Ashwagandha - Scientific Overview
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Introduction
Ashwagandha is a green shrub native to the drier parts of India, Sri Lanka, Congo, South Africa and Egypt (Jain et al, 2010). It is also known as Withania somnifera (Latin name), Indian Ginseng, and Winter cherry. Ashwagandha has a long history in India’s Ayurvedic system of healing. Ayurvedic medicine is based on a holistic view of balance achieved through the bodily systems using diet, herbal treatment, and yogic breathing.

Ashwagandha goes back nearly 3,000 years with a wide range of applications. Its nickname, “Queen of Ayurveda,” comes from its common use in Indian traditional home medicine. In Sanskrit, Ashwagandha means “smell of a horse,” which references not only the scent of the plant from the fresh roots, but the associated benefits of strength and stamina conferred to those individuals who take it (Milner 2016, Chandrasekhar et al 2012).

Ashwagandha has been linked to the following benefits (Tweed, 2017 & Wadhwa et al 2016):
• Cognitive enhancement
• Reduced stress & anxiety
• Improvements in sleep
• Reduction in food cravings & weight management
• Improved endurance during exercise & workouts
• Improvement in heart health

Adaptogen
Ashwaganda is classified as an adaptogen. What is an adaptogen? The concept of adaptogens has existed for nearly 60 years; they are herbs that help optimize an individual’s ability to manage stress (Panossian 2017). Also known as anti-stress agents, they help protect the body from stress and assist the body in addressing the effects of stress. Commonly used medicinal plants or adaptogens include: Bacopa monnieri, Centella asiatica, Passiflora incarnata, Valeriana officinalis, W. somnifera, Humulus lupulus, Matricaria chamomilla, Galphimia glauca, Melissa officinalis, Piper methysticum, Scutellaria lateriflora, and Ziziphus jujube (Gupta, 2016).

Cognitive Enhancement
The aging process often includes cognitive decline. Ashwagandha (Withania somnifera) has been linked to improvements in a variety of cognitive conditions involving memory and cognition. In an 8-week double-blind placebo-controlled study among 50 subjects, treatment with ashwaganda root aqueous extract was associated with significantly enhanced scores versus placebo in the general memory and immediate memory subset scores. Additionally, study results also indicated that ashwagandha might be effective in improving executive function, attention, and information processing speed in individuals with mild cognitive impairment (Choudhary et al, 2017).

Reduced Stress & Anxiety
According to the Stress in America Survey™, 2017 saw a significant increase in the percentage of Americans who experienced at least one symptom of stress in the past month at 75%, compared to 71% in 2016. The survey respondents reported their symptoms of stress fell into the following categories: 36% feeling nervous or anxious; 35% experiencing irritability or anger; and 34% experiencing fatigue (APA, 2017). Given the need for stress relief, scientists have studied
ancient remedies, and Ayurvedic medicine has long claimed that ashwagandha promotes stress relief, with studies indicating anti-stress activity (Bhattacharva & Muruganandam 2003, Jain et al, 2010). Ninety-eight chronically stressed humans completed a 60-day double-blind, randomized placebo-controlled study with Withania Somnifera extract (the root and leaf extract) showing a significant reduction in stress, anxiety, irritability, inability to concentrate, forgetfulness, sleeplessness, fatigue, and other subjective indicators of stress at all doses compared to placebo (Auddy et al, 2008).

**Improved Endurance During Exercise & Workouts**

Endurance sports such as cycling require aerobic capacity to thrive during long-duration events. Athletes look for ways to improve their aerobic capacity including such items as nutritional supplementation and ergogenic aids. Endurance athletes seek optimization of their VO2 Max – the maximal amount of oxygen that is consumed during exercise. Optimizing VO2 Max can positively impact the performance of the individual. Ashwaganda root extract has been tied to two recent clinical studies involving athletes and endurance. In a 12-week study with 50 adult athletes, improvements in heart and respiratory endurance along with enhancements in quality of life were observed among the treatment group using ashwagandha root extract versus the control group (Choudhary et al 2015). Moreover, in an 8-week study with elite Indian cyclists significant improvements in aerobic performance including VO2 Max and increased time to exhaustion were observed in the control (ashwagandha-treated) group vs. placebo group (Shenoy et al 2012).

**Improved Sleep**

Ashwagandha has been utilized in traditional Ayurveda medicine for sleep throughout the centuries. Its Latin name, somnifera means sleep-inducing. Researchers in Japan from the International Institute for Integrative Sleep Medicine, University of Tsukuba studied the various components of the ashwagandha leaf to elucidate the active component inducing sound sleep. Oral administration of the water extract from the ashwagandha leaf which contains triethylene glycol (TEG). This ingredient contributed to significant non-rapid eye movement sleep with a slight change in rapid eye movement sleep in mice. Conversely, the alcohol extract from the ashwagandha leaf (containing active withanolides) when administered orally to mice showed no effect on sleep. This study effectively demonstrated that the TEG component of ashwagandha leaves (Withania somnifera) was the active component responsible for sleep induction. (Kaushik et al 2017). In a 60-day double-blind, randomized, placebo-controlled study among 98 chronically-stressed men and women, improvements were observed at the 30 and 60 day time points in sleeplessness and fatigue scores using the modified Hamilton anxiety scale among all treatment groups of ashwagandha extract compared to placebo (Auddy et al 2008).

**Reduction in Food Cravings & Weight Management**

Stress has been linked to weight gain in several epidemiological studies (Lecerf 2006). Notably, stress can contribute to either under- or overeating; however, chronic life stress has been associated with the tendency to seek out energy dense foods i.e. high fat and high sugar (Torres and Nowson, 2007). Who hasn’t had their junk food binge of ice cream, potato chips, and M&M’s? With chronic stress, this binging behavior repeats itself over and over rather than occurring once in a while. In an 8-week double-blind, randomized, placebo-controlled clinical trial with 52 men and women, treatment with ashwagandha root extract showed significant improvements in well-being and happiness, food cravings, reactive eating, serum cortisol levels, and body weight measures vs. placebo. These results suggest that the ashwagandha root extract can be used among chronically-stressed adults for body weight management (Choudhary et al 2017).

**Patented Ashwagandha Root and Leaf Extract**

**Extract Description & Derivation**

Several published studies have been associated with the multi-patented ashwagandha root and leaf extract. Cultivated in the central and northern provinces of India, the ashwagandha root and leaf extract was derived from withaferin A and corresponding withanolide glycoside-predominant, genetically uniform chemotype. The ashwagandha root and leaf extract was processed using a proprietary water-based method using the roots and leaves of the withania somnifera. High performance thin layer chromatography analysis against standard references was utilized in accordance with the US Patent for the process to separate the fractions. This multi-patented ashwagandha root and leaf extract contains not less than 10% withanolide glycosides, not more than 0.5% of withaferin-A and not less than 32% of oligosaccharides.
Table 1 - Subjects’ Level of Perceived Stress
Overall Anxiety Level Over 60 Days*

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 30</th>
<th>Day 60</th>
</tr>
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<tbody>
<tr>
<td>Placebo</td>
<td>30</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>Ashwagandha extract (Twice daily) - 125 mg daily</td>
<td>30</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Ashwagandha extract (Once daily) - 125 mg daily</td>
<td>30</td>
<td>25</td>
<td>15</td>
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</tbody>
</table>

*Mean sum of total stress and anxiety scores based on modified Hamilton anxiety (mHAM-A) scale by treatment group with ashwagandha root and leaf extract or placebo at 0, 30, and 60 days. P<0.001 treatment vs. placebo (Auddy et al 2008).

Table 2
Percent Improvement in Select Individual Stress & Anxiety Measures Among Subjects Treated with Ashwagandha root and leaf extract & Placebo

<table>
<thead>
<tr>
<th></th>
<th>30 days</th>
<th>60 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatigue</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ashwagandha extract once daily – 125 mg</td>
<td>40.6%*⁺</td>
<td>53.1%*⁺</td>
</tr>
<tr>
<td>Ashwagandha extract twice daily – 125 mg</td>
<td>55.2%*⁺</td>
<td>79.3%*⁺</td>
</tr>
<tr>
<td><strong>Inability to Concentrate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ashwagandha extract once daily – 125 mg</td>
<td>34.4%*⁺</td>
<td>51.5%*⁺</td>
</tr>
<tr>
<td>Ashwagandha extract twice daily – 125 mg</td>
<td>50.0%*⁺</td>
<td>75.8%*⁺</td>
</tr>
<tr>
<td><strong>Sleeplessness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ashwagandha extract once daily – 125 mg</td>
<td>38.7%*⁺</td>
<td>38.7%*⁺</td>
</tr>
<tr>
<td>Ashwagandha extract twice daily – 125 mg</td>
<td>70.9%*⁺</td>
<td>67.7%*⁺</td>
</tr>
</tbody>
</table>

*Mean scores for select Stress & Anxiety measures based on a Modified Hamilton anxiety scale at 0, 30, and 60 days of treatment with ashwagandha extract or placebo. P<0.05 versus 30 days of treatment.
⁺ P<0.001 versus Placebo group.
ASHWAGANDHA ROOT AND LEAF EXTRACT BENEFITS

Cognitive Enhancements
A double-blind multi-dose ashwagandha root and leaf extract, placebo-controlled, crossover study was completed among 20 healthy male subjects over the course of the 42 day study. Simple reaction, choice discrimination, digit symbol substitution, digit vigilance, and card sorting test reaction times showed significant improvements versus placebo. These improvements suggest ashwagandha root and leaf extract can enhance cognitive and psychomotor performance (Pingali et al 2014).

Stress
98 healthy male and female chronically-stressed subjects completed a 60-day randomized, double-blind, placebo-controlled parallel clinical study with ashwagandha root and leaf extract. The results indicated that daily use of a standardized ashwagandha root and leaf extract decreased experiential feelings of stress and anxiety, reduced the concentration of serum cortisol and CRP (C-reactive protein), lowered blood pressure and pulse rate; and increased serum concentration of DHEAS in chronically stressed adults (Tables 1-2). Serum cortisol is the known as the stress hormone; DHEAS is a hormone associated with overall energy in the body. These results suggest that ashwagandha root and leaf extract can provide positive health benefits among chronically-stressed individuals (Auddy et al 2008).

Heart Health
In a double-blind placebo-controlled crossover study, 20 healthy male subjects completed treatments of either ashwagandha root and leaf extract or placebo over the course of 42-day study (14-day – phase I, 14-day wash out, 14-day phase II). As compared to baseline and the placebo treatment group, the ashwagandha root and leaf extract treatment group saw a significant decrease in aortic pressure and augmentation index as well as an increase in the subendocardial viability ratio. Treatment with ashwagandha root and leaf extract significantly lowered the elevated levels of hs-CRP caused by mental stress as compared to baseline and placebo. Increases in the CRP which is an inflammatory marker is associated with a higher incidence of coronary heart disease (CHD). Additionally, the ashwagandha root and leaf extract significantly decreased MDA levels versus baseline and the placebo treatment group. MDA levels are commonly used as indicators of lipid peroxidation; higher MDA levels are associated with a higher lipid peroxidation as seen in coronary heart disease patients. The ashwagandha root and leaf extract used during a period of short-term mental stress provided positive heart health benefits among healthy subjects (Pingali et al 2013).

Summary
Ashwagandha with its ancient roots in Ayurvedic traditional medicine has numerous benefits including improvements in stress and sleep. Numerous studies have been published throughout the world on ashwagandha which provide strong support for its touted benefits. With today’s on-the-go, hectic and stressful lifestyles, the inclusion in a dietary supplement of an ingredient such as ashwagandha provides a multi-functional and safe choice for consumers.


