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Therapeutic Use of Withania somnifera (Ashwagandha): A Review

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Abstract: ***Objectives*: *The objective of this paper is to review the literature regarding Withania somnifera (ashwagandha, WS) a commonly used herb in Ayurvedic medicine. Specifically, the literature was reviewed for articles pertaining to chemical properties, therapeutic benefits, and toxicity. Design: This review is in a narrative format and consists of all publications relevant to ashwagandha that were identified by the authors through a systematic search of major computerized medical databases; no statistical pooling of results or evaluation of the quality of the studies was performed due to the widely different methods employed by each study. Results: Studies indicate ashwagandha possesses anti - inflammatory, antitumor, antistress, antioxidant, immunomodulatory, hemopoetic, and rejuvenating properties. It also appears to exert a positive influence on the endocrine, cardiopulmonary, and central nervous systems. The mechanisms of action for these properties are not fully understood. Toxicity studies reveal that ashwagandha appears to be a safe compound. Conclusion: Preliminary studies have found various constituents of ashwagandha exhibit a variety of therapeutic effects with little or no associated toxicity. These results are very encouraging and indicate this herb should be studied more extensively to confirm these results and reveal other potential therapeutic effects. Clinical trials using ashwagandha for a variety of conditions should also be conducted.***

Keywords: ashwagandha, Ayurvedic medicine, therapeutic benefits, herbal safety, Withania somnifera

1. Introduction

Withania somnifera Dunal (ashwagandha, WS) is widely used in Ayurvedic medicine, the traditional medical system of India. It is an ingredient in many formulations prescribed for a variety of musculoskeletal conditions (e. g., arthritis, rheumatism), and as a general tonic to increase energy, improve overall health and longevity, and prevent disease in athletes, the eld erly, and during pregnancy.1, 2 Many pharmacological studies have been conducted to investi gate the properties of ashwagandha in an attempt to authenticate its use as a multi - purpose medicinal agent. For example, anti - inflammatory properties have been investigated to validate.

Anti - inflammatory Properties;

The effectiveness of ashwagandha in a variety of rheumatologic conditions may be due in part to its anti inflammatory properties, which have been studied by several authors. In a study by Anbalagan et al, 3 powdered root of WS (1 g/kg suspended in 2% gum acacia, 50 mg/mL) was given orally one hour before the induction of inflammation by injection of Freund's complete adjuvant in rats and continued daily for three days; phenylbutazone (100mg/kg) was given as a positive control. WS was found to cause considerable reduction in inflammation. Acute phase reactants of the blood monitored by crossed immuno electrophoresis showed changes in the concentration of many serum proteins (α2 - glycoprotein, major acute phase α1 protein, and pre - albumin) in the WS group. The α2 - glycoprotein found only in inflamed rat serum was decreased to undetectable levels in the WS group. Phenylbutazone, on the other hand, caused a considerable increase in the α2 glycoprotein in both arthritic and healthy rats. Another acute phase protein (peak 2, α - 1 major acute phase) which increased approximately 200 percent by inflammation was brought back to normal levels by WS treatment but only to 132 percent of normal by phenylbutazone. WS influenced several modulator proteins in normal rats, suggesting that several plant chemicals in WS possibly interact with the liver protein synthesis process.

Antitumor Properties

To investigate its use in treating various forms of cancer, the antitumor and radiosensitizing effects of WS have been studied. In one study, WS was evaluated for its anti - tumor effect in urethane - induced lung adenomas in adult male albino mice.11 Simultaneous administration of WS (ethanol extract of whole plant, 200 mg/kg daily orally for seven months) and urethane (125 mg/kg without food biweekly for seven months) reduced tumor incidence significantly (tumor incidence: untreated control, 0/25; urethane treated, 19/19; WS treated, 0/26, and WS plus urethane treated.

Antistress Effect

To evaluate the antistress effect of WS, an alcohol extract from defatted seeds of WS dissolved in normal saline was given (100 mg/ kg intraperitoneally as a single dose) to 20 - 25 g mice in a swimming performance test in water at 28º - 30ºC.10 Controls were given saline. The extracts approximately doubled the swimming time when compared to controls. In another study, WS prevented both a weight increase of the adrenals and a reduction in ascorbic acid content of the adrenals normally caused by this swimming test. The authors suggested that WS induced a state of nonspe cific increased resistance during stress. Glycosides of WS (sitoindosides VII and VIII, 50 to 100 mg/kg) exhibited significant antistress activity in forced swimming induced immobility in mice, restraint stress induced gastric ulcers in rats, restraint - induced Alternative Medicine. No Reprint Without Written Permission Withania somnifera (Ashwagandha) auto - analgesia in rats, restraint stress effect on thermic response of morphine in rats, and morphine - induced toxicity in aggregated mice.24 The alcohol extract of WS (100 mg/ kg, twice daily orally on day 1, 4 or 7) reduced stress - induced increases in blood urea nitro gen levels, blood lactic acid, and adrenal hy pertrophy, but did not affect changes in thymus weight and hyperglycemia in rats. reversed the cold swimming - induced increases in plasma corticosterone, phagocytic index, and avidity index to control levels. WS root powder (100 mg/kg orally as an aqueous sus

pension daily for seven days) given before the swimming test in water at 10ºC also increased total swimming time, indicating better stress tolerance in rats.8 These results indicated a significant increase in plasma corticosterone level, phagocytic index, and avidity index in control rats, whereas these levels were near normal in WS rats subjected to the same test. In a comparative study for antistress activity, finely powdered roots of WS and Panax ginseng (PG), suspended in 2 - percent acacia (100 mg/kg in 1.00 mL orally) were given to 18 - 20 g mice daily for seven days; the swimming test was given on day 8.25 Sig nificant antistress activity, as measured by the swimming endurance test, was found for both compounds.

Immunomodulatory Properties

The use of WS as a general tonic to increase energy and prevent disease may be partially related to its effect on the immune system. Glycowithanolides and a mixture of sitoindosides IX and X isolated from WS were evaluated for their immuno modulatory and central nervous system effects (antistress, memory, and learning) in Swiss mice (15 - 25 g, 5 - 6 months old) and Wistar strain albino rats (120 - 150 g and 250 - 300 g).31 Both materials produced statistically significant mobilization and activation of peritoneal macrophages, phagocytosis, and increased activity of the lysosomal enzymes. Both com pounds (50 - 200 mg/kg orally) also produced significant antistress activity in albino mice and rats, and augmented learning acquisition and memory retention in both young and old rats. Root extract of WS was tested for immunomodulatory effects in three myelosuppression models in mice: cyclophosphamide, azathioprin, or prednisolone.32 Significant increases.

Hemopoetic Effect

Administration of WS extract was found to significantly reduce leukopenia in duced by cyclophosphamide (CTX) treatment in Swiss albino mice.34 Total white blood cell count on the 12th day of the CTX - treated group was 3720/mm3; that of the CTX - plus - WS group was 6120/mm3. In the CTX - plus - WS mice, the cellularity of the bone marrow was significantly increased (13.1 x 106 /femur).

Rejuvenating Effect

The growth - promoting effect of WS was studied for 60 days in a double - blind study of 60 healthy children, age 8 - 12 years, who were divided into five groups of 12.35 Group 1 was given purified and powdered WS 2 g/day fortified in 100 cc of milk (no details about purification and powdering methods were disclosed). Similarly, Group 2 received 2 g daily of a mixture of equal parts WS and punarnava (Boerhaavia diffusa), Groups 3 and 4 were given ferrous fumarate 5 mg/day and 30 mg/day, respectively, and Group 5 received placebo. Group 1 experienced a slight increase in hemoglobin, packed cell volume, mean cor puscular volume, serum iron, body weight, and hand grip, and significant increases in mean corpuscular hemoglobin and total proteins.

Nervous System Effects

Total alkaloid extract (ashwagandholine, AG) of WS roots has been studied for its effects on the central nervous system.37 AG exhibited a taming effect and a mild depressant (tranquilizer) effect on the central nervous system in monkeys, cats, dogs, albino rats, and mice. AG had no analgesic activity in rats but increased Metrazol toxicity in rats and mice, amphetamine toxicity in mice, and produced hypothermia in mice. It also potentiated barbiturate-, ethanol -, and ure thane - induced hypnosis in mice. Effects of sitoindosides VII - X and withaferin isolated from aqueous methanol extract of roots of cultivated varieties of WS were studied on brain cholinergic, glutamatergic and GABAergic receptors in male Wistar rats.38 The compounds slightly enhanced acetylcholinesterase (AChE) activ ity in the lateral septum and globus pallidus, and decreased AChE activity in the vertical diagonal band. These changes were accompanied by enhanced M1 - muscarinic - cholinergic receptor - binding in lateral and medial septum as well as in frontal cortices, whereas the M2 muscarinic receptor - binding sites were increased in a number of cortical regions including cingulate, frontal, piriform, parietal, and retrospinal cortex. The data suggest the com pounds preferentially affect events in the cor tical and basal forebrain cholinergic - signal transduction cascade. The drug - induced increase in cortical muscarinic acetylcholine receptor capacity might partly explain the cognition - enhancing and memory - improving effects of WS extracts in animals and in humans.

2. Discussion

As outlined above, results from various studies indicate ashwagandha possesses many qualities, including anti - inflammatory, antitumor, and immunomodulatory properties, as well as exerting an influence on the endocrine, nervous, and cardiopulmonary systems. Further clinical studies should be conducted, as well as studies in multiple animal - based models using a variety of suitable biochemical markers (e. g., urinary excretion of pyridinoline and deoxypyridinoline) to understand its mechanism of action. Any protective or prophylactic effect it may have on the development of arthritis should also be investigated, as well as effects it may have on cartilage degradation or regeneration. As for its use in fighting cancer, confirmatory studies in several other animal tumor systems must be conducted for more definitive findings. Studies should also be carried out to determine the effects, if any, of WS on existing antitumor agents when given in combination with WS. Regarding the effects observed in animals on the endocrine and cardiopulmonary systems, the therapeutic significance of these biochemical markers is not clear. Studies point to a possible benefit of WS in central nervous system - related ailments. The lack of systematic toxicity studies is of some concern, as is the poor quality of the existing toxicity studies. The review indicates that WS may be useful in many ailments, including arthritis and other musculoskeletal disorders, stress - in duced nervous exhaustion, and hypertension. There are a few preliminary studies available on the effects of WS on the immune system, central nervous system, hemopoetic system, and general growth promotion to form a basis for further studies but not enough evidence to provide a firm scientific basis for definitive therapeutic uses.

3. Conclusion

Although the results from this review are quite promising for the use of ashwagandha as a multi - purpose medicinal agent, several limitations currently exist in the current literature.

While ashwagandha has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use. It is also important to recognize that WS may be effective not only in isolation, but may actually have a potentiating effect when given in combination with other herbs or drugs.

References

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