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Review Article

Ashwagandha As a Neutraceutical: A Review

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ABSTRACT

Withania somnifera, commonly known as Ashwagandha, is a well-established medicinal herb in ayurvedic medicine, has emerged as a promising neutraceutical due to its wide range of therapeutic effect. The Ashwagandha is known for its adaptogenic, anti-inflammatory, antioxidant, and neuroprotective properties, ashwagandha has been studied for its role in managing stress, enhancing cognitive function, enhancing cognitive function, supporting immune health and improving metabolic balance. The review highlights the current scientific understanding of Ashwagandha, focusing on its key phytochemical constituents specially withanolides and their biological activities. It also explores the underlying mechanism of action, available clinical evidence and safety considerations. Overall, Ashwagandha presents significant potential as a natural supplement in health maintenance and disease prevention, warranting further rigorous clinical research.

INTRODUCTION

Nutraceuticals

Nutraceuticals are food-derived products that provide health and medical benefits, including the prevention and treatment of disease. The term was coined by Dr. Stephen De Felice in 1989, merged as "nutrition" and "pharmaceutical". These products aim to enhance health, delay the aging process, prevent chronic diseases, and increase life expectancy. They are part of a growing field of nutrition that focuses on keeping people healthy, not just treating diseases. People often use other terms like "food supplements," "dietary supplements," or "functional foods." While these are similar, they can have small differences Nutraceuticals are foods or food parts that give extra health benefits. Functional foods are everyday foods that are changed a bit to make them healthier. Dietary supplements are vitamins, minerals, or other nutrients given in the pills,

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powders, or drinks. Nutraceutical is a marketing term used to imply a pharmaceutical effect from a compound or food product that has not been scientifically confirmed or approved to have clinical benefits. In the United States, nutraceuticals are considered and regulated as a subset of foods (such as dietary supplements) by the Food and Drug Administration (FDA). There are no internationally defined properties of nutraceuticals due to the vague, undiscriminating evidence for the biological effects of nutraceutical products.

Types of Nutraceuticals:

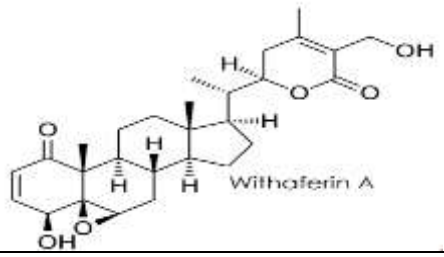
- **Functional Foods**: Foods modified to provide health benefits.
- **Dietary Supplements**: Concentrated nutrients which as been vitamins and minerals in pill, powder, or liquid form.
- **Nutraceuticals**: Bioactive food-derived products with therapeutic benefits.

Ashwagandha (Withania somnifera)

Figure – 1: Ashwagandha Plant and roots

Botanical Description [7]

Table No. 1: Botanical Description of Ashwagandha

Family	**Solanaceae**
Synonym	Withania somnifera
Common Name	Ashwagandha, Withania, Indian Ginseng
Biological Source	Ashwagandha is derived from the root of the Withania somnifera
Molecular Formula	$C_{28}H_{38}O_6$
Molecular weight	470.6 g/mol
Structure	
Habitat	India, the Middle East, and Africa
Chromosome number	Tetraploid (2n=48)
Reproduction	Self-pollinating with bisexual flowers

Traditional and Ayurvedic Significance

Ashwagandha (Withania somnifera), also known as Indian ginseng or winter cherry, is one of the most revered herbs in Ayurvedic medicine. Traditionally classified as a "Rasayana," it is used to promote overall health, longevity, and vitality. The term Ashwagandha translates to "smell of a horse," referring both to its unique odour and its reputation for bestowing the strength and Vigor of a horse. In Ayurvedic texts, it is used to manage stress, enhance stamina, support mental health, and rejuvenate the body. It has also been used in formulations for conditions such as arthritis, insomnia, respiratory disorders, and male infertility.

Traditional Significance. [23]

- **Stress and anxiety:** A 2022 systematic review and meta-analysis encompassing 12 randomized controlled trials with 1,002 participants found that ashwagandha supplementation significantly reduced anxiety and stress levels compared to placebo groups. Another meta-analysis in 2024, which included nine randomized controlled trials with 558 participants, reported significant improvements in stress and anxiety measures, including reductions in Perceived Stress Scale (PSS) scores, Hamilton Anxiety Scale (HAS) scores, and serum cortisol levels.

- **Male infertility:** Comprehensive review highlighted that Ashwagandha supplementation significantly increased sperm concentration, semen volume, sperm motility, testosterone, and luteinizing hormone levels, indicating its beneficial influence on male fertility. Enhanced Sperm Count and Motility: In a triple-blind randomized controlled trial, the group taking Ashwagandha showed a 12.5% mean increase in sperm count, a 21% improvement in progressive motility, and a 21% improvement in sperm morphology, suggesting its potential as a treatment for male infertility

- **Sleep disorders:** Ashwagandha (Withania somnifera) has been studied for its potential benefits in enhancing male fertility and supporting testosterone levels.

- **Arthritis and respiratory issues:** A systematic review and meta-analysis assessed the effects of Ashwagandha supplementation on physical performance. The findings indicated that Ashwagandha supplementation had been more efficacious than placebo in improving physical performance metrics, suggesting its potential as an ergogenic aid.

Historical and Ayurvedic significance [5]

Ashwagandha: An Ancient Herb with Modern Health Benefits. Ashwagandha has been used in traditional Indian medicine for almost 3,000 years. People have used its root as a natural remedy for many things, like boosting energy, helping with sleep, acting as a mild pain reliever, and improving overall health. While it originally comes from India, it is now also grown in other places like the Mediterranean, the Himalayas, Africa, the Canary Islands, South Africa, and Australia. Lately, scientists have become more interested in Ashwagandha because it may help with stress, brain function, and physical performance. Some studies suggest it can protect the brain, help with anxiety and OCD (obsessive-compulsive disorder), and fight inflammation and infections. Ashwagandha may also help with fertility, cancer, and diabetes. Other possible benefits include protecting the heart, helping with sleep problems, improving how the body handles stress, reducing anxiety, helping people with low thyroid, and building muscle strength and recovery. Even

though these benefits are exciting, more research is needed to understand exactly how Ashwagandha works and how effective it really is. This article looks at the current research, especially focusing on how Ashwagandha may help with stress, brain health, and physical fitness.

PURPOSE AND SCOPE

Purpose

To explore the pharmacological, therapeutic, and clinical significance of Ashwagandha as a nutraceutical, with emphasis on its phytochemical, adaptogenic, and neuroprotective effects. The primary purpose of this review is to provide a comprehensive understanding of Withania somnifera (Ashwagandha), a prominent herb in traditional Ayurvedic medicine. The review aims to evaluate its pharmacological properties, therapeutic benefits, mechanisms of action, and potential clinical applications based on scientific evidence. [6]

Scope

- Historical use
- Phytochemical composition
- Pharmacological properties
- Clinical and preclinical studies
- Safety and regulatory aspects
- Market trends and research gaps

PHYTOCHEMICAL COMPOSITION [8]

Table No. 2: Phytoconstituents of Withania somnifera

Compound Class	Examples	Source in Plant	Therapeutic Role
Withanolides	Withaferin A, Withanolide A/D	Roots, Leaves, Berries	Adaptogenic, anti-inflammatory, anticancer
Alkaloids	Anaferine, Isopelletierine	Roots and leaves	Neuroprotective, analgesic
Saponins	Glycosides	Whole plant	Immune-modulating, antioxidant

Therapeutic Effect:

Adaptogenic Effect [9]

- **Enhances stress resilience:** Withaferin stimulate the activity of antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase, which are responsible for neutralizing reactive oxygen species (ROS) produced during oxidative stress. This helps reduce oxidative damage to cells, DNA, and tissues, thereby maintaining cellular health and function during stress.
- **Modulates neurotransmitters (GABA, serotonin, dopamine):** Adaptogens help balance neurotransmitter levels, which can be disrupted during prolonged stress, affecting mood, cognition, and behaviour. Adaptogens like Withania somnifera (Ashwagandha) can influence serotonin and dopamine levels, supporting mood regulation and cognitive function. They also enhance the activity of GABA (gamma-aminobutyric acid), an inhibitory neurotransmitter that reduces neuronal excitability,
- **Reduces CRF (corticotropin-releasing factor), lowering anxiety:** Adaptogens reduce levels of corticotropin-releasing factor (CRF), a key molecule involved in anxiety and stress. This helps lower feelings of anxiety and promotes emotional stability during stressful situations.

Antioxidant Properties [10]

- **Activates enzymes like SOD, catalase:** Converts superoxide radicals to hydrogen peroxide. Converts hydrogen peroxide into water and oxygen. Detoxifies peroxides using glutathione. These enzymes protect cells from internal oxidative stress and maintain redox homeostasis.

- **Scavenges free radicals:** Free radicals (ROS/RNS) such as superoxide anion (O_2^-), hydroxyl radical (•OH), hydrogen peroxide (H_2O_2), and nitric oxide (NO•) are produced during cellular metabolism or from external sources (pollution, UV, drugs). Bioactive compounds act as electron or hydrogen donors, neutralizing these radicals and converting them into stable, non-toxic molecules.

- **Prevents lipid peroxidation:** Lipid peroxidation refers to the adaptive degradation of lipids in cell membranes, leading to loss of membrane fluidity and integrity. Antioxidants prevent the chain reaction of lipid peroxidation by scavenging lipid radicals (L•) and peroxyl radicals (LOO•). Reducing malondialdehyde (MDA).

- **Chelates metal ions (Fe^{2+}, Cu^{2+}):** Transition metals (like Fe^{2+} and Cu^{2+}) catalyse the generation of free radicals via Fenton reactions: Reducing malondialdehyde (MDA), a toxic end-product of lipid peroxidation. This action protects cell membranes, particularly in brain and liver tissues which are rich in polyunsaturated fatty acids (PUFAs)

Neuroprotective and Immunomodulatory Effects [25]:

Another significant mechanism is Ashwagandha's ability to promote neurogenesis, or the formation of new nerve cells. This contributes to enhanced cognitive function, including improved memory, learning, and mental clarity. It supports brain plasticity, which is essential for adapting to stress and recovering from neurological insults. In terms of immune health, Ashwagandha also exhibits potent immunomodulatory effects. It helps regulate immune responses by suppressing excessive inflammation, which is often associated with chronic disease and immune dysfunction. By balancing immune activity, Ashwagandha supports both resistance to infections and the prevention of autoimmune overactivation, making it a valuable herb for maintaining immune homeostasis.

Anti-inflammatory and Anticancer Potential [26,27]

An invitro study by Krishna Raju and et al states that a sustained-release formulation of Ashwagandha inhibited the expression of pro-inflammatory cytokines IL-1ß and TNF-a, as well as superoxide production. Reduction of Inflammatory Markers. According to the author, *Withania somnifera*, which has been studied extensively in cancer research, has demonstrated effectiveness as an antitumor agent due to its pleiotropic mechanism of action—simultaneously targeting multiple oncogenic pathways. Additionally, it has been shown to enhance the overall quality of life in cancer patients. The active compounds in ashwagandha target key oncogenic mediators such as NF-κB, MMP-2, MMP-9, the PI3K/Akt pathway, and the JAK/STAT pathway—factors that play a crucial role in inducing epithelial-mesenchymal transition (EMT), thereby facilitating cancer cell invasion and metastasis.

Ashwagandha As a Neutraceutical [11, 12, 19]

Ashwagandha, a traditional Ayurvedic herb, is known for its adaptogenic properties, helping the body manage stress. It has been studied for various

health benefits, including reducing anxiety, improving sleep, and enhancing cognitive function as a plant-based product with physiological effects.

Justification

i. **Botanical Origin:** Ashwagandha is a plant-derived ingredient with a long history of traditional use in Ayurveda. It is recognized for its adaptogenic properties, aiding in stress management and promoting overall well-being. According to the Food Safety and Standards Authority of India (FSSAI), nutraceuticals include products containing plant or botanical ingredients with a safe usage history.

ii. **FSSAI Compliance:** The FSSAI defines nutraceuticals as products derived from food sources that provide additional health benefits beyond basic nutrition. These products are formulated to supplement the diet with specific nutrients or naturally occurring bioactive compounds that have health benefits. Ashwagandha tablets, containing bioactive compounds like withanolides, align with this definition

iii. **Dosage Forms:** FSSAI regulations permit nutraceuticals to be manufactured in various dosage forms, including tablets, capsules, powders, and liquids. Ashwagandha tablets fall within these approved formats.

iv. **Labelling:** Nutraceutical products must comply with specific labelling provisions, such as Displaying the word "Nutraceutical" prominently. Declaring the amount of each nutraceutical ingredient present. Including advisory warnings like "NOT FOR MEDICINAL USE" and precautions regarding excessive

v. **Permissible Ingredient:** FSSAI's regulations specify certain schedules listing approved ingredients for nutraceuticals. Ashwagandha is included in these schedules, affirming its acceptance as a nutraceutical ingredient. Ashwagandha (Withania somnifera) stands out among herbal nutraceuticals for its adaptogenic properties, but it shares similarities and differences with other well-known herbs like ginseng and turmeric.

COMPARATIVE OVERVIEW [12]

Herbal medicines like Ashwagandha, Ginseng, and Turmeric have been integral to traditional healing systems such as Ayurveda and Traditional Chinese Medicine for centuries. These herbs are now gaining global attention for their diverse health benefits and are frequently used in modern wellness practices. While each possesses distinct active compounds and therapeutic actions, they share common roles in enhancing the body's response to stress, supporting immune function, improving cognitive performance, and reducing inflammation. The table below offers a comparative overview of their key characteristics, mechanisms, and health-promoting effects.

Table No. 3: Comparative overview with ginseng and turmeric

Property	Ashwagandha	Ginseng	Turmeric
Botonical name	*Withania somnifera*	*Panax ginseng* (Asian) / *Panax quinquefolius* (American)	Curcuma longa
Key Compounds	Withanolides	Ginsenosides	Curcumin
Mechanism	Adaptogen**:** regulates stress hormones (e.g., cortisol)	Adaptogen**:** boosts energy, modulates immune system	Anti-inflammatory, antioxidant, modulates enzymes
Primary Benefits	Reduces cortisol, supports calm, supports immune balance, Cognitive, may support thyroid & testosterone, Pain Relief Indirect via stress/inflammation	Mildly calming, but more energizing, Immune-modulating, Enhances brain function and clarity	Indirectly supportive stress and anxiety via inflammation control, Anti-inflammatory effects aid immunity, may protect neurons from oxidative damage
Side Effects	Drowsiness, GI upset, Headache	Insomnia, Nervousness, GI upset, Increased heart rate	GI discomfort, kidney stone risk
Safety Profile	Generally safe, some caution for hyperthyroidism	Generally safe, may cause insomnia or agitation in high doses	Safe, but high doses may cause GI upset or liver stress
Typical Dose	300–600 mg (standardized extract)	200–400 mg (standardized ginsenosides)	500–2000 mg curcumin (with black pepper for absorption)

CLINICAL EFFICACY AND SAFETY

Clinical Efficacy

- **Ashwagandha in Anxiety:** It is defined as ‘an emotion characterized by feelings of tension, worried thoughts and physical changes. High intake of a tasty and high-calories food is responsible for chronic positive energy balance when the ingestion of energy exceeds energy expenditure, cause to extra fat in body, weight gain, and obesity (*Dinh et al., 2015*). The ingestion of high-calorie food has also been associated with various neuropsychiatric disorders like the anxiety, mood disorders and binge eating (*Castanon et al., 2014*).

- **Ashwagandha in Alzheimer’s:** -Alzheimer’s disease is defined as neurodegenerative disease mainly characterized by the progressive memory loss or irreversible decline in cognitive functions. Various in vitro and in vivo studies highlighted the effect of Ashwagandha and its phytoconstituents in Alzheimer’s disorder. Recently, the research was performed to measure the anti-Alzheimer’s constituent present in the extract root of Ashwagandha and concluded that Withanone shows significant activity specifically by inhibition of amyloid β-42. Withanone also found to intensify the activity of acetyl choline, glutathione and secretase enzyme (β and γ) and improved the elevation in pro inflammatory cytokines levels *(Pandey et al., 2018).* Withanolide-A inhibited human acetyl cholinesterase by high binding affinity, predicted by docking simulation studies *(Grover et al., 2012).*

- **Ashwagandha in Parkinson’s:** - Parkinson’s disease is a progressive, age-dependent neurodegenerative disorder primarily

characterized by depletion of dopaminergic substantia nigra neurons caused by genetic and environmental factors. It is associated with oxidative stress, mitochondrial dysfunction and abnormality in aggregation of protein. Ashwagandha have been explored in various studies to 9 ameliorate Parkinson's disorder. *(Manjunath and Muralidhara, 2015).*

- **Ashwagandha in Depression:** - Depression is a heterogeneous disorder associated with brain health mainly mood swings and thoughts, misbehaviour, disappointments, sadness, hopelessness and loss of physical activities and self-worth. In case, depression is composed with disturbance in appetite, sleep pattern and other daily work with the help of symptoms of an anxiety *(Ahmed et al., 2017).* Experimental studies have reported the ameliorative effect of Ashwagandha in depression. In 2000, Bhattacharya et al., isolated the bioactive compound glycowithanolides from Ashwagandha roots and investigated its potential as antidepressant at the dose of 20 and 50mg/kg. Glycowithanolides has been found to exhibit comparable antidepressant effect to imipramine in behavioural despair and learned helplessness induced by forced swim tests Thereby, supporting with the uses of Ashwagandha as mood stabilizer *(Bhattacharya et al., 2000).*

Safety

The submitted scientific data supports to the Ashwagandha is a real potent regenerative tonic due to the its multiple pharmacological actions like anti-stress and neuroprotective. Which are useful for different types of neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases. The mechanism is responsible for Ashwagandha as neuroprotective to the larger degree is due to its antioxidant activity. Antioxidant activity is considerably due to a decrease or normalisation in reversed lipid peroxidation levels *(Bhattacharya et al., 2000)* and increase or normalisation of elevated superoxide dismutase levels (mainly in cerebellum, striatum, hippocampus, frontal cortex, etc) which has been must be followed by activity of enzymes catalase *(Prakash et al., 2013*) and glutathione peroxidise *(Gupta et al., 2003)* in striatum, cortex, hippocampus and other parts of brain. Ashwagandha also regulates non-enzymatic antioxidant levels by restoring the levels of glutathione which is an endogenous member of antioxidant defence system (Maher, 2005). Glutathione acts by reacting with oxygen free radicals, organic peroxides and also regulate enzymes (glutathione peroxidise and glutathione-S-transferase) by acting as substrate *(Raja Sankar et al., 2009).* Dopaminergic activity of a drug can enhance memory, and number of papers are published showing dopaminergic activity of Ashwagandha root (march, 2004; Prakash et al., 2014). A number of in vivo and clinical studies have proved the neurotropic activity of Ashwagandha and its extract *(Dhule, 2001; Chinappa et al., 2013; Pingali et al., 2014).* Neuroprotective effects of Ashwagandha supports its efficacy in Alzheimer's patients *(Kuboyama et al., 2014; Ven Murthy et al., 2010).* Ashwagandha and its extract have anti-stress and anxiolytic effect and these effects are involved in memory enhancing activity and used when normal mental activities of human are affected (*Eysenck et al., 2007*). Beside the Ashwagandha root, its leaf extract indicated probable effect on antioxidant induction in the Parkinson's disease mouse brain *(Raja Sankar et al., 2009).* The dopamine plays an important character in motor control.

Regulatory and Global Market Outlook

Market Size [18]

The expansion of the ashwagandha market is fostered by the increased emphasis on development of innovative products and growing consumer demand for naturally derived supplements. Furthermore, supportive government initiatives are creating opportunities for market growth.

- 2024**:** USD 766.24 million
- 2025**:** USD 837.50 million
- 2034**:** USD 1,864.51 million (CAGR**:** 9.3%)

Market Overview [19]

Ashwagandha also known as withania somnifera, poison gooseberry, winter cherry or Indian ginseng is an evergreen shrub which is extensively grown in the tropical and subtropical areas of Asia, Africa, and Europe. The roots of ashwagandha have been widely used in the traditional Ayurvedic and Unani medicine systems in India. The adaptogenic properties of the herb, applications for curing diseases such as diabetes and certain brain disorders such as Huntington's disease and increased use of ashwagandha extracts for managing anxiety and stress.

Ashwagandha Market Key Takeaways [20]

i. Asia Pacific led the global ashwagandha market with the highest share in 2024.North America is estimated to expand the fastest CAGR in the market over the forecast period Europe is seen to grow at a notable rate in the foreseeable future by formulation, powder segment held the largest market share in 2024.

ii. By formulation, capsules/tablets segment is anticipated to grow at a remarkable CAGR between 2025 and 2034.

iii. By application, the energy and stamina enhancement segment accounted for the largest market share in 2024.

iv. By application, the anxiety relief segment has grown at a notable rate in the market in 2024.

v. By distribution channel, retail pharmacies segment captured the largest market share in 2024.

vi. By distribution channel, online retail segment is expected to expand at a notable CAGR over the projected period Integration of Artificial Intelligence in Ayurveda.

Ashwagandha Market Growth Factors [21]

Launch of innovative products**:** With the increasing demand for ashwagandha products, manufacturers are focusing developing innovative product lines to cater to the specific needs of consumers and strengthen their market presence. Development of innovative delivery formats such as chewable, gummies and lozenges as well as combination of ashwagandha with additional ingredients like magnesium, Rhodiola and turmeric is fostering the market growth.

Global Regulations [22]

- **India (FSSAI):** According to the Food Safety and Standards Authority of India (FSSAI), a nutraceutical is a food product that provides a physiological benefit and helps maintain good health. In 2006, parliament passed the Food Safety and Security Act. Then, in 2008, FSSAI came into existence. For the implementation of the FSSAI Act process of pre-publication that handled food-related issues in various Departments. The FSSAI is responsible for setting standards for food so that there is one body to deal with and no confusion in the minds of consumers, traders, manufacturers, and investors.

- **Denmark (DVFA):** The DVFA's official website states**:** "Do not eat Ashwagandha or

supplements containing Ashwagandha because its root has negative effects on sex hormones and reproduction for both men and women. In addition, the plant can affect the metabolism, the immune system, and the central nervous system." Having researched and used Ashwagandha for over three decades, find that the statement is far from truth.

- **Australia (TGA):** Medicines and herbal supplements containing the herb Withania somnifera may cause serious side effects (known as 'adverse events') in some people. Withania somnifera is a widely used medicinal herb and can be bought in supermarkets, health food shops and pharmacies without a prescription. You should immediately stop taking it and seek medical advice if you experience any of the following symptoms**:**

- Yellowing of the skin or eyes
- Nausea and vomiting
- Unusual tiredness
- Weakness
- Stomach or abdominal pain
- Loss of appetite.
- If you currently have or have had liver problems, you should avoid medicines and herbal supplements containing Withania somnifera.

LIMITATIONS AND FUTURE DIRECTIONS

Challenges [23]

- **Lack of global harmonization in regulation:** - This term refers to the absence or insufficiency of studies that observe the safety, efficacy, or effects of a treatment, drug, or medical device over an extended period, typically years. While short-term trials may show promising results, long-term data is crucial for understanding sustained outcomes, rare side effects, or complications that may only emerge with time.

- **High quality control costs:** Developing and implementing quality control systems (like ISO 9001 or Six Sigma) requires significant investment in training, documentation, and auditing.

- **Limited long-term clinical safety data:** Some quality issues are not easily detectable with standard QC techniques and may only appear in long-term use.

Research Avenues [24, 25]

This term refers to the absence or insufficiency of studies that observe the safety, efficacy, or effects of a treatment, drug, or medical device over an extended period—typically years. While short-term trials may show promising results, long-term data is crucial for understanding sustained outcomes, rare side effects, or complications that may only emerge with time.

- Antibody-drug conjugates (ADCs)
- Dual-inhibitor therapies
- Nanoparticle-based delivery
- Herbal-drug combination therapies.

CONCLUSION

Medicinal plants with a wide range of therapeutic and nutraceutical properties are used mainly in developing countries to manage different disorders. Ashwagandha known for its adaptogenic properties and historical use in traditional medicine. It is recommended to strengthen physical as well as mental health and in stress disorders and to maintain a healthy long life. In Ayurvedic texts, it is used to manage stress, enhance stamina, support mental health, and rejuvenate the body. It has also been used in formulations for conditions such as arthritis, insomnia, respiratory disorders, and male infertility.

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