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RESEARCH ARTICLE

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Ashwagandha: THE HERO PLANT

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ABSTRACT

Withaniasomnifera L. is a multipurpose medicinal plant of family Solanaceae occurring abundantly in subtropical regions of the world. *W. somnifera* is rich in numerous treasured secondary metabolites such as steroids, withanolidealkaloids, flavonoids, phenolics, saponins, and glycosides. In recent years, there has been a significant surge in reports on the health-promoting benefits of winter cherry also known as Ashwagandha. The present review states its potential use as neuroprotective, sedative, adaptogenic anti-inflammatory, antimicrobial, cardioprotective and anti-diabetic properties. The antitumor and anticarcinogenic bio-functional compounds make it most sought after plant for pharmaceutical industries. It also has antioxidant, anxiolytic and adaptogenic properties, making it a Hero plant, but it is fast diminishing from the wild and its sustainable use and conservation is the need of the hour.

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INTRODUCTION

Nature has provided all the essentials to support and flourish the mankind. Being either food, fodder, shelter or medicines, nature nurtured and fulfilled our desires. When it comes to providing food, it gave us a wide range of crops. Also, nature is a treasure chest of large diversity of medicinal plants. The search for drugs in nature by man dates from the far east, and this search resulted the evolution of different modern medicinal systems. The curative powers of medicinal plants constitute the basis of all the indigenous systems of medicine namely Ayurveda, Unani, Siddha and Tibetan Medicine. Medicinal herbs have a great history in the realm of drug treatments, and are currently receiving attention as sources of synergistic combinations. More over medicinal plants made a lot of contribution towards the discovery of large number of new generation synthetic drugs. Recognition of the medicinal and the economic benefits of these plants are on increase in both developing and industrialized nations. Thus, in all aspects of research and development, the exploration and evaluation of phytopharmacological effect of herbal drugs are relevant. Also, we have to safely preserve the knowledge of medicinal plants and herbal remedies, which humankind has received from the past generations for posterity. *Withania somnifera* has been an important herb in the Ayurvedic and indigenous medical systems for over 3000 years. The roots of the plant are categorized as rasayanas, which are reputed to promote health and longevity by augmenting defense against disease, arresting the ageing process, revitalizing the body in debilitated conditions, increasing the capability of the individual to resist adverse environmental factors and by creating a sense of mental wellbeing [1]. It is in use for a very long time for all agegroups and both sexes and even during pregnancy without any side effects [2].

Its leaves are used in Ayurvedic and Unani systems for treatment of tumors and tubercular glands [3]. A number of steroids, isolated from the leaves of *W. somnifera* exhibit antibacterial, anti-fungal and antitumor properties [4]. Ashwagandha is used to calm the mind, relieve weakness and nervous exhaustion, build sexual energy and promote healthy sleep. The herb is termed a rasayana. in Ayurvedic practice, which means it acts as a tonic for vitality and longevity. It is also classified as an adaptogen [5].

Withania Somnifera: Family Solanaceae.

Common Name: Winter Cherry, Indian Winter Cherry, Indian Ginseng (English) Ashwagandha, *Withania somnifera* plant and Seeds [6].



Habit and Habitat: *Withania somnifera* is a small, erect, tomentose (covered with a dense mat of woolly), evergreen, woody shrub belonging to Solanaceae family that can grow up to 2-5 feet in height. It can be found growing in Africa, India, Baluchistan, Pakistan, Afghanistan, Sri Lanka, Congo, South Africa, Egypt, Morocco and

Jordan and the Mediterranean. In India, it is cultivated, commercially in drier parts of the country such as the states of Madhya Pradesh, Uttar Pradesh, plains of Punjab, and northwestern parts of India like Gujarat and Rajasthan [7]. Roots are stout fleshy, whitish brown; leaves simple ovate, glabrous, those in the floral region smaller and opposite; flowers inconspicuous, greenish or lubrid-yellow, in axillary, umbellate cymes; berries small, globose, orange-red when mature, enclosed in the persistent calyx; seeds yellow, reniform. The bright red fruit is harvested in the late fall and seeds are dried for planting in the following spring. Ashwagandha in Sanskrit means "horse's smell" probably originated from the odor of its root, which resembles that of sweaty horse. The species name *somnifera* means 'sleep-inducing' in Latin, indicating its sedating properties. Roots, leaves, stem, green berries, fruits, seeds, bark, in fact the whole plant is medicinally valuable and utilized in various disease treatments.

Uses in Ayurveda, Unani and Allopathy: More than 100 formulations in Ayurveda, Unani and Allopathy are known in which Ashwagandha is used as a major Ingredient [8]. It is one of the prime drugs of Ayurvedic medicines. Ancient Indian ayurvedic practioner Acharya Charak summarized its Balya and Brimhana-gana properties [9] (the term Balya in Ayurveda refers to those medications that are associated with enhancement of the "Bala" or strength while the term Brimhana, as described in charak Samhita, refers to nourishing and strengthening the depleted body parts). Apart from sedative properties, it has been also used for sexual vitality and as an adaptogen. Ethno-medicinally, decoction of the roots is used for colds and chills; and to increase the tone of uterus after miscarriage or birth. An infusion of the root bark has been used for asthma, a use also common to traditional herbal practices in India. In Ayurvedic medicine, its root is used as an anti-inflammatory drug for swellings, tumors, scrofula and rheumatism; and as a sedative and hypnotic in anxiety neurosis. Leaf possesses anti-inflammatory, hepatoprotective, antibacterial properties. Fruits and seeds are diuretic. As per ayurvedic literatures, Ashwagandha is used for various disease medications e.g. Murchha (syncope), Apasmara (epilepsy), Shosha (cachexia), Unmada (mania/psychosis), Karshya (emaciation), Arsha (piles), Pramehapidika (diabetic carbuncle), Arbuda (tumor), Gandamala (cervical lymphadenitis), Bhagandara (fistula-in-ano), Guhya-vrana (ulcer in genitalia), Vatarakta (gout), Kushtha (diseases of skin), Kilasa (vitiligo), Asthibhanga (bone fracture), Katigraha (stiffness in lumbo-sacral region), Gridhrasi (sciatica), Hanugraha (lockjaw), Janustabdhat (stiffness of the knee), Hrudgraha (cardiac failure), Yonidosha (disorders of female genital tract) and Vidradhi (abscess) [10,11].



Some Ayurvedic medications containing *Withania somnifera* as chief-constituent

It is used as an ingredient many formulations such as Ashwagandhadi-churna (Improves vitality), Ashwagandha-rasayana (helpful in nerves weakness, blood pressure, insomnia, cold, cough, psoriasis, and skin diseases, mental stress etc.), Ashwagandha-ghrita, Ashwagandha-rishta, Ashwagandha-taila, Madhyamanarayana-taila, Brihat

Ashwagandha-ghrita, Brihachchhagaladyaghrita, Saraswata-churna, Pramehamihira-taila [12], Nagabala-ghrita, Madhusnuhi-rasayana [13]. In Unani medical practices, as per the book "kitab-Ul-Hashaish", therapeutic properties of Asgard is useful in treatment of Endocrine, cardiopulmonary, central nervous system (Depression, Dementia, Anxiety, Insomnia) and sexual problems (low sperm count, low semen volume, low sperm production and mobility, abnormal sperm shape). The two varieties of *Withania* (Asgand) mentioned in classical Unani literature:

- 1) Asgard Nagori
- 2) Asgard Dakani.

Asgand Nagori is preferred for its more potential medicinal properties [14].

Chemical Composition: There are more than 35 chemical constituents found in the roots of *Withania somnifera* [15]. Some known biologically active chemical constituents are alkaloids (isopellertierine, anaferine), steroidal lactones (withanolides, withaferins), saponins containing an additional acyl group (sitoindoside VII and VIII), and withanoloides with a glucose at carbon 27 (sitoindoside XI and X) [16]. *Withania somnifera* is also rich in iron.

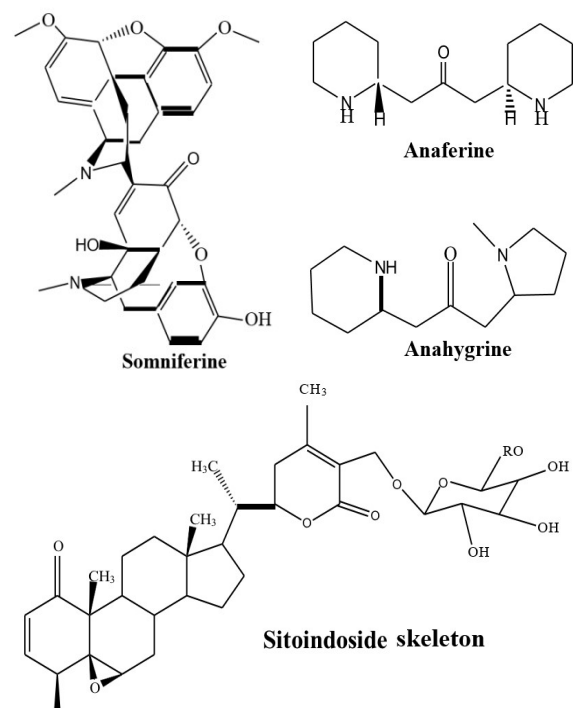
Chemical compounds Obtained from different parts of *W. somnifera*

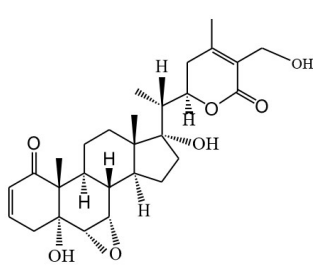
Root: 18 fatty acids, beta-sitosterol, polyphenols and phytosterols. The root contains several alkaloids, including withanine, withananine, withananine, pseudo-withanine, somnine, somniferine, nicotine, tropine, pseudotropine, choline, cuscudohygrine, anaferine, anahygrine, somniferine. The free amino acids present in the root include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid and cysteine [17].

Leaf: withanolides, including withaferin A, somnirol, somnitol. Withanine is sedative and hypnotic.

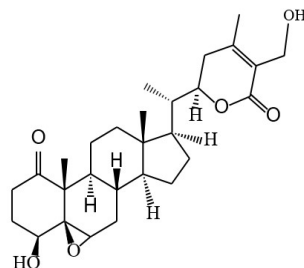
Seed: The seeds are known to contain many withanolides, withaferin A, and dihydro withaferin A1 and A2.

Structure of Some phyto-constituents of *Withania somnifera*

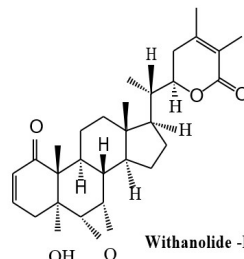




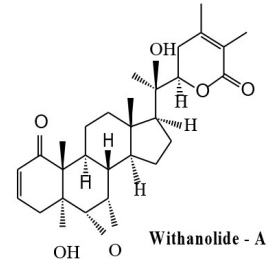
27-Hydroxywithanone



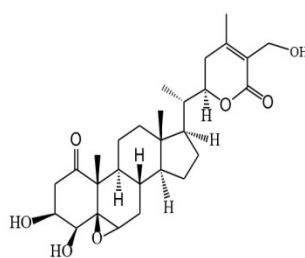
Dihydrowithaferine - A



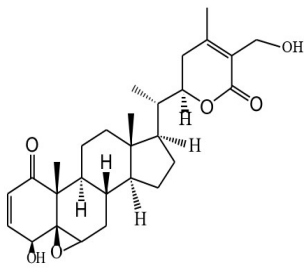
Withanolide - B



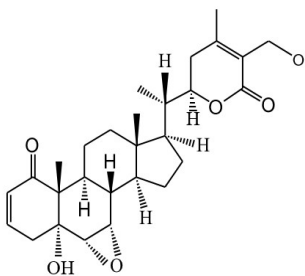
Withanolide - A



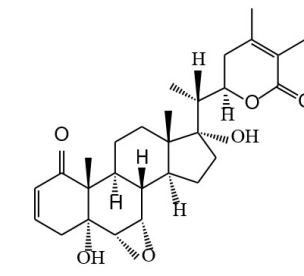
Viscosalactone - B



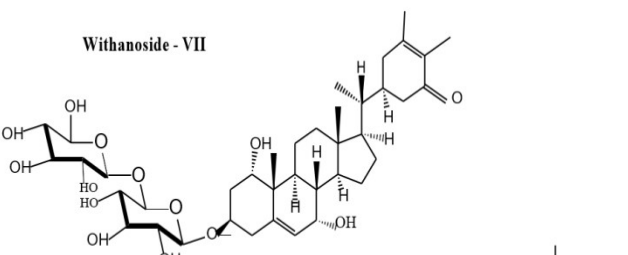
Withaferine - A



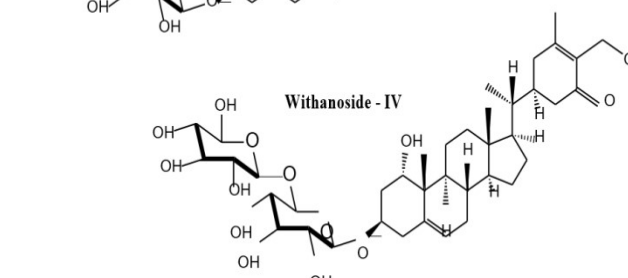
12-Deoxywithastramonolide



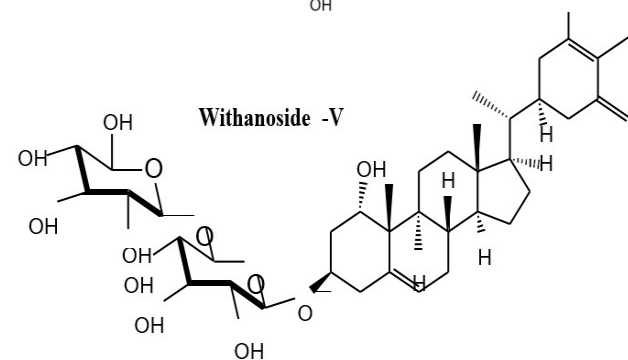
Withanone



Withanoside - VII



Withanoside - IV



Withanoside - V

COMPOUNDS	PHYTO-CHEMICALS
Alkaloids	Anaferine, Anahygrine, Cuscohygrine, Scopoletin, Withanine, Withananine, Somnine, Somniferine, Tropeltigloate, Somniferinine, Nicotine, Visamine, Withasomine, and Pseudotropine
Steroids	Cholesterol, β -sitosterol, Stigmasterol, Diosgenin, Stigmastadien, Sitosinoides VII, Sitosinoides VIII, Sitosinoides IX, and Sitosinoides X
Steroidal Lactones	Withaferin-A, Withanolide E, Withanolide F, Withanolide G, Withanolide H, Withanolide I, Withanolide J, Withanolide K, Withanolide L, and Withanolide M, Withanone

Two withanolides, withaferin A and withanolide D have been the most widely pharmacologically studied compounds. However, the presence of the following phyto-constituents has also been reported: Anaferine (Alkaloid), Anahygrine (Alkaloid), Beta-Sisterol, Chlorogenic acid (in leaf only), Cysteine (in fruit), Cuscohygrine (Alkaloid), Iron, Pseudotropine (Alkaloid), Scopoletin, Somniferinine (Alkaloid), Somniferine (Alkaloid), Tropanol (Alkaloid), Withanine (Alkaloid), Withananine (Alkaloid) and Withanolides A-Y (Steroidal lactones) [18,19]. The traditional uses of 'Ashwagandha' are to increase energy, youthful vigor, endurance, strength, health, nurture the time elements of the body, increase vital fluids, muscle fat, blood, lymph, semen and cell production. It helps to counteract chronic fatigue (Myalgic encephalomyelitis), weakness, dehydration (water loss in body), bone weakness, impotency, premature aging, emaciation (extremely absence of body fat and muscles due to malnutrition), debility (weakness due to illness), convalescence and muscle tension. These pharmacological activities are mainly contributed by the steroidal alkaloids, withaferin A and withanolide D.

Pharmacological Activity: As per Ayurvedic med literatures, the chief pharmacological value of *Withania somnifera* are as adaptogen, antibiotic, abortifacient, aphrodisiac, astringent, anti-inflammatory, deobstruent, diuretic, narcotic, sedative, and tonic. Ashwagandha has been found to:

- Provide potent antioxidant protection [20,21].
- Stimulates for activation of immune system [22,23].
- effective in stress treatment and generally promoting wellness [24].

Anti-inflammatory Activity: Withaferin A exhibits strong anti-arthritis and anti-inflammatory activities. Withaferin A is a major biologically active steroid component, attributed to Anti-inflammatory activity. It is as effective as hydrocortisone sodium succinate dose for dose [25]. It suppresses arthritic syndrome effectively. Another great feature of *Withania somnifera* is that in arthritic syndrome, the patients treated with hydrocortisone lose their body weight while the patients treated with *Withania somnifera* gain weight due to the pharmacological activity of withaferin A. In classical Ayurvedic literatures, *Withania somnifera* has been described as an anti-inflammatory herb, being used in the treatment of arthritis and asthma. The inflammatory response is a complex series that include an WBC activation and the production and release of inflammatory mediators.

Anti-stress: In an experimental study made on rodents by Institute of Basic Medical Sciences at Calcutta University about effects of stress on animals showed stress produced results like hyperglycemia,

glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression [26]. Researchers observed that animals that were treated with ashwagandha dose prior to the test, experienced a significantly reduced level of stress. This proved the assumption that Ashwagandha has a significant anti-stress adaptogenic effect [27]. In another research conducted at the Department of Pharmacology, University of Texas Health Science Center demonstrated that extracts of Ashwagandha produce anti-anxiety effects [28]. Certain researches have revealed that the herb produces an antidepressant and anti-anxiety effect [29]. It is one of the most widely used tranquilizers in Indian medicines.

Antibiotic Activity: several researches have experimentally shown the antibiotic activity of the roots as well as leaves of ashwagandha. Withaferin A blocks and retards the growth of various Gram-positive bacteria, acid-fast and aerobic bacilli, and fungi. It showed the protective action against systemic *Aspergillus* infection [30]. The unsaturated lactone-ring, responsible for the Antibiotic activity of Withaferin A showed strong therapeutic activity, somewhat stronger than that of Penicillin.

Antioxidant effect: In our body, the most susceptible parts for free radical damage are brain and nervous system than any other tissues because they are rich in lipids and iron content. This susceptibility is due to the fact that both of the systems (brain and nervous system) are involved in generating reactive oxygen species. Various normal aging and neurodegenerative diseases associated with free radical damage of nervous tissue are epilepsy, schizophrenia, Parkinson's, Alzheimer's, and other diseases. Sitoinosides VII-X and withaferin A (glycowithanolides), the active principle phyto-constituents of *Withania somnifera*, have been tested for antioxidant activity using the major free-radical scavenging enzymes, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) levels in the rat brain frontal cortex and striatum [31]. These enzymes control the toxic effects of free radicals. Decreased activity of these enzymes followed by accumulation of toxic oxidative free radicals in great concentration leads to neurodegenerative effects. An increase in these enzymes would represent increased antioxidant activity and a protective effect on neuronal tissue. Antioxidants play an important protective role against free radicals or reactive oxygen species. The potent antioxidant property of Ashwagandha extract is useful in Premature aging caused due to increased oxidative stress [32].

Antimalarial Potential: Malaria, caused by *Plasmodium falciparum* is an ongoing challenge to the scientists due to the resistance development of pathogen against chloroquine. Apart from the high cost, the side effects of the drug have led the researchers to look after a new potent antimalarial medicine with little or no side effects. In vivo investigation of antiplasmodial activity of *Withania somnifera* extracts showed significant inhibition of parasite [33]. The hot aq. root extracts of *W. somnifera* with chloroquine, showed improved disease potency against chloroquineresistant pathogens [34].

Neuroprotective Effects: The Neuroprotective effects of *Withania somnifera* includes protection and healing of neuro-degenerative diseases such as Parkinson's, Alzheimer's and Huntington's diseases which leads to structural and functional loss of neurons, leads to death of these messenger cells. In various research studies it was found that Ashwagandha can support the growth of neural dendrites. 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 [35, 36]. In an experiment carried out on Swiss albino rats, it was observed that *Withania* root extract was helpful in treating degenerating nerve cells [37]. The withanolide isolated from *Withania somnifera*, inhibited the chief enzyme causing breakdown of neural messenger cells [38, 39]. The study demonstrates that the extract of *Withania somnifera* may be helpful in protecting the neuronal injury in Parkinson's disease [40].

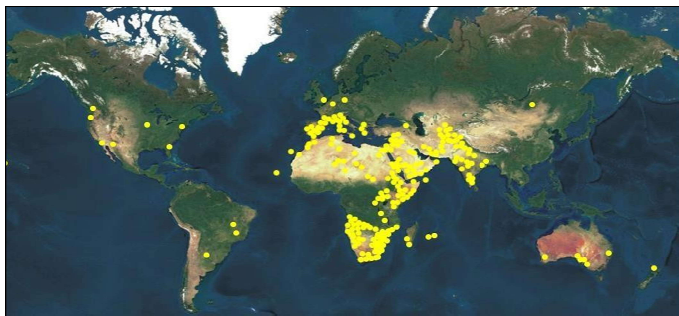
Cardiovascular protection: In an experimental study on cardiovascular and respiratory systems dogs and frogs the effect of *Withania somnifera* was found to have a prolonged hypotensive, brady cardiac, and respiratory stimulant action [41]. This hypotensive effect was mainly due to autonomic ganglion blocking action which also contributed to the hypotension. The alkaloids also stimulated the respiratory centers. The cardio-inhibitory action in dogs appeared to be due to ganglion blocking and direct cardio depressant actions.

Immunomodulatory Activity: Immune system in our body provides protection against invading pathogens. The immunomodulatory properties of *Withania somnifera* have been used in the formulations of 'rasayana', which makes the body resistant to diseases without any side effects. Several other scientific researches, carried out on immunomodulatory properties, support these findings. *Withania somnifera* also reported to possess immunopotentiating and myeloprotective effect, which increases the production of cytokine, stem cell proliferation and its differentiation. Scientific study carried on administration of *Withania* extract showed a significant increase ($P < 0.001$) of bone marrow cellularity, total WBC count and α -esterase positive cell number. Various withanolides (withanolide G, G, M, Q) have great potential to boost immunity. The herbal extracts of ashwagandha are used in prevention of COVID-19 infection [42]. Asgand showed a significant modulation of immune reactivity in animal models. *Withania* in association with three immunosuppressive drugs viz. cyclophosphamide, azathioprin, and prednisolone showed significantly increased level of immunosuppression action of the drug. In an experiment carried on mice, Asgand treatment was found to increase Hb concentration, RBC count, platelet count, and body weight [43]. Immunosuppressive effect of Withaferin A and Withanolide E are specially associated with human B and T lymphocytes and on mice thymocytes. Withanolide E had specific effect on T lymphocytes whereas Withaferin A affected both B and T lymphocytes [44, 45].

Anti-carcinogenic activity: Ashwagandha is reported to have anti-carcinogenic effects. The most exciting property of Ashwagandha is its capacity to fight cancers by reducing tumor size [46,47]. Research on animal cell cultures has shown that the herb decreases the levels of the nuclear factor kappa B, suppresses the intercellular tumor necrosis factor, and potentiates apoptotic signaling in cancerous cell lines [48]. *Withania somnifera* is reported to have antitumor, antioxidant, anti-inflammatory and immunoregulatory properties. The chemopreventive properties of *Withania somnifera* make it a potentially useful adjunct for patients undergoing radiation and chemotherapy. It not only supports the health of patients undergoing conventional cancer treatment and but also cures the after effects such as carbuncles, ulcers and painful swellings.

Other Therapeutic Properties: In addition to the modern medicinal properties, *Withania somnifera* traditionally used in the treatment of several other human ailments like osteoporosis [49]. Osteoporosis, often described by reduction in bone density, plays a major role in mortality rate in India. Ethanolic extract of *Withania somnifera* root contains withanolides, that is found to be effective for antiosteoporotic activity. The particular study concluded that Ashwagandha root extract may have some role in decreasing serum urea and creatinine levels and normalize the kidney weight against gentamicin toxicity, which may be due to its ability to inhibit free radicals [50]. This potency of Ashwagandha is a prove miracle for kidney patients. In rural parts of India, *Withania somnifera* extract is used for external applications as an antidote to snakebite.

IUCN Status: A research carried out by two scientists in Jharkhand state of India led to the conclusion that *W. somnifera* is undergoing at an alarming rate of disappearance in several districts like Lohardaga [51]. This disappearance was due to the local villagers and forests tribes using this species at a high risk rate.



WORLDWIDE DISTRIBUTION OF *Withania somnifera*

Urgent Need for Conservation: Due to overexploitation from natural resources, this plant has been reported to face a serious danger. Hence it is thought to come under Endangered Category for Asian countries. However, due to lack of enough data on a global scale it has been placed in data deficient category by IUCN. This over exploitation is due to its pharmacological as well as traditional values. The tribes and villagers that are dependent on forests for their daily needs sometimes over-use the specimen without considering its extinction rate. The major problem associated with its extinction is due to a large number of phytochemicals found in the plant root. To get those benefits, the whole plant is uprooted. This causes death of the plant as there are no chances of regeneration. This is the main reason for disappearance of the specimen in several parts of the world including India. Apart from that various multi-bagger pharmaceutical companies that are involved in medicine manufacturing exploit the plant to a greater extent wherever possible.

CONCLUSION

Withania somnifera, an herbaceous plant is known to play many crucial roles in medicinal field since time immemorial. The plant-based researches revealed that it is an important ingredient in Ancient Ayurveda, where it was an important remedy for diseases related to skin, endocrines, gastro, neural, as well as various other illnesses. Apart from Ayurveda it is widely used in Unani and allopathy formulations. The plant is known to be associated with various pharmacological activities like antioxidant, anxiolytic, adaptogen, memory enhancing, antiparkinsonian, anti-inflammatory, antitumor properties. Various other effects were also reported like immunomodulation, hypolipidemic, antibacterial, cardiovascular protection, sexual behavior etc. *Withania somnifera*, best known as Ashwagandha has been used for centuries for the treatment of vivid health disorders. Multiple health benefits featured in this herbal supplement makes it as a perfect rejuvenator of physical and psychological health. As per research, this medicinal herb is mainly found in the regions of North America and India. Powerful antioxidant compounds enriched in this herb scavenges free radicals and reduces aging impact on person. Apart from consuming this extract, diet taken by person plays an important role in increasing the level of antioxidants in body. In order to obtain good level of antioxidants, it is advised to include surplus amount of fruits and vegetables in diet. Apples, berries, onions and carrots are some among the top listed food items enriched with antioxidant compounds. Among the list of prestigious medicinal herbs, *Withania somnifera* holds a good place. Be it debility cure or sexual health or stressbuster properties, *W. somnifera* is a god gifted herb. The description of Ashwagandha in Ashtangahridaya (Sutrasthana) by Vagbhata and in Charaksamhita by ancient med-practitioner Charak speaks a lot about its values. Out of six pillars of Ayurveda, the balya and brimhana therapy merely uses ashwagandha extract in various medicinal formulations.

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