



## White Paper: Ashwagandha

### HISTORY AND TRADITIONAL USES OF ASHWAGANDHA

Used extensively in traditional Ayurvedic and Unani Indian medicine, Ashwagandha, sometimes referred to as 'Indian ginseng' due to exerting many similar effects to the Panax ginseng of traditional Chinese medicine, has been widely adopted in western herbal medicine. The historical roots of this herb, botanical name *Withania somnifera*, can be traced back to 6000BC in traditional Indian medicine. It was noted that the herb both had a horse-like smell and possibly gave the 'power' of a horse, hence 'ashwa' means horse and 'gandha' means smell in Sanskrit.<sup>2</sup> Various parts of the plant, including the root, seeds, leaves, berries and flowers, have an array of applications in traditional Indian medicine, including as a general tonic, diuretic, anthelmintic, aphrodisiac, anxiolytic, carminative, and cognition enhancer.<sup>2</sup>

Historically, the herb was classified as a 'rasayana' – a class of herbs in Ayurveda considered to be a tonic; promoting youthfulness, strength, longevity, energy, and alleviating pain and inflammation.<sup>3</sup>

### BOTANY AND ACTIVE CONSTITUENTS

Belonging to the botanical Solanaceae sub-family Solanoideae<sup>7</sup>, Ashwagandha can be typically found in arid areas of India, Sri Lanka, and certain parts of Africa and the Mediterranean, as well as the high altitudes of the Himalayas.<sup>6</sup>

Ashwagandha is a branched shrub with long, tuberous roots. Although the root of the plant is the most commonly utilised medicinally<sup>6</sup>, the berries, leaves, as well as the bark, may also be used in a variety of medicinal applications.<sup>1</sup>

The major groups of isolated chemical constituents identified in Ashwagandha thus far include steroidal lactones, flavonoids, tannins, saponins and alkaloids.<sup>7</sup> The chemical compounds identified from the aerial parts, berries and the roots include alkaloids, withanolides and sitoindosides. Further examination of the roots

has also isolated thiowithanolide (also known as ashwagandhanolide).<sup>7</sup>

The therapeutic properties of Ashwagandha are primarily attributed to the withanolides – biologically active steroidal lactones which have acquired much of the attention around the applications and efficacy of Ashwagandha; this is due, in large part, to the demonstrated biologically diverse activities in both *in vivo* and *in vitro* studies.<sup>8</sup> Withaferin A, a withanolide first identified in 1965, provides many of the pharmacological benefits ascribed to Ashwagandha and has been of particular interest in recent years due to its anti-inflammatory and anti-tumour effects.<sup>8</sup>

### ASHWAGANDHA AS AN ADAPTOGENIC HERB

Ashwagandha is often referred to and most widely prescribed as an adaptogen. Medicinal herbs with adaptogenic properties are unsurprisingly some of the most popular herbs in use today – this is because of their ability to improve the body's resistance to external stressors via a number of networks in the body, including the central nervous system, as well as the immune and endocrine systems. The term adaptogen was originally coined in 1940 to describe medicinal herbs that exerted a non-specific enhancing effect on the body – assisting in preventing an array of unfavourable conditions, resisting conditions brought on by stress, and encouraging homeostasis.<sup>9</sup> Put succinctly, adaptogens provide support for the body to adapt to a changing environment and changes to external stressors, improving resistance to negative impacts on the body's systems. Primary adaptogens must meet specific criteria, including having sufficient scientific evidence to support their efficacy, affording general resistance in the body, and maintaining or restoring homeostasis. Ashwagandha is considered a primary adaptogen as it meets all of the above criteria.<sup>9</sup>

The hypothalamic-pituitary-adrenal (HPA) axis is the main target of any primary adaptogen. Ashwagandha strengthens these glands in response to external stress,

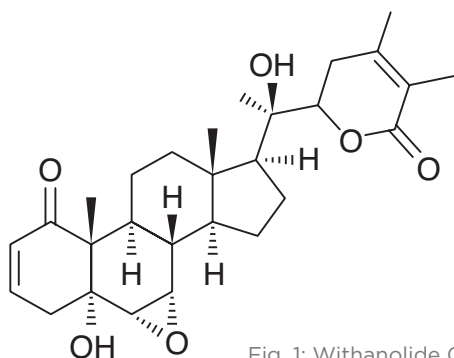


Fig. 1: Withanolide Glycoside

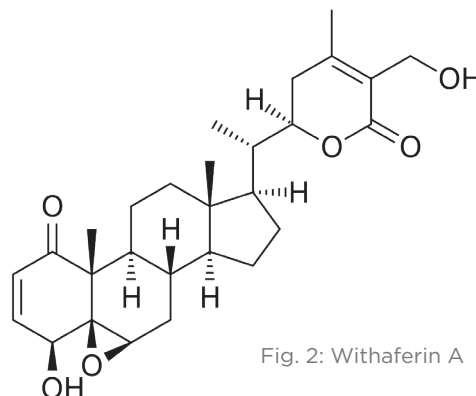


Fig. 2: Withaferin A



allowing for a positive stress response and healthy expression of associated hormones.<sup>9</sup> During times of heightened stress, the use of adaptogenic herbs such as Ashwagandha supports adrenal gland secretions, reducing excessive production of stress hormones. By increasing adenosine triphosphate production in the cells and inhibiting oxidative stress, adaptogens also aid in maintaining healthy adrenal functioning.<sup>9</sup>

## ACTIONS

- Adaptogenic<sup>9</sup>
- Cognitive enhancer<sup>10,11,12</sup>
- Anxiolytic<sup>13,14,15</sup>
- Neuroprotective<sup>15,18</sup>
- Anti-inflammatory<sup>15,16</sup>
- Immunomodulatory<sup>17,29</sup>
- Cardioprotective<sup>30,5</sup>
- Chemopreventive<sup>15,28,16</sup>
- Chondroprotective<sup>4,5</sup>

## CLINICAL USES

The clinical uses for Ashwagandha are increasing as further research emerges. The best *in vivo* and *in vitro* research supports the use of Ashwagandha for the following:

### Stress and anxiety

Several human trials have revealed positive results in using *Withania somnifera* extract (WSE) to improve stress response, with measures taken through both self-reporting questionnaires (Depression, Anxiety, and Stress Scale-21, Hamilton Anxiety Rating Scale) and clinically measured results, including serum DHEA-S, serum cortisol, C-reactive protein, heart rate and blood pressure. These trials provided evidence of the efficacy of Ashwagandha as anxiolytic, mood-enhancing, and adaptogenic.<sup>19,20,21</sup>

There is now further evidence to suggest a potential mechanism of action for Ashwagandha's anxiolytic and sleep inducing properties; a 2015 animal study utilising aqueous WSE revealed the herb to be a potent GABA<sub>A</sub>1 receptor agonist, although the bioactive compounds responsible for this effect were not able to be identified. The study forms a promising basis for further research into treating conditions involving GABAergic signalling dysfunction.<sup>22</sup>

### Memory and cognitive health

Ashwagandha has long been used in traditional Indian medicine to enhance memory and focus. These actions have been at the centre of numerous clinical trials, garnering positive results for not only memory and focus, but alertness, overall cognitive health and function, and prevention of cognitive decline.<sup>12,10,11</sup> An eight-week randomised, double-blind, placebo-controlled pilot study into the effects of Ashwagandha on general and immediate memory on 50 adults with mild cognitive

impairment (MCI) treated BID with 300mg Ashwagandha root extract or placebo was conducted in 2017. The results revealed vast improvements in the attention, information processing speed and general memory of the Ashwagandha treatment group, as measured by the Wechsler Memory Scale III subtest.<sup>12</sup>

### Joint pain and inflammation

The unregulated expression of inflammatory mediators is the target of treatment in rheumatoid arthritis (RA). The main bioactive compounds of Ashwagandha – withaferin A and withanolides, are responsible for the anti-inflammatory and immunomodulatory effects shown to inhibit nuclear factor kappa-B (NF-κB). NF-κB is one of the main transcription factors involved in the expression of pro-inflammatory cytokines and therefore a target objective for treatment of inflammatory conditions such as RA and osteoarthritis.<sup>4,5</sup>

### Sleep aid

Ashwagandha may target a number of the potential culprits underlying common sleep disorders; as it is shown to exert GABAergic effects, Ashwagandha is a potent anxiolytic and may be useful in disorders involving GABA dysregulation and/or deficiency.<sup>22</sup> Hyper-activation of the HPA axis is also a common driver of sleep disorders, particularly insomnia and obstructive sleep apnoea.<sup>23</sup> Ashwagandha is believed to work as a nervine tonic, in part, by regulating the HPA axis, thereby supporting restorative sleep.<sup>9</sup>

### Anaemia

Ashwagandha is considered to have haematopoietic potential and may therefore be useful in the treatment and prevention of iron deficiency anaemia. The results of a 2009 animal study provided preliminary evidence to support the use of Ashwagandha in the treatment of anaemia. Rats were divided into five groups, including a placebo group and an ethanolic WSE treated group administered 200mg per kilogram of body weight. The WSE treated group demonstrated increases in serum iron and protein. The increase in serum iron is likely to be partially due to the actual iron content present in Ashwagandha of around 947 micrograms per 50ml WSE. Furthermore, the WSE treated group also exhibited an acceleration of oxygen carrying capacity of red blood cells (RBC), and an increase in the actual number of RBCs.<sup>24</sup>

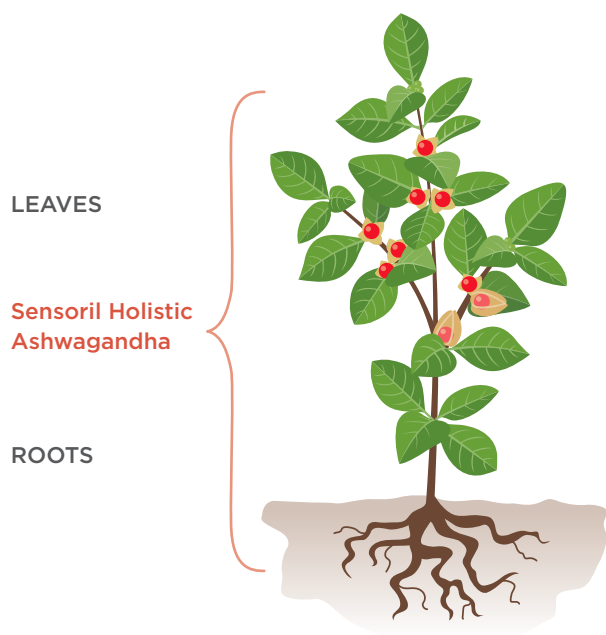
## CLINICALLY STUDIED ASHWAGANDHA EXTRACTS

### Sensoril®

Sensoril® is a patented combination of roots and leaves of the Ashwagandha plant containing > 10% withanolides. An aqueous extraction process is used to create Sensoril®, providing an extract that is 95% water soluble. Sensoril® has been the focus of 11 randomised, placebo-controlled, double-blind clinical trials in the United States and internationally and is certified organic. While the root is the focus of many Ashwagandha extracts on the market, Sensoril® places equal importance on the leaves, which



also contain bioactive compounds shown to provide many of the health benefits Ashwagandha is famous for. Due to the inclusion of the Ashwagandha leaves and the aqueous extraction method, the Sensoril® extract produces higher quantities of the standardised bioactives withanolide glycosides and withaferin A.<sup>26</sup>



## Strength

A 2018 study assessed the use of Sensoril® *Withania somnifera* to improve adaptations in strength training in healthy males aged between 18-45 years. Results showed that 500mg/day of Sensoril® extract significantly increased both upper and lower body maximal strength when compared to placebo.<sup>31</sup>

## Chronic stress

A 2008 clinical trial examined the effects of Sensoril® WSE in chronically stressed patients receiving 125mg BID. The WSE treated group had significantly reduced stress at 30 and 60 days, as evidenced by lowered serum cortisol, blood pressure, pulse rate, serum C-reactive protein, improved modified Hamilton anxiety scale rating, as well as increased serum DHEA-S and haemoglobin, when compared to the placebo group.<sup>32</sup>

## Joint health

The chondroprotective, analgaesic and anti-inflammatory actions of Ashwagandha formed the basis of a 2016 study to evaluate the efficacy of Sensoril® WSE in patients with knee joint pain and discomfort. WSE of 250mg given BID was shown to significantly reduce knee pain, swelling, stiffness and disability compared to both the placebo group and the group receiving 125mg WSE BID.<sup>5</sup>

## Shoden®

Shoden® is backed by clinical trials and utilises the roots and leaves of the Ashwagandha plant to create an extract containing 35% withanolide glycosides. The Shoden® extract also contains 21 bioactive withanolide glycosides, along with 4-5% bioactive withanolide aglycones (including withaferin A and withanone) – making Shoden® a market-leading high potency Ashwagandha extract.<sup>27</sup>

## Sleep

A 2020 clinical trial evaluated the effects of Ashwagandha extract as Shoden® on sleep quality in 144 adults experiencing non-restorative sleep (NRS). The results of the trial revealed that 120mg of Shoden® extract administered once daily over six weeks significantly improved NRS condition by reducing onset of sleep latency, wake after sleep onset, and average waking time, as well as improving total sleep time and quality of life.<sup>33</sup>

## Vitality and testosterone

A 16-week randomised, double-blind, crossover study using Shoden® beads containing 21mg of withanolide glycosides was undertaken to determine the efficacy of the extract on mild fatigue, vigour and steroid hormones in ageing, overweight men. The group receiving WSE as Shoden® beads had substantial increases to salivary DHEA-S and testosterone. Improvements were also seen in self-reported symptoms, including fatigue/energy, and sexual and psychological wellbeing.<sup>19</sup>

## NooGandha™

NooGandha™ extract provides full spectrum Ashwagandha root delivered via liposomal technology whereby the extract is bonded to phospholipids to enhance absorption and bioavailability, as well as allowing transport through the blood-brain barrier.<sup>34</sup>

## Cognition and memory

A randomised, placebo controlled study undertaken to assess the use of NooGandha™ in aiding cognition and memory found that the Ashwagandha groups given 400mg/day and 225mg/day, respectively, for 15 days noticeably increased cognitive flexibility, visual memory and reaction time compared to placebo.<sup>35</sup>

## Stress response

The same study also measured self-reported symptoms around mood, perceived stress, anxiety and food cravings, as well as serum cortisol levels. The Ashwagandha groups both reported significant reductions in perceived stress, anxiety, depression and food cravings throughout the study timeframe. Serum cortisol was also reduced in both Ashwagandha groups, but significantly more in the group receiving WSE of 225mg/day over 15 days.<sup>35</sup>

*References supplied on request.*