

Biochemical and Therapeutic Properties of *Withania Somnifera* in Traditional Medicinal System

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ABSTRACT

Withania somnifera (Ashwagandha) is a very important medicinal plant of Ayurveda. Roots are used as Rejuvenating drug, tonic, Alternative pungent, astringent, Aphrodisiac, anti-inflammatory agent. Root powder has been found to be effective against Asthma, bronchitis, leucoderma, Arthritis, emenagogue cold, asthma, Tuberculosis, fever. Leaves are effective against Ulcers, painful swelling Fever, chest pain, sores, swelling. Seeds contains Diuretic, narcotic and hypnotic properties. Ashwagandha contains anti-Diabetic, anti-cancer, anti-oxidant Effects, anti-inflammatory, antimicrobial, Anti-stress, Aphrodisiac, anti arthritic, Cardiovascular and Immunomodulatory effects. Biotechnological, and Modern Genomics tools may play an important role in the field of discovery of other secondary metabolites and development of improved plant varieties.

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Keywords: *Withania somnifera*, Diuretic, narcotic, anti-inflammatory effects, anti-cancer activity, anti-oxidant Effects, antimicrobial activity, Anti-stress activity, Aphrodisiac activity, anti arthritic activity, Cardiovascular and Immunomodulatory effects

INTRODUCTION

Out of a large number of medicinal plants known in present scenario, *Withania somnifera* (L.) Dunal (family Solanaceae) commonly known as Ashwagandha or Asgandh finds extensive use as a medicinal herb in the traditional system of medicine as a rasayana and medhya rasayana extends back over 3000 to 4000 years (Atal *et al.* 1961). *Withania somifera* is 30-75 cm high grayish, stellate-tomentose undershrub with long tuberous roots. Leaves on vegetative shoots are alternate or sub opposite, large, broad, elliptic ovate to oblong, petiolate, sub-acute, entire, with lamina 5 to 10cm long and 2.5-7 cm broad. Flowers are small, greenish, axillary, solitary or in few-flowered cymes and bisexual. The calyx is gamosepalous with five 3-5 mm lobes, accrescent and inflated in a fruit. The corolla is campanulate, greenish-yellow with five 5-8 mm lobes. There are five included stamens. The ovary is ovoid/globose, glabrous, and many ovuled. The style is filiform and stigma is 2-lobed. Fruit is a globose berry, orange-red when ripe and enclosed in the enlarged calyx. Seeds are many, discoid, yellow and reniform (Schonbeck-temsey *et al.* 1972, Hepper *et al.* 1991, Mir *et al.* 2012, Mozaffarian *et al.* 2003). Widely distributed in India, Pakistan, Afganistan, Bangladesh, Sri lanka and parts of north America. (Bano *et al.* 2013). Raimondo *et al.* (2009), described conservation status of *Withania somifera* as least

concern on the basis of W. Foden and L. Potte's (assessors) report.



Fig 1- *Withania somnifera*

Biochemical profile of *Withania somnifera*

Several biochemical constituents such as alkaloids, flavonoides, steroidal lactones, tannins, saponins etc has have been extracted, and identified from *Withania* species (Lavie *et al.* 1965, Kirson *et al.* 1977, Eastwood *et al.* 1977, Atta ur Rehman *et al.* 1991 & 93, Chaudary *et al.* 1996, Rastogi *et al.* 1998, Kapoor 2001, Bandopadhyay *et al.* 2007). Roots and leaf extracts of *W. Somnifera* indicates that it possesses anti-inflammatory, antitumor, anti stress, antioxidant, immune-modulatory properties (Singh *et al.* 2011). Udayakumar *et al.* (2009) reported antidiabetic activity in alloxan model mice.

The withanolide skeleton may be defined as a 22-hydroxyergostan-26-oic acid-26,22-lactone. Some variation in carbocyclic skeleton or the side chain and these have been studied and described as modified withanolides or ergostantype steroids related to withanolides. The characteristic feature of withanolides and ergosane-type steroids is one C8 or C9-side chain with a lactone or lactol ring but the lactone ring may be either six-membered or five-membered and may be fused with the carbocyclic part of the molecule through a carbon-carbon bond or through an oxygen bridge. Appropriate oxygen substituents may lead to bond scission, formation of new bonds, aromatization of rings and many other kinds of rearrangements resulting in compounds with novel structures [Tursunova *et al.* 1977, Glotter *et al.* 1991, Kirson *et al.* 1971].

Roots-

Dry root powder and various chemical root extracts are found to be effective against various illnesses. In Ayurvedic medicinal system roots are used as Rejuvenating drug, tonic, Alternative pungent, astringent, Aphrodisiac, Phthisis (Dutta 1877, Kumar *et al.* 1980, Sen Gupta 1984), in Siddha medicinal system it is effective against fever (SPC 1992), and inflammation and according to Unaani system it is found to be effective against Asthma, bronchitis, leucoderma, Arthritis, emenagogue (Stewart 1869, Maithani 1973 and according to Folklore system roots can be used against cold, asthma, Tuberculosis, fever (Dutta 1877), Kumar *et al.* 1980, Singh and Kumar 1998). Dry root powder contains Antiulcerogenic, Antistress, Anticancer & Radiosensitizer, Psycho-physiological, Pulmonary tuberculosis, Epilepsy, Nervinotonic, Easy abortion, General tonic in seminal disease, Glandular swellings in bubonic plague, Hypoglycemic diuretic properties. 70% Methanolic extract contains Antistress, GABA mimetic activity GABA receptor mediates anti-convulsant activity, Protective effect as amygdaloid kidlling Antiinflammatory effects. Chloroform-Methanol extract is effective against Alzheimers disease (Sehgal *et al.* 2012).

Leaves-

According to Ayurveda leaves are effective against Ulcers, painful swelling (Dutta 1877, Kumar *et al.* 1980, Singh and Kumar 1998, Mhaskar *et al.* 2000. Siddha system leaves are effective against Fever, chest pain, sores, swelling (SPC 1992), Unani- External pains, anti-inflammatory (UPC 1993) Folklore Cure eyesores, boils, diuretic Narcotic, treatment of syphilis and hemorrhoids (Shah and Gopal 1985, Sharma *et al.* 1985)

Seeds-

According to Ayurveda seeds contains Diuretic, narcotic and hypnotic properties (Dalzell and Gibson, 1861), Folklore

system seeds are found to be effective against open wounds and poison of a serpent rubbed on skin for ringworm in human beings and animals (Dalzell and Gibson 1861, Rao 1977, Sahu 1982, Shah and Gopal 1985, Dafni and Yaniv 1994).

Pharmacological Profile of *Withania sonifera***AntiDiabetic activity -**

Six withanolides isolated from *W. somnifera* were tested for anti-diabetic activity based on glucose uptake in skeletal myotubes. Withaferin A was found to increase glucose uptake, with 10 μ M producing a 54% increase compared with control, suggesting that withaferin A is at least partially responsible for *W. somnifera*'s anti-diabetic activity (Gorelick *et al.* 2015).

Anticancer activity -

Withaferin A and withanolide D are anti-tumor and radiosensitizing withanolides (Devi *et al.* 1992, 1993, 1999; Lyon and Kuttan, 2004). 1-oxo-5 β , 6 β -epoxy-witha-2-enolide reduces the UV induced skin carcinoma (Mathur *et al.* 2004). Withaferin A acts as a mitotic poison arresting the division of the cultured human larynx carcinoma cells at metaphase. It also produced a significant dose dependent retardation of the growth of Ehrlich ascites carcinoma, sarcoma 180, and sarcoma Black and E 0771 mammary adenocarcinoma (Davis and Kuttan, 1998). Methanolic extract of *W. somnifera* has been used in stem cell proliferation (Kuttan, 1996). It acts like a chemotherapeutic agent and inhibits the growth of breast, lung, central nervous system and colon cancer cell lines by decreasing their viability in doze dependent manner (Jayaprakasan *et al.* 2003). The withaferin A-mediated suppression of breast cancer cell viability correlated with apoptosis induction characterized by DNA condensation, cytoplasmic histone-associated DNA fragmentation, and cleavage of poly-(ADP-ribose)-polymerase (Silvia *et al.* 2008). Chemo-preventive activity is attributed partly to the antioxidant/free radical scavenging activity of the extract (Prakash *et al.* 2002)

Antioxidant Effects -

Brain and nervous tissues are rich in lipid and iron content which promotes the synthesis or generation of free oxygen species, so in comparison of other physiological system they are more susceptible to free radical damage. (Halliwell & Gutteridge, 1989). And this free radical or newly synthesized oxygen molecule may cause neural loss in cerebral ischemia, aging and neurodegenerative diseases, e.g., epilepsy, schizophrenia, Parkinson's, Alzheimer's and other diseases (Jesberger & Richardson, 1991, Sehgal *et al.*, 2012). *W. somnifera*, contains sitoindosides VII-X and withaferin A (glycowithanolides), is responsible to increase the amount of endogenous superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), and ascorbic acid and decreases the lipid peroxidation (Dhuley 1998, Bhattacharya *et al.* 2001, Jayaprakasan *et al.* 2004, Bhatnagar 2005, Mirjalali *et al.* 2009).

Anti inflammatory activity -

Ashwagandha acts as an anti-inflammatory agent in rheumatological conditions and by inhibiting the complement, lymphocyte proliferation, and delayed-type hypersensitivity (Rasool & Varalakshmi, 2006, Anbalagan *et al.* 1984, Al-Hindawi *et al.* 1992). Ashwagandha extract can 100 % decrease the glycosaminoglycans content in the granuloma tissue and may uncoupled the oxidative phospho-

rylation by reducing mitochondrial ADP/O ratio in mitochondria of granuloma tissue and may increase the Mg²⁺ dependent-ATPase enzyme activity and reduces the succinate dehydrogenase activity in mitochondria (Begum *et al.* 1988).

Antimicrobial effects -

The antibacterial properties of this multipronged medicinal plant were for the first time reported by Kurup (1956) against *Salmonella aurens*. In past one decade, antimicrobial activity against a range of bacteria and fungi ascribed to withanolide were reported (Dhuley, 1998, Ziauddin *et al.*, 1996, Dhuley, 1998, Mishra *et al.*, 2000, Owais *et al.*, 2005).

Anti-stress and Aphrodisiac activity -

Anti-stress activity associated with glycosides (sitoindosides VII and VIII) present in this plant was reported by Bhat-tacharya (1987; 2000 & 2003). Ashwagandha is also used as a tonic in the treatment of spermatopathia, impotence and seminal depletion (Nadkarni, 1976) and the men who used the herb enjoyed higher vigour performance (Boone, 1998). The higher concentrations of inorganic elements like Fe, Mg, K and Ni in the roots of this plant play a significant role in the diuretic and aphrodisiac activity of the drug (Lohar *et al.*, 1992). The decoction of the root boiled with milk and ghee is recommended for curing sterility in women (Singh & Kumar 1998).

Anti Arthritic properties -

Ashwagandha powder has been found useful in acute rheumatoid arthritis and reduces the discomfort associated with arthritis (Bector *et al.* 1968). This property has been attributed to the active principle withaferin A.

Cardiovascular effects -

Various extracts of *W. somnifera* has been reported that it shows hypotensive effect to autonomic ganglion blocking action as well as a depressant action on the higher cerebral centers. Recent study proves that *W. somnifera* act as a cardio-protective agent that provides a scientific reason for rationale of the use of this medicinal plant in Ayurveda as Maharashtra (Gupta *et al.* 2004, Mohanty *et al.* 2004, Sehgal *et al.* 2012).

Effects on nervous system -

The effects on nervous system are associated with Ashwagandholine (root extracts). It potentiates barbiturate-, ethanol- and urethane- induced hypnosis in mice and caused relaxant and antispasmodic effects against various agents that produce smooth muscle contractions in intestinal, uterine, tracheal and vascular muscles (Malhotra *et al.* 1965). The bioactive compounds are reported to preferentially influence the events in the cortical and basal forebrain cholinergic-signal transduction cascade. The cognition and memory enhancing effects of *W. somnifera* extracts can be partly explained by the drug-induced enhancement of cortical muscarinic acetylcholine receptor capacity (Schliebs *et al.* 1997). In general, Ashwagandha has been used traditionally as a tonic and nootropic agent (Sehgal *et al.*, 2012). It has also been associated with improvements in scopolamine-induced memory deficits in mice (Dhuley, 2001). *W. somnifera* extracts also show an antiparkinsonian effect on neuroleptic-induced catalepsy by inhibiting haloperidol or reserpine-induced catalepsy attributed to potent antioxidant, antiperoxidative and free radical

quenching properties (Ahmad *et al.*, 2005; Kumar & Kulkarni, 2006; Sehgal *et al.*, 2012).

Immunity -

Roots of *W. somnifera* shows an immuno-potentiating and myeloprotective effects by enhancing the levels of interferon (IFN)- γ , interleukin (IL)-2 and granulocyte macrophage colony stimulating factor in normal and cyclophosphamide-treated mice (Davis & Kuttan, 1999). As the plant is rich in iron, it contributes to red blood cell count. The effect of *W. somnifera* on the immune system is subtler than simply suppressing the immune/inflammatory response. The active compound (withanolide A) in the roots of *W. somnifera* significantly increases the expression levels of T-helper 1 (Th1) cytokines, as well as CD4 and CD8 counts. It also enhances natural killer (NK) cell activity in a dose dependent manner with a faster recovery of CD4+ T cells in immune suppressed animals (Davis & Kuttan, 2002, Khan *et al.*, 2006, Bani *et al.*, 2006, Singh *et al.*, 2008). Apart from the above activated macrophage functioning indicated by enhanced secretion of nitrite, IL-2 and TNF-2, decreases moderately IL-4 with no effect on IL-10 suggesting that it only influenced Th1 profile of the cytokines. Root powder of this plant is also reported to stimulate the cell-mediated immunity, IgM and IgG and a prominent enhancement in proliferation and differentiation of lymphocytes as indicated by lymphocyte surface markers of T cells (CD3+, CD4+ and CD8+) and B cells (CD19+) (Singh *et al.*, 2008).

Immunomodulatory effects -

Glycowithanolides and a mixture of sitoindosides IX and X isolated from *W. somnifera* were evaluated for their immunomodulatory and central nervous system effects (Ghosal *et al.*, 1989). Administered orally (50-200 mg/kg orally) both compounds also produced significant antistress activity in albino mice and rats. They also augmented learning, acquisition and memory retention in both young and old rats. Root extract of *W. somnifera* was tested for immunomodulatory effects in three myelosuppression models in mice: cyclophosphamide, azathioprin or prednisolone (Ziauddin *et al.* 1996). Significant increase in hemoglobin concentration, red blood cell count, white blood cell count, platelet count and body weight were observed in *W. somnifera* -treated mice compared to controls. A significant increase in hemolytic antibody responses toward human erythrocytes (which indicated immunostimulatory activity) was also reported.

Conclusion-

Withania somnifera is very important plant species from medicinal point of view. Dry root powder of Ashwagandha is commercially available as raw material of various ayurvedic formulations in market. These reviews are evidence that various other biochemical constituents of leaves and seeds of Ashwagandha should be study more extensively to reveal the other medicinal benefits. So that in future whole plant of ashwagandha will be utilize for the treatment of various illness.

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