

Aśvagandhā

Research Paper submitted in partial fulfillment
of the requirements for the degree of
Clinical Ayurvedic Specialist

California College of Ayurveda

California College of Ayurveda
700 Zion Street,
Nevada City,
CA 95959

Date Submitted: 11 April 2016

Table of Contents

Acknowledgements.....	3
Abstract.....	4
Introduction.....	5
Aśvagandhā - The Plant and its Distribution	5
Parts of the plant and their traditional therapeutic uses	6
Chemical Constituents of Aśvagandhā	6
Energetics and Ayurvedic properties of Aśvagandhā	7
Traditional uses of Aśvagandhā in Ayurvedic Medicine	7
Pharmacological and Clinical Studies.....	9
Adaptogenic and anti-stress Studies.....	9
Aśvagandhā	16
Hepato-protective Studies	10
Anti-tumoural Property Studies	11
Anti-inflammatory and anti-bacterial studies.....	13
Neuro-regenerative Potential Studies.....	14
Infertility and Sexual Dysfunction Studies	16
Toxicity and Safety Studies.....	17
Contra-indications of Usage.....	18
Conclusion.....	18
Bibliography.....	20

Acknowledgements

My salutations to the Divine for the eternal guidance and knowledge bestowed upon me and the numerous opportunities for learning that have appeared throughout this lifetime.

This research paper is in its present form with the encouragement and support, directly and indirectly, of many people. Most notably, Dr. Marc Halpern, for providing the opportunity to pursue the course of Ayurvedic Studies at the California College of Ayurveda. Special thanks also to my mentors and teachers of the AHP and CAS programs – Lisa Gallant and Mrunalini Patel.

I also thank all the immanent and transcendent Gurus for their divine guidance, inspiration and humourously imparted lessons for where I stand today.

Abstract

This research paper presents a summary of the review of literature available on *Withania Somnifera* (Aśvagandhā), an important herb of Ayurvedic pharmacology. The literature reviewed for this research paper includes Classical Ayurvedic texts, books by prominent authors in the field of ayurveda and several research articles and scientific/clinical studies that have been conducted with the aim of establishing a firm scientific basis and evaluation of the multiple pharmacological and therapeutic benefits proffered by *Withania Somnifera*. The classical ayurvedic literature was specifically reviewed for classical/traditional medicinal uses of Aśvagandhā and the conditions prescribed for. The published research articles and clinical studies were specifically reviewed for the scientific evaluation of the medicinal/therapeutic uses mentioned in the classical texts, as also other potential therapeutic uses within the paradigm of Western Medicine. Several digital and on-line medical databases were used to access the research articles and clinical studies. All the sources of reference are listed in the bibliography (End Notes). The literature reviewed indicate that *Withania Somnifera* possesses immunomodulatory, anti-stress, anti-tumoral, anti-oxidant, anti-inflammatory, thyroid regulating, cardio-pulmonary tonic, anti-anxiety, rejuvenative and haemopoetic properties. Some studies indicate the potential value of *Withania Somnifera* as an adjunct therapy with conventional western medicine. An important point to note is that not many of the mechanisms, of how *Withania Somnifera* exerts its therapeutic properties, are known. In conclusion, extensive and rigorous scientific studies are necessary to confirm the results of the preliminary and pilot studies thus far and to uncover other potential therapeutic benefits *Withania Somnifera* offers.

Introduction

Withania Somnifera is an important herb of the ayurvedic pharmacopoeia. It is also called Aśvagandhā (Sanskrit). Traditionally, it has been prescribed as a "*Rasayana*" and for other wide-ranging therapeutic benefits such as an alterative, an aphrodisiac, a nervine tonic, an adaptogen, an analgesic, in improving response to stress, an anti-inflammatory, for all vata deranged conditions, as a rejuvenative, to increase overall well-being, to increase endurance and for several musculo-skeletal conditions.^{1 2 3} According to Caraka, using a *rasayana*, *one obtains longevity, regains youth, vitality and vigour, a sharp memory, intellect, freedom from diseases, a lustrous complexion and the strength of a horse*. Sushruta clearly describes a *rasayana* as *anti-ageing, increases life-span, promotes intelligence and memory and increases resistance to disease*. Several pharmacological studies and clinical studies have been conducted to scientifically establish Withania Somnifera as a herb with multiple pharmacological uses. However, there is a paucity of studies on the toxicity and safety of Withania Somnifera. The results from all such studies have been summarized in this research paper. A short description of the plant, its habitat and distribution are mentioned, in addition to the chief chemical constituents of the plant that are the subject of several studies.

Aśvagandhā - The Plant and its Distribution

Withania Somnifera belongs to the Solanaceae family. It is an evergreen shrub that grows to about 150 cms in height. The leaves are simple, ovate, petiolate and glabrous, with inconspicuous flowers that are pale yellow or light green in colour. The fruits are orangish-red with yellow seeds. The roots of the wild plant are thicker and lower in starch content compared to those of cultivated plants.^{2, 3, 4}

The plant grows in the wild in the dry sub-tropical regions of India and Sri Lanka. It grows in Pakistan, Afghanistan, Jordan, Morocco, Egypt, the Congo and South Africa as well. It is also cultivated on a large scale in India and the United States. Aśvagandhā (Asva : horse, Gandha : Smell) gets its name from the fact that the

fresh root has a "horse-like" smell. In the various languages of India, *Withania Somnifera* (Latin) has several vernacular names - Aśvagandhā (Sanskrit), Asgandh (Hindi), Winter Cherry and Indian Ginseng (English), Ghodakun (Gujurati), Vajigandha (Telugu), Amukkuram (Tamil), Viremaddinagaddi (Kannada) and Chirpotan (Rajasthani)⁴. Aśvagandhā also has many synonyms in the classical texts, such as Vajigandha, Vatagni, Balya, Vrisya, Rasayani, Balada, Ponya, Hayagandha, Kusthagandhini, Varahakarni, Gokarana, Ashwarihaka, Sistagandha, Elaparni etc⁴.

Parts of the plant and their traditional therapeutic uses

The roots, leaves, flowers, fruits and seeds of WS are used in ayurvedic medicine. The roots are regarded to be tonic, aphrodisiac, anthelmintic, diuretic, astringent and thermogenic. The roots are prescribed for emaciation (in children), debility (in the elderly), rheumatism, leucoderma, constipation, insomnia, nervous debility, goiter, reduction of joint inflammations, Carbuncles, ulcers, painful swellings, leucorrhea, boils, pimples, flatulent colic, worms and haemorrhoids.^{1,4}

The leaves are prescribed for fevers and painful swellings, wounds, tumours, pustules and sores. The flowers are depurative, diuretic and aphrodisiac. The seeds are anthelmintic.^{1,4} An arishta (wine) prepared from the seeds is prescribed for hysteria, anxiety, memory loss, syncope and to increase sperm counts¹.

Chemical Constituents of Aśvagandhā

Aśvagandhā is chemically complex with 80 different constituents identified so far. The biologically active chemical constituents of Aśvagandhā are: Alkaloids (Ashwagandhine, Isopelletierine, Anaferine, Aiseohygrine, Anahygrine, Cuscohygrine, tropine and Withanine, Steroidal Lactones (Withanolides and Withaferins), Phytosterols (Sitoindosides, Beta-sitosterol), Saponins; several amino acids and Iron^{3,4}.

Energetics and Ayurvedic properties of Aśvagandhā

Aśvagandhā is described as possessing the following energetics³:

Rasa : Bitter, Astringent, Sweet; **Virya**: Heating; **Vipaka**: Sweet; **Guna**: Light, Unctous and **Dosha**: VK-

The ayurvedic description of the properties of Aśvagandhā are³:

Visaya: Increasing Sexual potency ; **Balya** : Increasing Strength; **Medhya** : Promotes intellect

Ojas Vardhana - Increases Ojas; **Nidranjana** - Promotes sleep; **Sukrala** – Increases sperm production

Sotahara - Prevents consumption and wasting; **Rasayana** – Rejuvenative;

Vatakaphahara - Reduces Vata and Kapha; **Vedanasthapana** - Reduces pain and

Svasa - Improves breathing

Traditional uses of Aśvagandhā in Ayurvedic Medicine

Aśvagandhā has traditionally been used as a rasayana to regain youthfulness and mental functioning and generally enhancing the quality of life by increasing energy, vigour, endurance and strength, increasing the vital fluids, muscle, blood, lymph, cells and semen. It has been used as an adaptogen to improve the physiological functioning of the body. Its rejuvenative properties have been used in treating conditions of nervous debility, insomnia, convalescence, exhaustion, thirst, premature ageing and weak memory. Traditionally, Aśvagandhā has also been used as an alterative, aphrodisiac, deobstruent, an analgesic and anti-inflammatory to treat arthritic conditions, an anabolic agent, a sedative, for treating rheumatism, for treating diseases of consumption and debility, enhancing immunity, improving memory and to counter the effects of stress, to regulate thyroid function, as a cardiac tonic and in resolving tumours, including cancers. Gynaecologically, it has been used to counter sterility and impotence, treat inflammations of the vagina and leucorrhoea.¹⁻⁴ Aśvagandhā has also been

used to treat asthma, coughs, and allergies induced by low immunity.

Sebastian Pole mentions in his book³ that Aśvagandhā is a rasayana specifically for mamsa dhatu and thus, finds use as a cardiac, lung and uterine tonic. Further, he mentions that Aśvagandhā has a "special affinity" for majja dhatu that tonifies the Central Nervous System, thus increasing tolerance to stress.

Many important ayurvedic formulations contain Aśvagandhā as a constituent. The typical formulations containing Aśvagandhā are Asvagandhadi Churna, Asgandh Pak and Aśvagandhā Ghrit. HS Puri mentions, in his book on rasayanas², the therapeutic indications for each of these formulations: Asvagandhadhi Churna is used to increase strength on the physical, mental and sexual fronts, increase resistance to stress and against infections, to improve memory and reverse the effects of premature ageing; Asgandh Pak is a general purpose tonic for all ages while Aśvagandhā Ghrit is specifically indicated for children and to strengthen the body, stimulate the nervous system, to cure sexual debility, all vata diseases, arthritis, back-aches, insomnia and depression. Asvagandharishta is a classical herbal wine formulation indicated for nervous debility, epilepsy, memory loss and insanity⁵.

The Samhitas of Ayurveda - Caraka, Susrutha, Astangahridayam, Carakadatta, Chikitsa Kalika, Cakradatta, Sarangadhara Samhita, Bhaisajya Ratnavali - contain several references to Aśvagandhā as an ingredient of formulations for treating several conditions. The various Nighantus also mention Aśvagandhā and contain several synonyms of Aśvagandhā. Some of these synonyms are: Vajigandha, Vatagni, Balya, Vrisya, Hayagandha, Kusthagandhini, Elaparni, Vajikari etc⁶.

Caraka Samhita and Susruta Samhita mention specific recipes for specific illnesses that mention Aśvagandhā as a constituent of these recipes^{7 8}.

Aśvagandhā, as a tonic, is used in combination with other herbs to target specific organs and systems of

the body. Frawley and Ranade⁹, list the following combinations of Aśvagandhā with other herbs:

- a) Aśvagandhā with Arjuna - Tonic for the Heart
- b) Aśvagandhā with Bala - Tonic for Lungs and Muscles
- c) Aśvagandhā with Gokshura - Tonic for Kidneys and Bladder
- d) Aśvagandhā with Gotu Kola - Tonic for the Brain and Nerves
- e) Aśvagandhā with Kapikacchu - Excellent Aphrodisiac
- f) Aśvagandhā with Shatāvri - Tonic for the reproductive system (Male & Female)
- g) Aśvagandhā with Vidari Kand - Tonic for the Bones and anti-arthritis.

Pharmacological and Clinical Studies

Many clinical and pharmacological studies have been conducted, and continue to be conducted, on Aśvagandhā with the intent of scientifically confirming the wide-ranging therapeutic uses of this important herb of ayurvedic medicine. Clinical studies, conducted all over the world, have established and confirmed, scientifically, the studied therapeutic actions of Aśvagandhā. Many of these studies are based on animal (in vivo and in vitro) models, while others are based on human models. The following are summarized findings from several of these pertinent studies, arranged categorically by the property of Aśvagandhā that was studied.

Adaptogenic and anti-stress Studies

Animal model studies indicate that Aśvagandhā enhances physical endurance while reducing the effects of stress-induced gastric ulcers. Stress-induced reductions of cortisol and ascorbic acid levels in the adrenal gland were also prevented by Aśvagandhā¹. In another study on the effects of Aśvagandhā on the psychophysiology of trainee mountaineers, who ascended to heights of 7000 meters and then descended,

Aśvagandhā was found to have altered the psychophysical behaviours related to their sleeping patterns, states of awareness, alertness and general physical capabilities². In another study to determine the effects of Aśvagandhā on the cardio-respiratory endurance (aerobic capacity) of cyclists, a eight-week supplementation of 500mg aqueous extract of Aśvagandhā roots, twice daily, was found to increase the cardio-respiratory endurance of the cyclists by about 13%. In comparison, the control group showed no improvement in endurance¹⁰.

Aśvagandhā increases resistance to stress and thus reduces anxiety, imparting a general feeling of well-being. This was the finding of a controlled study on the effects of Aśvagandhā on subjects with a history of chronic stress. After being on a protocol of 300mg, twice a day, of full spectrum, high concentration extract of the root of Aśvagandhā for sixty days, the subjects had significantly reduced scores on stress assessment measures, indicating that their resistance to stress had improved substantially. Their serum cortisol levels were also found to be significantly reduced¹¹. Aśvagandhā also appeared to induce a state of non-specific increase in resistance (SNIR) to stress¹².

Hepato-protective Studies

The steroidal lactone constituent of the roots of Aśvagandhā, Withanolide, protects the liver against toxicity induced by several chemicals, such as, bromobenzene (C₆H₅Br), Carbon tetrachloride (CCl₄) and ammonia. These chemicals are the constituents of certain drugs. Aśvagandhā protects the liver against the damage that these chemicals cause. It is hypothesized that this hepato-protective effect is exerted by the withanolides and other bioactive compounds, that the root extract of Aśvagandhā contains, in addition to its anti-oxidant properties and free-radical scavenging capabilities. However, the exact mechanism underlying the hepato-protective property of Aśvagandhā needs more study.^{13 14 15}

A rather interesting study was found which indicates that exposing the Aśvagandhā plant to supplemental ultraviolet-B radiation changed the metabolite profile and the free-radical scavenging capabilities

of the plant. It was found that exposure to such radiation altered the composition of the plant metabolites resulting in a higher free-radical scavenging capability!!¹⁶

Anti-tumoural Property Studies

Many animal model studies observed that Aśvagandhā inhibits the growth of cancer cells and also disrupts the colony-forming efficiency of the cancer cells. In clinical studies at the International Institute of Herbal Medicine, Lucknow, India, Aśvagandhā has been found to be effective in preventing and treating many different cancers such as colon cancer, lung cancer, skin cancer, blood cancer, breast cancer, renal cancer, prostate cancer, pancreatic cancer, endodermal carcinoma and fibrosarcoma. Singh, et al. contend that, Aśvagandhā works through its many bio-active constituents and their wide-ranging therapeutic properties (as "adaptogens, anabolic agents, anti-oxidants, immuno-modulators and detoxification agents") to inhibit the cancer rather than just inhibiting the cancer cell division. This occurs as Aśvagandhā protects normal cells and boosts immunity, both of which are compromised in chemotherapy or radiotherapy. Aśvagandhā also has a radio-sensitizing effect, which means that it enhances the effects of radiation on tumour regression and inhibits tumour growth. Therefore, Aśvagandhā can be used alone in treating cancer or it can be used as an adjunct therapy with radiotherapy or chemotherapy. This contention by Singh, et al., however, can only be verified by long-term clinical trials and studies in which participation of Oncologists will be of importance. Aśvagandhā also finds use as an anti-tumour and immuno-modulatory agent in the treatment of uterine fibroids and tumours¹⁷.

Ravikumar, et al., conducted a study on the changes in biological and molecular functions and the immuno-modulatory processes induced by treatment of prostate cancer cells with Aśvagandhā. It was found that Aśvagandhā dynamically regulated the pro-inflammatory cytokines, thus playing the role of an immuno-modulator. (Pro-inflammatory cytokines play a crucial role in inflammatory response and other cellular processes). Aśvagandhā also regulated the expression of certain proteins that are responsible for cell

proliferation and immunity. Additionally, Aśvagandhā was found to activate the signalling pathway of apoptosis of the cancer cells. Based on these results, this study points out that Aśvagandhā could be used as complementary therapy in oncology care^{18, 19}.

A water extract of Aśvagandhā leaves were found to arrest the growth and induce cell differentiation in glioma cells at concentrations of $\leq 0.5\%$ while at higher concentrations of $>1\%$, cytotoxicity and apoptosis of the glioma cells occurred. (Glioma is a brain tumour that has very limited treatment options). These were the findings of a study by Hardeep Kataria, et al²⁰. An interesting study presents evidence, at a molecular level, that an extract of the Aśvagandhā leaf selectively arrests tumour cell growth and causes apoptosis²¹. Both in vivo (in mice) and in vitro studies were conducted. In vitro studies were conducted on the following human tumour cells : Normal diploid fibroblasts, osteogenic sarcoma, breast carcinoma, fibrosarcoma, colon carcinoma and lung carcinoma. A component from the leaf extract, that the authors call i-Factor, selectively killed human tumour cells without affecting normal cells. NMR (Nuclear Magnetic Resonance) analysis and electro-spray mass spectroscopy of i-Factor determined it to be a withanone that is potentially an anti-cancer drug.

Another study on the effect of an extract of Aśvagandhā on human melanoma cells (Melanoma is a type of skin cancer) indicates that Aśvagandhā regulates the synthesis of melanin by interrupting the intracellular signalling and reduces their response to the melanocyte master transcription factor, consequently, suppressing the expression of melanin synthesis proteins²².

Aśvagandhā has been suggested as an adjunct therapy with chemotherapy or radio therapy for cancer. In a study on breast cancer patients, it was determined that the extract of Aśvagandhā root, at dosages of 2 gms, thrice a day, with parallel chemotherapy/radio therapy, the quality of life of these patients improved and significantly reduced cancer treatment-related fatigue²³.

In vitro and in vivo studies, by Su-Hyeong Kim and Shivendra V. Singh, on mammary cancer showed that withaferin A, one of the main steroidal lactones in Aśvagandhā roots, inhibited the self-renewal capability of breast cancer stem cells. This suggests that Aśvagandhā may have a potential role in the prevention and treatment of mammary cancer, pending large scale clinical investigations²⁴.

Based on the above studies, it can be inferred that Aśvagandhā shows a lot of promise in the prevention and treatment of tumour-related conditions, including cancer, with the added note that large-scale, long-term and rigorous clinical trials are necessary to confirm Aśvagandhā's use in such treatment and the optimal dosages that are to be used.

Anti-inflammatory and anti-bacterial studies

In a study by SoRelle, et al., conducted to evaluate the ability of Withaferin A, (WA), to protect mouse and human pancreatic islets from the effects of pro-inflammatory cytokines following transplantation, it was determined that treating the islets with WA inhibited inflammatory response in the islets and protected them against cytokine-induced damage, thus improving the survival rate of the transplanted islets. These results suggest the potential use of Aśvagandhā as an adjunct therapy to improve the success rates of islet transplants²⁵.

In another study, Aśvagandhā was compared with hydrocortisone for its anti-inflammatory properties. Here, the acute anti-inflammatory effect of Aśvagandhā, in carrageenan-induced paw edema, in rats used in the study, was comparable to the results that were achieved with hydrocortisone. The chronic anti-inflammatory effect of Aśvagandhā, in Freund's adjuvant induced arthritis, again, was comparable to the results obtained with hydrocortisone. Additionally Aśvagandhā significantly inhibited secondary lesions and their spreading, exhibiting an efficacy comparably close to that of hydrocortisone²⁶.

A clinical trial involving humans to determine the safety and efficacy of Aśvagandhā in managing

rheumatoid arthritis, found that the anti-inflammatory and analgesic properties of Aśvagandhā reduced pain, stiffness and swelling in the patients²⁷.

An extract of the leaves of Aśvagandhā showed selective anti-bacterial action against intestinal microbiota, i.e., human pathogenic bacteria and intestinal bifidobacteria. An acetone extract of the leaves of Aśvagandhā exhibited selective anti-bacterial action against the pathogens while not affecting the bifidobacteria²⁸.

Neuro-regenerative Potential Studies

Several studies have focused on studying herbs that exhibit neuro-regenerative properties in the quest to find cures for neuro-degenerative diseases, most notable among these being studies conducted in Japan. These studies noted that neurite atrophy in the brain is a common feature of neuro-degenerative diseases such as Alzheimer's, Parkinson's, Huntington's and Creutzfeldt-Jakob's diseases. Such atrophy ends in destruction of the neuronal networks and ultimately, a fatal dysfunction of the brain. The hypothesis behind this quest is that the recovery of functions in the injured brain would be feasible with neuritic regeneration and synaptic reconstruction.

Tohda, et al.²⁹ in their study with Aśvagandhā, ginseng and coffee bean arrived at the following conclusion: certain saponins in Ginseng were able to reconstruct neuronal networks and induced recovery from memory impairment in mice; Compounds Withanolide A, withanoside IV and withanoside VI, isolated from Aśvagandhā, were able to regenerate axons and dendrites and reconstruct synapses even though the neurons were severely damaged; Trigonelline, an active constituent of coffee, also exhibited axonal and dendritic regeneration and improved memory retention.

In another study, Tohda, et al.³⁰, investigated the effect of Withanolide A on memory-deficient mice that

showed neuronal atrophy and synaptic loss in the brains. The memory impairment was induced in the mice by Ab(25-35) a partial fraction of Amyloid b (Amyloid b is the pathological cause of Alzheimer's disease). Treatment with Withanolide A reversed the Ab(25–35)-induced memory deficit in the mice. The authors suggest that this could be a result of the reconstruction of the neuronal network. It was also observed that the neuronal atrophy was reversed, with the regeneration of axons and dendrites in the cerebral cortex and hippocampus, in addition to the reconstruction of neuronal pre- and post-synapses.

In the same study, cultured cortical neurons of rats were also studied. Dendritic and axonal atrophy and pre- and post-synaptic loss were induced by treating them with Ab(25–35). The same results were observed - the regeneration of axons and dendrites and the reconstruction of pre- and post-synapses in the cultured neurons.

The authors of this study also note that Withanolide A did not prevent the death of neurons induced by Ab(25–35) in vitro. This is attributed to the fact that Amyloid b has several mechanisms of inducing neuronal death, which differ from the mechanism that Amyloid b uses to induce neuronal atrophy.

The results of these studies indicate that Withanolide A could be a potential drug that can be an adjunct in treating neuro-degenerative diseases in combination with medicines that could prevent pathogenesis and neuronal death.

Kuboyama, et al.³¹, conducted a study to determine how various extracts of Aśvagandhā and the different withanolide compounds affect in vitro and in vivo models of neurodegenerative diseases and spinal cord injury. The several extracts and withanolide compounds exhibited axonal and dendritic regenerative actions, synaptic reconstruction, memory improvement, neuroprotective effect and recovery of functionality of the neuronal system. Additionally, the effect of "denosomin", a derivative of Withanoside IV was synthesized by the authors of this study and used to determine its effect on spinal cord injuries on mice. A contusion injury at L1

spinal cord was affected. An hour later, oral administration of denosomin was started. After 14 days of administration, motor function of the hind limb was recovered. In a note on the safety of several compounds of Aśvagandhā, the authors note that withaferin A and withanolide D demonstrated neurotoxicity in cultured cells and normal neuronal cells. They caution that this toxicity should be taken note of, particularly at high doses. The study concludes with the hope that further studies on Aśvagandhā will meet the urgent necessity of cures for neuro-degenerative diseases.

Infertility and Sexual Dysfunction Studies

Aśvagandhā has traditionally been prescribed to treat conditions related to infertility and other conditions of sexual dysfunction. Dongre S et al. conducted a pilot study on female sexual dysfunction which demonstrates that supplementation with a high-concentration root extract of Aśvagandhā could possibly improve sexual function in healthy women³². The conclusions drawn were that Aśvagandhā improved sexual function by i) reduction of stress, which directly contributes to sexual dysfunction and ii) increasing levels of testosterone, a factor in androgen deficiency, which affects sexual dysfunction. Of note is that both the control group and placebo group received counselling. So, it can be concluded that Aśvagandhā could be an adjunct to the counselling program, helping to resolve some, if not all the issues associated with sexual dysfunction.

Some studies show that male infertility (Oligospermia) can be reversed with the use of a high concentration root extract of Aśvagandhā. In one pilot study³³ that was conducted for a duration of 90 days, treatment of oligospermic males with the root extract of Aśvagandhā resulted in marked improvement in semen parameters and sexual hormone levels. Increases in sperm concentration, ejaculate volume, motile sperm count and serum levels of testosterone were in evidence. However, rigorous scientific study is necessary, from a western medicine perspective, for acceptance of the efficacy and safety of Aśvagandhā in treating oligospermia.

Ahmad MK, et al.³⁴ conducted another study investigating the effects of a root extract of Aśvagandhā on

the reproductive hormone levels, oxidative biomarkers and semen profile of infertile men. Before the study, serum levels of testosterone (T), Follicle stimulating hormone (FSH), Lutenizing hormone (LH) and Prolactin (PL), biochemical parameters of seminal plasma and antioxidant enzymes were measured for a baseline. After the study, measures of the same parameters indicated that treatment with the root extract of Aśvagandhā raised levels of antioxidant enzymes in seminal plasma, decreased serum levels of FSH and PL, increased serum levels of T and LH. Sperm count and motility also increased. This results points to the reduction of oxidative stress, which negatively affects sperm concentration and motility. Further studies are necessitated as the mechanisms of action of Aśvagandhā on infertility are not well known.

Toxicity and Safety Studies

There is a dearth of studies regarding the toxicity of Aśvagandhā and its safety or side-effects when used with different medications. Very few studies were found on this topic.

A reference to the observed toxic effects of specific compounds of Aśvagandhā, Withaferin A and Withanolide D, is the study by Kuboyama et al.³¹ where the authors caution on the neurotoxicity of these two compounds, on normal and cultured neuronal cells.

At doses of up to 2000mg per kilogram of body weight per day, oral administration of Aśvagandhā root extract was found to be safe³⁵. No mortalities were observed at this dosage even after 28 days. In a study conducted on pregnant rats, no toxic effects were seen in the rats or the foetuses, thus concluding that up to a dosage of 2000mg/kg of body weight/day, oral administration of Aśvagandhā root extract is safe³⁶. However, another recent study by Sahni et al. on acute and chronic toxicity studies on albino rats observed that at a dosage of 1000 mg per Kg body weight of hydro-alcoholic extract of the root of Aśvagandhā, there was some initial excitement followed by mild depression, reduced respiration, dullness and a reduction in spontaneous motor activity. But no mortalities occurred. The conclusion arrived at was that Aśvagandhā appears to be safe as it

does not present acute or chronic toxicity³⁷.

Contra-indications of Usage

As per Ayurveda, rasayanas are always administered after cleansing the external and internal (Panchakarma) organs, making the organ systems more receptive to receive the maximum benefits of the rasayanas administered. In conditions of high pitta and if ama with congestion is present, Aśvagandhā should not be prescribed.

Although traditionally prescribed in India to strengthen the uterus and to maintain good health of the mother and the child, Aśvagandhā is contra-indicated for pregnant and lactating women in the West³.

Conclusion

In conclusion, several preliminary studies and clinical trials have been conducted to scientifically confirm and verify the multiple therapeutic benefits proffered by Aśvagandhā. Although the results of these studies and trials point to the potential use of Aśvagandhā as a panacea for several diseases, large scale and rigorous scientific studies and clinical trials are necessary to firmly establish a scientific basis for the therapeutic uses of Aśvagandhā within the paradigm of Western medicine. Another important note is that many of the mechanics of how Aśvagandhā exerts its therapeutic actions at the cellular and molecular levels are unknown. Uncovering these exact mechanisms will also necessitate rigorous and detailed studies to determine, not only which of the specific compounds of Aśvagandhā can be used to effect a cure for each disease, but also the optimal dosages that might be required to do so. In short, there is high optimism of finding cures for several diseases, solely with Aśvagandhā, or with Aśvagandhā as an adjunct with conventional therapy.

Bibliography (End Notes)

- 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 Suppl): 208–213. Published online 2011 Jul 3. doi: 10.4314/ajtcam.v8i5S.9; PMID: PMC3252722; <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3252722/>
- 2 Puri HS. RASAYANA: Ayurvedic Herbs of Rejuvenation and Longevity. Taylor & Francis, London. 2003; p. 46-58.
- 3 Sebastian Pole. Ayurvedic Medicine: The Principles of Traditional Practice - Churchill Livingstone Elsevier 2006. ISBN-044310090X. P. 313 - 315
- 4 Veena Sharma, Sadhana Sharma, Pracheta, Ritu Paliwal; Withania somnifera: A Rejuvenating Ayurvedic Medicinal Herb for the Treatment of various Human ailments. International Journal of PharmTech Research, Vol. 3, No.1, pp 187-192, Jan-Mar 2011.
- 5 Frawley D, Ayurvedic Healing - A Comprehensive Guide; Motilal BanarsiDass Publishers Private Limited, Delhi. 3rd Reprint, 2012. ISBN:978-81-208-1003-7 pp 372-373.
- 6 Chaudhary SP, An Ayurvedic review of Ashwagandha from Samhitas and Nighantus. World Journal of Pharmaceutical Research, Vol. 4, Issue 10, 2736 - 2745; ISSN-2277-7105. www.wjpr.net
- 7 Agnivesa's Caraka Samhita, Vol. IV Chikitsa Sthan; By Dr. Sharma RK, Vaidya Das B; Chowkhamba Snaskrit Series Office, Varanasi, 2009 Reprint.
 1. Linctus(Lehya) recipe for hiccup and Asthma. Ch. XVII, p 147, Verse 117
 2. Ingudi-tvagadi Dhuma recipe for vatika Kasa. Ch. XVIII, p 176, Verse 75
 3. Granthi Visarpa recipe of paste for external application. Ch. XXI, p 295, Verse 123.
 4. Gandha-Hasti recipe of paste for curing poisons, unmada, apasmara, etc. Ch. XXIII, p 345, Verse 70.
 5. Maha-Gandha-Hasti recipe for curing eye diseases. Ch. XXIII, p 347, Verse 80.

6. Amrta-Ghrta recipe for curing Udara, gulma, poisons, etc. Ch. XXIII, p 382, Verse 244.

Agnivesa's Caraka Samhita, Vol. V Chikitsa Sthan; By Dr. Sharma RK, Vaidya Das B; Chowkhamba Snaskrit Series Office, Varanasi, 2009 Reprint.

1. Kusthadya Taila recipe for Urusthamba. Ch. XXVII, p 12, Verse 43.
2. Recipe for Utsadana therapy for Urusthamba. Ch. XXVII, p 14, Verse 50.
3. Recipe for Rasna taila for vataroga. Ch. XXVIII, p 64, Verse 166.
4. Recipe for Vrsa-mulakadya-taila for bone fractures & Osteoporosis caused by vayu. Ch. XXVII, p 65, Verse 170.
5. Recipe of paste forvata-rakta (gout). Ch. XXIX, p 106, Verse 73.

- 8 Susrutha Samhita, Vol I, Sutrasthana. Translated & edited by Sharma PV; Chaukhamba Visvabharati Oriental Publishers & distributors. 2013 Reprint. ISBN: 978-93-81301-25-8. 1. Formula for Lepa (paste) for Karnapali Vriddhi. Ch. XVI, pp 180, Verse 18.
2. Formula for Kalka and taila for Karnapali Vriddhi. Ch. XVI, pp 181, Verse 21.

Susrutha Samhita, Vol II, Chikitsasthana. Translated & edited by Sharma PV; Chaukhamba Visvabharati Oriental Publishers & distributors. 2013 Reprint. ISBN: 978-93-81301-25-8.

1. Formula for Kalka for Vata rakta. Ch. V, pp 316, Verse 10.
2. Recipe for Bala taila for Vata vyadhis. Ch. XV, pp 414, Verse 33.
3. Formula for Lepa for Kaphaja Visarpa (Erysipelas). Ch. XVII, pp 427, Verse 14.
4. Formulas for lepas for Paripotaka (Karnapali roga). Ch XXV, pp 513-514. Verses 15 & 18.
5. Formulas of tailas for Vata rogas. Ch. XXXVII, pp 617-619. Verses 12, 16 & 20.
6. Formula for enema preparation for vatavyadhis, grahani, etc.Ch. XXXVIII, pp 644. Verse 43.

- 9 Frawley D, Ranade S - Ayurveda - Nature's Medicine; Motilal Banarsidas Pub. Pvt. Ltd. ISBN:978-81-208-2040-1. Chapter on Ayurvedic Herbology, pp 158-159.
- 10 Shenoy S, Chaskar U, Sandhu JS, Paadhi MM. Effects of eight-week supplementation of Ashwagandha on cardiorespiratory endurance in elite Indian cyclists. J Ayurveda Integr Med [serial online] 2012 [cited 2016 Mar 28];3:209-14. Available from: <http://www.jaim.in/text.asp?2012/3/4/209/104444>
- 11 Chandrasekhar K, Kapoor J, Anishetty S. 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 J Psychol Med [serial online] 2012 [cited 2016 Mar 28];34:255-62. Available from: <http://www.ijpm.info/text.asp?2012/34/3/255/106022>
- 12 Singh, R. Nath, A. Lata, S. P. Singh, R. P. Kohli & K. P. Bhargava pages 29-35; Withania Somnifera (Ashwagandha), a Rejuvenating Herbal Drug Which Enhances Survival During Stress (an Adaptogen) - <http://www.tandfonline.com/doi/pdf/10.3109/13880208209083282>
- 13 Mahima VEDI, Mahaboobkhan Rasool, Evan Prince Sabina; Amelioration of bromobenzene hepatotoxicity by Withania somnifera pretreatment: Role of mitochondrial oxidative stress; Toxicology Reports Volume 1, 2014, Pages 629–638. <http://www.sciencedirect.com/science/article/pii/S2214750014000729>
- 14 B. HARIKRISHNAN, P. SUBRAMANIAN and S. SUBASH; Effect of Withania Somnifera Root Powder on the Levels of Circulatory Lipid Peroxidation and Liver Marker Enzymes in Chronic Hyperammonemia; E-Journal of Chemistry Vol. 5, No.4, pp. 872-877, October 2008; <http://www.e-journals.net>
- 15 Praveen Kumar, Raghavendra Singh, Arshed Nazmi, Dinesh Lakhnopal, Hardeep Kataria, and Gurcharan Kaur; Glioprotective Effects of Ashwagandha Leaf Extract against Lead Induced Toxicity; Hindawi Publishing Corporation, BioMed Research International, Volume 2014, Article ID 182029, 15 pages.

<http://www.hindawi.com/journals/bmri/2014/182029/>; <http://dx.doi.org/10.1155/2014/182029>

- 16 Swabha Takshak, S. B. Agrawal. Alterations in metabolite profile and free radical scavenging activities of *Withania somnifera* leaf and root extracts under supplemental ultraviolet-B radiation. Franciszek Górski Institute of Plant Physiology, Polish Academy of Sciences, Kraków, in cooperation with Warsaw University of Life Sciences - SGGW, Department of Plant Physiology. <http://link.springer.com/article/10.1007/s11738-015-2014-5?no-access=true>
- 17 N. Singh, P. Verma, B. R. Pandey, M. Gilca. Role of *Withania somnifera* in Prevention and Treatment of Cancer: An Overview. *International Journal of Pharmaceutical Sciences and Drug Research* 2011; 3(4): 274-279, Review Article. ISSN 0975-248X. <http://www.ijpsdr.com/volumethree-issue4.html>
- 18 Ravikumar Aalinkeel, Zihua Hu, Bindukumar B. Nair, et al., “Genomic Analysis Highlights the Role of the JAK-STAT Signaling in the Anti-Proliferative Effects of Dietary Flavonoid—‘Ashwagandha’ in Prostate Cancer Cells,” *Evidence-Based Complementary and Alternative Medicine*, vol. 7, no. 2, pp. 177-187, 2010. doi:10.1093/ecam/nem184; <http://www.hindawi.com/journals/ecam/2010/267039/cta/>
- 19 Marie Winters, ND, *Ancient Medicine, Modern Use: Withania somnifera and its Potential Role in Integrative Oncology*; *Altern Med Rev* 2006;11(4):269-277; <http://www.altmedrev.com/publications/11/4/269.pdf>
- 20 Hardeep Kataria, Navjot Shah, Sunil C. Kaul, Renu Wadhwa, and Gurcharan Kaur, “Water Extract of Ashwagandha Leaves Limits Proliferation and Migration, and Induces Differentiation in Glioma Cells,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2011, Article ID 267614, 12 pages, 2011. doi:10.1093/ecam/nep188; <http://www.hindawi.com/journals/ecam/2011/267614/cta/>
- 21 Nashi Widodo, Kamaljit Kaur, Bhupal G. Shrestha, Yasuomi Takagi, Tetsuro Ishii, Renu Wadhwa and Sunil C. Kaul - Selective Killing of Cancer Cells by Leaf Extract of Ashwagandha: Identification of a Tumor-Inhibitory Factor and the First Molecular Insights to Its Effect; doi: 10.1158/1078-0432.CCR-06-0948; *Clin Cancer Res* April 1, 2007 13; 2298; <http://clincancerres.aacrjournals.org/content/13/7/2298.full.pdf+html>
- 22 Hiroaki Nakajima, Katsunori Fukazawa, Yuki Wakabayashi, Kazumasa Wakamatsu, Genji Imokawa; *Withania somnifera* extract attenuates stem cell factor-stimulated pigmentation in human epidermal equivalents through interruption of ERK phosphorylation within melanocytes; Original Paper, *Journal of Natural Medicines*, July 2012, Volume 66, Issue 3, pp 435-446, First online: 16 November 2011; <http://link.springer.com/article/10.1007%2Fs11418-011-0604-0/fulltext.html>
- 23 Biswal BM, Sulaiman SA, Ismail HC, Zakaria H, Musa KI - Effect of *Withania somnifera* (Ashwagandha) on the development of chemotherapy-induced fatigue and quality of life in breast cancer patients. *Integr Cancer Ther*. 2013 Jul;12(4):312-22. doi: 10.1177/1534735412464551. Epub 2012 Nov 9.
- 24 Su-Hyeong Kim and Shivendra V. Singh - Mammary Cancer Chemoprevention by Withaferin A Is Accompanied by In Vivo Suppression of Self-Renewal of Cancer Stem Cells. *Cancer Prev Res*; 7(7) July 2014, American Association for Cancer Research. DOI: 10.1158/1940-6207.CAPR-13-0445. <http://cancerpreventionresearch.aacrjournals.org/content/7/7/738.full.pdf+html>
- 25 J. A. SoRelle, T. Itoh, H. Peng, M. A. Kanak, K. Sugimoto, S. Matsumoto, M. F. Levy, M. C. Lawrence, B. Naziruddin - Withaferin A inhibits pro-inflammatory cytokine-induced damage to islets in culture and following transplantation; *Diabetologia*, April 2013, Volume 56, Issue 4, pp 814-824; <http://link.springer.com/article/10.1007%2Fs00125-012-2813-9>
- 26 Dr. Kiran R Giri, Comparative study of anti-inflammatory activity of *Withania somnifera* (Ashwagandha) with hydrocortisone in experimental animals (Albino rats); *Journal of Medicinal Plants Studies* 2016; 4(1): 78-83;
- 27 Sufiyan Ahmad Ghawte, Shaikh Nikhat, Jalis Ahmad and Ghazala Mulla; *Withania somnifera* L. Dunal: A potential herb for the treatment of rheumatoid arthritis; *Annals of Phytomedicine* 3(1): 98-102, 2014;
- 28 K. HALAMOVA, L. KOKOSKA, Z. POLESNY, K. MACAKOVA, J. FLESAR AND V. RADA; SELECTIVE IN VITRO GROWTH INHIBITORY EFFECT OF WITHANIA SOMNIFERA ON HUMAN PATHOGENIC BACTERIA AND BIFIDOBACTERIA ; *Pak. J. Bot.*, 45(2): 667-670, 2013. <http://www.pakbs.org/pjbot/PDFs/45%282%29/45.pdf>

- 29 Chihiro Tohda, Tomoharu Kuboyama, Katsuko Komatsu - Search for Natural Products Related to Regeneration of the Neuronal Network. *Neurosignals* 2005;14:34–45; DOI: 10.1159/000085384; <http://content.karger.com/Article/FullText/85384>
- 30 Kuboyama, T., Tohda, C. and Komatsu, K. (2005), Neuritic regeneration and synaptic reconstruction induced by withanolide A. *British Journal of Pharmacology*, 144: 961–971. doi: 10.1038/sj.bjp.0706122
- 31 Tomoharu Kuboyama, Chihiro Tohda, and Katsuko Komatsu - Effects of Ashwagandha (Roots of *Withania somnifera*) on Neurodegenerative Diseases. *Biol. Pharm. Bull.* 37(6) 892–897 (2014), The Pharmaceutical Society of Japan. https://www.jstage.jst.go.jp/article/bpb/37/6/37_b14-00022/html.
- 32 Swati Dongre, Deepak Langade, and Sauvik Bhattacharyya, “Efficacy and Safety of Ashwagandha (*Withania somnifera*) Root Extract in Improving Sexual Function in Women: A Pilot Study,” *BioMed Research International*, vol. 2015, Article ID 284154, 9 pages, 2015. doi:10.1155/2015/284154
- 33 Vijay R. Ambiyé, Deepak Langade, Swati Dongre, Pradnya Aptikar, Madhura Kulkarni, and Atul Dongre, “Clinical Evaluation of the Spermatogenic Activity of the Root Extract of Ashwagandha (*Withania somnifera*) in Oligospermic Males: A Pilot Study,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 571420, 6 pages, 2013. doi:10.1155/2013/571420
- 34 Mohammad Kaleem Ahmad, M.Sc., Abbas Ali Mahdi, M.A., M.S., Ph.D., Kamla Kant Shukla, M.Sc., Najmul Islam, Ph.D., Singh Rajender, Ph.D., Dama Madhukar, M.V.Sc., Satya Narain Shankhwar, M.Ch., and Sohail Ahmad, M.D; *Withania somnifera* improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males; *Fertility and Sterility* Vol. 94, No. 3, Pages 989–996, August 2010; American Society for Reproductive Medicine, Published by Elsevier Inc. <http://www.fertstert.org/article/S0015-0282%2809%2901014-0/fulltext>
- 35 Prabu PC, Panchapakesan S, Raj CD. Acute and sub-acute oral toxicity assessment of the hydroalcoholic extract of *Withania somnifera* roots in Wistar rats. *Phytother Res.* 2013 Aug;27(8):1169-78. doi: 10.1002/ptr.4854. Epub 2012 Sep 21.
- 36 P. C. Prabu & S. Panchapakesan (2015) Prenatal developmental toxicity evaluation of *Withania somnifera* root extract in Wistar rats, *Drug and Chemical Toxicology*, 38:1, 50-56. <http://dx.doi.org/10.3109/01480545.2014.900073>
- 37 Y.P. Sahni, M. Sharma and G.P. Pandey. STUDIES ON PHYTOCHEMISTRY AND TOXICITY OF WITHANIA SOMNIFERA; *International Journal of Animal, Veterinary, Fishery and Allied Sciences IJAVFAAS* 2014, Vol. 1(1): 12-16.