

EXPLORING THE PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF WITHANIA SOMNIFERA - A REVIEW

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ABSTRACT

Ashwagandha (*Withaniasomnifera*) is a widely used herb in traditional Ayurvedic medicine, known for its adaptogenic properties. It has been extensively studied for its pharmacological effects and therapeutic potential. The herb exhibits various bioactive compounds, including alkaloids, steroidal lactones (withanolides), and saponins, which contribute to its diverse medicinal properties. Research indicates that ashwagandha possesses antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, and anti-stress properties. Additionally, it has shown promising effects in improving cognitive function, enhancing stamina and endurance, modulating hormonal balance, and supporting overall health and well-being. Furthermore, clinical studies have highlighted its potential in managing conditions such as anxiety, depression, insomnia, and cognitive decline. Despite its wide-ranging therapeutic benefits, further research is warranted to elucidate its mechanisms of action and optimize its therapeutic applications. Overall, ashwagandha stands as a promising natural remedy with significant potential for promoting health and treating various ailments.

Key Words: *Withania somnifera*, Ashwagandha, Indian Winter cherry, Ginseng and Withanolides

INTRODUCTION

Common names for ashwagandha include "Indian Winter cherry" and "Indian Ginseng." Another name for it is *Withania somnifera*¹. Ashwagandha is a member of the Solanaceae family². This plant was given the Sanskrit names "Ashva," which means horse, and "Gandha," which means smelling, because of the roots' similarity to a sweaty horse's scent³. With several health advantages, it has been used as a Rasayana for millennia, making it one of the most significant herbs in Ayurveda, the traditional medical system of India. Rasayana is defined as a herbal or metallic preparation that enhances happiness and supports a young condition of physical and mental health. These kinds of medicines are taken by the middle-aged and elderly to lengthen their lives, and they are also given to young children as tonics. Of all the herbs used in Ayurvedic Rasayana, Ashwagandha is the most important. The herb is specified as "Sattvic Kapha Rasayana". The majority of Rasayana plants have adaptogenic or anti-stress properties⁴

The most popular form of ashwagandha is churna, which is a finely ground powder that may be combined with honey, ghee (clarified butter), or water. It helps memory and the way the brain and nervous system work. It enhances the reproductive system's functionality, supporting a balanced sexual and reproductive life. As a potent adaptogen, it increases the body's ability to withstand stress. Ashwagandha enhances cell-mediated immunity, which strengthens the body's resistance to illness. Additionally, it has strong antioxidant qualities that aid in preventing cellular damage brought on by free radicals⁵

This native medicinal plant has a significant role in treating a number of illnesses, including stress⁶, anxiety⁷, rheumatoid arthritis⁸, and other conditions involving the central nervous system (CNS), such as Parkinson's⁹ and Alzheimer's disease¹⁰.

TAXONOMY

Kingdom	Plantae (plants)
Subkingdom	Tracheobionta (vascular plants)
Super division	Spermatophyta(seed plants)
Division	Angiosperma
Class	Dicotyledons
Order	Tubi florae
Clade	Solanaceae
Genus	Withania
Species	Somnifera,Dunal



Fig 1: Ashwagandha plant¹¹



Fig 2: Ashwagandha fruits¹¹

Table 1: Common names of Ashwagandha¹²

Language	Name
English	Winter cherry, Indian ginseng
Sanskrit	Ashvagandha (Horse smelling)
Hindi	Asgandh
Urdu	Asgandanagori
Rajasthani	Sarvgandha
Marathi	Askandha, Kanchuki
Konkani	Fatarfoda
Bengali	Ashvaganda
Oriya	Asugandha
Assamese	Asgandhisrol
Kannada	Amangura, Sogadeberu
Malayalam	Amukkiram, Pevetti
Tamil	Amkulan-kalang, Achuvagandhi
Telugu	Penneru gaddalu

ORIGIN, GEOGRAPHICAL DISTRIBUTION

It can be found in many dry and subtropical regions of India, including the plains of Bombay, Gujarat, Rajasthan, Madhya Pradesh, Uttar Pradesh, and Punjab. It can also be found in mountainous areas of Himachal Pradesh and Jammu & Kashmir, where it can reach elevations of up to 1800 meters above mean sea level. The plant is found in a range of phyto-geographic zones with varying edaphic characteristics and climates. The Neemuch District of Madhya Pradesh serves as the primary hub for the selling of dried ashwagandha roots. It is found in regions with different soil, rainfall, temperature, and altitudinal gradients, including Pakistan, Afghanistan, Palestine, Egypt, Jordan, Morocco, Spain, Canary Island, Eastern Africa, Congo, Madagascar, and South Africa, according to reports.¹³

BOTANICAL DESCRIPTION

The plant typically grows up to 1.25 meters tall and is an upright, green, branching or unbranched herb. Fine hairy tomentum is sporadically coated throughout the aerial section, particularly on the stem, leaves, and calyx. The plant has rounded branches, simple, petiolated, ovate, whole, glossy, smooth, and opposite leaves; tiny, flat, yellow, reniform, and extremely light seeds; bisexual, inconspicuous flowers in axillary umbellate cymes; berries in a persistent calyx; and fruit in the shape of a berry. The crop is often planted in the Kharif season, and the plant has tap roots that are light yellow in color and are 15 to 25 centimeters in length. The branches are between 60 and 120 cm long and are upright. Dry weather is necessary for the growth of higher alkaloid content and improved root quality.¹³

Propagation

As ashwagandha naturally spreads through seeds, commercial ashwagandha production has been advised to use the broadcast method of seed planting. Numerous variations in phytochemical characteristics result from seed propagation.¹⁴

Cultivation

There is great potential to grow this plant commercially due to the plant's widespread curiosity and the significant demand for its roots. Additional cultivation opportunities include the following: the crop can be integrated with traditional crops through crop sequencing; the crop can be grown under rainfed conditions with ease; the crop offers economically remunerative returns in comparison to traditional crops; by-products can be profitably used; value addition can increase profits; however, current exports are limited and large-scale exports of roots and value-added products need to be explored.¹⁵

Cultivation practices for Ashwagandha

In India, the districts of Kota in Rajasthan; Bhanpura, Manasa, Neemuch, and Jawad tehsils in the Mandsaur district in Madhya Pradesh; and Anantapur, Kurnool, Mahabubnagar, Warangal, and Prakasam in Andhra Pradesh are among those that commercially farm ashwagandha as a rainfed crop. In a few places in Karnataka, cultivation has begun. Details on the cultivation are provided below.¹⁵

Soil and climate

It is widespread in India between 230 and 330 N, or 180 and 1700 m above mean sea level. This crop may be grown in semi-arid tropical regions with 500–750 mm of rainfall. During its growth season, it needs a dry season. A late winter rain or two is ideal for the healthy growth of roots. The crop thrives on pH 7.5–8.0 light-textured reddish-black soils, sandy loams, and well-drained sandy soils.¹⁵

Varieties

High yielding varieties Poshita and Rakshita were released by CSIR-CIMAP, Lucknow. Maharashtra is the home of Jawahar 20 cultivation. Another variant offered by the CSIR-Regional Research Laboratory in Jammu is called WSR. A native variant with starchy roots is called Nagoya.¹⁵

Harvesting

After 180–210 days of seeding, the crop is ready for harvesting. A crop that is 150–180 days old is harvested in some areas. The crop's maturity is indicated by the berries becoming red and the leaves drying off. The entire plant is removed, and the roots are separated by chopping the stem 1-2 cm above the crown. After being washed, the roots are either chopped into 7–10 cm lengths and dried in the sun, or they are dried whole and preserved. The seeds are saved for the following harvest after the berries are hand-picked, dried, and threshed.¹⁵

GRADING OF ROOTS

To break off thin, fragile lateral rootlets and remove any clinging dirt, the dried roots are hammered with a club. Using a knife, lateral branches, the root crown, and the stem remnants are carefully cut. The following grades are subsequently assigned to the root parts.

1) A grade

Root portions that are solid cylindrical, smooth on the outside, and completely white on the interior, measuring up to 7 cm in length and 1 to 1.5 cm in diameter.

2)B grade

Root portions that are firm, brittle, and white within that measure up to 5 cm in length and 1 cm or less in diameter.

3)C grade

chunks of solid root, little more than 1 centimeter in diameter and 3–4 cm in length.

4)D grade

tiny, less than a centimeter in diameter, semisolid or hollow, thin, and have a yellowish inside. Farmers are now classifying the roots into seven or more classes.¹⁵

PHYTOCHEMICAL DISTRIBUTION

Roots

Alkaloids, amino acids, steroids, volatile oil, starch, reducing sugars, glycosides, dulcitol, withaniol, and hentriacontane are all found in roots. Although substantially larger yields (up to 4.3%) have been observed elsewhere, the total alkaloidal content of Indian roots has been found to fluctuate between 0.13 and 0.31 percent.

A few examples of basic alkaloids include cuscohygrine, anahygrine, tropine, pseudotropine, anaferine, isopelletierine, withananine, withananine, pseudo-withanine, somnine, somniferine, and somniferinine. Other alkaloids are visamine, withanine, and assomnine. Aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid, and cystine are among the free amino acids found in the root.¹⁶

Leaves

According to reports, the plant (Indian chemotype) contains 12 withanolides, 5 unidentified alkaloids (yield, 0.09%), condensed tannins, glucose, glycosides, chlorogenic acid, and flavonoids in addition to a large number of free amino acids. The most significant withanolide found in the extract of *Withaniasomnifera's* dried roots and leaves is withaferin A, a steroidal lactone.¹⁷

Fruits

The green berries contain amino acids, a proteolytic enzyme, condensed tannins, and flavonoids. They contain a high proportion of free amino acids which include proline, valine, tyrosine, alanine, glycine, hydroxyproline, aspartic acid, glutamic acid, cystine and cysteine. The presence of a proteolytic enzyme, chamase, in the berries may be responsible for the high content of the amino acid.¹⁸

Other Parts

Tender shoots that lack fibrousness and are high in crude protein, calcium, and phosphorus. They are said to include scopoletin. The plant's stem is rich in flavonoids and condensed tannins. There are many free amino acids in the bark.¹⁸

CHEMICAL CONSTITUENTS

The plant is made up of a variety of chemical substances in different areas. Following is a list of a few of them:

• Alkaloid

Ashwagandhine, anahygrine, anaferine, cuscohygrine, tropine, isopelletierine, pseudotropine, 3-tigloyloxtropine, dlisopelletierine, hygrine, mesoanaferine, choline, somniferine, withanine, withananine, etc.

• Steroidal compounds

Ergostane

• Steroidal lactones

withanone, asomidienone, asomniferols A–C, withanolides A–Y, withaferin A, etc.

• Saponins

including sitoindosides VII and VIII, which are extra acyl groups

• Withanolides

Containing sitoindoside IX and X having a glucose at carbon 27.

• Withanolide glycosides

withanosides I, II, III, IV, V, VI and VII.

• Pyrazole derivatives

ashwagandhine and pseudowithanine in addition to the aforementioned components, the plant also includes a high concentration of iron, withaniol, acylsteryl glucosides, starch, reducing sugar, hantreacotane,

ducitol, and a range of amino acids, like aspartic acid, proline, tyrosine, alanine, glycine, cystine, glutamic acid and tryptophan.¹⁹

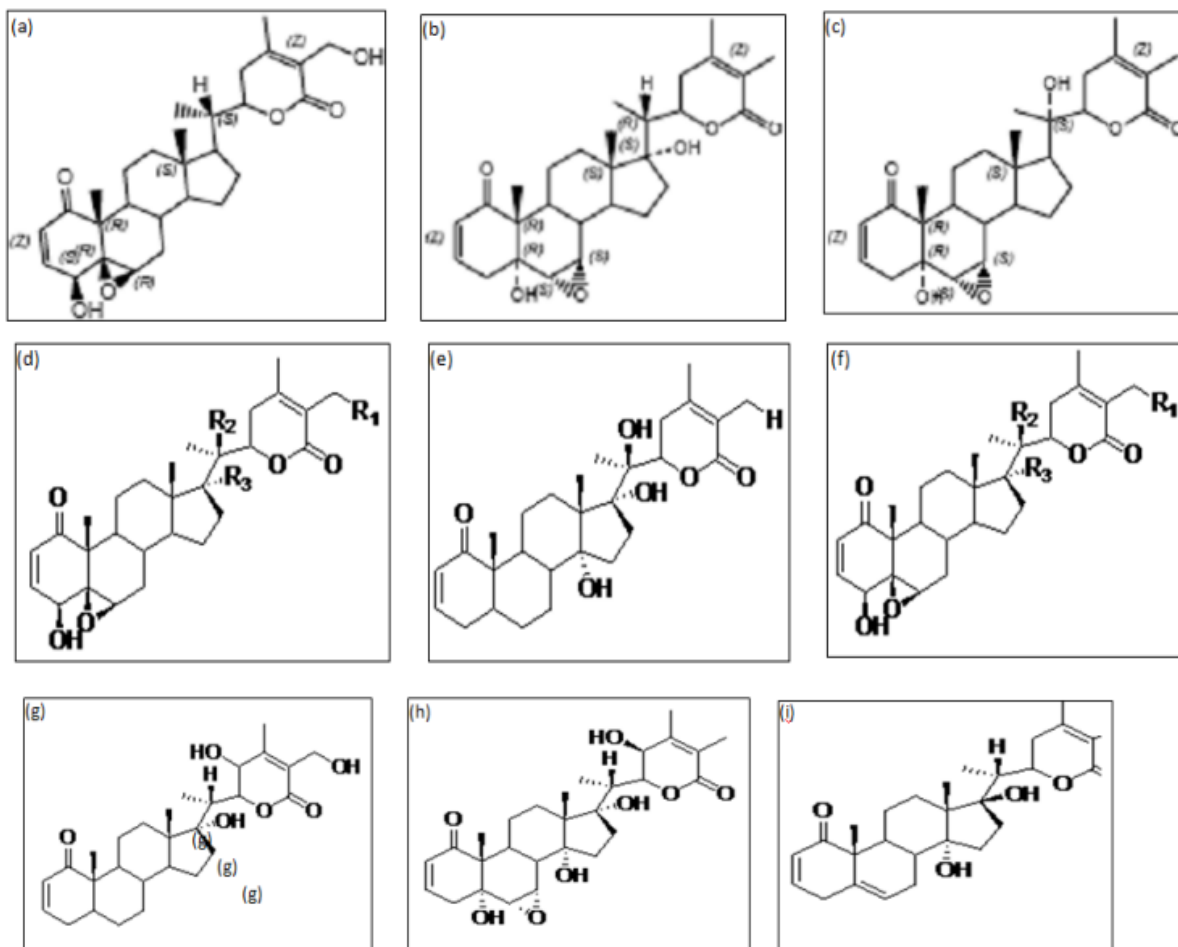


Fig 3: structures of chemical constituents[Ashwagandha]¹⁹

(A) Withaferin A, (B) Withanone, (C) Withanolide A, (D) Withanolide D, (E) Withanolide E, (F) Withanolide G, (G) Withanolide Q, (H) Withanolide R, (I) Withanolide P, (J) 7-Hydroxy withanolide B and

PHARMACOLOGICAL PROFILE

1. Effect on nervous system

Ashwagandha is an excellent medication for tiredness and nervous irritation since it is said to have a sedative rather than a stimulative effect on the central nervous system. The concentration of neurotransmitters that are known to be crucial for brain functions like memory is changed by ashwagandha. Root extracts of ashwagandholine are linked to effects on the neurological system. It produces relaxing and antispasmodic effects against numerous drugs that elicit smooth muscle spasms in intestinal, uterine, tracheal, and vascular muscles. It also amplifies the hypnosis that is produced in mice by barbiturates, ethanol, and urethane.

Traditionally, ashwagandha has been utilized as a nootropic and tonic herb. Additionally, it has been linked to improvements in mice's scopolamine-induced memory deficiencies. Because *Withaniasomnifera* extracts have strong antioxidant, antiperoxidative, and free radical quenching qualities, they also have an

antiparkinsonian action on neuroleptic-induced catalepsy by preventing the effects of haloperidol or reserpine.

Table 2: Biological activity of root extracts of *Withania somnifera*²⁰

Root extract	Biological activity
Alcoholic extract	Neurological, Radiosensitizer, Anticonvulsant, Anti-inflammatory, Sedative, Antitumour, Antibacterial.
Methanolic extract	GABA mimetic activity GABA receptor mediates anti-convulsant activity, Protective effect as amygdaloid kidling Anti-inflammatory (70% extract), Antistress.
Chloroform-Methanol extract	Prevention of Alzheimers disease Immunomodulatory, Anti-inflammatory, Nematicidal, Hepatoprotective,
Water extract	Nephroprotective, Antistress, Antianxiety, Hypothyroidism. Anti-convulsnt, Anti-inflammatory, Antiarthritic, Hepatoprotective,
Root powder	Antiulcerogenic, Antistress, Anticancer & Radiosensitizer, Pscophysiological, Pulmonary tuberculosis, Epilepsy, Nervinetic, Easy abortion, General tonic in seminal disease, Glandular swellings in bubonic plague, Hypoglycemic diuretic.
Decoction	Anticonvulsant, Cold & Chills, Health restorative to old & pregnant.
Petroleum ether extract	Insecticidal

2. Anticancer activity

Significant anti-tumor effects have been found for withaferin A and withanolide D.²¹ Additionally, *withania somnifera* contains oxo-5 β , 6 β -epoxy-witha-2-enolide, which has been shown to prevent skin carcinomas caused by UV exposure.²² Withaferin A functions as a mitotic toxin, halting the cultivated human laryngeal carcinoma cells' division during metaphase. Additionally, it resulted in a notable dose-dependent inhibition of the development of sarcoma 180, sarcoma Black, Ehrlich ascites carcinoma, and E 0771 mammary adenocarcinoma.²³ *Withaniasomniferamethanolic* extract has been used to stem cell proliferation.²⁴ It also showed potential as a chemotherapeutic drug by reducing the viability of colon, breast, lung, and central nervous system cancer cell lines in a dose-dependent manner.²⁵ The activation of apoptosis, which is characterized by DNA condensation, cytoplasmic histone-associated DNA fragmentation, and poly-(ADP-ribose)-polymerase cleavage, is coupled with the withaferin A-mediated

lowering of breast cancer cell survival.²⁶ Part of the extract's chemopreventive action is ascribed to its antioxidant and free radical scavenging properties.²⁷

3. Antioxidant effects

The brain and nervous system are relatively more susceptible to free radical damage than other tissues because they are rich in lipids and iron, both known to promote the generation of reactive oxygen species.²⁸ Free radical damage of nervous tissue may be responsible for neural loss in cerebral ischemia and may be involved in aging and neurodegenerative diseases, e.g., epilepsy, schizophrenia, Parkinson's, Alzheimer's and other diseases.²⁹ It has been claimed that the active components of *Withaniasomnifera*, sitoindosides VII-X and withaferin A (glycowithanolides), raise endogenous levels of SOD, CAT, glutathione peroxidase (GPX), and ascorbic acid while simultaneously lowering lipid peroxidation.³⁰

4. Anti-inflammatory properties

By suppressing complement, lymphocyte proliferation, and delayed-type hypersensitivity, ashwagandha reduces inflammation.³¹ *Withaniasomnifera* extracts have demonstrated anti-inflammatory properties in a range of rheumatological disorders.³² It was discovered that the extract increased the activity of the Mg²⁺ dependent ATPase enzyme, which in turn reduced the activity of succinate dehydrogenase in the mitochondria of the granuloma tissue. Additionally, the extract significantly reduced the ADP/O ratio in the mitochondria of the granuloma tissue, uncoupling the oxidative phosphorylation.³³

5. Anti-microbial activities

Kurup (1956) described the antibacterial activity of this multipurpose medicinal herb against *Salmonella aurens* for the first time. Withanolide has been linked to antibacterial action against a variety of bacteria and fungi during the last ten years. The body of research on this plant suggests that further research is necessary to see whether or not it can also be used to treat other infectious disorders.³⁴

6. Anti-arthritic properties

It has been shown that ashwagandha powder helps with acute rheumatoid arthritis and lessens arthritis pain. Withaferin A. has been identified as the active principle responsible for this characteristic.³⁵

7. Immunity

Withaniasomnifera shows an immuno-potentiating and myeloprotective effects know roots by enhancing the levels of interferon (IFN)- γ , interleukin (IL)-2 and granulocyte macrophage colony stimulating factor in normal and cyclophosphamide-treated mice.³⁶ As the plant is rich in iron, it contributes to red blood cell count. The effect of *Withaniasomnifera* on the immune system is subtler than simply suppressing the immune/ inflammatory response. The active compound (withanolide A) in the roots of *Withaniasomnifera* notably increases the expression levels of T-helper 1 (Th1) cytokines, also 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.³⁷ Apart from the above activated macrophage functioning

indicated by enhanced secretion of nitrile, 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 extract of this plant is also noted to stimulate the cell-mediated immunity, IgM and IgG and a prominent improvement in proliferation and differentiation of lymphocytes as indicated by lymphocyte surface markers of T cells (CD3+, CD4+ and CD8+) and B cells (CD19+).³⁸

8. Cardiovascular Protection

Ashwagandha has a cardioprotective effect due to its anti-apoptotic properties and due to its restoring of the oxidative balance. The cardioprotective effect of withaferin A, a component of Ashwagandha known for its anticancer properties, was also studied.³⁹

USES OF PLANT PARTS:⁴⁰

Table 3: Plant parts and uses:

Plant Part	System of medicine	Uses
Roots	Ayurveda	Rejuvenating drug, tonic, Alternative pungent, astringent, Aphrodisiac, Phthisis
	Siddha	Aphrodisiac, fever, inflammation
	Unani	Asthma, bronchitis, leucoderma, Arthritis, emmenagogue
	Folklore	Abortifacient, cold, asthma, Tuberculosis, fever
Leaves	Ayurveda	Aphrodisiac, carbuncle, Ulcers, painful swelling
	Siddha	Fever, chest pain, sores, swelling
	Unani	External pains, anti-inflammatory
	Folklore	Cure eyesores, boils, diuretic, treatment of syphilis and hemorrhoids
Seeds	Ayurveda	Diuretic, narcotic and hypnotic
	Siddha	Siddha
	Unani	Unani
	Folklore	To coagulate milk, applied on open wounds, Relieving the poison of a serpent rubbed on skin for ringworm in human beings and animals
Fruits		antihelmantic, ulcers and tubercular glands

9. DISCUSSION AND CONCLUSION

Due to its numerous pharmacological activities, including those that are anti-stress, neuroprotective, anticancer, anti-arthritic, analgesic, and anti-inflammatory, the existing scientific evidence support the assertion that ashwagandha is a really effective regeneration tonic (Rasayana of Ayurveda). Numerous illnesses, including Parkinson's, dementia, memory loss, illnesses brought on by stress, malignoma, and others, might benefit from it. Indians utilize ashwagandha as a home treatment; they believe it to be the ideal tonic for children and the elderly, while young people take it as an aphrodisiac. It is among the most effective nervine tonics found in Ayurveda, the oldest medical science system. Our clinical experience demonstrated that, in addition to the above neurological diseases, long-term ashwagandha therapy also improves brain strokes that cause paralysis and neuronal deficiency. We also use it to treat other cancers, such as lung and prostate cancer, especially in the later stages when it can provide patients substantial health benefits. When we used ashwagandha therapy, some of our lung cancer patients who refused modern treatment recovered both clinically and radiologically. During a recent lecture on the essential drug concept, topics such as cancer and neurological diseases were covered.⁴¹

REFERENCES:

1. Narendra Singh, Mohit Bhalla, Prashanti de Jager and Marilena Gilca. An Overview on Ashwagandha: A Rasayana (Rejuvenator) Of Ayurveda. Afr J Tradit Complement Altern Med. 2011; 8(5); 208-213.
2. Madhu Prakash Srivastava, Shashi Gupta, Sonal Dixit, Namita Yadav, Vandana Yadav, Hina Singh, Pankaj Kanaujia¹, Yogesh Kumar Sharma. *Withaniasomnifera* (Ashwagandha): A wonder herb with multiple medicinal properties, multiple medicinal properties. Asian Journal of Pharmacy and Pharmacology. 2018; 4(2); 123-130.
3. Rajeswara Rao B., Rajput D.K., Nagaraju G. And Adinarayana G. Opportunities and Challenges In The Cultivation Of Ashwagandha {*WithaniaSomnifera* (L.)Dunal. Journal Of Pharmacognosy. Issn: 0976-884x & E-Issn: 0976-8858,2012; Volume 3, Issue 2 ;88-91.
4. Narendra Singh, Mohit Bhalla, Prashanti de Jager and Marilena Gilca. An Overview on Ashwagandha: A Rasayana (Rejuvenator) Of Ayurveda. Afr J Tradit Complement Altern Med. 2011; 8(5);208-213.
5. Narendra Singh, Mohit Bhalla, Prashanti de Jager and Marilena Gilca. An Overview on Ashwagandha: A Rasayana (Rejuvenator) Of Ayurveda: Afr J Tradit Complement Altern Med. 2011; 8(5);208-213.
6. Bhattacharya.A, Ghosal.S and Bhattacharya.SK. Anti-oxidant effect of *Withaniasomniferaglycolwithanolides* in chronic foot-shock stressinduced perturbations of oxidative free radical scavenging enzymes and lipid peroxidation in rat frontal cortex and striatum. Journal of Ethnopharmacology.200: 74(1);1-6.
7. Gupta.A and Singh.S. Evaluation of anti-inflammatory effect of *Withaniasomnifera* root on collagen-induced arthritis in rats. Pharm Biol.2014: 52(3); 308-320.
8. Prakash.J, Chouhan.S, Yadav.SK, Westfall.S, Rai.SN, Singh.SP. *Withaniasomnifera* Alleviates Parkinsonian Phenotypes by Inhibiting Apoptotic Pathways in Dopaminergic Neurons. Neuro chem Res.2014:39(12);2527-2536.
9. Manjunath.MJ and Muralidhara. Standardized extract of *Withaniasomnifera* (Ashwagandha) markedly offsets rotenone-induced locomotor deficits, oxidative impairments and neurotoxicity in *Drosophila melanogaster*. J Food Sci Technol.2013:52(4);1971-81.
10. Jayaprakasam.B, Padmanabhan.K, Nair.MG. Withanamides in *Withaniasomnifera* Fruit Protect PC-12 Cells from β -Amyloid Responsible for Alzheimer's Disease. Phytother. Res.2010: 24(6); 859-863.

11. Lalit Krishan Meena, A.K. Gupta, JanakPate.l, Mohammad Yunus Khan and Sunil Kumar.Ashwagandha(*WithaniasomniferaL.*).<https://www.researchgate.net/publication/346032613>.
12. Rajeswara Rao. B.R, Rajput. D.K, Nagaraju. G And Adinarayana. G. Opportunities and Challenges in The Cultivation of Ashwagandha {*Withaniasomnifera (L.) Dunal*}. Journal of Pharmacognosy. 2012: Volume 3, Issue 2; 88-91.
13. Lalit Krishan Meena, A.K. Gupta, Janak Patel, Mohammad Yunus Khan and Sunil Kumar.Ashwagandh(*WithaniasomniferaL.*).<https://www.researchgate.net/publication/34603261>.
14. Lalit Krishan Meena, A.K. Gupta, Janak Patel, Mohammad Yunus Khan and Sunil Kuma.Ashwagandha (*WithaniasomniferaL.*) <https://www.researchgate.net/publication/346032613>.
15. Singh S. and Kumar S. *WithaniaSomnifera: The Indian Ginseng Ashwagandha*.1998: 293.
16. Abdel-Kader.MM, El-Mougy.NS, Lashin.SM. Essential Oils and as *Trichoderma harzianum* Integrated Control Measuzre against Faba Bean Root Rot Pathogens. Research, Journal of Plant Protection.2011: 51;306-3133.
17. Araujo.L, Padilla.N, Llanos GG, Bazzocchi IL, Moujir L. Antimicrobial activity of withanolides from the leaves of *Withaniaaristata* Planta Medica.2008: 74: PB70.
18. Madhu Prakash Srivastava, Shashi Gupta, Sonal Dixit , Namita Yadav, Vandana Yadav , HinaSingh,PankajKanaujia, Yogesh Kumar Sharma, *Withaniasomnifera (Ashwagandha): A wonder herb with multiple medicinal properties*, Asian Journal of Pharmacy and Pharmacology 2018;4(2); 123-130.
19. Rajeswara Rao B.R., Rajput D.K., Nagaraju G. And Adinarayana G. Opportunities and Challenges in The Cultivation of Ashwagandha {*Withaniasomnifera (L.) DUNAL*} Journal of Pharmacognosy.2012: Volume 3, Issue 2; 88-91.
20. Bilal Ahmad Mir, JabeenaKhazir, Nisar A. Mir, Tanvir-ul Hasan and Sushma Koul:Botanical,chemicalandpharmacologicalreviewof*Withaniasomnifera*(Indianginseng: an ayurvedic medicinal plant.2012:vol:1/Issue:6;2278-2958.
21. Leyon PV and Kuttan G. Effect of *Withaniasomnifera* on B16F-10 melanoma induced metastasis in mice. *Phytother*.2004: Res. 18; 118-122.
22. 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 *Withaniasomnifera*, in a rat model. *Phytomed*.2004: 11; 452-460.
23. Davis L and Kuttan G. Suppressive: Effect of cyclophosphamide-induced toxicity by *Withaniasomnifera* extract in mice. *J. Ethnopharmacol*.1998: 62; 209-214.
24. Kuttan G. Use of *WithaniasomniferaDunal* as an adjuvant during radiation therapy. *Ind. J. Exp. 0000*;34; 854-856.
25. Jayaprakasam B, Zhang Y. Seeram NP and Nair MG. Growth inhibition of human tumor cell lines by withanolides from *Withaniasomnifera* leaves. *Life Sci*. 2003: 7; 125-132.
26. Silvia DS, Eun RH, Renaud W and Shivendra VS. Withaferin A Causes FOXO3a- and Bim- dependent Apoptosis and Inhibits Growth of Human Breast Cancer Cells s In vivo. 2008: 68;7661-7669.
27. Prakash J, Gupta SK and Dinda AK. *Withaniasomnifera* root extract prevents DMBA-induced quamous cell carcinoma of skin in Swiss albino mice. *Nutr. Cancer*.2002: 42, 91-97.
28. Halliwell B and Gutteridge JMC *Free radicals in biology & medicine*. 2nd ed. Oxford: clarendon press.1989.
29. Jesberger JA and Richardson JS. Oxygen free radicals and brain dysfunction. *Int. J. Neurosci*.1991: 57; 1-17.
30. DhuleyJN.Effect of ashwagandha on lipid peroxidation in stress-induced animals. *J Ethnopharmacol*.1998: 60; 173- 178.
31. Rasool M and Varalakshmi P. Immunomodulatory role of *Withaniasomnifera* root powder on experimental induced inflammation: an in vivo and in vitro study. *Vascul. Pharmacol*.2006: 44;406-410.
32. Anbalagan K and Sadique J Role of prostaglandins in acute phase proteins in inflammation. *Biochem*.1984: Med. 31; 236-245.

33. Begum VH and Sadique J (1988) Long term effect of herbal drug *Withaniasomnifera* on adjuvant induced arthritis in rats. *Ind. J. Exp.* 1988: 26; 877-882.
34. Dhuley JN. Effect of ashwagandha on lipid peroxidation in stress-induced animals. *J Ethnopharmacol.* 60;1998: 173- 178.
35. Bector NP, Puri AS, Sharma D. Role of *Withaniasomnifera* (Ashwagandha) in various types of Arthropathies. *Ind. J. Med.* 1968: 56;1581-1583.
36. Devi. *Withaniasomniferadunal* (ashwagandha): Potential plant source of a promising drug for cancer chemotherapy and radiosensitisation. *Ind. J. Exp. Biol.* 34 (10); 927–932.
37. Khan B, Ahmad SF and Bani S. Augmentation and proliferation of T lymphocytes and Th-1 cytokines by *Withaniasomnifera* in stressed mice. *Int. Immunopharmacol.* 2006: 6; 1394-1403.
38. Singh B, Saxena AK, Chandan BK, Gupta DK, Bhutani KK and Anand KK. (2001) Adaptogenic activity of a novel, withanolide-free aqueous fraction from the roots of *Withaniasomnifera* Dun. *Phytother.* 2001: 15 (4); 311-318.
39. Khalil M, Ahmmed I, Ahmed R, Tanvir E.M, Afroz R, Paul S, Gan S.H, Alam N. Amelioration of isoproterenol-induced oxidative damage in rat myocardium by *Withaniasomnifera* leaf extract. *Biomed Res. Int.* 2015:2015;624159.
40. Bilal Ahmad Mir, JabeenaKhazir, Nisar A. Mir, Tanvir-ul Hasan1 and Sushma Koul. Botanical, chemical and pharmacological review of *Withaniasomnifera* (Indian ginseng): an ayurvedic medicinal plant. 2012: Vol:1 Issue:6;2278- 2958.
41. Narendra Singh, Mohit Bhalla, Prashanti de Jager and Marilena Gilca. An Overview on Ashwagandha: A Rasayana (Rejuvenator) Of Ayurveda. *Afr J Tradit Complement Altern Med.* 2011:8(5);208-213.

