

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

Neha Singh¹, Dr. Anita R. J. Singh²

¹PhD Scholar, ²Associate Professor & Dean of Research

^{1,2}PG & Research Department of Biotechnology, Women'S Christian College, Chennai, Tamil Nadu, India

How to cite this paper: Neha Singh | Dr. Anita R. J. Singh "Biochemical and Therapeutic Properties of *Withania Somnifera* in Traditional Medicinal System" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-3 | Issue-3, April 2019, pp.551-556, URL: <http://www.ijtsrd.com/papers/ijtsrd21715.pdf>



IJTSRD21715

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.

Copyright © 2019 by author(s) and International Journal of Trend in Scientific Research and Development Journal. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0) (<http://creativecommons.org/licenses/by/4.0>)



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 10 cm 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 Unani 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 10µM 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 radio-sensitizing withanolides (Devi *et al.* 1992, 1993, 1999; Lyon and Kuttan, 2004). 1-oxo-5ß, 6ß-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, Jayaprakasam *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 aureus*. 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 Bhattacharya (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 Maharasayana (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 nitric oxide, IL-2 and TNF- α , 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, azathioprine 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 studied more extensively to reveal the other medicinal benefits. So that in future whole plant of ashwagandha will be utilized for the treatment of various illness.

References-

- [1] Al Hindawi M.K, Al Khafaji S.H and Abdul-Nabi M.H. Anti-granuloma activity of Iraqi *Withania somnifera*. *J. Ethnopharmacol.* (1992) 37, 113-116.
- [2] Ahmad, M., Saleem, A., Ahmad, S., Ansari, M., A., Yousuf, A., Hoda, M., N., and Islam, F. Neuroprotective effects of

- Withania somnifera on 6-hydroxydopamine induced Parkinsonism in rats. *Hum. Exp. Toxicol.* (2005). 24(3): 137-147.
- [3] Anbalagan K, Sadique J. Role of prostaglandins in acute phase proteins in inflammation. *Biochem Med.* (1984) 19:245-24.
- [4] Atal, C. K. and Schwarting, A. E. Ashwagandha, an ancient drug. *Economic Botany*, (1961). 15,256-263
- [5] Atta-ur-Rahman, Jamal, A.S., Choudary, M.I., Asif, I. Two withanolides from *Withania somnifera*. *Phytochemistry*, (1991). 30, 3824-3825.
- [6] Atta-ur-Rahman, Abbas, S., Dur-e-Shawar, Jamal, A.S., Choudhary, M.I. New withanolides from *Withania* spp. *J. Nat. Prod.*, (1993). 56, 1000-1006.
- [7] Bandopadhyay M., Jha S., Tepfer D. Changes in morphological phenotypes and withanolide composition of Ri -Transformed roots of *Withania somnifera*. *Plant cell Rep.* (2007). 26, 599-609.
- [8] Bano A, Ayub M, Rashid S, Sultana S and Sadia H. Ethnobotany and conservation status of floral diversity of Himalayan range of Azad Jammu and Kashmir Pakistan. *Pakistan Journal of Botany*. (2013). 45: 243-251.
- [9] Bector N.P, Puri A.S, Sharma D. Role of *Withania somnifera* (Ashwagandha) in various types of Arthropathies. *Ind. J. Med. Res.* (1968). 56, 1581-1583.
- [10] Begum V. H. and Sadique J. Long term effect of herbal drug *Withania somnifera* on adjuvant induced arthritis in rats. *Ind. J. Exp. Biol.* (1988). 26, 877-882.
- [11] Bhatnagar M, Sisodia SS and Bhatnagar R Antiulcer and antioxidant activity of *Asparagus racemosus* WILLD and *Withania somnifera* DUNAL in Rats. *Ann. NY Acad. Sci.* (2005) 1056, 261-278.
- [12] Bhattacharya SK, Goel RK, Kaur R, Ghosal S. Anti-tress activity of sitoinsosides VII and VIII, new acylsteryl glucosides from *Withania somnifera*. *Phytother. Res.* (1987). 9: 10-13.
- [13] Bhattacharya A, Ghosal S and Bhattacharya S.K. Antioxidant effect of *Withania somnifera* glycowithanolides in chronic footshock stress-induced perturbations of oxidative free radical scavenging enzymes and lipid peroxidation in rat frontal cortex and striatum. *J. Ethnopharmacol.* (2001) 74: 1-6.
- [14] Bhattacharya A, Ramanathan M, Ghosal S, Bhattacharya SK. Effect of *Withania somnifera* glycowithanolides on iron-induced hepatotoxicity in rats. *Phytother Res.* (2000) 14(7):568-570.
- [15] Bhattacharya, S., K., Muruganandam, A., V. Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress. *Pharmacol. Biochem. Behav.* (2003) 75(3): 547-555.
- [16] Boone K. *Withania*-The Indian ginseng and anti-aging adaptogen. *Nutr. Healing*. (1998). 5, 5-7.
- [17] Choudary, M.I., Abbas, S., Jamal, A.S. and Atta-ur-Rahman. *Withania somnifera*- A source of exotic withanolides. *Heterocycles* (1996). 42, 555-563.
- [18] Dafni A. and Yaniv Z. Solanaceae as medicinal plants in Israel. *Journal of Ethnopharmacology*. (1994). 44, 11-18.
- [19] Dalzell N. A. and Gibson A. In the Bombay flora together with a supplement of induced species (Bombay). (1861).
- [20] Davis L and Kuttan G. Suppressive: Effect of cyclophosphamide-induced toxicity by *Withania somnifera* extract in mice. *J. Ethnopharmacol.* (1998) 62, 209-214.
- [21] Davis L, Kuttan G. Effect of *Withania somnifera* on cytokine production in normal and cyclophosphamide treatment mice. *Immunopharmacol & Immunotoxicol.* (1999). 21(4):695-703.
- [22] Devi P. U, Sharada A. C, Solomon F. E and Kamath M. S. In vivo growth inhibitory effect of *Withania somnifera* (Ashwagandha) on a transplantable mouse tumor, Sarcoma 180. *Ind. J. Exp. Biol.* (1992) 30, 169-172.
- [23] Devi P. U, Sharada A. C and Solomon F. E. Antitumor and radiosensitizing effects of *Withania somnifera* (ashwagandha) on a transplantable mouse tumor, Sarcoma-180. *Ind. J. Exp. Biol.* (1993) 31, 607-611.
- [24] Devi P.U. *Withania somnifera* dunal (ashwagandha): Potential plant source of a promising drug for cancer chemotherapy and radiosensitisation. *Ind. J. Exp. Biol.* (1999). 34 (10), 927-932.
- [25] Dhuley J. N. Effect of Asgand on lipid peroxidation in stress induced animals. *J. Ethnopharmacol.* (1998). 7:173-178.
- [26] Dhuley, J., N. Nootropic-like effect of Ashwagandha (*Withania somnifera* L.) in mice. *Phytother. Res.* (2001). 15(6): 524-528.
- [27] Dutta U. C. and King G. *Materia medica of Hindus*. Calcutta Machine Press. (1877).
- [28] Eastwood FW, Kirson I, Lavie D and Abraham A. New withanolides from a cross of a South African chemotype by chemotype II (Israel) in *Withania somnifera*. *Phytochem.* (1980). 19, 1503-1507.
- [29] Ghosal S, Lal J and Srivastava R. Immunomodulatory and CNS effects of sitoindosides IX and X, two new glycowithanolides from *Withania somnifera*. *Phytother. Res.* (1989) 3, 201-206.
- [30] Glotter, E. Withanolides and related ergostane-type steroids. *Nat. Prod. Rep.* (1991). 8, 415-440.
- [31] Gorelick J, Rosenberg R, Smotrich A, Hanus L and Bernstein N. Hypoglycemic activity of withanolides and elicited *Withania somnifera*. *Phytochemistry*. (2015).
- [32] Gupta M.L, Mishra A.K and Khanduja S.P.S Root rot and wilt: A new disease of Ashwagandha (*Withania somnifera*) caused by *Fusarium solani*. *Journal of Medicinal and Aromatic plant sciences*. (2004). 26, 285-287.
- [33] Halliwell B and Gutteridge, J.M.C. Free radicals in biology & medicine. (2nd ed. Oxford: clarendon press. (1989).
- [34] Hepper, F.N. In *Solanaceae III: taxonomy, chemistry, evolution*; Hawkes, J.G., Lester, R.N., Nee, M., Estrada, E.,

- Eds.; Royal Botanic Gardens, Kew: UK. (1991) pp. 211-227.
- [35] Jayaprakasam B, Zhang Y. Seeram N.P and Nair M.G. Growth inhibition of human tumor cell lines by withanolides from *Withania somnifera* leaves. *Life Sci.* (2003) 74, 125-132.
- [36] Jayaprakasam, B.; Strasburg, G.A.; Nair, M.G. Potent lipid peroxidation inhibitors from *Withania somnifera* fruits. *Tetrahedron* (2004). 60, 3109-3121.
- [37] Jesberger J. A and Richardson J. S. Oxygen free radicals and brain dysfunction. *Int. J. Neurosci.* (1991). 57, 1-17.
- [38] Kapoor, L.D. *Handbook of Ayurvedic Medicinal Plants*; CRC Press: London, UK. (2001). pp. 337-338.
- [39] Kirson, I, Glotter, E, Lavie, D and Abraham, A. Constituents of *Withania somnifera* Dun. XII. The withanolides of an Indian chemotype. *J. Chem. Soc. C*, (1971). 2032-2044.
- [40] Kirson I., Abraham A. and Lavie D. Chemical analysis of hybrids of *W. somnifera* L. (Dunal) chemotype I and III Israel by Indian I (Delhi). *Israel. J. Chem.* (1977) 16, 20-24.
- [41] Kumar S, Tiwari, A. And Dwivedi R. The use of aphrodisiacs in Medieval India. *Nagarjun*, (1980). 23:170-174.
- [42] Kumar, S.K. Kulkarni. Effect of BR-16A (Mentat), a polyherbal formulation drug-induced catalepsy in mice. *Indian J. Exp. Biol.* (2006). 44(1): 45-48.
- [43] Kurup P.A. Antibiotic principals of the leaves of *Withania somnifera*. *Curr. Sci.* 25, 57-60.
- [44] Kuttan G (1996) Use of *Withania somnifera* Dunal as an adjuvant during radiation therapy. *Ind. J. Exp. Biol.* (1956) 34, 854-856.
- [45] Lavie D, Glotter E, Shro Y. Constituents of *Withania somnifera*. Dun IV. *J Chem Soc.* (1965). 12:7517.
- [46] Leyon PV and Kuttan G. Effect of *Withania somnifera* on B16F-10 melanoma induced metastasis in mice. *Phytother. Res.* (2004) 18, 118-122.
- [47] Lohar DR, Chaturvedi D and Varma P. N. Mineral elements of a few medicinally important plants, *Ind. Drugs.* (1992). 29, 271-273.
- [48] Maithani B. P. Medicinal plants of western garhwal. *Khadi gramodyog.* (1973). 19, 269-278.
- [49] Malhotra C. L, Mehta V. L, Das P. K, Dhalla N. S. Studies on *Withania-ashwagandha*, Kaul (Part-V) The effect of total alkaloids (ashwagandhadholine) on the central nervous system. *Ind J Physiol Pharmacol.* (1965). 9:127-136.
- [50] Mathur S, Kaur P and Sharma M. The treatment of skin carcinoma induced by UV B radiation, using 1-oxo-5beta, 6beta -epoxy-with a-2-enolide, isolated from the roots of *Withania somnifera*, in a rat model. *Phytomed.* (2004). 11, 452-460
- [51] Mhaskar KS, Blatter E, Caius J F Indian Medicinal Plants (Sri Satguru Publications, Delhi, India). (2000). Vol 8, 2447-2449.
- [52] Mir B A., Khazir J., Mir N A., Hasan T., Koul S. Botanical, chemical and pharmacological review of *Withania somnifera* (Indian ginseng) : an ayurvedic medicinal plant. *Indian Journal of Drugs and Diseases.* (2012). 1 [6] 147-160.
- [53] Mirjalili MH, Moyano E, Bonfill E, Cusido RM and Palazón J. Steroidal Lactones from *Withania somnifera*, an an-cient plant for novel medicine. *Molecule*, (2009) 14, 2373-2393.
- [54] Mishra L.C, Singh B.B and Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (Ashwagandha): A Review. *Altern Med. Rev.* (2000) 5(4), 334-346.
- [55] Mohanty I, Arya D.S, Dinda A, Talwar K.K, Joshi S, Gupta S.K. Mechanism of cardioprotective effect induced myocardial infarction. *Bas & Clin Pharm & Toxicol.* (2004). 94(4):184-190.
- [56] Mozaffarian, V. *Trees and shrubs of Iran*; Farhange Moaser: Tehran, Iran, (2003). pp. 874-877.
- [57] Nadkarni K. M. Indian materia medica, (Popular Prakashan Limited: Bombay, India. (1976). 1291.
- [58] Owais, M., Sharad K.S., Shehbaz, A. and Saleemuddin M. Antibacterial efficacy of *Withania somnifera* (Ashwagandha) an indigenous medicinal plant against experimental murine salmonellosis. *Phytomedicine.* (2005) 12(3): 229-235.
- [59] Prakash J, Gupta S K. and Dinda A K. *Withania somnifera* root extract prevents DMBA-induced quamous cell carcinoma of skin in Swiss albino mice. *Nutr. Cancer.* (2002) 42, 91-97.
- [60] Raimondo D, Von Staden L, Foden W, Victor J.E, Helme N. A, Turner R. C, Kamundi D. A, and Mayama P. A Red list of south African national biodiversity institute Pretoria. (2009).
- [61] Rao R. R. Medicobotany of some Mysore plants. *J. Res. Ind. Med. Yoga Homoeo.* (1977). 12: 53-58.
- [62] Rasool M and Varalakshmi P. Immunomodulatory role of *Withania somnifera* root powder on experimental induced inflammation: an in vivo and in vitro study. *Vascul. Pharmacol.* (2006) 44, 406-410.
- [63] Rastogi, R.P. and Mehrotra, B.N. *Compendium of Indian Medicinal Plants*; Central Drug Research Institute: New Delhi, India. (1998).
- [64] Sahu T.R. An ethnobotanical study of Madhya pradesh1: plants used against various disorders among tribal women. *Ancient science of life*(1982). 1, 178-181.
- [65] Schliebs R, Liebmann A, Bhattacharya S.K, Kumar A, Ghosal S, Bigl V. Systematic administration of defined extracts from *Withania somnifera* (Indian Ginseng) and Shilajit differentially affects cholinergic but not glutamatergic and GABAergic markers in rat brain. *Neurochem Int.* (1997) 30:181-190.
- [66] Sehgal N, Gupta A, Khader R, Shanker V, Joshi D, Mills JT, Hamel E, Khanna P, Jain S.C, Thakur S.S, and Ravindranath V. *Withania somnifera* reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in liver. *Proc. Nat. Acad. Sci.* (2012) 109(9), 3510-3515.
- [67] Sen Gupta N. N. K. The ayurvedic system of medicine. (Delhi, Neeraj Publishing House) Vol II.

- [68] Shah, G. L., and Gopal, G. V. (1985). Ethnomedical notes from the tribal inhabitants of the North Gujarat (India). *Journal of Economic and Taxonomic Botany* (1984). 6(1): 193-201.
- [69] Sharma S., Dahanukar S., Karandikar S.M. Indian drugs, (1985) 23, 133.
- [70] Singh N, Bhalla M, De Jager P and Glica M. An overview on ashwagandha : A rasayana (Rejuvenator) of ayurveda. *African journal of Traditional, complementary and alternative medicines: AJTCAM*. (2011). 8(5), 208-213.
- [71] Singh S, Kumar S. Withania somnifera The Indian Ginseng- Ashwagandha. CIMAP, Lucknow, India. (1998).
- [72] **Silvia D.S., Eun R.H., Renaud W and Shivendra V. S.** Withaferin A Causes FOXO3a- and Bim-Dependent Apoptosis and Inhibits Growth of Human Breast Cancer Cells *In vivo*. *Can. Res.* **(2008)**. 68, 7661-7669.
- [73] Schonbeck-Temesy, E. In *Flora Iranica*; Rechinger, K.H., Ed. Akademische Druck-u. Verlagsanstalt: Graz, Austria. No. (1972). 100, pp. 29-26.
- [74] SPC (The Sidha Pharmacopoeia Committee). Compound formulations in the Sidha formulary of India. Part-I. (New Delhi Ministry of Health and Family Welfare) First edition. (1992).
- [75] Stewart L. Punjab plants comprising Botanical and vernacular names and uses of most of the trees, shrubs, and herbs of economical value, growing within the province (Lahore, British India: The Government Press). (1969).
- [76] Tursunova, R.N.; Maslennikova, V.A.; Abubakirov, N.K. Withanolides in the vegetable kingdom. *Chem. Nat. Comp.* (1977). 13, 131-138.
- [77] Udayakumar R, Kasthuriengan S, Mariashibu T. S, Rajesh M, Anbazhagan V. R, Kim S. C, Ganapathi A, Choi C. W. Hypoglycaemic and hypolipidaemic effects of *Withania somnifera* root and leaf extracts on alloxan-induced diabetic rats. *Int J Mol Sci.* (2009). 10(5):2367-2382.
- [78] UPC (The Unani Pharmacopoeia Committee). Compound formulations in the National formulary of Unani medicine. Part- I. (New Delhi Ministry of Health and Family Welfare) (1983). First edition.
- [79] Ziauddin M, Phansalkar N, Patki P, Diwanay S, Patwardhan B. Studies on the immunomodulatory effect of Asgandh. *J Ethnopharmacol.* (1996). 50(2):69-76.

