THERAPEUTIC USES OF WITHANIA SOMNIFERA (ASHWAGANDHA) WITH A NOTE ON WITHANOLIDES AND ITS PHARMACOLOGICAL ACTIONS

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ABSTRACT

Withania somnifera is a medicinal plant extends over a large area, from the Atlantic ocean to South East Asia and from the Mediterranean region to South Africa. The medicinal plants are widely used by the traditional medical practitioners for curing various diseases in their day to day practice. In traditional systems of medicine, different parts (leaves, stem, flower, root, seeds, bark and even whole plant) of Withania somnifera (known as Ashwagandha in Hindi), a small herb seen throughout India, have been recommended for the treatment of aphrodisiac, liver tonic, anti-inflammatory agent, astringent, and more recently to treat bronchitis, asthma, ulcers, emaciation, insomnia, and senile dementia etc. Clinical trials and animal research support the therapeutic use of ashwaganda for anxiety, cognitive and neurological disorders, inflammation, and Parkinson’s disease. Ashwaganda’s chemopreventive properties make it a potentially useful adjunct for the patients undergoing radiation and chemotherapy. Ashwaganda is also used therapeutically as an adaptogen for patients with nervous exhaustion, insomnia, and debility due to stress, and as an immune stimulant in patients with low white blood cell counts in blood. The major biochemical constituents of ashwaganda root are steroidal alkaloids and steroidal lactones in a class of constituents called withanolides.

Keywords: Withania somnifera, Withanolides, Medicinal plants, Ashwaganda

INTRODUCTION

Plants are one of the most important sources of medicines in world. Today the large numbers of drugs in use are derived from plants, like morphine from Papaver somniferum, Eugenol from Ocmum sanctum, Ephedrine from Ephedra vulgaris, Atropine from Atropa belladonna, Reserpine from Roulphia serpentina etc. The medicinal plants are rich in secondary metabolites and essential oils of therapeutic importance.

The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability [1,2]. Because of these advantages the medicinal plants have been widely used by the traditional medical practitioners in their day to day practice. According to a survey (1993) of World Health Organization (WHO), the practitioners of traditional system of medicine treat about 80% of patients in India, 85% in Burma and 90% in Bangladesh [2,3].

In traditional systems of medicine the Indian medicinal plants have been used in successful management of various disease conditions like bronchial asthma, chronic fever, cold, cough, malaria, dysentery, convulsions, diabetes, diarrhea, arthritis, emetic syndrome, skin diseases, insect bite etc. and in treatment of gastric, hepatic, cardiovascular & immunological disorders [2-4].

The medicinal use of plants is very old. The writings indicate that therapeutic use of plants is as old as 4000–5000 B.C. and Chinese used first the natural herbal preparations as medicines. In India, however, earliest references of use of plants as medicine appear in Rigveda which is said to be written between 3500–1600 B.C. Later the properties and therapeutic uses of medicinal plants were studied in detail and recorded empirically by the ancient physicians in Ayurveda (an indigenous system of medicine) which is a basic foundation of ancient medical science in India [9].

Withania somnifera

A plant from genus Withania

Among the plants known for medicinal value, the plants of genus Withania belonging to family Solanaceae are very important for their therapeutic potentials. Withania coagulens, Withania simonii, Withania adunensis, Withania riebeckii are examples of known...
important species of genus Withania which grow in different parts of the world and are known to have medicinal properties [4-12]. Withania somnifera Dunal and Withania somnifera Kaul are the two sub-species of the plant.

Therapeutic uses of Withania somnifera

Withania somnifera is one of the major herbal components of geriatric tonics mentioned in Indian systems of medicine. In the traditional system of medicine Ayurveda, this plant is claimed to have potent aphrodisiac rejuvenative and life prolonging properties. It has general animating and regenerative qualities and is used among others for the treatment of nervous exhaustion, memory related conditions, insomnia, tiredness, potency issues, skin problems and coughing. It improves learning ability and memory capacity.

The traditional use of ‘Ashwagandha’ was to increase energy, youthful vigour, endurance, strength, health, nurture the time elements of the body, increase vital fluids, muscle fat, blood, lymph, semen and cell production. It helps counteract chronic fatigue, weakness, dehydration, bone weakness, loose teeth, thirst, impotency, premature aging emaciation, debility, convalescence and muscle tension. It helps invigorate the body by rejuvenating the reproductive organs, just as a tree is invigorated by feeding the roots [10-14].

Immunomodulation and Hematopoiesis

A series of animal studies show ashwagandha to have profound effects on the hematopoietic system, acting as an immunoregulator and a chemoprotective agent [15, 16]. In a mouse study, administration of a powdered root extract from ashwagandha was found to enhance total white blood cell count. In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocytic activity of macrophages when compared to a control group [17].

Recent research suggests a possible mechanism behind the increased cytotoxic effect of macrophages exposed to W. somnifera extracts [18]. Nitric oxide has been determined to have a significant effect on macrophage cytotoxicity against microorganisms and tumor cells. Iwone et al demonstrated Withania somnifera increased. No production in mouse macrophages in a concentration-dependent manner. This effect was attributed to increased production of inducible nitric oxide synthase, an enzyme generated in response to inflammatory mediators and known to inhibit the growth of many pathogens [19].

Ashwagandha exhibited stimulatory effects, both in vitro and in vivo, on the generation of cytotoxic T lymphocytes, and demonstrated the potential to reduce tumor growth [20]. The chemopreventive effect was demonstrated in a study of ashwagandha root extract on induced skin cancer in Swiss albino mice given ashwagandha before and during exposure to the skin cancer-causing agent 7,12-dimethylbenz[a]anthracene. A significant decrease in incidence and average number of skin lesions was demonstrated compared to the control group. Additionally, levels of reduced glutathione, superoxide dismutase, catalase, and glutathione peroxidase in the exposed tissue returned to near normal values following administration of the extract. The chemopreventive effect is thought to be due in part to the antioxidant/free radical scavenging activity of the extract [21].

An in vitro study showed withanolides from Withania somnifera inhibited growth in human breast, colon and liver tissue cells compared to doxorubicin. Witherifer A more effectively inhibited growth of breast and colon cancer cell lines than did doxorubicin. These results suggest Withania somnifera extracts may prevent or inhibit tumor growth in cancer patients, and suggest a potential for development of new chemotherapeutic agents [22].

Anti-Aging

In a double-blind clinical trial, ashwagandha was tested in a group of 101 healthy males, 50-59 years old, at a dosage of 3 grams daily for one year. A significant improvement in hemoglobin, red blood cell count, hair melanin, and seated stature was observed. Serum cholesterol decreased and calcium was increased. Erythrocyte sedimentation rate decreased significantly and 71.4% reported improvement in sexual performance [23].

Chronic Stress

Chronic stress (CS) can result in a number of adverse physiologic conditions including cognitive deficit, immunosuppression, sexual dysfunction, gastric ulceration, irregularities in glucose homeostasis, and changes in plasma corticosterone levels. In a rat model of chronic stress Withania somnifera and Panax ginseng extracts were compared for their ability to attenuate some effects of chronic stress. Both botanicals were able to decrease the number and severity of CS-induced ulcers, reverse CS-induced inhibition of male sexual behavior, and inhibit the adverse effects of CS on retention of learned tasks. Both botanicals also reversed CS-induced immunosuppression, but only the Withania extract increased peritoneal macrophage activity in the rats. The activity of the Withania extract was approximately equal to the activity of the Panax ginseng extract. Withania somnifera, however, has an advantage over Panax ginseng in that it does not appear to result in ginseng-abuse syndrome, a condition characterized by high blood pressure, water retention, muscle tension, and insomnia [24].

Cardiovascular Protection

Hypoglycemic, diuretic, and hypcholesterolemic effects of ashwagandha root were assessed in human subjects, in which six type 2 diabetes mellitus subjects and six mildly hypercholesterolemic subjects were treated with a powder extract for 30 days. A decrease in blood glucose comparable to that of an oral hypoglycemic drug was observed. Significant increases in urine sodium, urine volume, and decreases in serum cholesterol, triglycerides, and low-density lipoproteins were also seen [25].

Hypothyroidism

Animal studies reveal ashwagandha has a thyrotropic effect [26, 27]. An aqueous extract of dried Withania root was given to mice via gastric intubation at a dose of 1.4 g/kg body weight daily for 20 days. Serum was collected at the end of the 20-day period and analyzed for T3 and T4 concentrations and lipid peroxidation was measured in liver homogenate via antioxidant enzyme activity. Significant increases in serum T4 were observed, indicating the plant has a stimulatory effect at the glandular level. No changes in T3 levels were observed. Withania may also stimulate thyroid activity indirectly, via its effect on cellular antioxidant systems. Withania extract significantly decreased lipid peroxidation in the liver homogenate via antioxidant enzyme activity. Significant increases in serum T4 were observed, indicating the plant has a stimulatory effect at the glandular level. These results indicate ashwagandha may be a useful botanical in treating hypothyroidism [28].

Anxiety and Depression

In an animal study assessing the anxiolytic and antidepressive actions of ashwagandha compared to commonly prescribed pharmaceuticals, an extract of the root was administered orally to rats once daily for five days. The results were compared to a group administered the benzodiazepine lorazepam for anxiolytic activity, and the tricyclic antidepressant imipramine for antidepressive investigation.

Both the ashwagandha group and the lorazepam group demonstrated reduced brain levels of a marker of clinical anxiety. Ashwagandha also exhibited an antidepressant effect comparable to that induced by imipramine in the forced swim-induced "behavioral despair" and "learned helplessness" tests. Other similar studies confirm these results, lending support to the use of ashwagandha as an antistress adaptogen [29, 30].

Studies show ashwagandha to be effective in the treatment of osteoarthritis [30], inflammation [31, 32], stroke [33], and tardive dyskinesia [34]. Studies also reveal ashwagandha to be a potential...
antimicrobial agent, with antifungal activity [35, 36] and moderate antibacterial activity against Staphylococcus aureus and Pseudomonas aeruginosa [37].

Pharmacological actions of withanolides

The roots of Withania somnifera consist primarily of compounds known as withanolides, which are believed to account for its extraordinary medicinal properties. Withanolides are steroidal and known as withanolides, which are believed to account for its achieving these effects.

The withanolides serve as important hormone precursors that can convert into human physiologic hormones as needed. Ashwagandha is thought to be amphoteric; i.e., it can help regulate important physiologic processes.

The theory is that when there is an excess of a certain hormone, the plant-based hormone precursor occupies cell membrane receptor sites so the actual hormone cannot attach and exert its effect. If the hormone level is low, the plant-based hormone exerts a small effect. Ashwagandha is also considered to be an adaptogen, facilitating the ability to withstand stressors, and has antioxidant properties as well. Other studies have shown ashwaganda to have an immunostimulatory effect.

CONCLUSION

As modern medicine continues to expand, so do the uses of botanical medicines. Withania somnifera shows great potential as a safe and effective in Immunomodulation and Hematopoiesis. More research is needed to determine if Withania somnifera can duplicate this activity in humans, and to determine an optimal dosage range for achieving these effects.

The potential beneficial effects of Withania in anxiety, cognitive and neurological disorders, inflammation, and Parkinson’s disease. Experienced natural medicine practitioners, working hand-in-hand with oncologists, could increase effectiveness and decrease side effects of conventional treatments with the use of Withania somnifera.

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