Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Scholars Research Library

Annals of Biological Research, 2010, 1 (3) : 56-63
(http://scholarsresearchlibrary.com/archive.html)

Annals of Biological Research
Scholars Research Library

ISSN 0976-1233
CODEN (USA): ABRNBW

Biological activities of *Withania somnifera*

G. Singh*, P. K. Sharma, R. Dudhe and S. Singh

Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, Meerut, U.P., India

---

ABSTRACT

Withania somnifera (Ashwagandha) is a plant used in medicine from the time of Ayurveda, the ancient system of Indian medicine. The dried roots of the plant are used in the treatment of nervous and sexual disorders. From chemistry point of view, the drug contains group of biologically active constituents known as withanolides. The chemical structures of withanolides have been studied and they are widely distributed in family Solanacae. Withaferin- A is therapeutically active withanolide reported to be present in leaves. In animal studies, withaferin-A has shown significant anticancer activity. Majority of the anticancer drugs like Vinblastine, Vincristine, and Taxol have been derived from green flora. Today there is much interest in natural products with anticancer activity. Withanolides are of under research potential as far treatment of cancer is concerned. The article reviews the scope of studies published in favor of anticancer potential of withaferin-A.

Key words: *Withania somnifera*, Biological activities, antibiotic, aboritifacient, anti-inflammatory.

INTRODUCTION

Plants have been the major source of drugs for the treatment of diabetes mellitus (DM) in Indian medicine and other ancient systems in the world, and for a long time DM has been treated orally with herbal medicines or their extracts [1].Because plant products are frequently considered to be less toxic and more free from side effects than synthetic ones [2]. Furthermore, after the recommendations made by the WHO on DM, investigations on hypoglycaemic agents from medicinal plants have become more important and the search for more effective and safer hypoglycaemic agents has continued to be an important area of active research. World ethnobotanical information about medicinal plants reports that almost 800 plants could be used

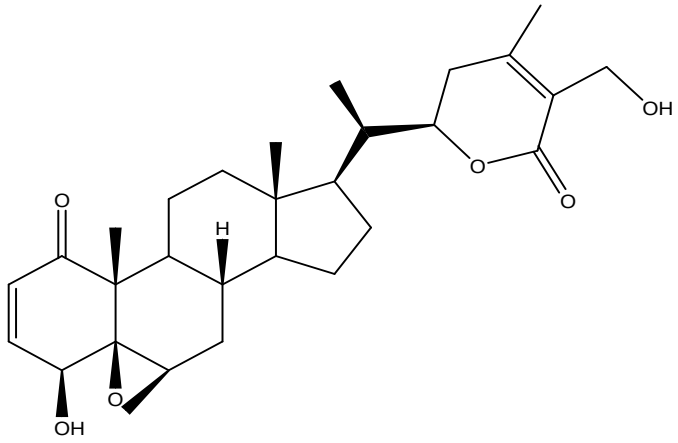
to control DM. Many herbs and plants have been described as possessing hypoglycaemic activity when taken orally [1,3]. Some of these plants have also been pharmacologically tested and shown to be of some value in human diabetes treatment. *Withania somnifera* (L.) Dunal, commonly known in Sanskrit as Ashwagandha, is a perennial plant belonging to the order Solanaceae. The pharmacological effects of the roots of *W. somnifera* are attributed to the presence of withanolides, a group of steroidal lactones [4]. Its leaves are used in Ayurvedic and Unani systems for treatment of tumors and tubercular glands [5]. A number of withanolide steroidal lactones have been isolated from the leaves of *W. somnifera* [6]. and exhibit antibacterial, anti-fungal and antitumor properties.[7] There are a number of reports elucidating the chemical and pharmacological properties of *W. somnifera* [8,9]. *Withania somnifera*, (Ashwagandha), is a shrubby plant cultivated in India, parts of East Asia and Africa which offers tremendous potential as an energizing medicinal herb. Ayurvedic practitioners have used the roots of this plant for centuries with success as a tonic to increase vitality and longevity, as well as to treat health conditions as diverse as tumors and arthritis. Recent laboratory studies have begun to confirm what Ayurvedic practitioners have known for years – that *Withania somnifera* deserves attention as an herbal therapy to ease or even eliminate many of today's common health problems. Sometimes referred to as .Indian ginseng. because of its stimulating effects, 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 [10].

Chemical Composition

Laboratory analysis has revealed over 35 chemical constituents contained in the roots of *Withania somnifera* [11]. The biologically active chemical constituents are alkaloids (isopellertierine, anferine), steroidal lactones (withanolides, withaferins), saponins containing an additional acyl group (sitoindoside VII and VIII), and withanoloides with a glucose at carbon 27 (sitonidoside XI and X). *Withania somnifera* is also rich in iron.

The roots of *Withania somnifera* consist primarily of compounds known as withanolides, which are believed to account for its extraordinary medicinal properties. Withanolides are steroidal and bear a resemblance, both in their action and appearance, to the active constituents of Asian ginseng (Panax ginseng) known as ginsenosides. Ashwagandha's withanolides have been researched in a variety of animal studies examining their effect on numerous conditions, including immune function and even cancer[12]. Chemical analysis of Ashwagandha show its main constituents to be alkaloids and steroidal lactones. Among the various alkaloids, withanine is the main constituent. The other alkaloids are somniferine, somnine, somniferinine, withananine, pseudo-withanine, tropine, pseudo-tropine, 3-a-gloyloxytropane, choline, cuscohygrine, isopelletierine, anaferine andanahydrine. Two acyl steryl glucoside viz. sitoindoside VII and sitoindoside VIII have been isolated from root. The leaves contain steroidal lactones, which are commonly called withanolides. The withanolides have C28 steroidal nucleus with C9 side chain, with a six membered lactone ring [13]. Twelve alkaloids, 35 withanolides, and several sitoindosides from *Withania somnifera* have been isolated and studied. A sitoindoside is a withanolide containing a glucose molecule at carbon 27. Much of Ashwaganda's pharmacological activity has been attributed to two main withanolides, withaferin A and withanolide D. Further chemical analysis has shown the presence of the following:

Anaferine (Alkaloid), Anahygrine (Alkaloid), Beta-Sisterol, Chlorogenic acid (in leaf only), Cysteine (in fruit), Cuscohygrine (Alkaloid), Iron, Pseudotropine (Alkaloid), Scopoletin, Somniferinine (Alkaloid), Somniferiene (Alkaloid), Tropanol (Alkaloid), Withanine (Alkaloid), Withananine (Alkaloid) and Withanolides A-Y(Steroidal lactones) [14,15].



Withaferin A

Pharmacological Activity

Centuries of Ayurvedic medical experience using *Withania somnifera* have revealed it to have pharmacological value as an adaptogen, antibiotic, aboritifacient, aphrosidiac, astringent, anti-inflammatory, deobstruent, diuretic, narcotic, sedative, and tonic.

Ashwagandha has been found to:
Provide potent antioxidant protection [16][17].
Stimulate the activation of immune system cells, such as lymphocytes and phagocytes [18][19].
Counteract the effects of stress and generally promote wellness [20].

Anti-stress

A study conducted by the Institute of Basic Medical Sciences at Calcutta University examined the effects of Ashwagandha on chronic stress in rodents. For a period of 21 days, the animals received a mild electric shock to their feet. The resulting stress on the animals produced hyperglycemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression [21]. Researchers using *Withania somnifera* discovered the animals given the herb an hour before the foot shock experienced a significantly reduced level of stress. This research confirms the theory that Ashwagandha has a significant anti-stress adaptogenic effect [22].

Research conducted at the Department of Pharmacology, University of Texas Health Science Center indicated that extracts of Ashwagandha produce GABA-like activity, which may account for the herb's anti-anxiety effects [23]. GABA (Gamma Amino-butyric acid) is an inhibitory neurotransmitter in the brain. Its function is to decrease neuron activity and inhibit nerve cells from over firing. This action produces a calming effect. Excessive neuronal activity can lead to restlessness and insomnia, but GABA inhibits the number of nerve cells that fire in the brain, and helps to induce sleep, uplift mood, and reduce anxiety.

Ashwagandha has traditionally been used to stabilize mood in patients with behavioral disturbances. Research has revealed that the herb produces an anti-depressant and anti-anxiety effect in rodents comparable to the anti-depressant drug imipramine and the anti-anxiety drug lorazepam (Ativan) [24].

In fact, Ashwagandha is one of the most widespread tranquillizers used in India, where it holds a position of importance similar to ginseng in China. It acts mainly on the reproductive and nervous systems, having a rejuvenative effect on the body, and is used to improve vitality and aid recovery after chronic illness [25].

Chronic stress can cause conditions such as cognitive deficit, immunosuppression, sexual dysfunction, gastric ulceration, irregularities in glucose homeostasis, and changes in plasma corticosterone levels. In a rat model of chronic stress syndrome, *Withania somnifera* and Panax ginseng extracts were compared and contrasted for their abilities to relieve some some of the adverse effects of chronic stress [26].

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. Both botanicals also reversed stress-induced immunosuppression, but only the Withania extract increased peritoneal macrophage activity. The activity of the Withania extract was about the same as the activity of the ginseng extract. *Withania somnifera*, however, has an advantage over Panax ginseng in that it does not appear to result in .ginseng-abuse syndrome., a condition characterized by high blood pressure, water retention, muscle tension, and insomnia [27].

Anti-oxidant activity

Researchers from Banaras Hindu University in Varanasi, India, have discovered that some of the chemicals found in *Withania somnifera* are powerful antioxidants. Studies conducted on rats' brains showed the herb produced an increase in the levels of three natural antioxidants-superoxide dismutase, catalase and glutathione peroxidase [28].

These findings are consistent with the therapeutic use of *Withania somnifera* as an Ayurvedic rasayana. The antioxidant effect of active principles of *Withania somnifera* root may explain the reported anti-stress, cognition-facilitating, anti-inflammatory and anti-aging effects produced by them in experimental animals, and in clinical situations [29].

Anti-carcinogenic activity

Ashwagandha is reported to have anti-carcinogenic effects. Research on animal cell cultures has shown that the herb decreases the levels of the nuclear factor kappaB, suppresses the intercellular tumor necrosis factor, and potentiates apoptotic signalling in cancerous cell lines [30]. One of the most exciting of the possible uses of Ashwagandha is its capacity to fight cancers by reducing tumor size [31,32]. To investigate its use in treating various forms of cancer, the antitumor effects of *Withania somnifera* have been studied by researchers. In one study, the herb was evaluated for its anti-tumor effect in urethane-induced lung tumors in adult male mice[33]. Following administration of Ashwagandha over a period of seven months, the histological

appearance of the lungs of animals which received the herb was similar to those observed in the lungs of control animals.

Anti-inflammatory activity

Research has explored the capacity of Ashwagandha to ease the symptoms of arthritis and other inflammatory conditions These studies have proven that the herb acts as an effective anti-inflammatory agent. Its naturally occurring steroidal content is much higher than that of hydrocortisone, a commonly-prescribed anti-inflammatory [34]. The effectiveness of Ashwagandha in a variety of rheumatologic conditions may be due in part to its anti-inflammatory properties. Rats given powdered root of *Withania somnifera* orally one hour before being given injections of an inflammatory agent over a three day period showed that Ashwagandha produced anti-inflammatory responses comparable to that of hydrocortisone sodium succinate [35].

Anti-aging activity

Ashwagandha was tested for its anti-aging properties in a double-blind clinical trial. A group of 101 healthy males, 50-59 years old were given the herb at a dosage of 3 grams daily for one year. The subjects experienced significant improvement in hemoglobin, red blood cell count, hair melanin, and seated stature. Serum cholesterol decreased and nail calcium was preserved. Seventy percent of the research subjects reported improvement in sexual performance [29].

Cardioprotective activity

Ashwagandha has been evaluated in clinical studies with human subjects for its diuretic, hypoglycemic, and hypocholesterolemic effects [36]. Six type 2 diabetes mellitus subjects and six mildly hypercholesterolemic subjects were treated with a powder extract of the herb for 30 days. A decrease in blood glucose comparable to that which would be caused by administration of a hypoglycemic drug was observed. Significant increases in urine sodium, urine volume, and decreases in serum cholesterol, triglycerides, and low-density lipoproteins were also seen.

Hypothyroid activity

Animal studies have shown that Ashwaganda may have a effect on thyroid activity. An aqueous extract of dried Withania root was given to mice daily for 20 days. Significant increases in serum T4 were observed, indicating the plant has a stimulating effect at the glandular level. *Withania somnifera* may also stimulate thyroid activity indirectly, via its effect on cellular antioxidant systems. These results indicate ashwaganda may be a useful botanical in treating hypothyroidism [37,38].

ImunomodulImatory activity

A series of animal studies have demonstrated Ashwagandha to have profound effects on healthy production of white blood cells, which means it is an effective immunoregulator and chemoprotective agent [39,40]. In a study using mice, administration of powdered root extract from Ashwagandha was found to enhance total white blood cell count. In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocytic activity of macrophages when compared to a control group [41]. Recent research suggests a possible mechanism behind the increased cytotoxic effect of macrophages exposed to *W. somnifera* extracts [42]. Nitric oxide has been determined to have a significant effect on macrophage

cytotoxicity against microorganisms and tumor cells. Iuvone et al demonstrated *Withania somnifera* increased no production in mouse macrophages in a concentration-dependent manner. This effect was attributed to increased production of inducible nitric oxide synthase, an enzyme generated in response to inflammatory mediators and known to inhibit the growth of many pathogens [43]. Research has also shown Ashwagandha to have stimulatory effects, both in vitro and in vivo, on the generation of cytotoxic T lymphocytes, and a demonstrated potential to reduce tumor growth [44]. The chemopreventive effect was demonstrated in a study of ashwagandha root extract on induced skin cancer in Swiss albino mice given ashwagandha before and during exposure to the skin cancer-causing agent (7,12-dimethylbenz[a]anthracene) [31]. A significant decrease in incidence and average number of skin lesions was demonstrated compared to the control group. Additionally, levels of reduced glutathione, superoxide dismutase, catalase, and glutathione peroxidase in the exposed tissue returned to near normal values following administration of the extract. The chemopreventive activity is thought to be due in part to the antioxidant/free radical scavenging activity of the extract.

Other Therapeutic Benefits

Further studies have also shown ashwagandha to be effective in the treatment of osteoarthritis,[45] inflammation [46], stroke [47], and tardive dyskinesia [48]. Ashwagandha has been shown to be a potential antimicrobial agent, with antifungal activity[49], and moderate antibacterial activity against Staphyloccus aureus and Pseudomonas Aeruginosa bacteria strains [50].

CONCLUSION

The studies so far indicate that *W. somnifera* could prove to be a good natural source of a potent and relatively safe radiosensitizer/chemotherapeutic agent. *Withania somnifera* (Ashwagandha) is a plant used in medicine from the time of Ayurveda, the ancient system of Indian medicine. Ashwagandha has been used as an aphrodisiac, liver tonic, anti-inflammatory agent, astringent, and to treat bronchitis, asthma, ulcers, emaciation, insomnia, and senile dementia. Clinical trials and animal research support the use of ashwaganda for anxiety, cognitive and neurological disorders, inflammation, and Parkinson's disease

REFERENCES

[1] Akhtar, F.M.; Ali, M.R; *J. Pak. Med. Assoc*. **1984**, 34, 239-244.
[2] Brinker, F. Herb contraindications and drug interactions, 2nd Ed.; Eclectic Medical Publications: Sandy, OR, USA, **1998**, 36-82.
[3] Pepato, M.T.; Baviera, A.M.; Vendramini, R.C.; Perez, M.P.M.S.; Ketelhut, I.C.; Brunetti, I.L.J. *Biotechnol. Appl. Biochem*. **2003**, 37, 15-20.
[4] Budhiraja, R.D.; Sudhir, S. *J. Sci. Ind. Res*. **1987**, 42, 488-491.
[5] Chopra, R.N. Glossary of Indian medicinal plants; Academic Publishers: New Delhi, India, **1994.**
[6] Glotter, E.; Kirson, I.; Abraham, A.; Lavie, D. *Tetrahedron* **1973**, 29, 1353-1364.
[7] Devi, P.U.; Sharada, A.C.; Solomon, F.E. *Indian J. Exp. Biol.* **1993**, 31, 607-611.
[8] Nittala, S.S.; Lavie, S. *Phytochemistry* **1988**, 20, 2741–2748.
[9] Kandil, F.E.; Elsayeh, N.H.; Abou-Douh, A.M.; Ishak, M.S.; Mabry, T.J. *Phytochemistry* **1994**, 37, 1215-1216. Int. J. Mol. Sci. **2009**, 10

[10] "*Withania somnifera*". Alternative Medicine Review. FindArticles.com. 13 Oct. **2008**.
[11] Rastogi RP, Mehrotra BN, Compendium of Indian Medicinal Plants, Vol. 6. Central Drug Research Institute, New Delhi, **1998**.
[12] Grandhi, A. *Journal of Ethnopharmacology* (Ireland), **1994**: vol. 3, 131-135
[13] Dr. Ajay Padmawar; *Withania somnifera*. Monograph for Anruta Herbals, LTD.
[14] Bone K; Clinical Applications of Ayurvedic and Chinese Herbs. Queensland, Australia: Phytotherapy Press, **1996**, 137-41.
[15] Elsakka M; Grigorescu E; Stanescu U et al; *Rev Med Chir Soc Med Nat lasi* **1990**, 94, 385-387.
[16] Abou-Douh AM. *Arch Pharm* **2002**, 335, 267-276.
[17] Panda S; Kar A; *Indian Journal Physiological Pharmacology*. **1997** , 424-426.
[18] Wagner H; Norr H; Winterhoff H; Plant adaptogens, *Phytomed* **1994**, 1, 63-76.
[19] Singh B; Saxena AK; Chandan BK; et al. *Phytother Res* **2001**, 15, 311-318.
[20] Singh B; Chandan BK; Gupta DK; *Phytother Res*. **2003**, 531-536.
[21] Bhattacharya SK; Muruganandam AV; *Pharmacol Biochem Behav*. **2003,** 547-555.
[22] Bhattacharya A; Ghosal S; Bhattacharya SK; *J Ethnopharmacol* **2001**, 74 ,1-6.
[23] Mehta AK; Binkley P; Gandhi SS; Ticku MK; *Indian J Med Res.* **1991** , 94, 312-5.
[24] Archana R; Namasivayam A; *J Ethnopharmacol* **1999**,64,91-93.
[25] Bhattacharya, S; Goel R; Kaur R; Ghosal S; *Phytotherapy Res* **1987**, 1, 32-39.
[26] Bhattarcharya SK; Muruganandam AV; *Pharmacol Biochem Behav* **2003**, 75, 547-555.
[27] Bhattacharya SK; Bhattacharya A; Sairam K; Ghosal S; *Phytomedicine* **2000**, 7, 463-469.
[28] Dhuley JN; *J Ethnopharmacol* **2007**, 57-63.
[29] Bone K; Clinical Applications of Ayuvedic and Chinese Herbs. Queensland, Australia: Phytotherapy Press, **1996**, 137-41.
[30] Ichikawa H; Takada Y; Shishodia S; Jayaprakasam B; Nair MG; Aggarwal BB . *Molecular Cancer Therapeutics* **2006** , 1434-45.
[31] Prakash J; Gupta SK; Dinda AK; *Nutr Cancer* **2002**, 42, 91-97.
[32] Jayaprakasam B; Zhang Y; Seeram N; Nair M. *Life Sci* **2003**, 74, 125-132.
[33] Singh N;Singh SP; Nath R; et al. *International Journal Crude Drug Research* **1986**, 24, 90-100.
[34] Anbalangan K; Sadique J; *Indian Journal of Experimental Biology* **1981**, 19,245-249.
[35] Begum VH; Sadique J; *Indian J Exp Biol* **1988**, 26, 877-882.
[36] Andallu B; Radhika B; *Indian Journal of Experimental Biology* **2000**, 3, 607-609.
[37] Panda S; Kar A; *J Ethnopharmacol* **1999**, 67, 233-239.
[38] Panda S; Kar A; *J Pharm Pharmacol* **1998**, 50, 1065-1068.
[39] Kuttan G; *Indian J Exp Biol* **1996**, 34, 854-856.
[40] Ziauddin M; Phansalkar N; Patki P; et al. *J Ethnopharmacol* **1996**, 50, 69-76.
[41] Davis L; Kuttan G; *J Ethnopharmacol* **2000**, 71, 193-200.
[42] Iuvone T; Esposito G; Capasso F; Izzo A. *Life Sci* **2003**, 72, 1617-1625.
[43] Bogdan C; *Nature Immunol* **2001**, 2, 907-916.
[44] Davis L; Kuttan G; *J Exp Clin Cancer Res* **2002**, 21, 115-118.
[45] Kulkarni RR; Patki PS; Jog VP et al. *J Ethnopharmacol* **1991**, 33, 91-95.
[46] Angalagan K; Sadique J; *Indian J Exp Biol* **1981**, 19, 245-249.
[47] Chaudhary G; Sharma U; Jagannathan N; Gupta Y; *Clin Exp Pharmacol Physiol* **2003**, 30, 399-404.
[48] Bhattacharya SK; Bhattacharya D; Sairam K; Ghosal S; *Phytomedicine* **2002**, 9, 167-170.

[49] Choudhary MI; Dur-e-Shahwar; Parveen Z *et al*. *Phytochemistry* **1995**, 40, 1243-1246.
[50] Ali NA; Julicch WD; Kusnick C; Lindequist U; *J Ethnopharmacol* **2001**, 74, 173-179.