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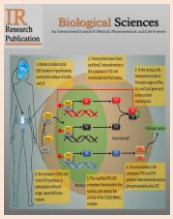

A literature review on pharmacological activities of *Withania somnifera*

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ABSTRACT

Withania somnifera, is a well-known medicinal herb in the Solanaceae family that has been used for over 3,000 years all over the world. It's also known as "Indian ginseng" and winter cherry, and it's an Ayurvedic and indigenous medicine. The fragrance is described by the word "*Withania somnifera*", which means "horse." In India, the Middle East, and portions of Africa, it is grown. Isopellertierine, anferine, withanolides, withaferins, and withanolides are the main components of *Withania somnifera*. It has the ability to treat a variety of health conditions, including anxiety, stress, antioxidant, anti-inflammatory, and antidepressant properties, as well as increase fertility and testosterone in males and regulate brain activities. Despite the fact that *Withania somnifera* has been used for a long time, further clinical trials are needed to improve therapeutic efficacy.

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 (18,19,20,28,29,8). Among ancient cultures, India has long been renowned as a rich storehouse of natural treatments (24,25,26,27). It's an Ayurvedic and traditional medication that's been used all over the world for over 3,000 years. Traditional medicine practitioners use natural active compounds found in medicinal plants to treat a variety of diseases. *Withania somnifera*, also known as *Withania somnifera*, 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*. From the Mediterranean to South Africa, and from the Atlantic Ocean to Southeast Asia, WS spans a large area. The presence of tannins, phenolics, terpenoids, flavonoids, saponins, glycosides, and, most critically, alkaloids and steroids is revealed by phytochemical screening of extractions. Withanolides are a term used to describe steroidal lactones and steroidal alkaloids. These bioactive chemicals are responsible for their diverse therapeutic potential as well as their economic significance. *Withania somnifera*, has been shown in studies to help with anxiety, cognitive and

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neurological illnesses like Parkinson's and Alzheimer's disease. Anti-tumour, anti-inflammatory, anti-oxidant, sedative, adaptogenic, antispasmodic, hypoglycemic, and diuretic properties have been documented for *Withania somnifera*. It may be a useful supplement for people receiving radiation or chemotherapy because of its chemopreventive characteristics. In patients with a low white blood cell count, *Withania somnifera*, can be utilized as an immunomodulatory and hematopoietic drug (30,31,32,33).

Taxonomic classification

Domain: Eukaryota
Kingdom: Plantae; Plants
Sub-kingdom: Tracheobionta; Vascular plants
Super-division: Spermatophyta; Seed-bearing plants
Division: Angiosperma; Flowering plants
Class: Dicotyledons
Order: Tubiflorae/Solanales; Tubular flowers
Family: Solanaceae
Genus: Withania
Species: Somnifera (16).

Vernacular names

Arabic: Kaknaj-e-Hindi
Bengaali: Ashvaganda, Asvagandha
English: Winter cherry
Gujarati: Asan, Asana, Asado, Asundha, Ghadaasoda
Hindi: Asgandh, Punir
Malayalam: Amukkiram, pevetti
Marathi: Askandha, Kanchuki, Tilli
Odiya: Ashgandha
Persian: Kaknaj-e-Hindi, Asgand Nagaori
Sanskrit: Ashvagandha, Ashvakandika, Gandhapatri
Tamil: Amukkira, Asubam, Asuvagandi, Asvagandhi
Telugu: Asvagandhi, Penneru, Dommadolu
Urdu: Asgand, Asgand Nagori

Description

Macroscopic

Stems: Brownish dark color and erect, sometimes leaves are absent or less on the lower part of the stem.

Leaves: Simple ovate, glabrous, and those in the floral region these are smaller and opposite.

Flowers- Green or yellow, born in axillary fascicles, giving rise to red globose fruits when mature.

Fruits- Round hairless berry, 5– 8 mm across, orange-red to red in ripped condition and is enveloped by the enlarged calyx.

Roots- Stout fleshy, whitish brown, more or less brown tuberous which are used for medicinal purposes.

Seeds- Yellow, reniform.

Microscopic

- Vascular bundles of root and stem are open.
- The cross-section view of the stem is circular with shallow ridges.
- The leaf is bifacial, dorsiventral.
- Fruit is mainly parenchymatous, resembling the spongy mesophyll of leaves (35).

Chemical constituents

The active chemical constituents of *Withania somnifera*, are withaferin A, ashwagandhine, withasomniferin-A, isopelletierine, withasomidienone, tropine, withanone, cuscohygrine, anahygrine etc (21,10).

Pharmacological activities of *Withania somnifera*

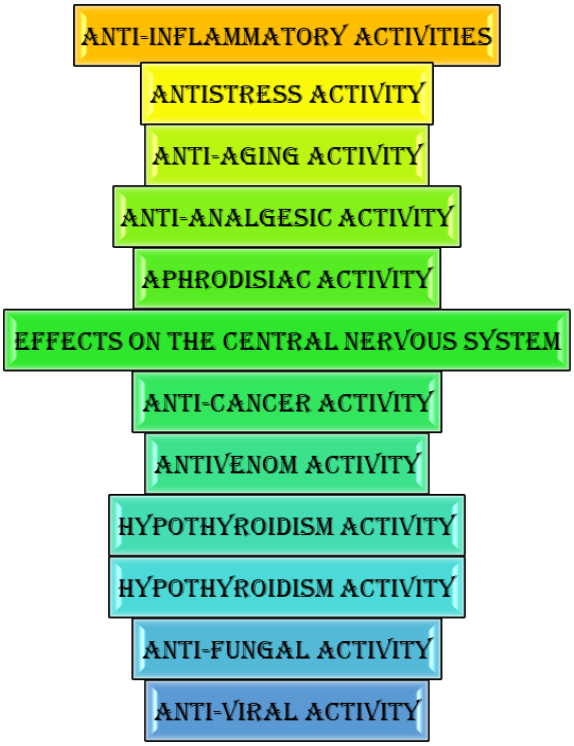

Figure 1. Pharmacological activities of *Withania somnifera*.

Anti-inflammatory activities

Withania somnifera, is an anti-inflammatory plant that can aid in the treatment of arthritis, asthma, and other inflammatory diseases. It has a far higher concentration of naturally occurring steroids than hydrocortisone, a commonly prescribed anti-inflammatory medicine. In one study, rats were administered orally a powdered root extract of *Withania somnifera*, one hour before getting anti-inflammatory injections for up to three days. The findings revealed that the components of *Withania somnifera* elicited anti-inflammatory responses (2). Using the human keratinocyte cell line HaCaT, the current study studied the antiinflammatory efficacy of *Withania somnifera* root water extract on skin. In HaCaT cells, *Withania somnifera* root water extract dramatically decreased mRNA expression of inflammatory cytokines such as interleukin (IL) 8, IL 6, tumor necrosis factor (TNF), IL1, and IL12, while promoting mRNA expression of the anti-inflammatory cytokine transforming growth factor (TGF). Furthermore, the lipopolysaccharide-induced phosphorylation of p38 and cJun N-terminal kinase, as well as nuclear translocation of nuclear factor (NF)B p65, were reduced by *Withania somnifera* root water extract. In vivo, after *Withania somnifera* root water extract treatment of mouse skin, there was a decrease in TNF mRNA and an increase in TGF1 mRNA. The anti-inflammatory action of *Withania somnifera* root water extract may be attributed to its capacity to decrease the NFB and mitogen-activated protein kinase pathways, as well as modulate cytokine expression, according to the findings. These findings imply that *Withania somnifera* root water extract may have anti-inflammatory properties (36).

Antistress activity

The effects of *Withania somnifera*, on chronic stress in rodents were investigated in a study conducted by Calcutta University's Institute of Medical Science. A small electric shock was applied to the animal's feet for 21 days. As a result of the stress, the animals acquired hyperglycemia, glucose sensitivity, increased male sexual dysfunction, stomach ulcers, plasma corticosterone levels, cognitive deficits, mental depression, and immunosuppression (5). According to researchers who utilized *Withania somnifera*, the animals who were given *Withania somnifera*, one hour before the foot shock were significantly less anxious. This investigation confirmed that *Withania somnifera* has a potent anti-stress and adaptogenic effect (6). Adaptogens improve non-specific resistance to stress and reduce sensitivity to stressors, resulting in stress protection and extending the resistance phase (stimulatory effect). *Withania somnifera*, an adaptogenic Ayurvedic plant, has long been used to battle and relieve stress, as well as to improve overall health. Other studies have documented the use of *Withania somnifera*, for stress resistance, but this is the first (37).

GABA-like activity has been found in *Withania somnifera*, extracts, which may explain the herb's anti-anxiety benefits (15). GABA is an inhibitory neurotransmitter in the brain. Its goal is to minimize neuronal activity and keep nerve cells from firing too much. This type of behavior has a calming effect on the human body. Excessive neural activity can induce agitation and insomnia, but GABA can help you fall asleep faster, reduce anxiety, and enhance your mood by lowering the number of nerve cells in your brain.

Withania somnifera, is an adaptogen that has anti-depressant and anti-anxiety properties in rodents, similar to imipramine (an anti-depressant) and lorazepam (an anti-anxiety drug) (4) *Withania somnifera*, is the most widely used tranquilizer/sedative in India.

Anti-analgesic activity

Withania somnifera, is a pain reliever that also helps to relax the neurological system (23). *Withania somnifera*, is well-known for its anti-arthritic qualities, but it's also used as an analgesic and antipyretic. The analgesic efficacy of *Withania somnifera*, was significantly boosted by cyproheptadine, but not by paracetamol, showing that serotonin, not prostaglandins, is involved in *Withania somnifera* 's analgesic effect (14).

Anti-aging activity

In a double-masked clinical trial, the anti-aging benefits of *Withania somnifera* were explored. The herb *Withania somnifera* was given to 101 healthy males aged 50 to 59 years old at a dose of 3 grams per day in a one-year double-masked clinical research. As a result, hemoglobin concentration, RBC count, seated posture, and hair melanin all improved significantly. Cholesterol levels in the blood were lowered, while calcium levels in the nails were retained. The incidence of erythrocyte sedimentation fell considerably, and 7.14 percent of individuals said their sexual performance had improved (7).

Aphrodisiac activity

Withania somnifera is an effective aphrodisiac. Men who take *Withania somnifera* produce more nitric oxide in their systems (NO). As a result, the blood vessels supplying blood to the genitals dilate, resulting in an increase in sexual appetite and

pleasure. As men age, the amount of testosterone produced in their bodies decreases drastically. The herb *Withania somnifera* has been demonstrated to boost testosterone levels considerably (1). Men's libido is known to be improved by *Withania somnifera*, which helps to increase sperm counts and endurance. *Withania somnifera* also aids in the improvement of sperm quality.

Effects on the central nervous system

The effects of a full alkaloid extract (Ashwagandholine, AG) derived from *Withania somnifera* roots have been examined (13). On the CNS (central nervous system) of cats, dogs, and mice, ashwagandholine had a calming and mild depressant (tranquilizer) effect. The effects of Sitoindosides VII-X and Withaferin isolated from *Withania somnifera* roots aqueous methanol extract on brain cholinergic, glutamatergic, and GABAergic receptors were investigated. It's possible that the ability of cortical muscarinic acetylcholine receptors to respond to medicines explains why *Withania somnifera* extracts improve cognition and memory in both animals and humans. Many medicines that generate smooth muscle spasms in the gut, trachea, uterus, and vascular muscles produced relaxing and antispasmodic effects when combined with Ashwagandholine (13).

Antivenom activity

Venom hyaluronidases aid in the rapid dissemination of poisons by interfering with the integrity of the extracellular matrix of victim tissues. A glycoprotein that inhibits hyaluronidase has been isolated from *Withania somnifera*. The hyaluronidase function of Cobra (Naja naja) and Viper (Daboia russelii) venoms is inhibited by the glycoprotein. The plant extract of *Withania somnifera* is used as an antidote for snakebite sufferers in rural India (9).

Anti-cancer activity

Withania somnifera has been demonstrated to have anti-cancer effects. Using animal cell cultures, researchers showed that the herb reduces nuclear factor kappaB (NF-B) levels, decreases intercellular tumor necrosis factor (TNF), and improves apoptotic signaling in malignant cell lines (11). One of the most exciting applications of *Withania somnifera* is its ability to fight cancer by decreasing tumors. In tests, withaferin, a component present in *Withania somnifera*, was demonstrated to aid in the induction of apoptosis in tumor cells. In a variety of situations, this also prevents the spread of new tumor cells.

To begin with, Withaferin is hypothesized to aid the production of reactive oxygen species (ROS) within tumor cells, which disrupts their function. Second, it may render tumor cells more susceptible to apoptosis. In animals, it appears to help fight cancers such as breast, brain, lung, colon, and ovarian cancer. Researchers investigated the anti-cancer properties of *Withania somnifera* to see if it may be utilized to treat various cancers. In one study, adult male mice with urethane-induced lung tumors were given *Withania somnifera* to see if it had anti-tumor capabilities (22). The lungs of animals given *Withania somnifera* for seven months had a histological appearance similar to that of control animals. Mice with ovarian cancer were given Withaferin alone or in combination with an anti-cancer drug in another study, and tumor growth was reduced by 70-80%. The medicine also prevented cancer from spreading to other parts of the body.

Hypothyroidism activity

Roots of *Withania somnifera* were given to human volunteers to see if they have hypoglycemic, diuretic, or hypocholesterolemic effects. Six persons with moderate NIDDM and six people with mild hypercholesterolemia received Withania somnifera root powder treatment for 30 days. Suitable criteria were examined in the subjects' blood and urine samples, as well as their dietary patterns, before and after the treatment. Blood glucose levels were brought down to the same level as with oral hypoglycemic medication. The root of *Withania somnifera* was found to have a significant increase in urinary sodium and volume, as well as a significant decrease in triglycerides, serum cholesterol, LDL (low-density lipoproteins), and VLDL (very low-density lipoproteins) cholesterol, suggesting that it could be a source of hypoglycemic, diuretic, and hypocholesterolemic agents.

Hypothyroidism activity

Animal studies have demonstrated that *Withania somnifera* has thyrotropic properties. Mice were stomach intubated and given an aqueous extract of dried *Withania somnifera* root every day for 20 days. The concentrations of T3 and T4 in serum collected at the end of the 20-day cycle were measured. T4 levels in the blood increased considerably, indicating that the plant had a stimulating effect at the glandular level. T3 levels did not improve in any way. *Withania somnifera* can indirectly enhance thyroid activity by affecting cellular antioxidant systems. These data suggest that *Withania somnifera* may be useful in the treatment of hypothyroidism (3,17).

Anti-fungal activity

By suppressing spore formation and hyphal development in phytopathogenic fungi (e.g., Aspergillus flavus and Fusarium verticilloides), a glycoprotein from *Withania somnifera* acts as a fungistatic agent. Candida albicans has been proven to be resistant to flavonoids derived from *Withania somnifera*. Aspergillus flavus and Aspergillus niger also showed resistance to *Withania somnifera* (9,21).

Anti-viral activity

Chikungunya, herpes simplex virus (HSV), human papillomavirus (HPV), parainfluenza-3, hemagglutinin type 1, and neuraminidase type 1, hepatitis C virus, SARS-CoV & SARS-CoV-2 virus have all been demonstrated to be effective with phytochemicals from *Withania somnifera*. *Withania somnifera* bioactive substances (such as Withaferin A and Withanolides) have significant antiviral action, making them effective in the treatment of COVID-19 patients (12).

Conclusion

Despite the fact that *Withania somnifera* has been used in Ayurvedic medicine for centuries, further clinical research is needed to back up its efficacy. The results of this study can be used to build cost-effective formulations of active chemical compounds in natural medicines to treat a variety of neurological and inflammatory conditions in the future. Synthetic chemicals are high cost as compared to natural plants. For a long time, there has been a tremendous disagreement between Ayurvedic treatment and Western medicine. While biomedicine and modern medications are primarily concerned with reducing pathology, Ayurveda is known for taking a holistic approach to ailments and general wellness. *Withania somnifera* is one of the most well-known medicinal plants, with immunomodulatory, anti-cancer, anti-depressant, neuroprotective, and other biological activities. Increased resistance, unavoidable adverse effects, efficacy loss due to continuous usage, and high cost are all issues that modern conventional medicines face. Researchers have been driven to derive bioactive medicinal chemicals and medications from natural sources such as herbal plants. *Withania somnifera* can provide overall protection to mental and neuronal health.

Contribution of authors

The author has done exhaustive literature survey from google scholar, pubmed, shodhganga etc, and various search engines to put best knowledge.

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Conflict of interest

There is no conflict of interest by the author.

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