

TRENDS IN CURRENT BIOLOGY ISSN 2584-2080 (online) Vol 2(4): 10-17 https://doi.org/10.14719/tcb.4431

REVIEW ARTICLE



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An in-depth exploration of ethnomedicinal applications, phytochemical profiles and pharmacological potentials: unveiling Withania somnifera

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OPEN ACCESS 6

ARTICLE HISTORY

Received: 23 July 2024 Accepted: 07 September 2024 Available online Version 1.0:01 October 2024

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https:// horizonepublishing.com/journals/ index.php/TCB/open_access_policy

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Balkrishna A, Kumud, Chaurasia SK, Goswami P, Arya V. An In-Depth Exploration of Ethnomedicinal Applications, Phytochemical Profiles and Pharmacological Potentials: Unveiling Withania somnifera. Trends in Current Biology. 2024; 2 (4): 10-17.https://doi.org/10.14719/tcb.4431

Abstract

Researchers have extensively studied Withania somnifera (L.) Dunal, a woody shrub renowned for its multifaceted medicinal attributes such as antibacterial, antiinflammatory, adaptogenic, aphrodisiac and tonifying properties, because of its medicinal and traditional values. However, comprehensive information about its medicinal uses and pharmacological implications is scattered across various sources. Thus, this study aims to provide a comprehensive review of its ethnomedicinal uses, phytochemistry and pharmacological attributes, consolidating information from diverse data sources. Systematic investigations have revealed the presence of diverse phytochemicals in W. somnifera, including major alkaloids, withanolides, flavonoids, tannins, oils, phytosterols and amino acids. Extracts, fractions and bioactive compounds derived from W. somnifera exhibited potent antibacterial, antiinflammatory, anti-aging, anti-analgesic, anti-cancer, antivenom, anti-fungal and anti -viral activities. W. somnifera serves as a valuable source of phytochemicals with diverse biological activities, offering significant therapeutic benefits globally. However, further studies are needed to assess potential side effects. Additionally, while several isolated compounds have demonstrated notable bioactivities, future research should focus on elucidating their mechanistic features to facilitate their integration into drug discovery endeavors.

Keywords

Withania somnifera; Ashwagandha; medicinal applications; phytochemistry; pharmacological properties

Introduction

Researchers are increasingly fascinated by plant-based bioactives for their health benefits derived from rich secondary metabolites. Over 80% of the global population, particularly in developing nations, rely on phytomedicines because of their minimal side effects and affordability, which helps sustain traditional healing systems such as Ayurveda, Greco-Arab and Chinese medicine. Within the Solanaceae family, Withania plants, notably W. somnifera (Ashwagandha) hold medicinal value and are prevalent across Africa, the Mediterranean, Sri Lanka, Pakistan and India. Ayurveda recognizes its roots and leaves as potent phototherapeutic agents for treating various ailments (Fig. 1).

Clinical trials underscore W. somnifera's effectiveness against conditions such as hepatotoxicity, neurological disorders, anxiety, Parkinson's disease and hyperlipidemia. Its fruits and leaves contain significant saponins and exhibit insect repellent properties. It is found to be a potential source of various pharmacologically active compounds namely withanolides, withanine, alkaloids,

कंदिनी वाजिगंधा स्यात् क्षुपा पर्पेटिवत् फला । वनजा वृत्तपर्णी च कंदो वाजीकरः स्मृतः ॥ (शि.)

The fruit of the *kandini* is like the fragrance of a horse and is stirred like a crust. The forest tree is known as *V*_{*i*}*ttapar*_{*n*}*i* and the tuber is known as *V*_{*i*}*ttapar*_{*n*}*i*.

गंधान्ता वाजिनामादिराश्वगंधा हयाव्या वराहकर्णी वरदा बलदा कुष्ठ गंधिनी । अश्वगन्धानिलश्लेष्मश्वित्रशोधक्षयापहा। बल्या रसायनी तिक्ता कषायोष्णातिशुक्रला ॥ (भा. प्र.) Gandhanta is the origin of the names of Ashwagandha, Hayahvya, Varahakarni, Varada, Balada, Kushtagandini and Baji. Its two synonyms are Bajigandha and Hyagandha. Ashwagandha is a remedy for anti-aging, mucus, leukoderma, sweating and inflammation. It manages many problems associated with emaciation. It is very sweet, bitter, and astringent in taste, pungent in smell, and hot in potency. It is energy provider and enhances the spermatogenesis.

पीताश्वगंधा पयसार्धमासं घृतेन तैलेन सुखाम्बुना वा । कृशस्य पुष्टिं वपुषो विधत्ते बालस्य सस्यस्य यथाम्बुवृष्टिः ॥ (च. द.) Yellow Ashwagandha milk mixed with ghee, oil, or pleasant water for half a month is beneficial. Just as a shower of water nourishes a child's body when it is lean, this mixture rejuvenates and strengthens the body.

शिशिरं योऽश्वगंधायाः कन्दचूर्णम् पलोन्मितम् । मासमत्ति समध्वाज्यं स वृद्धोऽपि भवेद्युवा ॥ (रा. मा.) During winter, those accustomed to consuming powdered Ashwagandha tubers will retain their youthful vigor, even in old age.

पादकल्केऽश्वगंधायाः क्षीरे दशगुणे पचेत् । घृतं पेयं कुमाराणां पुष्टिकृद्वलवर्धनम् ॥ (च. द.) Boil the limestone in ten times the amount of Ashwagandha milk. Ghee is a drink that nourishes and increases the strength of young men.

Fig. 1. Ancient verse on Withania somnifera in Ayurvedic texts

sterol and phenolics, flavonoids, and glycoside for its immense therapeutic applications. Despite existing literature, a comprehensive review encompassing *W. somnifera*'s phytochemical composition, medicinal uses, and nutraceutical potential is necessary to bridge knowledge gaps among professionals in pharmacy and medicine, fostering a deeper understanding and application of its beneficial properties.

For centuries, medicinal plants and their derived natural products have been primary sources of healthcare for millions of individuals. Scientists have extensively validated and documented the therapeutic efficacy of many of these plants through research (1-5). Among these plants, the genus *Withania* stands out, with taxonomically recognized species predominantly found on the Indian subcontinent and widely distributed in regions including India, Pakistan and Sri Lanka. *Withania* species are utilized across various nations for their reputed exceptional medicinal properties.

W. somnifera, a woody shrub typically reaching heights of 1-2 m, is rich in phytochemicals including alkaloids, withanolides, sitondosides, flavonoids, tannins, oils and phytosterols. Numerous pharmacological studies have demonstrated its remarkable therapeutic potential, including anti-inflammatory, anti-stress, anti-aging, analgesic, aphrodisiac, anti-cancer, anti-venom, hypothyroidism, anti-fungal and anti-viral activities.

The large number of phytochemicals present in *W.* somnifera holds immense therapeutic benefits and exhibits impressive pharmacological actions. However, some compounds have undergone limited pharmacological investigation, with scattered and inadequate data available regarding their traditional uses (3,6-9). Moreover, there is a lack of correlations between the pharmacological attributes of this plant and its ethnobotanical applications. Safety profiles and specific formulations also remain insufficiently researched. Despite several studies on the biological activities of *W. somnifera* and its phytoconstituents, researchers have not yet published a comprehensive review that details both its pharmacological activities and extensive insights into its medicinal uses (10,11). Consequently, we have undertaken this study to provide a comprehensive overview encompassing botanical description, taxonomy, geographic distribution, medicinal applications, phytochemistry and pharmacological properties of *W. somnifera*. We anticipate that this knowledge will benefit the research community, facilitating the organization of secure experiments with bioactive compounds.

Botanical Classification

The taxonomical classification of *W. somnifera* (12) is listed below-

Kingdom	Plantae
Subkingdom	Tracheobionta
Super-Division	Spermatophyta
Division	Angiosperm
Class	Dicotyledons
Order	Tubiflorae
Family	Solanaceae
Genus	Withania
Species	somnifera

Vedic Name

अश्वगंधकः स्वापकर: (Aśvagandhakaḥ svāpakaraḥ)

Vernacular Names

W. somnifera is known by several names based on the different regions and languages. Some of the commonly spoken names are listed in Table 1.

Botanical Description

W. Somnifera, also known as Ashwagandha or Indian

Language	Names
Sanskrit	Ashwagandha, Baji, Balda, Gandhpatri, Hyahriya, Kamrupini, Kusthgandhini, Turangi-gandha, Varda, Vajini and Vrahkarni.
Hindi	Asgandh, Asgandha and Ashwagandha
English	Winter Cherry and Indian Ginseng
Tamil	Amukkara, Amukura, Askulang and Kizhangu
Urdu	Asgandh and Nagori
Marathi	Asandh, Ashwagandhika and Doragunj
Bengali	Amangura and Asvagandha
Punjabi	Asgandh
Gujarati	Aasandha, Asundha and Ghoda Aakun
Telugu	Penneru Gadda and Dommadolu Gadda
Malayalam	Amukkura and Amukkuram
Kannada	Asvagandhi and Punir
Oriya	Ajagandha
Kashmiri	Asgand

ginseng, is a perennial shrub belonging to the nightshade family. Originating from the Indian subcontinent, including regions of India, Pakistan and Sri Lanka (15), this plant has been integral to traditional Ayurvedic medicine for centuries due to its diverse therapeutic qualities (Fig. 2).

Characteristics:

Form: Ashwagandha is a small woody shrub that typically grows to a height of about 1 to 2 meters (3 to 6 feet). The tree has a central trunk with many branches, giving it a bushy appearance. The stems are covered with fine hairs, giving them a bluish-gray color.



Fig. 2. Withania somnifera (Courtesy: Patanjali Research Foundation, Haridwar)

Leaves: Its leaves are simple, elliptical and arranged alternately along the branches. Possessing short petioles, they measure approximately 5 to 10 centimeters (2 to 4 inches) in length, exhibiting a vibrant green coloration with a relatively smooth surface, occasionally featuring slight hairiness underneath.

Flowers: Ashwagandha yields petite, bell-shaped flowers, typically colored yellow-green to greenish-white. These blooms congregate in clusters at branch terminations, forming terminal inflorescences. The corolla is tubular with five lobes, while the calyx remains inconspicuous.

Fruits: Following flowering, the plant bears diminutive, spherical berries initially green in hue, later maturing to a vivid orange-red shade. Each berry contains small, flattened seeds.

Roots: The most valuable part of the Ashwagandha plant is its fleshy, tuberous root. The roots are light brown in color and have a characteristic odor often described as that of a horse, giving rise to the name "Ashwagandha", which means "smell of a horse" in Sanskrit.

Culture: Ashwagandha prefers well-drained sandy loam soils and is commonly grown in warm tropical regions. It can withstand high temperatures but is sensitive to frost. Propagate mainly by seeds or cuttings (16).

Materials and Methods

The current review study was conducted using a complete and organized search of the available literature and research articles. The searches were performed using various databases, including PubMed (http://www.ncbi.nlm.nih.gov/ pubmed), Science Direct (http://www.sciencedirect.com/), Scopus (http://www.sco pus.com/) and Google Scholar (http://www.scholar.google.com/) using the terms, for example Withania phytochemistry, somnifera, pharmacological activity, Withania, antibacterial, antimicrobial and traditional uses. Scientific names and synonyms were validated through www.worldfloraonline.org.

Traditional Uses

Ashwagandha has an extensive historical background across various cultures, with traditional practices recognizing its potential health advantages. Within systems such as Ayurveda and Unani, it has been a staple, serving diverse purposes. While the roots are predominantly utilized and hold the majority of bioactive compounds responsible for its benefits, other parts like leaves, berries and aerial segments also find application in different traditional methodologies. Some of the traditional applications of Ashwagandha are enlisted in Table 2.

Phytochemistry

W. somnifera, contains a wide range of natural chemicals that make it a valuable plant for medicinal purposes. This ancient herb has a complex mixture of bioactive compounds that are responsible for its healing effects. Researchers have identified numerous compounds in *W. somnifera* that play essential roles in its medicinal properties. These chemicals include alkaloids and flavonoids among others, each contributing to the herb's diverse health benefits. This variety highlights how *W. somnifera* works holistically to promote wellness. Studying how these compounds interact provides insight into the full range of healing capabilities that *W. somnifera* offers, enhancing our understanding of its importance in medicine (Table 3 and Fig. 3).

The presence and concentration of these phytochemicals can vary depending on factors such as the plant's growing conditions, geographical location and the part of the plant used (roots, leaves or berries). **Table 2.** Traditional uses of *W. somnifera*

Ashwagandha's diverse bioactive compounds contribute to its adaptogenic, anti-inflammatory, antioxidant and other medicinal properties, making it a valuable medicinal herb. tradition and is an active area of research in modern pharmacology.

Pharmacology

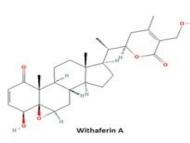
Several pharmacological studies showed that extracts, fractions and compounds derived from the roots, leaves, stems, berries and other aerial parts of *W. somnifera* exhibited significant anti-inflammatory, antistress, antiaging, anti-analgesic, aphrodisiac, anticancer, antivenom, antifungal, anti-viral, hyperthyroidism, hypothyroidism activities and various effects on central nervous system. The notable pharmacological activities are also described as follows:

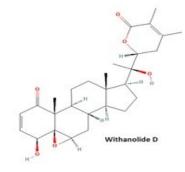
Anti-inflammatory Activities

The indigenous medicine system has used Indian ginseng and winter cherry for over 3,000 years. For a variety of chronic conditions, such as osteoarthritis, antiinflammatory drugs are highly beneficial. *W. somnifera*, containing primary components called withanolides renowned for their remarkable therapeutic properties, is utilized. The primary components of withanolides, which have extraordinary therapeutic qualities, are *W. somnifera*. In order to distinguish its anti-inflammatory action from that of hydrocortisone, ethanolic root decoction is used. Asthma, arthritis and other inflammatory conditions can all be treated with the help of the anti-inflammatory herb *W. somnifera* (33,34).

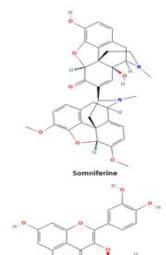
Plant Part		Uses	References
	Adaptogen	Manages stress and fosters equilibrium.	(17)
	Stress and Anxiety Relief	Mitigates stress, anxiety and nervous tension.	(18)
Roots	Energy and Vitality	Increases energy levels, vitality and endurance.	(19)
	Sexual Health Support	Enhances reproductive health and fertility.	(20)
	Muscle Strength and Recovery	Bolsters muscle strength and improves recovery.	(21)
Leaves	Topical Applications	Treats wounds and skin concerns.	(22)
Demine	Tonifying Properties	Elevates overall health; used for rejuvenation.	(23)
Berries	Rasayana	Utilized for rejuvenation and longevity in Ayurveda.	(24)
	External Preparations	Used for poultices, ointments and external applications.	(25)
Aerial Parts	Pain Alleviation	Relieves joint pain and arthritis.	(26)
	Sleep Enhancement	Improves sleep quality and addresses insomnia.	(24)
	Skin Health Promotion	Aids in maintaining a healthy complexion.	(27)
able 3. Phytochemic	cal compounds of W. somnifera		
Compound	Description		Reference
Withanolides	Natural steroid lactones, pivotal for Ashwagandha's healing properties, including adaptogenic and anti-inflammatory effects. Withaferin A and withanolide D are notable examples.		(28)
Alkaloids	Various alkaloids like somniferine, sominine and anaferine, contributing to the plant's pharmacological activities.		(26)
Sitoindoside	Unique steroid glycoside, consisting of a steroid aglycone attached to glucose molecules. Common examples include Sitoindosides VII and VIII.		(25)
Flavonoids	Several flavonoids like quercetin, kaempferol and rutin, known for their antioxidant properties and overall healing effects.		(29)
Tannins	Polyphenolic compounds giving Ashwagandha its acrid taste, possessing antioxidant and anti-inflammatory properties.		(30)
Phytosterols	Various phytosterols like stigmasterol, β-sitosterol and campesterol, structurally akin to cholesterol with health benefits.		(31)
Oil	Essential oils lending Ashwagandha its characteristic aroma, potentially contributing to its healing properties.		(32)
Amino Acids/ Sugars	Various amino acids and sugars enhancing Ashwagandha's nutritional value and overall chemical composition.		(30)

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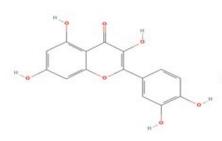


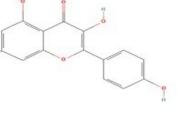






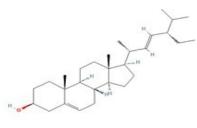
Rutin

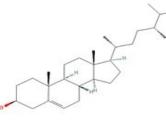




Quercetin

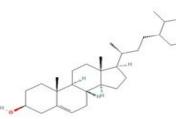
Kaempferol





Stigmasterol

Campesterol



Beta-Sitosterol

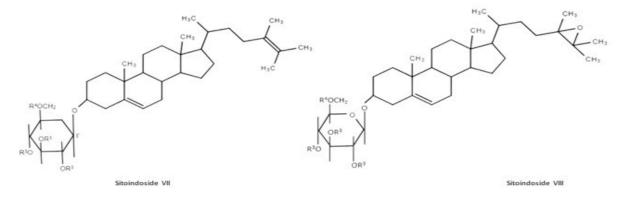


Fig. 3. Molecular structure of various phytochemicals extracted from different parts of W. somnifera (PubChem)

Anti-stress Activities

A study conducted by the Institute of Medical Science at Calcutta University explored the effects of W. somnifera on chronic stress in rats. Over a period of 21 days, the rats were subjected to mild electric shocks on their feet, resulting in various adverse effects including hyperglycemia, increased glucose sensitivity, heightened male sexual dysfunction, stomach ulcers, elevated plasma corticosterone levels, cognitive impairments, mental distress and immunosuppression due to the induced stress (35). However, administration of W. somnifera one hour prior to the foot shocks significantly alleviated anxiety in the animals, as observed in studies involving this botanical. This investigation suggests that *W. somnifera* possesses potent adaptogenic and anti-stress properties (36).

Adaptogens increase generalized stress resistance and decrease sensitivity to stressors, which results in increased resistance to stress and an extension of the resistance phase (stimulatory effect). The ayurvedic herb, *W. somnifera* has long been utilized to combat and relieve stress as well as to enhance general health. This is the first study to examine the usage of *W. somnifera* for stress resistance (37).

Anti-aging Activities

During a double-blind clinical trial, researchers evaluated the anti-aging effects of ashwagandha. Over the course of a year, 101 healthy men aged 50 to 59 received a daily dose of 3 grams of the herb. The study observed significant enhancements in participants' haemoglobin levels, red blood cell count, hair pigmentation and sitting stature. Furthermore, nail calcium levels were maintained and serum cholesterol decreased. Notably, 70% of the participants reported improvements in their sexual performance (38).

Anti-analgesic Activities

W. somnifera, known for its effectiveness in alleviating arthritis symptoms, also serves as both a pain reliever and a relaxant for the nervous system. Cyproheptadine, but not paracetamol, greatly increased the analgesic effectiveness of *W. somnifera*, demonstrating that serotonin, not prostaglandins, is responsible for the analgesic impact of this plant (39).

Aphrodisiac Activities

The herb *W. somnifera* works well as an aphrodisiac. Men who consume *W. somnifera* have higher levels of nitric oxide (NO) in their bodies. The blood arteries that feed blood to the genitals enlarge as a result, increasing sexual desire and pleasure. The quantity of testosterone generated by men's bodies dramatically declines with age. It has been proven that the plant *W. somnifera* significantly increases testosterone levels (40). With its reputed ability to enhance sperm count, endurance and overall quality, *W. somnifera* is believed to be beneficial in boosting male libido.

Anti-cancer Activities

In various experimental settings, both in laboratory conditions and within living organisms, the active compounds of *W. somnifera* have demonstrated properties

that combat cancer, enhance sensitivity to radiation therapy, and prevent the onset of cancer. Moreover, *W. somnifera* contributes to alleviating the adverse effects of chemotherapy and aids in patients' recovery. Among the prevalent forms of cancer, skin cancer ranks high. When tested on Swiss albino mice induced with skin cancer using 7,12-dimethylbenz[α]anthracene(DMBA), the hydroalcoholic root extract of *W. somnifera* exhibited a significant decrease in both the occurrence and average number of skin lesions (41).

Anti-venom Activities

Disrupting the structural stability of the extracellular matrix within affected tissues, venom hyaluronidases facilitate the rapid diffusion of toxins. *W. somnifera* contains a glycoprotein known to impede hyaluronidase activity. This glycoprotein effectively counters the hyaluronidase properties of cobra (*Naja naja*) and viper (*Daboia russelii*) venoms. In rural India, extracts from *W. somnifera* are employed as a treatment for individuals bitten by snakes (42).

Anti-fungal Activities

In a study, crude extracts derived from *W. somnifera* demonstrated both antibacterial and antifungal properties against 20 bacterial and 17 fungal strains. These extracts were particularly effective against *Corynebacterium*, *Bacillus*, *Streptococcus* and *Staphylococcus* species. Additionally, in a mouse model of aspergillosis caused by *Aspergillus fumigatus*, they exhibited protective effects against infection. The potential mechanism behind Ashwagandha's preventive action against systemic *Aspergillus* infection might involve its ability to enhance macrophage activity, thereby facilitating phagocytosis (41.43).

Anti-viral activities

Phytochemicals derived from *W. somnifera* demonstrate efficacy against a range of viruses including chikungunya, herpes simplex virus (HSV), human papillomavirus (HPV), parainfluenza-3, hemagglutinin type 1, neuraminidase type 1, hepatitis C virus, as well as SARS-CoV and SARS-CoV-2. Due to their potent antiviral properties, *W. somnifera* bioactive compounds (such withaferin A and withanolides) are useful in the treatment of COVID-19 patients (44,45).

Hyper and Hypo thyroidism

conducted on Research animals suggests that ashwagandha could influence thyroid function. In a study lasting 20 days, mice received a water-based extract derived from dried W. root. The results indicated notable rises in serum T4 levels, indicating that the plant activates glands at cellular level. By affecting cellular antioxidant а mechanisms, W. somnifera may potentially enhance thyroid function indirectly. These observations imply that ashwagandha could serve as a promising herbal treatment for thyroid disorders (46-48).

Conclusion

In many countries throughout the world, W. somnifera, an ayurvedic herb, is used to treat a variety of neurological and inflammatory diseases. The herb W. somnifera can offer comprehensive defence for the brain and nervous system. Various plant components have been employed in thorough the therapy. More scientific clinical investigations are required, nonetheless, to substantiate its medicinal use. There is currently a lack of knowledge on the mechanism of action of W. somnifera, despite its extensive pharmacological research for its effects against stress, cancer, fungus, inflammation and other conditions. The identification of the chemical substances that make up the mechanisms of action and are accountable for the therapeutic activity should be the focus of future study.

Acknowledgements

The authors are humbly grateful to H. H. Swami Ramdev Ji for guidance, extreme support and Blessings. The authors also thank Patanjali Research Foundation Trust, Haridwar, Uttarakhand, (India), for its robust support and assistance.

Authors' contributions

AB and VA were involved in planning and supervising the work, K, SKC and PG drafted the manuscript and tables with input from all authors, and SKC designed the figures.

Compliance with ethical standards

Conflict of interest: The authors declare that there is no conflict of interest.

Ethical issues: None.

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