

PHARMACOLOGICAL PROFILE OF WITHANIA SOMNIFERA – A REVIEW

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ABSTRACT

Withania somnifera (Ws) belonging to the family Solanaceae is traditionally known as *Amukkara Kizhangu* in Siddha system of medicine. It is a short herb that grows naturally around the Indian subcontinent. It has been used for centuries in India as an adaptogenic herbal remedy to improve overall health, vitality and longevity. Use of *Amukkara kizhangu* can be traced back to at least 4000 years. It has been used predominantly as an adaptogen for therapeutic purposes in Siddha. It benefits our health in various ways. The plant is believed to improve memory, support the immune system and generally aid in optimizing the physiological functions of the body. Historically, the

herb has also been used as a sex enhancing tonic owing to its potent activity as an aphrodisiac. It also possesses Antiparkinsonism, Antioxidant, Anti inflammatory, Anti tumour, Hypnotic, Sedative, Memory enhancing, Aphrodisiac, Diuretic, Febrifuge properties. Various other effects like Hypolipidemic, Antibacterial cardiovascular protection also been studied. This review article is presented to compile all the updated information on its phytochemical and pharmacological activities.

KEYWORDS: *Withania somnifera*, *Ashwagandha*, *Amukkara kizhangu*, Siddha Medicine, Herbal medicine, Traditional medicine.

INTRODUCTION

The plant kingdom has been an intimate companion to mankind down through the ages. In the yester years, when the synthetic drug epoch was not existent, man found a solace in plants for all his basic and therapeutic needs. In India, Ayurveda and Siddha were the two chief

therapeutic systems that had their foundation laid on the plant kingdom. The early physicians explored the heterogeneous nature of each therapeutic plant in detail. *Withania somnifera* is one such plant whose diverse salubrious activities were investigated by the early physicians. The plant is widely used in the treatment of diverse ailments in India. Dioscorides (78 AD) the early Greek philosopher and physician described the pharmacological efficacy of this plant in his research book '*Kitab-ul-Hashaish*'.^[1]

NOMENCLATURE AND GENERAL HABITAT

The plant belongs to the nightshade family of Solanaceae. It is called as *Ashwagandha* in Sanskrit, *Amukara* in Tamil, *Ashgandh* in Hindi, *Rasbhari* in Kannada, *Vajigandha* in Telugu and *Amukkuram* in Malayalam. The herb is also popularly known as Winter cherry or Indian ginseng and is a common habitat of parched lands. The Sanskrit name '*Ashwagandha*' means 'smell of a horse' denoting its horse like odour of the roots.^[2] The plant is a native of India, Sri Lanka and other Mediterranean countries like South Africa and the Canary islands. In India, the herb is commonly found in Western India, Punjab, Madhya Pradesh and some parts of Rajasthan.^[3,4] The shrub is also seen in the Himalayas at a high altitude of about 5500 feet above sea level. But throughout the country, the plant has been cultivated owing to its rich therapeutical properties.

ASHWAGANDHA IN INDIAN SYSTEM OF MEDICINE

The plant has been used to treat a myriad of infections and diseases since time immemorial. Both vegetative and reproductive parts of the plant are used in Ayurveda, Siddha and Unani systems of medicine. The shrub is highly recommended for treating multiple arthritis like lupus, Rheumatoid and Psoriatic arthritis. It is also used to treat generalized inflammation, involuntary ejaculation, sexual weakness, memory loss, mental instability, scabies, ulcer of different kinds and leucorrhoea.^[1] In addition, the plant has antibacterial, antioxidant and adaptogenic properties. The plant is often called as the '*Rasayana* herb' and the different extracts of the plant is used traditionally to surge the vital fluids of the body. The plant is also long been used as an ayurvedic adaptogen.^[5]

PHYTOCHEMISTRY

Withania somnifera (Ws) is one of the plant kingdom's exchequer of phytochemicals. Phytochemical research has proven that the plant possess more than 35 bio efficient chemical constituents. Majority of these phytochemicals are alkaloids, steroidal lactones, saponins and withanolides. Some of the alkaloids present in the plant are Anaferin, Anahygrine,

Cusohygrine, Pseudotropine, Somniferinine, Somniferinine, Tropanol, Withanine and Withananine. Withanolides are steriodals resembling ginsenosides in Asian ginseng and are active components of research in animal studies for various medical conditions like cancer and auto immune disorder.^[6]



Fig.1: Withania somnifera plant.

PHARMCOLOGICAL PROPERTIES

Ayurvedha, Siddha and other traditional system of medicine have done extensive research on the plant in view of its pharmacological efficacy. The plant is highly valued as adaptogen, sexual enhancer, astringent, anti-inflammatory, diuretic, narcotic, sedative and tonic.^[7,8]

ANTI - INFLAMMATORY PROPERTY

The plant acquires high anti arthritic and anti inflammatory activities. This is because of the rich presence of steroids like Withaferin. In a research study, the arthritis induced animals treated with the plant extract gained weight in contrast to the hydro cortisone treated animal models which lost weight during the study period. This study illustrates the ameliorating effects of Withania when compared to the standard synthetic drug hydrocortisone. In addition the dose response was relatively higher in the range of 12-25mg/kg body weight in oedema inhibition test.^[9] A single intraperitoneal dose showed commendable changes in inflammation reduction within short duration. Begum and Sadique (1987) reported the effect of Ws on glycosaminoglycan production of granulation induced air pouch granuloma. When 1000mg kg⁻¹ Ws root powder was administered, glycosaminoglycan content was substantially reduced to 92% in comparison with hydrocortisone and phenylbutazone.^[10]

Anabalagan and Sadique studied in detail the release of serum β -1 globulin during inflammation by adjuvant induced arthritis and formaldehyde-induced arthritic animal models. The results showed the plant extracts suppressed the inflammation to a greater degree.^[11]

ANTI-STRESS AND ANTI-ANXIETY ACTIVITY

Bhattacharya *et al.*, (2001) studied the antistress efficacy of Ws extract on stress induced rats using periodical mild electric foot shock for 21 days. This disturbed the normal levels of superoxide dismutase (SOD) and lipid peroxidation (LPO) activity, with concomitant decrease in catalase (CAT) and glutathione peroxidase (GPX) activities in both the brain regions. The administration of the plant extract (10, 20, 50 mg/kg) one hour before the administration of the shock was found to induce a dose dependent reversal of the stress outcome. The plant extract tried to normalize high levels of SOD and LPO activities and increased the CAT and GPX. This preclinical study supports the antistress adaptogenic efficacy of Ws.^[12] Another study reported the GABA-mimetic pharmacological activity of Ws root extract on GABA receptor complex. The results showed inhibition of [3H] GABA and [35S] TBPS binding to their respective sites by the root extract. The efficacy increased with concentration. In addition, the root extracts increased ³⁶Cl-influx in the absence of GABA (Gamma Amino-butyric acid) during functional studies using ³⁶Cl-influx assay in spinal cord neurons of mammals.^[13] Research has revealed that GABA is the inhibitory neurotransmitter of the brain which reduces the neuronal activity and inhibits the nerve cells from excess pressure which leads to anxiety and sleeplessness.

These studies indicate that extract of *Ashwagandha* produce GABA-like activity, which may account for the herb's anti-anxiety effects. *Ashwagandha* has long been used in traditional system of medicine to fortify mood swings in depressed patients. In a rat model of chronic stress syndrome, *Withania somnifera* and *Panax ginseng* extracts were compared and contrasted for their abilities to relieve some of the adverse effects of chronic stress. Research results showed that both *Ashwagandha* and *Panax ginseng* decreased the frequency and severity of stress-induced ulcers, reversed stress-induced inhibition of male sexual behavior and inhibited the effects of chronic stress on retention of learned tasks. In another preclinical study, *Withania somnifera* showed superior ameliorating effects related to stress induced immunosuppression and peritoneal macrophage activity compared to *Panax ginseng*. In addition Ws did not produce the 'ginseng abuse syndrome' a condition characterized due to

over consumption of ginseng leading to hypertension, water retention, muscle stress, and sleeplessness.^[14]

Many studies have revealed that the medicinal plant elicits an anti-depressant and anti-anxiety effect in animal models comparable to anti-depressant drug imipramine and the anti-anxiety drug lorazepam (Ativan). Ws has been well known in India as a natural sedative and calmative drug and is comparable to the Chinese ginseng which is a well known tranquillizer. Long term stress develop chronic debilities like deficit in logical thinking, low resisting power, sexual impairment, gastritis, irregular glucose levels etc. The herb is often used to treat sexual and neural disorders and is generally considered as a convalescing medication.^[15]

ANTIMICROBIAL ACTIVITY

Many microbiological studies have revealed the antimicrobial activity of vegetative parts of Ws. The plant extract elicits phagocytosis and intracellular destruction of peritoneal macrophages in mice models. The chemical compound isolated from Ws namely Withaferin A restrains the growth of many Gram-positive bacteria, acid-fast and aerobic bacilli, and pathogenic fungi at a concentration of 10 μ g/ml. The compound also inhibited the growth of Ranikhet virus. The plant's whole extract actively restrained Vaccinia virus and the parasite *Entamoeba histolytica*.^[16] Ws also exhibited antifungal activity against systemic *Aspergillus* infection. The microbicidal activity of Withaferin A owes to the presence of the unsaturated lactone-ring. This lactone presented rich therapeutic activity compared to the well known antibiotic Penicillin in experimental rabbits. These preclinical studies suggest that the plant can be a prospective antimicrobial drug candidate.

RADICAL SCAVENGING EFFICACY

Owing to the high concentration of iron and fatty acids, the brain and nerves are more prone to oxidative damage by free radicals leading to several neurodegenerative diseases like paralysis, schizophrenia, amnesia, Alzheimer's, and other diseases. In another study, the aqueous root extract inhibited the aggravation of lipid peroxidation in stress induced rodents by administration of 0.2 μ g/kg of lipopolysaccharide from *Klebsiella pneumonia* and 100 μ g/kg of peptidoglycan from *Staphylococcus aureus*.^[17] The active compound glycowithanolides present in Ws administered for 21 days in stress induced rodents enriched the activities of some of the antioxidant enzymes like glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT) in rat brain frontal cortex and striatum. The active compound was efficacious than the synthetic antioxidant agent deprenyl.^[18]

Bhattacharya *et al.*, in 2000 studied the ameliorating efficacy of glycowithanolides on hepatotoxicity induced rats. This active compound containing sitoindosides VII-X and withaferin A isolated from *Ws* root was given in different doses of 10, 20 and 50 mg/kg) to rats previously overloaded with iron to induce hepatotoxicity. The glycowithanolides abated the increase in lipid peroxide and serum levels of alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase and was equally efficacious as the antioxidant standard Silymarin (20mg/kg, p.o.). These animal studies warrant the antioxidant efficacy of the plant.

ANTI-AGING PROPERTY

A double blind trial of 101 healthy male volunteers of age 50-59 years were given the *Ws* extract at a dosage of 3 grams daily for a year. Commendable improvement in hemoglobin, red blood cell count, hair melanin and reduction in serum cholesterol was evident in a majority of patients. In addition, a major population of the research subjects (70%) reported improvement in sexual performance.^[19]

ANTICONVULSANT ACTIVITY

The root extract (100mg/kg) of *Ashgandh* reduced jerks (70%) and muscular spasms (10%) in animals. In addition, pentylene tetrazole (PTZ)-induced convulsions was significantly reduced from EEG wave pattern. The root extract also exhibited alleviation in severity of motor seizures induced by electrical stimulation in right basilateral amygdaloid nuclear complex through bipolar electrodes. Research has revealed that this defensive effect of the plant in convulsions has been reported to involve GABAergic mediation.^[20]

HYPOLIPIDEMIC EFFECT

The free radicals are primary cause for the overall breakdown of the entire biological system. The oxidative stress leads to a cascade of medical conditions which eventually leads to chronic diseases. *Withania somnifera* with its repository of therapeutic constituents is a panacea to a myriad of medical conditions. *Ws* root powder or extract greatly reduced total lipids, cholesterol and triglycerides in hypercholesteremic animals. Besides the extract significantly increased plasma HDL-cholesterol levels, HMG-CoA reductase activity, bile acid content of liver, cholesterol and neutral sterol excretion in the hypercholesteremic animals with *Ws* administration. A significant reduction in lipid-peroxidation was evident in *Ws* administered hypercholesteremic animals in comparison to the normal animals. The root powder also decreased the lipid profiles in normal subjects.^[21] Hemalatha *et al.* studied the

hypoglycemic, diuretic and hypocholesterolemic efficacy of the roots of *Ws* on human volunteers. Six borderline NIDDM subjects and six mild hypercholesterolemic subjects were treated with the powder of roots of *Ws* for 30 days. Various blood and urine parameters were studied with dietary pattern before and at the end of treatment period. Hypoglycemic levels were comparable to that of a synthetic oral hypoglycemic drug. Increase in urine sodium, urine volume and decrease in serum cholesterol, triglycerides, LDL (low density lipoproteins) and VLDL (very low density lipoproteins) cholesterol were noticed indicating that root of *Ws* is a prospective source of hypoglycemic, diuretic and hypocholesterolemic agent.^[22]

APHRODISIAC ACTIVITY

About 50% of infertility accounts for male infertility with unknown etiology. A pilot study to estimate the spermatogenic activity of Ashwagandha root extract in was performed in 46 male patients with oligospermia (sperm count < 20 million/mL semen). They were administered with extract of Ashwagandha root (675 mg/d in three doses for 90 days). The study results revealed highly significant increase in sperm concentration t ($P < 0.0001$) and also 17% and 34% improvement in testosterone and LH Hormone levels respectively after 90 days of therapy²³. Therefore *Withania somnifera* can be concluded to have aphrodisiac activity by enhancing the libido, sexual performance, sexual vigour and penile erection.

CONCLUSION

The traditional system of medicines consists of many therapeutic mysteries that need to be unravelled. The ancient physicians depended entirely upon the plant kingdom for their medicinal needs. *Withania somnifera* is in itself a rich reservoir of natural phytochemicals which are both therapeutic and preventive. Much research has been done on the therapeutic efficacy of the plant as a whole. Most of them are in pre clinical phase with animal models. More clinical trials with human subjects are warranted to study the complete therapeutic efficacy of the plant.

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