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Benefits of Withania somnifera (Ashwagandha) supplementation in obesity

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Abstract

Introduction and purpose: Ashwagandha (fam. Solanaceae) also known as *Withania somnifera*, is an herb commonly used in traditional Ayurvedic medicine. It is sometimes called Indian ginseng or winter cherry and it is used for its extensive health benefits for millennia as a Rasayana. Ashwagadha supplementation is playing an increasing role not only as an adaptogen, but is beneficial in the context of health in individuals struggling with obesity. This is a growing field of research and the aim of this brief review is to provide an update on the positive effects of Ashwagandha supplementation on the health of those dealing with obesity.

Description of the state of knowledge: Ashwagandha has a wide range of positive effects, most common are sedative, anti-stress, immunomodulatory and anti-cancer effects. The literature also draws attention to other results such as binding insulin sensitivity, increasing endurance, effects on adipogenesis and lipogenesis. Ashwagandha lowers blood cortisol levels, inhibits fat accumulation and the expression of genes involved into excessive fat tissue accumulation.

Summary: Regular intake of Ashwagandha is associated with health benefits in people struggling with obesity. As an adaptogen with adipogenic potential, Ashwagandha has great potential to participate in future adjunctive obesity therapy and the prevention of other similar and obesity-related diseases, but further research is needed in this area.

Keywords: *Withania somnifera*; Solanaceae; withanolide; withaferin A, obesity

Introduction

By implementing Ashwagandha in a group of obese patients, it seems that many health benefits can be achieved. This is caused by the association of obesity with health problems such as reduced physical performance, fat accumulation, increased mood or depression-like conditions and other problems such as promoting diabetes, cardiovascular disease and cancer. The anti-stress and sedative effects of Ashwagandha through its supplementation are well studied. It also seems that by reducing stress, eating behaviour could be improved. The literature also highlight other less common actions that could bring benefit for people struggling with obesity.

Obesity

Obesity is a major, worldwide health problem due to the impact of obesity in promoting diabetes, hypertension, cardiovascular disease and cancer. Numbers of people dealing with obesity continue to rise, making this disease a major public health concern globally. [1] Medically, we can define obesity as a condition of increased body weight, with excessive accumulation of adipose tissue. Genes, environmental factors, lifestyle and diet are among the many factors that influence the development of obesity [2]. Fat tissue growth is caused by the differentiation of preadipocytes in adipose tissue into adipocytes and the production and accumulation of lipid droplets in adipocytes [3, 4]. In today's society, it is increasingly common for people to lead sedentary lifestyles, experience psychological stress and use work-saving devices, which can lead to an imbalance of energy gains and expenditure ending in obesity. It also influences increased consumption of palatable foods and high-calorie diets, resulting in increased out-of-normal BMI values and obesity-like conditions. In addition to the more common cardiovascular and metabolic risk, a high-calorie diet also has a high incidence of neuropsychiatric disorders such as compulsive overeating, depression like behavior and cognitive dysfunction [5, 6, 7]. A successful obesity therapy must

impact energy intake, energy expenditure, or both [8]. Also should be focus on treatment health problems, effects of obesity. There is a growing interest among scientists to discover active substances that prevent adipogenesis and lipogenesis, which could have a role in the prevention of obesity and metabolic disease and can be used as a potential therapeutic method. What has particularly caught the attention of researchers is the finding of natural compounds with anti-adipogenic potential [9]. In experimental studies, researchers have suggested that the withanolides identified in *Withania somnifera* have anti-adipogenic potential and may be considered for the development of strategies to manage obesity. In addition, the mechanisms affecting adipogenesis and lipogenesis were described in the above-described studies, which provided a background for the potential use of Indian winter cherry as a therapeutic agent in obesity and metabolic diseases [10]

Withania somnifera

Withania somnifera (fam. Solanaceae) also known as Ashwagandha, is an herb commonly used in traditional Ayurvedic medicine. It is sometimes called „Indian ginseng” or „Indian winter cherry” and it is used for its extensive health benefits for millennia as a Rasayana. It occurs in dry regions of India, Sri Lanka, South Africa, and the Mediterranean [8, 9]. Many medicinal benefits of Ashwagandha have been reported in the literature, including anti-cancer, anti-inflammatory, antioxidant and hypoglycaemic effects [11]. Ashwagandha contains a large amount of chemically active substances such as withanolides, sitoindosides and many useful alkaloids. Used for centuries to treat a wide range of diseases, it is considered by scientists as a candidate for a multifunctional therapeutic agent [12]. Methanolic extracts from various parts of Ashwagandha are known to show therapeutic potential against different types of cardiovascular disease and are also successful against hyperlipidaemia and obesity [13]. Ashwagandha comes in various forms such as churna, a finely sieved powder that can be mixed with water, ghee (clarified butter) or honey. Strengthens and improves the function of many systems and organs. In the nervous system and brain function, it improves memory, has anxiolytic effects and improves energy levels. In the Reproductive System, it promotes healthy sexual and reproductive balance. It increases the body's resistance to stress and has a positive effect on the immune system, especially cellular immunity. It is also a powerful antioxidant [8]. Withaferin A, one of the more recognised and most frequently described in the literature of the withanolides isolated in *W. somnifera*, have recently been found to exhibit anti-adipogenic effects in 3T3-L1 adipocytes by reducing lipid accumulation and down-regulating the expression of key activators of adipogenesis, peroxisome proliferator-activated receptor gamma

(PPAR γ) and CCAAT/enhancer binding protein alpha (C/EBP α), as well as fatty acid-binding protein in adipocytes [10].

Anti-stress effect of Ashwagandha and impact of stress on obesity

Stress is a common experience that can have significant effects on our physical and mental health. It is linked to a range of health issues such as cardiovascular disease, immune dysfunction, and mental disorders like anxiety and depression [14]. Stress can trigger a complex set of physiological responses involving the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) [15]. These responses include the release of stress hormones like cortisol, adrenaline, and noradrenaline. Chronic stress can lead to dysregulation of the HPA axis, resulting in elevated cortisol levels and other changes that can have negative effects on our health [16]. However, there are many ways to manage stress, such as physical exercise, mindfulness, and relaxation techniques. In fact, a growing body of research has demonstrated the beneficial effects of mind-body interventions, such as yoga and meditation, on stress reduction [17,18]. It is a growing field to find methods to manage stress through natural products. There were many research conducted on adults aged 18-75 years to evaluate the anti-stress activity of *Withania somnifera*. Study populations included healthy individuals, stressed individuals, overweight or obese individuals experiencing chronic work stress, diagnosed with anxiety, and diagnosed with schizophrenia or schizoaffective disorder. In these research Ashwagandha was administered as capsules of commercially available preparations, with daily doses ranging from 240 mg to 1000 mg. Stress was assessed via serum cortisol levels and three questionnaires: the Depression Anxiety Stress Scale (DASS), the Perceived Stress Scale (PSS), and the General Health Questionnaire-28 (GHQ-28). Ashwagandha supplementation improved stress markers and symptoms in the majority of the human trials, as evidenced by statistically significant declines in PSS, DASS, and GHQ-28 scores, as well as decreased serum cortisol levels compared to placebo. [19] Recent research has shown that cortisol responsiveness is a crucial factor in the metabolic consequences of stress. The hypothalamo-pituitary-adrenal axis and energy homeostasis are closely linked, and activation of the former can affect the latter. Specifically, glucocorticoids are known to increase the consumption of foods that are high in fat and sugar. [20] The literature highlights the causal relationship of psychological stress to weight gain, increased food intake and obesity. External stressors and, in response, increased negative mood is strongly correlated with changes in eating habits with a prevalence of cravings for sugary and fried foods, soft drinks and alcoholic beverages, which are ultimately associated with increased calorie intake and consequently higher body mass index. Another crucial

hormone in maintaining a healthy weight which level is low in stress is leptin. Its role is satiety signalling. Reduction of stress normalize leptin level and help maintain healthy eating habits. [21, 22] Ashwagandha is known for its anti-stress and calming effects. From studies conducted, researchers indicate that Ashwagandha root extract reduces serum cortisol levels resulting in reduced feelings of stress, improved mental wellbeing and consequently improved eating behaviour and reduced intake of food cravings.

Impact of sleep on obesity

Body weight and metabolism may be influenced significantly by the duration of sleep. Large population studies have reported a correlation between shorter habitual sleep duration and higher body mass index (BMI). Reduced levels of leptin and increased levels of ghrelin were found in individuals with short sleep duration. This may lead to increased appetite, which could potentially explain the higher BMI observed in individuals with inadequate sleep. [23]

Studies indicate that Ashwagandha may have positive effects on sleep quality and accordingly may ameliorate BMI rate. In a double-blind, randomized, placebo-controlled study was found that participants who took Ashwagandha extract for 10 weeks had improved sleep quality and reduced symptoms of insomnia compared to those who had a placebo. [24]

Anti-cancer effect of Ashwagandha

Obesity is also associated with an increased risk of certain malignancies. The correlation between high body weight and an elevated risk of certain cancers is supported by compelling evidence. These cancers include: endometrial adenocarcinoma, oesophageal cancer, pancreatic cancer, hepatocellular carcinoma, gastric cancer, colorectal cancer, postmenopausal breast cancer, ovarian cancer, gallbladder cancer and thyroid cancer. [25] The relationship between obesity and cancer risk is believed to be linked to several pathways, including those related to insulin resistance, inflammation, and sex hormones. [26] There is some evidence to suggest that Ashwagandha may have anti-cancer properties. In particular, studies have suggested that Ashwagandha extracts may be able to reduce the growth and spread of cancer cells in various types of cancer, including breast, lung, colon, ovarian, and brain cancer. One study found that an Ashwagandha extract was able to inhibit the growth of breast cancer cells by inducing apoptosis and growth arrest in the cancer cells. [27] Based on another scientific study, it is also known that Ashwagandha may modulate several

signalling pathways that can inhibit the growth and spread of colorectal tumours. Studies indicate that WS may reduce the transcriptional activity of STAT3, resulting in reduced proliferation and migration of colorectal cancer cells. [28] While these studies are promising, more research is needed to determine the potential anti-cancer benefits of Ashwagandha in humans.

Benefits of Ashwagandha in obese individuals

Research on benefits of *Withania Somnifera* has been carried out for more than a several years. The present review was aimed to elucidate the potential beneficial effect of *Withania somnifera* (Ashwagandha) in obese individuals. It has been proven that significant metabolic improvements in hepatic insulin sensitivity, adipocytokines with improved glucose tolerance were observed after administration of Ashwagandha with diet [29]. In the first case, the researchers found that withasomniferol D, isolated from *Withania somnifera* inhibited adipogenesis and suppressed the enlargement of lipid droplets. Additionally, mRNA expression levels of the adipocyte markers *Fabp4* and *Adipsin* decreased noticeably after administration of 25 μ M withasomniferol D. In the second case, *Withania somnifera* ethanolic extract was reported to reduce weight gain, serum and liver lipid accumulation and promote browning of subcutaneous adipose tissue in mice by increasing the expression of mitochondrial uncoupling protein 1 (UCP1). In other studies, significant reductions in BMI and body weight were observed in patients treated with Ahwagandha root extract compared to placebo [30]. It also was found to increase energy expenditure by increasing mitochondrial activity in brown adipose tissue (BAT), oxygen consumption and thermogenesis in mice fed the High Fat Diet. In summary, these results provided experimental rationale active coumpounds isolated from *W. somnifera*, have anti-adipogenic potential and may be considered for the development of therapeutical strategies to manage obesity and related with obesity diseases [31, 32, 33]. Furthermore, in addition to the benefits mentioned above, Ashwagandha may be a key regulator in maintaining synaptic plasticity, which is reduced in obesity induced by a high-fat diet, and may be used in the future with its nootropic effect against obesity-induced cognitive impairment [6].

Summary

Obesity is a disease with many complications, occurring worldwide. It is a significant health risk factor, reducing productivity and life expectancy. A tailored diet focusing on providing the right amount of calories and more active lifestyle are effective in losing weight. However, for many patient sruggling with obesity, implemening and maintaining these changes is too challenging. A

number of clinical trials have been undertaken among natural products for weight management with varying effectiveness [34]. The current review found that Ashwagandha, its active ingredients may have a role in obesity management. The use of natural anti-obesity products may provide an alternative and safer tool in achieving weight loss goals. The most important benefits of using Ashwagandha in obese people are improved eating habits, improved mood and stamina, which will allow patients to be consistent in improving BMI rate and reducing weight. In addition to this, it seems that patients could be able to achieve faster results due to its anti-adipogenic effects and decreased fat accumulation. As obesity is associated with an increased risk of certain cancers, it appears that using Ashwagandha in these individuals it is possible to reduce this risk by the reduction of the occurrence of this risk factor. Literature has also cited an Ashwagandha effect on reducing cancer cells through apoptosis and decreasing the proliferation of cancer cells e.g. in colon cancer and breast cancer. Despite a number of important reports on the positive effects of Ashwagandha in the treatment of disorders in many areas of medicine, it is necessary to deepen research with its participation and the emergence of recommendations for its use in order to safely introduce the adaptogen into common clinical practice.

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