Withania somnifera (Ashwagandha) a plant of many possibilities

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SUMMARY:
Introduction: Ashwagandha (Withania somnifera) has been long used in the traditional Ayurvedic system of medicine to enhance various kinds of disease processes and specially as a nervine tonic. Nowadays, its beneficial activities are still being searched.
Objective: This article summarizes the currently available knowledge of Ashwagandha extensive use in medicine.
Abbreviated description of the state of knowledge: Withania somnifera, an admired herb which is also known as Ashwagandha of the family solanaceae. For about thousands of years it has been a part of a traditional system of the Indian Ayurvedic Medicine. Many studies have been conducted on Ashwagandha, proving its anti-cancer, immunomodulating, analgesic, adaptogenic, —such as anxiolytic, antidepressant, and increasing physical and mental strengths.
**Conclusions:** Ashwagandha therapy is a promising method for more effective anti-cancer therapy not only as a drug that helps to fight cancer directly, but also to reduce the negative effects of chemotherapy, such as decreased immunity and physical and mental exhaustion. In addition, Ashwagandha can be helpful for overworked people by adding mental and physical strength. Research results show that this plant can also be used in diseases of old age to reduce cognitive defects.

**Key words:** Withania somnifera; Vitanoside IV; Glycowithanolides withaferin-A; Sitoindosides IX and X; Isopelletierine; Solanaceae

**ARTICLE**

1. **Introduction**

The global society suffers from different kinds of environmental diseases such as mental and physical fatigue, sleep disorders, depression and anxiety states. Evidence based on knowledge sheds a light on the unhealthy lifestyle, ranging from unbalanced diet, to a variety of stress factors that can contribute to development of mentioned dysfunctions and various types of cancer as well. [1] Ashwagandha (Withania somnifera, fam. Solanaceae) may be an underestimated solution for previously mentioned problems. This plant grows naturally in East Africa and India. It is called "Indian ginseng" due to the area of its occurrence and similar stimulant properties to ginseng. Researches on Ashwagandha have shown the presence of 35 chemical compounds, including alkaloids (Isopelletierine, Anaferine), steroidal lactones (withanolides, vitaferins), saponins with an additional acyl group (VII and VIII sitoindosides) and with 27-carbon glucose (Sitoindosides IX and X). [2] Literature has attributed different types of biological and pharmacological actions of Ashwagandha, such as: anxiolytic, antioxidant, antitumor, adaptogenic, analgesic and neuroprotective properties. That contributes its possible usefulness in treatment variety of diseases including dyskinesia, infertility, memory disorders and Alzheimer disease. [2,3,4]

**Objective:**

Various studies have been conducted on Ashwagandha over the years. In this work, we presented the most important of them and their promising results, showing some of its usefulness properties. The purpose of this manuscript is elaborating currently available data on PubMed and Scopus.

2. **The state of knowledge**

2.1. **Adaptogenic properties**

Ashwagandha is known primarily for its adaptogenic properties. Tests on adult mice showed, that they achieve better results in swimming while they Ashagandha were supplemented.[3] At the beginning of the experiment, the animals withstood an average of 385 minutes while swimming, and after administering Ashwagandha, they withstood 740 minutes. A significant increase in swimming time indicates an increase in energy. Blood cortisol levels after swimming were tested as well. It turned out that the animals that got Ashwagandha had 5 times lower concentration of cortisol, the stress hormone, in relation to the mice that did not get the plant extract. This experiment proves the anxiolytic effect of Withania Somnifera. [4] In addition, Ashwagandha has been shown to reduce the levels of tribulin, a stress marker in the rat brain that was elevated by the administration of pentylenetetrazole. [3,4]
2.2 Neuroprotective effects
The Bhattacharya research group proved that Ashwagandha stops the atrophy of neurons and synapses responsible for cognitive defects in the course of neurodegenerative diseases such as Alzheimer, Parkinson and Huntington. It was proved that responsible for this activity is Glycowithanolides withaferin-A and sitoindosidides VII-X isolated from the Withania Somnifera root. These compounds decreased cognitive defects in Alzheimer disease, through significant reversing of ibotenic acid level. [4,5]

Kuboyama and colleagues in 2006 administered amyloid peptide Aβ(25–35) in mice, inducing the axonal, dendritic and synaptic losses and memory deficits. At the same time, mice which were given Vitanoside IV isolated from Ashwagandha, revealed attenuation of the Aβ - amyloid effect. This knowledge may be used in the treatment of dementia. [4,6]

It was proved that the root extract of the Withania somnifera may support a GABA - mimetic activity. After 7 days supplementation the growth of nerves was observed. [4] It can be used to reduce the side effects of neuroleptics such as dyskinesia. [4]

Scientists led by Abdel-Magied in 2001 addressed Ashwagandha's anti-depressive activity. They conducted research on, for example, "learned helplessness" or "behavioral despair" caused by forced swimming. Promising research results were obtained. [7]

2.3 Anticancer properties
There have been many studies investigating the effect of Ashwagandha on anti-cancer activity. The tests conducted by Singh et al. in 1979, 1981, 1986 and 2010 showed that Withania somnifera prevents lung adenoma and leukocytopenia caused by urethane which is a chemical stressor. [8-15]

Further research was undertaken by Abbas in 2005 and colleagues, who showed that Ashwagandha contributes to a decrease in the tendency to uterine bleeding and to the reduction of muscle wasting in the course of uterine fibroids. [16]

Dixit and colleagues demonstrated the immunomodulatory effects of Withania. [17]

These results give a great hope for including Ashwagandha in anti-cancer therapy. Immunomodulatory properties can be very readily used in oncological patients as the decline in immunity after chemotherapy is another important problem in cancer treatment.

2.4 Analgesic properties
Pain is an unpleasant sensory and emotional experience localised to a part of the body and associated with actual or potential tissue damage. Pain can be debilitating. It has a huge role in quality of life, sleep comfort and socio-economic factors, as well as, ability to adequately perform at work.

Randomised, double-blind study, conducted by Murthy et al. in which 12 healthy male participants aged 18-40 years divided into two groups (1000 mg Withania somnifera or placebo) were supplemented in a single oral dose, shows a significantly increased pain tolerance force and time compared. Pain threshold force and time were also increased [18].

Symillarly, a study carried out by Mazen and colleagues confirmed Ashwagandha’s anti-pain activity. A hot plate test was performed on mice and was conducted to know the mechanism of herb’s activity. The scientists observed that a 1000 mg/kg dose of Ashwagandha resulted in a significant analgesic activity. This effect was potentiated by a 10 mg/kg dose of cyproheptadine what suggests the involvement of serotonin in the analgesic activity of Ashwagandha [19].
3. Recapitulation

Withania somnifera (Ashwagandha) is a highly respectable herb in Ayurvedic medicine, which might be the solution to many health problems of people in the 21st century. Its properties could be helpful in mental and physical fatigue, sleep disorders, depression and anxiety states treatment. Ashwagandha’s adaptogenic, neuroprotective, anticancer and anti-stress activity were carried out in detail in many scientific studies. Its beneficial effects have been demonstrated in many researches. However, future studies, with large sample size are required to substantiate the current findings.

4. References

[1] Doughty KN, Del Pilar NX, Audette A, Katz DL. Curr Cardiol Rep. 2017 Oct 4;19(11):116.
[2] P. C. Shah*, N. A. Trivedi, J. D. Bhatt And K. G. Hemavathi, Effect of Withania Somnifera on forced swimming test induced immobility in mice and its interaction with various drugs; Indian J Physiol Pharmacol 2006; 50 (4) : 409–415
[3] Salve J, Pate S, Debnath K, Langade D. Adaptogenic and Anxiolytic Effects of Ashwagandha Root Extract in Healthy Adults: A Double-blind, Randomized, Placebo-controlled Clinical Study. Cureus. 2019;11(12):e6466.
[4] Narendra Singh, Mohit Bhalla, Prashanti de Jager, Marilena Gilca, An Overview on Ashwagandha: A Rasayana (Rejuvenator) of Ayurveda, Afr J Tradit Complement Altern Med. 2011; 8(5 Suppl): 208–213.
[5] Bhattacharya SK, Goel RK, Kaur R, Ghosal S. Anti - stress activity of Sitoidosides VII and VIII. New Acylsterylglucosides from Withania somnifera. Phytother Res. 1987;1:32–37.
[6] Kuboyam A T, Tohda C, Komatsu K. Withanoside IV and its active metabolite, sominone, attenuate A beta(25–35)-induced neurodegeneration. Eur J Neurosci. 2006;23(6):1417–1426.
[7] Abdel-Magied EM, Abdel-Rahman HA, Harraz FM. The effect of aqueous extracts of Cynomorium coccineum and Withania somnifera on testicular development in immature Wistar rats. J Ethnopharmacol. 2001;75:1–4.
[8] Singh N, Agarwal AK, Lata A, Kohli RP. Evaluation of ‘adaptogenic’ properties of Withania somnifera. Proc Indian Pharmacological Society. 1976;17
[9] Singh N, Agarwal AK, Lata A, Kohli RP. XIIth Scientific Seminar on Indian Medicine. Vol. 4. Varanasi: Institute of Medical Sciences; 1977. Experimental evaluation of ‘adaptogenic’ properties of Withania somnifera.
[10]. Singh N. A new concept on the possible therapy of stress disease with ‘Adaptogens’ (Anti-stress drugs) of indigenous plant origin. Curr Med Prac. 1981;25:50–55.
[11] Singh N, Singh SP, Sinha JN, Shanker K, Kohli RP. Withania somnifera (Ashwagandha) A rejuvenator herbal drug which enhances survival during stress (An adaptogen) Int J Crude Drug Res. 1982;3:29–35.
[12]. Singh N, Singh SP, Nath C, Kohli RP, Bhargava KP. 5 th Sepal Congress of Rheumatology. Bangkok: 1984. Anti-stress plants as anti-rheumatic agents; p. 37.
[13] Singh N. A pharmaco-clinical evaluation of some Ayurvedic crude plant drugs as anti-stress agents and their usefulness in some stress diseases of man. Ann Nat Acad Ind Med. 1986;2(1):14–26.
[14] Singh N, Singh SP, Dixit KS, Saxena RC, Kohli RP. A Placebo Controlled Clinical Trial of Cypruss rotundus, Withania somnifera and their Combination in cases of Rheumatoid Arthritis. Proc International Seminar. 1986a;2:18–21.
[15] Singh N, Gilca M. Herbal Medicine - Science embraces tradition - a new insight into the ancient Ayurveda. Germany: Lambert Academic Publishing; 2010. pp. 51–67.
[16] Abbas SS, Bhalla M, Singh N. Proc workshop on essential medicines, adverse drug reactions and therapeutic drug monitoring. Lucknow: Scientific Convention Centre; 2005. A clinical study of Organic Ashwagandha in some cases of uterine tumors (fibroids) and dermatofibrosarcoma; pp. 143–144.

[17] Dixit KS, Agarwal AK, Seth PK, Singh N. World Congress on Biotech Dev Med Subs Plants &amp; Marine Origin. Lucknow (India): King George Medical College; 1995. Effect of Withania somnifera, Panex ginseng and Cannabis indica and radio ligand binding with neurohumoral in the CNS; p. 141.

[18] MURTHY MNK, GUNDAGANI S, NUTALAPATI C, PINGALI U. Evaluation of Analgesic Activity of Standardised Aqueous Extract of Withania somnifera in Healthy Human Volunteers using Mechanical Pain Model. Journal of Clinical & Diagnostic Research. 2019;13(1):1-4.

[19] Sakka Mazen E, Pavelescu M, Grigorescu E. Contributions to the pharmacodynamic study of roots of Withania somnifera Dun species of Pakistani origin. Note III: Testing of analgesic activity of dichlormethanic and methanolic extract from Withania somnifera roots. Rev Med Chir Soc Med Nat Iasi. 1990;94(3-4):603-605.