease (Choudhary et al., 2004, 2005; Johri et al., 2005; Kambizi et al., 2006). Important constituent withanolides, withanosides can be isolated and purified by various techniques mainly by Ultra High Performance Liquid Chromatography (UHPLC) and spectrometry.

Immunomodulatory Effects: Immune system provides protection from invading pathogens and various cancers. The regulation of the immune system has been a major challenge for the management of autoimmune disorders, tumor immunity, infectious diseases and organ transplants. The immunomodulatory properties of *Withania somnifera* are well known and have been used in the formulations of 'rasayana', which makes the body resistant to diseases without any side effects. Trivedi et al (2017) studied immunomodulatory properties of *W. somnifera* based formulations in Sprague Dawley rats. They found noteworthy increase in CD4+ and CD8+ T-Cell populations in rats. In addition the concentrations of IgM and IgG antibodies were also improved. Besides, other supportive parameters like antioxidant profile and hematology was also improved.

A glycoprotein Glycowithanolides, commonly known as *Withania somnifera* glycoprotein (WSG), 28 kDa isolated from the *W. somnifera* root has demonstrated potent antimicrobial activity against the pathogenic fungi and bacteria. WSG protein shows fungicidal activity by inhibiting fungal spore germination and reduction of hyphal growth of *Fusarium oxysporum*, *F. verticilloides* and *Aspergillus flavus*. Antibacterial effect has also been seen against *Clavibacter michiganensis* subsp. *Michiganensis* bacteria. In vitro antibacterial property of *Withania* plant in laboratory plant cell culture is also on hand. These findings persuade further studies to explore wide horizons of WSG as a budding therapeutic agent against various fungi and bacteria (Girish et al., 2006; Jamil et al., 2007;).

Anti-Viral Properties :- Some study highlights the importance of natural origin phytochemicals in controlling COVID-19 entry into host cells, and provides an attractive and alternative means for the management of COVID-19 infection. *W. somnifera* could

will be the first choice of ayurvedic medicine in these directions, to control the COVID-19 infections. Studies done by Cai et al (2015) demonstrated that Withaferin-A (WA) has the potential to attenuate the neuraminidase (NA) of H1N1 influenza. Their docking and simulation results predicted high binding affinity of the WA toward NA and revealed several interesting molecular interactions with the residues which are catalytically important during molecular dynamic simulations. Many studies have revealed that withaferin A is a potential ligand to target/inhibit DNA polymerase of the Herpes simplex virus, thus can be used to develop potential drug against Herpes (Grover et al 2011).

Anti-inflammatory effects: In Ayurveda, Ashwagandha is considered as an anti-inflammatory herb traditionally used for the treatment of arthritis and asthma. The inflammatory response is a complex cascade of steps that include an activation of white blood cells and the production and release of inflammatory mediators. Ashwagandha reported to possess anti-inflammatory property in different pharmacological animal models of inflammation such as carrageenan-induced inflammation, cotton pellet granuloma and adjuvant-induced arthritis. It inhibited the granuloma formation in cotton-pellet implantation in rats similar to that of hydrocortisone sodium succinate (Uddin et al., 2012; Hindawi et al 1986; Hindawi et al 1992).

Anti-cancer effects: Studies reveals that *W. somnifera* can be used as synergizer to support conventional chemotherapy or radiation therapy due to its long term tumor growth inhibition property. Anti-carcinogenic effects are mainly on account of decreased expression of nuclear factor-kappa-B, suppression of intercellular Tumor Necrosis Factor (TNF) and potentiation of apoptotic signaling in cancerous cells of animals or cell lines (Singh et al., 2010; Dhama et al., 2013e).

Role against neurodegenerative disorders or Neuroprotective Effects: Neurodegeneration is the progressive loss of structure or function of neurons, including death of neurons. Parkinson's, Alzheimer's and Huntington's diseases occur as a result of neuro-degenerative processes. Researchers found that ashwagandha can support the growth of nerve cell dendrites, which allow these cells to receive communications from other cells. Thus ashwagandha can heal the brain tissue changes that accompany dementia and also promote the growth of both normal and damaged nerve cells, suggesting that the herb may boost up healthy brain cell function as well as benefit diseased nerve cells

CONCLUSION

The uses of ayurvedic medicines continue to grow in Covid-19 period with the expansion of modern medicine. The wonder herb *W. somnifera* (Ashwagandha) potentiates the immune functions, enhances the longevity and facilitates the restoration of homeostasis

by reducing the stress. Withaferin A (WA), an active constituent of *Withania somnifera* has been shown to have a broad range anti-viral activity with little or no side effects. The trusted reputation of Ashwagandha as an immunity enhancer forms the basis of researches for developing drugs for combating novel Coronavirus infections. Because of its wide pharmacological activities, Ashwagandha is considered as an important component of various polyherbal preparations. Thus the plant has got immense practical applicability in biomedicine as well as veterinary medicine focusing its potent role in the maintenance of sound health.

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