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POTENTIAL CLINICAL USAGE OF ASHWAGANDHA ROOT EXTRACT: A REVIEW

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ABSTRACT

INTRODUCTION AND OBJECTIVE

Ashwagandha, an herb commonly used in traditional Indian medicine, has been gathering attention as a potential drug in various specialties such as psychiatry, neurology, or endocrinology and even as a possible cancer treatment. In this review we aim to summarize reports form recent years on potential clinical usage of Ashwagandha.

REVIEW METHODS

The literature review was conducted using PubMed and Google Scholar online databases.

THE STATE OF KNOWLEDGE

Several studies evaluating potential pharmacological uses of Ashwagandha root extract has been published. There are clinical trials conducted in India using the plant in treatment of insomnia that resulted in improved sleep quality. Ashwagandha root extract has been successfully administered in stress-related disorders. There are reports of improvement in cognitive functions in patients with mild cognitive impairment and better symptom control in obsessive-compulsive disorder after Ashwagandha supplementation. Ashwagandha has been studied in endocrine diseases, showing potential in alleviating climacteric symptoms during perimenopause and in subclinical hypothyroidism. The study aimed to assess effect of Ashwagandha on vitality and hormonal changes in elderly men showed mixed results, with improvement in some hormonal levels and not statistically significant improvement in quality of life compared to placebo group. It has also been noted that Ashwagandha root extract has positive effect on cardiovascular system, as well as enhancing muscle strength and recovery in otherwise healthy adults.

SUMMARY

Ashwagandha root extract seems to possess beneficial properties that allow for its use in several branches of medicine. However as current findings are reported from small sample studies, further research on a larger scale is needed.

KEYWORDS: Ashwagandha; Withania somnifera; Review; Clinical trial; herbal;

INTRODUCTION AND OBJECTIVE

In recent years the Ashwagandha root extract has been gathering attention as a potential treatment for several disorders. Mainly it has been administered for psychiatric conditions such as insomnia[1] or anxiety[2] and neurodegenerative[3] such as Parkinson's and Alzheimer's diseases, however in the last couple of years several studies have been conducted exploring its possible benefits in treatment of some endocrine dysfunctions, cardiovascular conditions or even cancer[4]. In this review of literature, we aim to summarize current knowledge about potential therapeutical uses of Ashwagandha root extract.

Withania somnifera, more commonly known as Ashwagandha, is an herb used in Indian Ayurvedic medicine[5]. Its composition of several bioactive compounds provides various pharmacological effects: anti-stress, narcotic, tonic and anti-inflammatory to name a few.[6] In India it has been widely used to improve cognitive function, relieve stress and anxiety, improve sleeping. Due to anti-inflammatory properties, it is also used topically as a treatment for carbuncules, ulcers and swelling[7]. The wide range of pharmacological effects led to several clinical trials examining possible role of Ashwagandha root extract in treatment. The aim of this systematic review is to present recent findings in potential usage of Ashwagandha root extract as a medical treatment.

REVIEW METHODS

The literature review was conducted using PubMed and Google Scholar online databases. The main search words included 'Ashwaganda', 'clinical use', 'clinical trial', 'root' 'root extract'. A total of 70 articles has been read in preparation for this review, with 10 being chosen. The articles published before 2015, comparative studies of different substances such as matcha and trials using other parts of Withania somnifera such as leaves were excluded.

THE STATE OF KNOWLEDGE

Sleep

In 2019 a study[8] to assess efficacy and safety of Ashwagandha root extract in treatment of insomnia and anxiety was published. It was a randomized, double-blind, placebo-controlled study conducted at Prakruti Hospital in Kalwa, Maharashtra, India between November 2014 and March 2015. Sixty patients were randomly divided

into two groups, with test group receiving a capsule containing 300mg of Ashwagandha root extract twice a day for 10 weeks. Both groups were evaluated at the 5 and 10 weeks of the study. The primary outcome of the study was sleep onset latency (SOL) assessed using Philips Respironics actigraphy and it showed a statistically significant decrease in SOL in the test group compared to the placebo. The secondary outcomes included total sleep time (TST), sleep efficiency (SE) and wake after sleep onset (WASO), total time in bed (sleep log), mental alertness on rising, sleep quality, Pittsburgh Sleep Quality Index (PSQI), and Hamilton Anxiety Rating Scale (HAM- A). A significant increase was recorded in TST, TIB, and SE as well as a decrease in WASO. The overall results of the study showed significant improvement in sleep quality in the test group receiving Ashwagandha root extract capsule compared to the placebo. The authors thus concluded that the Ashwagandha root extract has potential use in treatment for insomnia, however larger scale studies are needed.

Another randomized, double-blind, placebo-controlled trial[9] was conducted at International Institute of Sleep Sciences, NEST Hospital in Thane, Maharashtra, India with aim to assess the effects of ashwagandha (*Withania somnifera*) extract on sleep quality in healthy adults. In this study 150 participants were randomly divided into two groups. The test group were given 120mg of Ashwaganda root extract once daily for a period of six weeks. The participants were assessed after 6 weeks through the Restorative Sleep Questionnaire-weekly version and World Health Organization Quality of Life-Bref (WHOQOL) scale. Sleep actigraphy was used to measure the onset of sleep latency, sleep efficiency, total sleep time and wake after sleep onset. The study showed significant improvement in sleep efficiency, total sleep time, sleep latency and wake after sleep onset (WASO) in test group compared to placebo after six weeks. The authors drew conclusion that Ashwagandha extract administered for six weeks helped to improve the overall quality of sleep.

The two studies show the potential for use of Ashwagandha root extract in treatment of insomnia and possibly other sleep-related disorders. The difference in dosage system and duration of administered treatment suggests the need for further studies to examine a potential dosage and time period for the most effective treatment.

Stress

In 2019 Lopresti et al. published their findings on anxiolytic properties of Ashwagandha root extract. It was a randomized, double-blind, placebo-controlled study[10] aimed to investigate the stress-relieving and pharmacological activity of an Ashwagandha root extract in stressed, otherwise healthy adults. Sixty participants were randomly divided into two groups. The treatment group was given 240 mg of Ashwagandha extract once daily for 60 days. Outcomes were measured using the Hamilton Anxiety Rating Scale (HAM-A), Depression, Anxiety, and Stress Scale -21 (DASS-21), and by marking the levels of cortisol, dehydroepiandrosterone- sulphate (DHEA-S), and testosterone. The results showed a statistically significant reduction in HAM-A and a significant reduction in morning cortisol and in DHEA-S levels compared to the placebo group. The conclusion was drawn that Ashwagandha has a potential anxiolytic effect, however further studies on larger sample size and using different dosages are needed.

Mild cognitive disfunction

An article published in 2017 Journal of Dietary Supplements[11] reported on a study to assess the impact of Ashwagandha root extract on improving memory and cognitive function in adults with mild cognitive impairment. It was a prospective, randomized, double-blind, placebo-controlled study that was conducted in 50 adults divided into two study groups. The test group was given 300mg of Ashwagandha root extract twice daily for 8 weeks. The outcome was evaluated using Wechsler Memory Scale III which is comprised of subtests for logical memory, verbal paired associates, face recognition and family pictures and it showed a statistically significant improvement in immediate and general memory in the test group compared to the placebo group.
Secondary outcomes were measured using the Eriksen Flanker task, Wisconsin Card sort test, Trail-Making Test part A and the Mackworth Clock test which showed significantly greater improvement in executive function, sustained attention and information-processing speed in the test group. The authors concluded that Ashwagandha root extract has a potential use as a supplementary treatment for mild cognitive dysfunction.

Obsessive-compulsive disorder

In 2015 S.P. Jahanbakhsh et al.[12] conducted a clinical trial to test potential use of Withania somnifera root extract in treatment for obsessive-compulsive disorder. It was a randomized double-blind placebo-controlled trial. 30 patients were randomly divided into two groups. The test group was given daily 120mg of Ashwagandha root extract with a dosing system of 4 capsules, each containing 30mg of Ashwagandha per day for 6 weeks. The OCD symptoms were assessed by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

symptom checklist at the baseline and after 6 weeks. The results showed statistically significant improvement in managing the symptoms in the test group compared to the placebo group. The authors have concluded that Ashwagandha root extract has potential as a possible therapy for obsessive-compulsive disorder.

Subclinical Hypothyroidism

A prospective, randomized, double-blind, single-center placebo-controlled study[13] was performed at Sudbhawana Hospital in Varanasi, India between May 2016 and September 2016. 50 patients with elevated serum thyroid stimulating hormone (TSH) levels were randomly divided into two groups of 25 patients. The test group were given 600mg of Ashwagandha root extract once daily for a period of 8 weeks. The outcome measures included serum levels of TSH, T4, and T3. The assessment of hormonal levels at 8 weeks showed a statistically significant improvement in the test group compared to the placebo group. The authors concluded that Ashwagandha root extract may be beneficial in treatment of hypothyroidism, however more studies on a larger scale are needed.

Climacteric symptoms during perimenopause

A study[14] published in 2021 examined the effect of Ashwagandha root extract on alleviating climacteric symptoms. In this randomized, double-blind, placebo-controlled study, 100 women with climacteric symptoms were randomly divided into two groups. The test group was given 300 mg of an Ashwagandha root extract twice daily for duration of 8 weeks. Outcomes were measured using the menopause rating scale (MRS), menopause- specific Quality of Life (MENQoL), hot flash score, and hormonal changes in estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone. The study found that the Ashwagandha root extract contributed to statistically significant reduction in climacteric symptoms as established by evaluating the questionnaires. Increase in serum estradiol and reduction in serum FSH were also noted. The authors concluded that Ashwagandha may be beneficial in relieving climacteric symptoms in women during perimenopause.

Vitality, hormonal effects in elderly men

In 2019 Lopresti et al. published their report[15] on a trial aimed to assess the hormonal and vitality effects of Ashwagandha in aging, overweight men. It was a randomized, double-blind, placebo-controlled, crossover study. 57 participants were divided randomly into two groups. The test group was given a capsule containing 10,5mg of Ashwagandha root extract twice daily for 8 weeks. The outcome was measured using The Profile of Mood States, Short Form (POMS-SF), Aging Males' Symptoms (AMS) questionnaire and salivary levels of DHEA-S, testosterone, cortisol and estradiol. There was a statistically significant difference in increased DHEA-S and testosterone levels in the test group compared to the placebo group, however no such difference was observed in levels of cortisol and estradiol. The evaluation of the outcomes found improvement in vitality, fatigue, psychological and sexual well-being in both Ashwagandha test group and the placebo group, with no significant differences between the groups. There were no complaints of adverse effects among the test group receiving Ashwagandha root extract indicating its safety to use. The authors of the study suggest that small number of participants, baseline mild symptoms and the recruitment of participants through social media may have played a role in those results and recommend further studies on a larger scale to better assess the potential benefits of Ashwagandha root extract.

Cardiorespiratory endurance

A study[16] published in May 2021 presented its findings on the effect of Ashwagandha root extract in improving cardiorespiratory endurance and recovery in healthy athletic adults. A double-blind, randomized, placebo-controlled trial was performed on a group of 50 participants that were randomly divided into two equal groups. The test group received 300 mg of Ashwagandha root extract twice daily for 8-weeks. Cardiorespiratory endurance was assessed by measuring the maximum aerobic capacity (VO2 max). The outcome showed a statistically significant improvement in VO2 max in the test group compared to the placebo group. The secondary outcomes observed during the study included estimation of stress management through Total Quality Recovery Scores (TQR), Recovery-Stress Questionnaire for Athletes (RESTQ), and Daily Analysis of Life Demands for Athletes (DALDA) questionnaires along with the antioxidant level measurement. The questionnaire analysis showed statistically significant improvement especially for fatigue recovery, lack of energy, and fitness analysis. The antioxidant level was significantly enhanced in the test group. The authors drew a conclusion that Ashwagandha root extract can significantly improve cardiorespiratory endurance.

Muscle strength and recovery

	Title	Medical condition	Year of publishment	Number of participants	Intervention (dose of Ashwagandha root extract in milligrams)	Duration	Outcome measures	Main results
1.	Evaluation of the efficacy of Withania somnifera (Ashwagandha) root extract in patients with obsessive-compulsive disorder: A randomized double- blind placebo-controlled trial	Obsessive-compulsive disorder	2016	30	30mg, 4 times daily	6 weeks	the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)	The Y-BOCS score was reduced by 8 units in the treatment group and 2 units in the placebo group. The observed findings were statistically significant with P <0.001.
2.	Efficacy and Safety of Ashwagandha (Withania somnifera) Root Extract in Insomnia and Anxiety: A Double-blind, Randomized, Placebo-controlled Study	Insomnia and anxiety	2019	60	300mg, twice daily	10 weeks	Sleep onset latency (SOL), total sleep time (TST), sleep efficiency (SE), wake after sleep onset (WASO), total time in bed (TIB), mental alertness on rising, sleep quality, Pittsburgh Sleep Quality Index (PSQI), the Hamilton Anxiety Rating Scale (HAM- A)	A statistically significant decrease in SOL and WASO; increase in TST, TIB, and SE was found in the test group compared to placebo.

A study[17] published in 2015 in Journal of the International Society of Sports Nutrition reported its findings on the effect of Ashwagandha root extract on muscle strength and recovery. It was a randomized, prospective, double-blind, placebo-controlled clinical trial. 57 participants were randomly divided into two groups. The test group was given 300mg of Ashwagandha root extract twice daily for 8 weeks. During course of the study both groups underwent the same resistance training regiment for 8 weeks. The outcome measurements included muscle strength which was assessed by the 1-RM load for the bench press and leg extension exercises; muscle recovery which was evaluated by obtaining serum creatine kinase level as a marker of muscle injury from the effects of exercise; muscle size, body composition and serum testosterone levels. The study found that supplementation of Ashwagandha root extract significantly improved the increase in muscle strength, provided better recovery, enhanced the growth in muscle size, the decrease of body fat percentage and increase in

testosterone level compared to the placebo group. No serious adverse effects were reported in the test group indicating the safety of Ashwagandha root extract. The conclusion was drawn that supplementation of Ashwagandha may enhance muscle strength and recovery.

3.	A randomized, double blind, placebo- controlled study to evaluate the effects of ashwagandha (Withania somnifera) extract on sleep quality in healthy adults.	Sleep quality	2020	150	120mg, once daily	6 weeks	the Restorative Sleep Questionnaire-weekly version, World Health Organization Quality of Life-Bref (WHOQOL) scale sleep onset latency (SOL), sleep efficiency (SE), total sleep time (TST), wake after sleep onset (WASO)	A statistically significant improvement in SE, TST, SOL and WASO in test group compared to placebo after six weeks
4.	An investigation into the stress-relieving and pharmacological actions of an ashwagandha (Withania somnifera) extract	Stress	2019	60	240mg, once daily	60 days	the Hamilton Anxiety Rating Scale (HAM-A), Depression, Anxiety, and Stress Scale -21 (DASS- 21), cortisol, dehydroepiandrosterone- sulphate (DHEA-S), and testosterone levels	A statistically significant reduction in the HAM-A and a near- significant reduction in the DASS-21; greater reductions in morning cortisol and DHEA- S in test group compared to the placebo
5.	Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions.	Mild cognitive impairment	2017	50	300mg, twice daily	8 weeks	Wechsler Memory Scale III; the Eriksen Flanker task, Wisconsin Card sort test, Trail-Making Test part A, the Mackworth Clock test	A statistically significant improvement in immediate and general memory

6.	Efficacy and Safety of Ashwagandha Root Extract in Subclinical Hypothyroid Patients: A Double-Blind, Randomized Placebo-Controlled Trial	Subclinical Hypothyroidism	2016	50	600mg, once daily	8 weeks	TSH, T4, T3 serum levels	A statistically significant improvement in serum TSH ($p < 0.001$), T3 ($p = 0.0031$), and T4 ($p = 0.0096$) levels in the test group compared to placebo
7.	Effect of an ashwagandha (Withania Somnifera) root extract on climacteric symptoms in women during perimenopause: A randomized, double-blind, placebo-controlled study	Climacteric symptoms	2021	100	300mg, twice daily	8 weeks	the menopause rating scale (MRS), menopause-specific QoL (MENQoL), hot flash score, hormonal changes in estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone	A statistically significant reduction in total MRS score ($p < 0.0001$), significant reduction in the psychological ($p = 0.0003$), somato- vegetative ($p = 0.0152$), and urogenital ($p < 0.0001$) areas. A statistically significant reduction in total MENQoL scores ($p < 0.0001$) A statistically significant increase in serum estradiol ($p < 0.0001$) and a significant reduction in serum FSH ($p < 0.0001$) and serum LH ($p < 0.05$) compared with the placebo

8.	A double-blind, randomized, placebo- controlled trial on the effect of Ashwagandha (Withania somnifera dunal.) root extract in improving cardiorespiratory endurance and recovery in healthy athletic adults	Cardiorespiratory endurance and recovery	2021	50	300mg, twice daily	8 weeks	the maximum aerobic capacity (VO2 max)	A statistically significant improvement in VO2 max in the test group compared with the placebo group
9.	A Randomized, Double-Blind, Placebo-Controlled, Crossover Study Examining the Hormonal and Vitality Effects of Ashwagandha (Withania somnifera) in Aging, Overweight Males	Vitality, vigor, sexual well-being in aging overweight males	2019	57	10,5mg twice daily	16 weeks	the Profile of Mood States, Short Form (POMS-SF), Aging Males' Symptoms (AMS) questionnaire, and salivary levels of DHEA- S, testosterone, cortisol, and estradiol	A statistically significant increase in levels of DHEA-S and testosterone, An improvement in cortisol, estradiol, fatigue, vigor, or sexual well-being was observed in both the test and the placebo groups, with
								no statistically significant differences between the two groups.
10.	Examining the effect of Withania somnifera supplementation on muscle strength and recovery: a randomized controlled trial	Muscle mass and strength in healthy young men engaged in resistance training.	2015	57	300mg twice daily	8 weeks	Muscle strength (the 1- RM load for the bench press and leg extension exercises) muscle size, body composition, serum testosterone levels, muscle recovery (serum creatine kinase level as a marker of muscle injury from the effects of exercise)	A significant increase in muscle mass and strength; greater reduction of exercise-induced muscle damage (assessed by the stabilization of serum creatine kinase); a significant increase in testosterone level, a significant decrease in body fat percentage

SUMMARY

In this systematic review 10 studies have been presented in order to summarize current findings on potential usage of Ashwagandha root extract as medical treatment. The studies showed a generally favorable outcomes indicating there are possible health benefits in the drugs derived from the plant however there are several limitations that need to be taken into consideration before implementing Ashwagandha root extract into widespread use. These limitations include small sample sizes, as the trials presented in this review included only between 30 to 150 participants, which offer limited view making it difficult to draw definitive conclusions. To obtain more precise results large scale studies involving bigger sample groups are needed. Varying doses used in presented trials suggest the need for more precise evaluation of dosage regiment in order to find doses of maximum efficacy with minimal risk of adverse effects. Similarly further studies examining different time intervals of Ashwagandha supplementation are essential to establish the optimal duration of treatment.
Withania somnifera root extract has been used in traditional medicine for centuries, but only recently its pharmacological effects are being tested in evidence-based medicine. Some studies have been published that show potential for clinical usage of the plant. While majority of studies focus on psychiatric disorders such as anxiety or insomnia and neurodegenerative conditions, there are some trials researching the usage of ashwagandha root extract in treatment for disorders from other specialties including endocrinology, gynecology and cardiology. The studies on Ashwagandha root extract show promising results for it to be used as a potential therapy for stress-related diseases and insomnia due to its anxiolytic properties. It was found to improve cognition and memory in patients with mild cognitive dysfunction. In endocrinology the study on hypothyroidism established that Ashwagandha root extract has effect on thyroid hormones regulation. In gynecology it was observed to help in relieving climacteric symptoms. In healthy adults Withania somnifera extract improves cardiorespiratory endurance and stimulates muscle strength and recovery. In conclusion recently conducted research allows to consider the possibility of using Ashwagandha root extract as medical treatment however further large-scale studies are needed to more accurately assess the potential place of Ashwagandha root extract in modern medicine.

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