Biological Activities Of Withania Somnifera

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Abstract

In the Ayurvedic system, *Withania somnifera* is a tonic herb.It's used to cure a variety of ailments, but it's most commonly utilized as a nerve tonic. Diverse studies have been conducted as a result of its various facts, and its various biological actions have been thoroughly investigated. This review covers a wide range of studies on *W. somnifera*, including anti-cancerous activity, anti-immunomodulatory activity, antioxidant activity, anti-inflammatory activity, anti-aging activity,anti-stress activity, and many others. This review also covers its botanical classification, localism names, morphological description, chemical constituents, and medicinal uses which are very useful for further studies.

Keywords: Withania somnifera, Biological-activity, Botanical classification, Chemical Constituents. Medicinal uses.

1.Introduction

Plants are the major source of pharmaceuticals on the planet. The first country to use herbal preparations as medicines is China(Girme et al. 2020). Plants as medicine were first mentioned in India's Rigveda, and later in Ayurveda(Bano et al. 2015). More than twenty thousand medicinal plants species are listed by WHO, which are used globally. According to the World Health Organization, traditional herbal remedies are used by almost 80% of the world's population("Herbal Remedies of District Attock.Pdf," n.d.). For millennia, *Withania somnifera* is a prominent traditional medicative plant used as a medicine from the family of Solanaceae which includes around 23 species, and the rest of its botanical classifications are given in Table 1(Ujwala et al. 2015). In the Hindi language, it is known as ashwagandha and the rest of its local names are given in table 2. It mainly constitutes Steroidal Lactones (Withanolides). It is used to treat a variety of ailments such as asthma, bronchitis, ulcers, and stomach disorders, among others.Various pharmacological experiments have convincingly signified the potential of *Withania somnifera* to exhibit anti-inflammatory, anti-oxidative, anti-ulcer, anti-diabetic, anti-cancer, and many more life-saving properties. It also helps to treat neurological disorders like Parkinson, and Alzheimer's(Scarfiotti et al. 1997)(S. K. Bhattacharya and Muruganandam 2003)(Arora et al. 2004)(Kuboyama, Tohda, and Komatsu 2005)(Harikrishnan, Subramanian, and Subash 2008)(Sandhu et al. 2010). Withaferin A, Withanolide A, and withanolide D Are isolated from this plant and are bioactive molecules and their structures are given in fig 1, 2, and 3.It is a highly regarded herb in Indian Ayurvedic medicine as a tonic (Rasayana). It boosts energy levels and mitochondrial health due to its anxiolytic action. Its anti-inflammatory and anti-arthritic qualities have been demonstrated to be beneficial in Rheumatoid and Osteoarthritis clinical situations. It also posseses anti-stress activity (Gajarmal, Shende, and Chothe 2014).In 74 Ayurvedic, 9 Siddha, 3 Unani, and 126 herbal formulations, ashwagandha is one of the components(Srivastava et al. 2018).

Table 1: Botanical classification of *W. Somnifera*

KINGDOM	PLANTAE
GENUS	WITHANIA
SPECIES	SOMNIFERA
DIVISION	ANGIOSPERMS
FAMILY	SOLANACEAE
CLASS	DICOTILEDONEAE

Table 2: Localism names of *W.somnifera*

ARABIC	KAKNAJ- E- HINDI
BENGALI	ASVANGANDA
ENGLISH	WINTER CHERRY
GUJRATI	ASAN, ASODA

ODIYA	ASUGANDHA
SANSKRIT	ASHVAGANDHA, PALASHAPARNI
URDU	ASGAND NIGORI
TAMIL	ASUBAM
TELEGU	PENNERU

1.1 Geographical Distribution

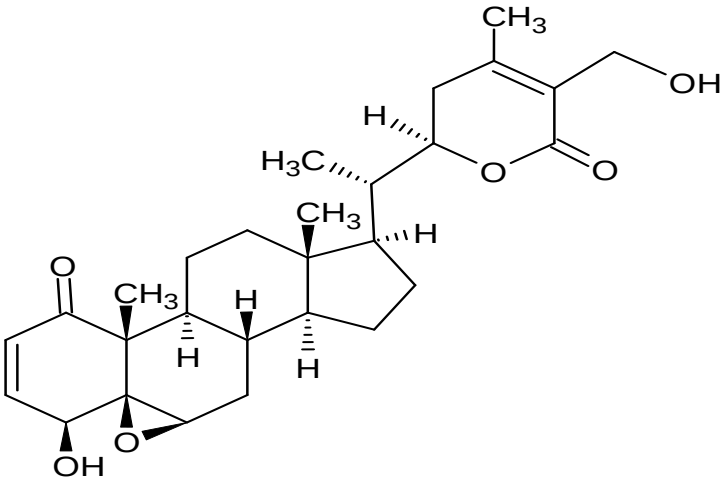
W. somnifera can be found all over the world, from the southern Mediterranean to the Canary Islands, and from South Africa to East Africa. Israel, Jordan, Egypt, Sudan, Iran, Afghanistan, Baluchistan, and Pakistan are all home to this species. In India, the plant can be found growing wild at heights of up to 1,500 meters in the northern regions of Punjab, Himachal Pradesh, and Jammu. (Srivastava et al. 2018).

1.2 Morphologic elucidation

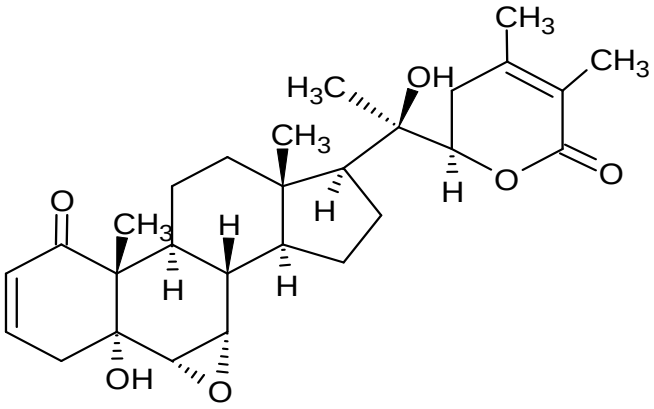
W. somnifera is a tall, greenish, branching, or unbranching herb that can reach a height of 1.25 meters. Fine hairy tomentum covers the aerial components such as the stem, leaves, and calyx. The leaves are simple, petiolate, oval, entire, shining smooth, and opposite; the flowers are inconspicuous, greenish or yellow, in axillary umbellate cymes, bisexual; the fruit is a berry in persistent calyx, and the seeds are small, flat, yellow, reniform, and extremely light(Saleem et al. 2020). Seeds are planted at a spacing of 60 cm x 30 cm from each other in June or July(Purohit and Purohit 2018). The plant enjoys a sunny site. Bacterial, fungal, viral, phytoplasma, and parasite illnesses are all probable(Alwadi and Baka 2001).Comparative morphological analyses of wild accessions have also been thoroughly explored to discover new cytomorphotypes from North Indian wild germplasm(Sharma et al. 2014).

1.3 Chemical constituents

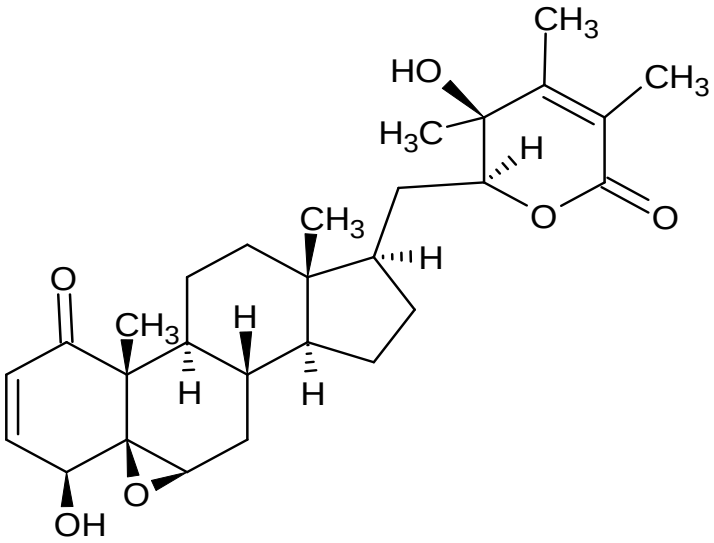
Alkaloids and withanolides are the two major secondary categories identified in *Withania somnifera*, and both are medicinally important(Bano et al. 2015). A considerable variety of withanolides have been synthesized from the roots and leaves of this plant, which are responsible for its therapeutic benefits.Withaferin A was the first natural lactone of the withanolide class to be isolated from its shoots(G. L. Gupta and Rana, n.d.). Withaferin A and withanolide D are responsible for the majority of *Withania somnifera's* pharmacological activities (G. Singh et al. 2010). The structure of various chemical constituents of *W. somnifera* is given in Fig 1. Its roots are a rich source of phytochemicals that are beneficial to humans. The presence of a C-28 basic Skelton with a nine-carbon atom side chain in which C-22 and C-26 oxidised to create a six-membered lactone ring distinguishes withanolides (CS-8).Withanolides are thought to have a cholestane-like structure, with an additional methyl group at C-24 and other oxygenated groups or double bonds positioned at various places along with the Skelton, according to biogenetics(Afewerky et al. 2021).Using GC-MS and NMR spectroscopy, researchers discovered 82 chemically varied metabolites in *W. somnifera* fruits, including fatty acids, organic acids, aliphatic and aromatic acids, polyols, sterols, sugars, phenolic acids, and withanolides. Squalene and tocopherol, the most effective natural chemicals with antioxidant qualities, have been discovered for the first time in the fruit. Analysis of roots and callus confirm the presence of 17 alkaloids out of which maximum present in roots followed by callus(Bhatia et al. 2013).



Withaferin A



Withanolide A



Withanolide D

Fig 1 Various Chemical constituents of *W. somnifera*

1.4 Medicinal uses

Table 3 The pathophysiological conditions and the part of *W. somnifera* that is used to treat the condition

Nutrition	Young shoots
Eye treatments	Leaf
Sedatives	Roots
Kidneys, Fever	Leaf, Roots
Skin infection	Leaf, Stem, and Berry
Pulmonary troubles	Leaf, Root
Asthma	Leaf sap
Malaria	Leaf sap
Hemorrhoids	Green fruit
Anthrax	Dried roots
Gynecological	Leaf, fruit, and root

2. Scientific studies on ashwagandha

W. somnifera (L.) (Ashwagandha) is a common constituent in Ayurvedic medicines and is used to treat several musculoskeletal diseases such as arthritis and rheumatism.It's also used as a general tonic to help people feel more energized, improve their overall health, and live longer. Many pharmacological studies have been undertaken to examine the properties of Ashwagandha, including immunomodulatory, cardioprotective, neuroprotective, anti-aging, and anti-oxidant investigations, among others(N. Singh et al. 2011). Few workers have also reviewed and offered information regarding diverse pharmacological activities in their respective reviews. It is one of the most important plants in Indian and worldwide pharmacopeia. The fundamental purpose of this research is to gather as much information about W. somnifera as possible so that other researchers can quickly obtain reliable data.

2.1 Anti-stress activity

This study was conducted at Risk Care Hospital in Thane, Maharashtra, India, and was a prospective, double-blind, randomized, placebo-controlled trial. Two arms of the treatment group received two dosages of Ashwagandha root extract, while the third arm received a placebo. The treatment groups received 250 mg/day and 600 mg/day of Ashwagandha root extract, respectively, whereas the placebo group received 250 mg/day of starch for the whole eight-week research. Participants aged 18 to 55 years old of either gender were assessed for study eligibility using the inclusion and exclusion criteria.participants having a Perceived Stress Scale (PSS) score of more than 20 and no other mental problems were included in the study. Pregnant women and people who are taking some other medicines and treatments are excluded from this study.A total of 60 people were chosen based on their qualifications. During the follow-up process, two participants were lost. Then the study was done for 58 participants.Participants were given bottles containing either the active therapy component or a placebo, which they were instructed to ingest two times a day. There are two active treatment groups: one that had to take 125 mg of ashwagandha root extract and the other that had to take 300 mg of the root extract in capsules. Participants in the placebo group were given capsules containing 125mg of starch. One capsule was taken two times a day, after meals, with water or milk. The placebo and ashwagandha capsules had the same color, size, and shape. The results of the ranking data and scores analysis are reported as a mean with standard deviation (SD). Wherever possible, 95 percent confidence intervals (CI) were used throughout the analyses. The Friedman test within the group was used to compare baseline scores to post-treatment ratings for the various scales in this study. Table 4 shows the perceived stress scale (PSS).

Table 4 The perceived stress scale is given here

250mg/Per day ashwagandha				**600mg/Per day ashwagandha**			**Placebo**			**Reference**
	N	**Mean (SD)**	**95%CI**	**N**	**Mean (SD)**	**95%Confidence interval**	**N**	**Mean (SD)**	**95%Confidence intervals**	
Baseline	20	22.6 (1.75)	21.83-23.47	20	22.9 (1.57)	22.2-23.6	20	22.70 (2.17)	21.6-23.7	(Chandrasekhar, Kapoor, and Anishetty 2012)
4 Week	19	18.7 (2.20)	17.7-19.8	20	18.8 (2.05)	17.8-19.8	19	19.8 (2.30)	18.7-21.0	
8 Week	19	15.00 (2.21) *	13.93-16.07	20	14.15 (2.62) **	12.92-15.38	19	16.63 (3.13)	15.12-18,14	

Here N= number of participants

Relative to the values in the table it is clear that at baseline the mean value PSS of ashwagandha 250mg and 600mg is lower than that of the placebo group. From the table, it is also clear that the ashwagandha 250mg/day treatment is more effective than the ashwagandha 600mg/day treatment.

From this, it is clear that ashwagandha helps in reducing stress levels.

Another study conducted by Culcutta university's institute of basic medical sciences surveyed the effect of *Withania somnifera* on chronic stress disease.For 21 days, the animals were subjected to a modest electric shock to their feet. The results of stress due to this shock on animals developed various problems like

gastric ulceration, depression, intolerance of glucose, etc. The rats administered *Withania somnifera* an hour before the foot shock had a considerably lower degree of stress, according to the researchers. This study backs up the idea that Ashwagandha has a powerful anti-stress adaptogenic impact(S. K. Bhattacharya and Muruganandam 2003).

2.2 Antioxidant activity

Some of the compounds present in *Withania somnifera* are potent antioxidants, according to researchers at Banaras Hindu University in Varanasi, India. The plant increased the amounts of three natural antioxidants enzymes that are catalase, Superoxide dismutase, and glutathione in the brains of rats, according to studies(Dhuley 2000).

2.3 Anti-cancerous activity

Ashwagandha is said to have anti-cancer properties. The herb reduces the levels of the nuclear factor kappaB, lowers the intercellular tumor necrosis factor, and potentiates apoptotic signaling in tumorigenic lines, per the research undertaken on animal cell culture(Yadav et al. 2010).*Withania somnifera* (L.) Dunal was examined in adult male albino mice for its tumor-preventive activity against urethane-induced lung adenomas. The rats all developed lung adenomas after being given urethane subcutaneously biweekly for seven months at a dose of 125 mg/kg. Urethane caused a considerable loss in body weight, a rise in mortality, leucopenia, and a drop in lymphocyte percentage when compared to untreated controls. Simultaneous oral administration of *W.somnifera*given at a dose of 200 mg/kg per day in combination with urethane protected the rats from the tumor-inducing effects of the urethane. By producing a condition of nonspecific increase in resistance (adaptogen) and immunostimulant characteristics, it also reduced the drop in body weight and the rise in mortality caused by urethane. adenomas. Significant increases in total leucocyte count and lymphocyte percentage revealed that the hematological abnormalities had been reversed.These hematological changes were also observed in animals who had very recently been administered *W. somnifera*. By creating a nonspecific increase in resistance (adaptogen) and immunostimulant properties, *W. somnifera* appears to protect against urethane-induced lung adenomas (Pediat 1967).

2.4Anti-inflammatory activity

Ashwagandha's ability to relieve the symptoms of arthritis and other inflammatory disorders has been studied. The plant possesses anti-inflammatory qualities, according to these studies. It contains far more naturally occurring steroids than hydrocortisone, a commonly prescribed anti-inflammatory (Saleem et al. 2020)(Sikandan, Shinomiya, and Nagahara 2018). *W. somnifera* root powder (600 mg kg1) successfully suppressed arthritis symptoms and increased functional recovery of motor activity and radiological score in arthritic rats.

In rats, the root of *W. somnifera* protects them from collagen-induced arthritis (CIA). The findings imply that *W. somnifera* root powder reduces arthritic symptoms in collagen-induced arthritic mice by acting as an anti-inflammatory and antioxidant agent(A. Gupta and Singh 2014).

2.5 Anti-aging activity

In a double-blind clinical trial, Ashwagandha was evaluated for its anti-aging qualities.For one year, a group of one hundred one fit males aged fifty to fifty-nine was given 3 grams of the plant daily. Red blood count, hemoglobin, hair melanin, and sitting height all improved significantly in the participants. The amount of cholesterol in the blood was reduced, while the calcium in the nails was conserved. Seventy percent of the study participants said their sexual performance had improved (Bonilla et al. 2021).

2.6 Hypothyroid activity

In a study, 28 albino mice were given a dose of 1.4 g/kg weight of aqueous extract of *Withania somnifera* by gastric intubation for 20 days, with the results showing that *Withania somnifera* appears to improve thyroid function in female mice without inducing hepatotoxicity. Hypothyroidism can be treated with these plant extracts. Further research will, however, be beneficial to optimize the dose and duration of treatment (Panda

and Kar 1999).

2.7 Immunomodulatory activity

Babl/c mice were given a powdered root extract from the plant *Withania somnifera*, which enhanced immunological activity. The overall WBC count (17125 cells/mm(3)) increased on the tenth day after treatment with five doses of Withania root extract (20 mg/dose/animal; i.p.). Bone marrow cellularity (27x10(6) cells/femur) and alpha-esterase positive cell number (1800/4000 cells) both increased significantly after taking the Withania extract (P0.001). After treatment with Withania extract and the antigen, the circulating antibody titer and the number of plaque-forming cells (PFC) in the spleen increased (SRBC). The maximum number of PFC (985 PFC/10(6) spleen cells) was recorded on the fourth day. Withania extract inhibited the delayed-type hypersensitivity reaction in mice (Mantoux test). When compared to the control (31.5/200 cells), the injection of Withania extract boosted the phagocytic activity of peritoneal macrophages (76.5 pigmented cells/200). The immunomodulatory characteristics of *W.somnifera* extract, a well-known immunomodulator in traditional medicine, are supported by these findings

Withanolides and steroidal lactones have been found in *W. somnifera*. At this time, we don't know if these compounds are responsible for the extract's immunostimulatory properties. More isolated chemical research is being done(Davis and Kuttan 2000).

2.8 Adaptogenic effect

Shade dried roots of *W. somnifera* were powdered and turned into 0.5-gram tablets, which were administered to healthy individuals in doses of 2 pills taken 3 times a day with milk in a one-year double-blind trial. When compared to the control group, there was a significant increase in hemoglobin, RBC, hair melanin, and seated height in the treated group. Serum cholesterol and calcium levels in the nails were also reduced in the treated group(Priyanka et al. 2020).

2.9 Effect on sexual behavior

The root extract of *W. somnifera* can help to improve libido and sexual performance, sexual vitality, and penile erection problems. The roots include iron, potassium, Magnesium, and Nickel, which have diuretic and aphrodisiac properties and are used to treat spermatopathia and seminal depletion. These effects are somewhat reversible when therapy is stopped, and are related to the extract's hyperprolactinemic, Gamma Amino Butyric Acid (GABA), serotonergic, or sedative actions rather than changes in testosterone levels. The roots of W. somnifera hurt male sexual competence, which is contradictory. The libido is severely suppressed by the **gamma-Aminobutyric acid(**GABA) mimetic effects of *W. somnifera* roots as well as serotonergic systems(Chauhan et al. 2014).

2.10 Effect of ashwagandha on alcohol- addiction

A study was conducted to study the effect of ashwagandha on alcohol addiction in albino mice in which the mice were given doses of ashwagandha for 21 days. The concludes that ashwagandha helps to reduce alcohol addiction and also the anxiety due to alcohol. The GABAergic and serotonergic systems were discovered to be the major mechanism responsible for ashwagandha's anti-addictive activity (Bansal and Banerjee 2016).

2.11 Anticonvulsant property

In both the maximal (electroshock)MES and (pentylenetetrazole) PTZ methods, the alcoholic extract of W. somnifera (Dunal) has shown a considerable anticonvulsant effect at 300 mg/kg body weight, although the anticonvulsant action is considerably less at 200 mg/kg and 100 mg/kg doses. The test chemical was prepared by dissolving 3g of alcoholic extract of *W. somnifera* in 50ml of propylene glycol concentration of about 14 mg/ml. has a better protection rate against pentylenetetrazol seizures than MES, indicating that it is likely more useful in the absence (petit mal) seizures rather than generalized tonic-clonic (grand mal) seizures, and its action may be similar to sodium valproate. More research is needed to confirm and isolate the extract active ingredient contained in *W. somnifera's* alcoholic extract, which is responsible for its anticonvulsant properties(Raju et al. 2017).

2.12 Antidiabetic property

Sarangi and colleagues investigated the efficacy of *W. somnifera* leaf and root extracts in the treatment of

diabetes mellitus (DM), as well as their hypoglycaemic and hypolipidaemic effects in streptozotocin-induced diabetic mice(Jena 2018). The extract has hypoglycaemic and hypolipidaemic characteristics, making it effective in the treatment of diabetes mellitus. Another study found that *W. somnifera* has a strong anti-diabetic effect in diabetic rats when compared to the conventional medication Glibenclamide. Anti-diabetic effectiveness could be aided by enhanced hepatic metabolism, increased insulin release from pancreatic -cells, or insulin sparing action(Khatak, Sehrawat, and Khatak 2013). *W. somnifera* root (WSREt) and leaf (WSLEt) extracts show hypoglycaemic and hypolipidaemic effects in alloxan-induced diabetic rats (Udayakumar et al. 2009). Andallu and Radhika tested the hypoglycemic, diuretic, and hypocholesterolemic effects of *W. somnifera* roots on six mild NIDDM and mild hypercholesterolemic human subjects (2000). The plant could be a source of hypoglycemic, diuretic, and hypocholesterolemic drugs, according to their research. There were no side effects found in clinical trials(Andallu and Radhika 2000).

2.13 Other benefits of *W. somnifera*

Ashwagandha has also been demonstrated to be useful in the treatment of osteoarthritis (Kulkarni et al. 1991), stroke (Chaudhary et al. 2003), and tardive dyskinesia(Salil K. Bhattacharya et al. 2002) in other research. Antifungal(Iqbal Choudhary et al. 1995)and antibacterial properties of ashwagandha have been demonstrated against Staphylococcus aureus and Pseudomonas Aeruginosa bacteria strains(Ali et al. 2001).

3. Conclusion

Owing to its various pharmacologic properties,*W. somnifera* is regardedas a real ‘Rasayana of Ayurveda.It can increase immunity while also lowering stress levels. From the time of Ayurveda, the plant *Withania somnifera* (Ashwagandha) has been employed in Indian medicine. *Withania somnifera* is a substantial source of a range of pharmaceutically and remediallyvital chemicals, including withaferins, sitoindosides, and other beneficial alkaloids, according to the literature review.Ashwagandha has been used to treat bronchitis, asthma, ulcers, emaciation, sleeplessness, and senile dementia as well as an aphrodisiac, liver tonic, anti-inflammatory agent, and astringent. The use of ashwagandha for anxiety, cognitive and neurological disorders, inflammation, and Parkinson's disease is supported by clinical trials and animal research. As a result of the above-mentioned facts, it is obvious that Ashwagandha's traditional use has a logical and scientific basis. To prove the herb's therapeutic value, large-scale clinical trials are needed, especially in stress-related diseases, neurological disorders, and cancer.

Acknowledgements

The author is grateful to department of applied sciences, Chandigarh University, Mohali Punjab for valuable support and guidance throughout this work.

Competing Interest

The author declare no competing interest

References

Afewerky, Henok Kessete, Ayeni Emmanuel Ayodeji, Bashir Bolaji Tiamiyu, Joshua Iseoluwa Orege, Emmanuel Sunday Okeke, Aanuoluwapo Opeyemi Oyejobi, Petuel Ndip Ndip Bate, and Sherif Babatunde Adeyemi. 2021. “Critical Review of the Withania Somnifera (L.) Dunal: Ethnobotany, Pharmacological Efficacy, and Commercialization Significance in Africa.” *Bulletin of the National Research Centre* 45 (1). https://doi.org/10.1186/s42269-021-00635-6.

Ali, N. A.Awadh, W. D. Jülich, C. Kusnick, and U. Lindequist. 2001. “Screening of Yemeni Medicinal Plants for Antibacterial and Cytotoxic Activities.” *Journal of Ethnopharmacology* 74 (2): 173–79. https://doi.org/10.1016/S0378-8741(00)00364-0.

Alwadi, Hussien M., and Zakaria A.M. Baka. 2001. “Microorganisms Asssociated with Withania Somnifera Leaves.” *Microbiological Research* 156 (4): 303–9. https://doi.org/10.1078/0944-5013-00094.

Andallu, B, and B Radhika. 2000. “Hypoglycemic, Diuretic and Hypocholesterolemic Effect of Winter Cherry (Withania Somnifera, Dunal) Root.” *Indian Journal of Experimental Biology* 38 (6): 607–9.

Arora, S., S. Dhillon, G. Rani, and A. Nagpal. 2004. "The in Vitro Antibacterial/Synergistic Activities of Withania Somnifera Extracts." *Fitoterapia* 75 (3–4): 385–88. https://doi.org/10.1016/j.fitote.2004.01.002.

Bano, Anisha, Navdeep Sharma, Harcharan Dhaliwal, and Vivek Sharma. 2015. "A Systematic and Comprehensive Review on Withania Somnifera (L.) Dunal- An Indian Ginseng." *British Journal of Pharmaceutical Research* 7 (2): 63–75. https://doi.org/10.9734/bjpr/2015/17102.

Bansal, Priya, and Sugato Banerjee. 2016. "Effect of Withinia Somnifera and Shilajit on Alcohol Addiction in Mice." *Pharmacognosy Magazine* 12 (46): 121. https://doi.org/10.4103/0973-1296.182170.

Bhatia, Anil, Santosh K. Bharti, Shri K. Tewari, Om P. Sidhu, and Raja Roy. 2013. "Metabolic Profiling for Studying Chemotype Variations in Withania Somnifera (L.) Dunal Fruits Using GC-MS and NMR Spectroscopy." *Phytochemistry* 93: 105–15. https://doi.org/10.1016/j.phytochem.2013.03.013.

Bhattacharya, S. K., and A. V. Muruganandam. 2003. "Adaptogenic Activity of Withania Somnifera: An Experimental Study Using a Rat Model of Chronic Stress." *Pharmacology Biochemistry and Behavior* 75 (3): 547–55. https://doi.org/10.1016/S0091-3057(03)00110-2.

Bhattacharya, Salil K., D. Bhattacharya, K. Sairam, and S. Ghosal. 2002. "Effect of Withania Somnifera Glycowithanolides on a Rat Model of Tardive Dyskinesia." *Phytomedicine* 9 (2): 167–70. https://doi.org/10.1078/0944-7113-00089.

Bonilla, Diego A., Yurany Moreno, Camila Gho, Jorge L. Petro, Adrián Odriozola-Martínez, and Richard B. Kreider. 2021. "Effects of Ashwagandha (Withania Somnifera) on Physical Performance: Systematic Review and Bayesian Meta-Analysis." *Journal of Functional Morphology and Kinesiology* 6 (1). https://doi.org/10.3390/jfmk6010020.

Chandrasekhar, K., Jyoti Kapoor, and Sridhar Anishetty. 2012. "A Prospective, Randomized Double-Blind, Placebo-Controlled Study of Safety and Efficacy of a High-Concentration Full-Spectrum Extract of Ashwagandha Root in Reducing Stress and Anxiety in Adults." *Indian Journal of Psychological Medicine* 34 (3): 255–62. https://doi.org/10.4103/0253-7176.106022.

Chaudhary, Geeta, Uma Sharma, Naranamangalam R. Jagannathan, and Yogendra K. Gupta. 2003. "Evaluation of Withania Somnifera in a Middle Cerebral Artery Occlusion Model of Stroke in Rats." *Clinical and Experimental Pharmacology and Physiology* 30 (5–6): 399–404. https://doi.org/10.1046/j.1440-1681.2003.03849.x.

Chauhan, Nagendra Singh, Vikas Sharma, V. K. Dixit, and Mayank Thakur. 2014. "A Review on Plants Used for Improvement of Sexual Performance and Virility." *BioMed Research International* 2014. https://doi.org/10.1155/2014/868062.

Davis, Leemol, and Girija Kuttan. 2000. "Immunomodulatory Activity of Withania Somnifera." *Journal of Ethnopharmacology* 71 (1–2): 193–200. https://doi.org/10.1016/S0378-8741(99)00206-8.

Dhuley, Jayant N. 2000. "Adaptogenic and Cardioprotective Action of Ashwagandha in Rats and Frogs." *Journal of Ethnopharmacology* 70 (1): 57–63. https://doi.org/10.1016/S0378-8741(99)00177-4.

Gajarmal, Amit Ashok, M.B. Shende, and D.S. Chothe. 2014. "Antistress Activity Od Ashwagandha (Withania Somnifera Dunal) – A REVIEW." *International Ayurvedic Medical Journal* 2 (3): 386–93.

Girme, Aboli, Ganesh Saste, Sandeep Pawar, Arun Kumar Balasubramaniam, Kalpesh Musande, Bhaumik Darji, Naresh Kumar Satti, et al. 2020. "Investigating 11 Withanosides and Withanolides by UHPLC-PDA and Mass Fragmentation Studies from Ashwagandha (Withania Somnifera)." *ACS Omega* 5 (43): 27933–43. https://doi.org/10.1021/acsomega.0c03266.

Gupta, Apurva, and Surendra Singh. 2014. "Evaluation of Anti-Inflammatory Effect of Withania Somnifera Root on Collagen-Induced Arthritis in Rats." *Pharmaceutical Biology* 52 (3): 308–20. https://doi.org/10.3109/13880209.2013.835325.

Gupta, Girdhari Lal, and A C Rana. n.d. "Withania Somnifera (Ashwagandha): A Review PHCOG MAG.: Plant

Review Withania Somnifera (Ashwagandha): A Review." *Pharmacognosy Reviews*. Vol. 1.

Harikrishnan, B., P. Subramanian, and S. Subash. 2008. "Effect of Withania Somnifera Root Powder on the Levels of Circulatory Lipid Peroxidation and Liver Marker Enzymes in Chronic Hyperammonemia." *E-Journal of Chemistry* 5 (4): 872–77. https://doi.org/10.1155/2008/589394.

"Herbal Remedies of District Attock.Pdf." n.d.

Iqbal Choudhary, M., Dur-e-Shahwar, Zeba Parveen, Abdul Jabbar, Irshad Ali, and Atta-Ur-Rahman. 1995. "Antifungal Steroidal Lactones from Withania Coagulance." *Phytochemistry* 40 (4): 1243–46. https://doi.org/10.1016/0031-9422(95)00429-B.

Jena, Somanatha. 2018. "ANTI-DIABETIC EFFECTS OF Withania Somnifera ROOT AND LEAF EXTRACTS ON STREPTOZOTOCIN INDUCED DIABETIC RATS ANTI-DIABETIC EFFECTS OF Withania Somnifera ROOT AND LEAF EXTRACTS ON STREPTOZOTOCIN INDUCED," no. January.

Khatak, Mamta, Renu Sehrawat, and Sunil Khatak. 2013. "A Comparative Study : Homoeopathic Medicine and a Medicinal Plant Withania Somnifera for Antidiabetic Activity" 2 (3): 109–12.

Kuboyama, Tomoharu, Chihiro Tohda, and Katsuko Komatsu. 2005. "Neuritic Regeneration and Synaptic Reconstruction Induced by Withanolide A." *British Journal of Pharmacology* 144 (7): 961–71. https://doi.org/10.1038/sj.bjp.0706122.

Kulkarni, R. R., P. S. Patki, V. P. Jog, S. G. Gandage, and Bhushan Patwardhan. 1991. "Treatment of Osteoarthritis with a Herbomineral Formulation: A Double-Blind, Placebo-Controlled, Cross-over Study." *Journal of Ethnopharmacology* 33 (1–2): 91–95. https://doi.org/10.1016/0378-8741(91)90167-C.

Panda, S., and A. Kar. 1999. "Withania Somnifera and Bauhinia Purpurea in the Regulation of Circulating Thyroid Hormone Concentrations in Female Mice." *Journal of Ethnopharmacology* 67 (2): 233–39. https://doi.org/10.1016/S0378-8741(99)00018-5.

Pediat, Indian J. 1967. "Indian J. Pediat. 34 : 245, 1967."

Priyanka, G., B. Anil Kumar, M. Lakshman, V. Manvitha, and B. Kala Kumar. 2020. "Adaptogenic and Immunomodulatory Activity of Ashwagandha Root Extract: An Experimental Study in an Equine Model." *Frontiers in Veterinary Science* 7 (September): 1–11. https://doi.org/10.3389/fvets.2020.541112.

Purohit, Abhilasha, and Ashok Purohit. 2018. "Eltroxin like Mimic Action of Withania Somnifera Leaf Extract in Hypothyroid-Induced Rats." *Asian Journal of Pharmaceutical and Clinical Research* 11 (11): 280–84. https://doi.org/10.22159/ajpcr.2018.v11i11.27424.

Raju, Santhosh Kumar, P. L. Basavanna, H. N. Nagesh, and Ajay D. Shanbhag. 2017. "A Study on the Anticonvulsant Activity of Withania Somnifera (Dunal) in Albino Rats." *National Journal of Physiology, Pharmacy and Pharmacology* 7 (1): 17–21. https://doi.org/10.5455/njppp.2016.6.0615112072016.

Saleem, Sumaira, Gulzar Muhammad, Muhammad Ajaz Hussain, Muhammad Altaf, and Syed Nasir Abbas Bukhari. 2020. "Withania Somnifera L.: Insights into the Phytochemical Profile, Therapeutic Potential, Clinical Trials, and Future Prospective." *Iranian Journal of Basic Medical Sciences* 23 (12): 1501–26. https://doi.org/10.22038/ijbms.2020.44254.10378.

Sandhu, JaspalSingh, Biren Shah, Shweta Shenoy, MM Padhi, Suresh Chauhan, and GS Lavekar. 2010. "Effects of Withania Somnifera (Ashwagandha) and Terminalia Arjuna (Arjuna) on Physical Performance and Cardiorespiratory Endurance in Healthy Young Adults." *International Journal of Ayurveda Research* 1 (3): 144. https://doi.org/10.4103/0974-7788.72485.

Scarfiotti, C., F. Fabris, B. Cestaro, and A. Giuliani. 1997. "Free Radicals, Atherosclerosis, Ageing, and Related Dysmetabolic Pathologies: Pathological and Clinical Aspects." *European Journal of Cancer Prevention*. https://doi.org/10.1097/00008469-199703001-00007.

Sharma, Vivek, Harcharan S. Dhaliwal, Raghbir C. Gupta, and Bikram Singh. 2014. "Comparative Evaluation of Cytomorphological Studies on 27 Accessions of 'Indian Ginseng' Withania Somnifera (L.) Dunal from North

India." *Revista Brasileira de Botanica* 37 (4): 583–96. https://doi.org/10.1007/s40415-014-0094-x.

Sikandan, Abudubari, Takahisa Shinomiya, and Yukitoshi Nagahara. 2018. "Ashwagandha Root Extract Exerts Anti-Inflammatory Effects in HaCaT Cells by Inhibiting the MAPK/NF-KB Pathways and by Regulating Cytokines." *International Journal of Molecular Medicine* 42 (1): 425–34. https://doi.org/10.3892/ijmm.2018.3608.

Singh, G, P K Sharma, R Dudhe, and S Singh. 2010. "Biological Activities of Withania Somnifera." *Annals of Biological Research* 1 (3): 56–63.

Singh, Narendra, Mohit Bhalla, Prashanti de Jager, and Marilena Gilca. 2011. "An Overview on Ashwagandha: A Rasayana (Rejuvenator) of Ayurveda." *African Journal of Traditional, Complementary and Alternative Medicines* 8 (5 SUPPL.): 208–13. https://doi.org/10.4314/ajtcam.v8i5S.9.

Srivastava, Abhilasha, Anil K. Gupta, Karuna Shanker, Madan M. Gupta, Ritu Mishra, and Raj K. Lal. 2018. "Genetic Variability, Associations, and Path Analysis of Chemical and Morphological Traits in Indian Ginseng [Withania Somnifera (L.) Dunal] for Selection of Higher Yielding Genotypes." *Journal of Ginseng Research* 42 (2): 158–64. https://doi.org/10.1016/j.jgr.2017.01.014.

Udayakumar, Rajangam, Sampath Kasthurirengan, Thankaraj Salammal Mariashibu, Manoharan Rajesh, Vasudevan Ramesh Anbazhagan, Sei Chang Kim, Andy Ganapathi, and Chang Won Choi. 2009. "Hypoglycaemic and Hypolipidaemic Effects of Withania Somnifera Root and Leaf Extracts on Alloxan-Induced Diabetic Rats." *International Journal of Molecular Sciences* 10 (5): 2367–82. https://doi.org/10.3390/ijms10052367.

Ujwala, T K, Shawn Tomy, Sandra Celine, and J Sam Johnson. 2015. "A Systematic Review of Some Potential Anti-Diabetic Herbs Used in India Characterized By Its Hypoglycemic Activity." *International Journal Of Pharmaceutical Sciences And Research* 6 (12): 13040. https://doi.org/10.13040/IJPSR.0975-8232.6(12).4940-57.

Yadav, B., A. Bajaj, M. Saxena, and A. K. Saxena. 2010. "In Vitro Anticancer Activity of the Root, Stem and Leaves of Withania Somnifera against Various Human Cancer Cell Lines." *Indian Journal of Pharmaceutical Sciences* 72 (5): 659–63. https://doi.org/10.4103/0250-474X.78543.