WHITE PAPER SERIES

SENSORIL® HOLISTIC ASHWAGANDHA:

Harnessing the Power of Leaf & Root to Optimize Health Benefits

Sensoril®

CREATED BY

NATREON, INC.
OCTOBER 2018

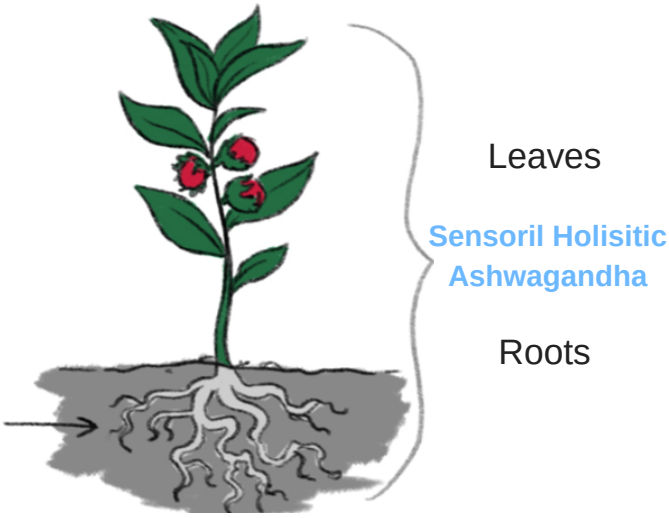
Natreon
Trusted Science, Naturally ™
natreoninc.com

SENSORIL HOLISTIC ASHWAGANDHA

Sensoril Ashwagandha is an adaptogen derived from a unique blend of both leaves and roots of the *Withania somnifera* plant, by a totally aqueous extraction process, to provide optimal efficacy and bioactive diversity. This proprietary extract, with water-solubility more than 95%, has been studied in more than ten randomized, double-blind, placebo-controlled human clinical trials. It supports many health benefits, and has excellent applications in supplements, foods, beverages, and personal care products. Sensoril is the trusted and original holistic ashwagandha extract in the market, and is GRAS affirmed, Non-GMO Project Verified, and Organic certified.

SENSORIL HOLISTIC ASHWAGANDHA VS ASHWAGANDHA

Ashwagandha is one of the most well-studied adaptogens, defined as a plant extract that helps support the body's ability to resist the effects of everyday stress and promote normal physiological functioning (Merriam-Webster Dictionary). Ashwagandha has **adaptogenic properties of "warming", "soothing", and "energizing."** It has been used in traditional Ayurveda for thousands of years to **promote longevity, enhance vitality, support a healthy immune response, enhance focus and to help reduce everyday stress and fatigue** (1-8).



LEAF & ROOT POWER HOUSE

Initial scientific and commercial endeavors have focused only on the root, excluding the benefits from the **"power house"** of health benefits, the Ashwagandha leaf. Recent research has been extensively focusing on both the root and the leaf of the Ashwagandha plant because both plant parts contribute to a variety of health benefits. **The leaves from the Ashwagandha plant contain bioactives, which are shown to support improvement in cognition, sleep and oxidative stress as well as a healthy immune response** (9-20). The roots from Ashwagandha are most commonly used to promote longevity, enhance vitality and support a healthy immune system (21,22).

Generic ashwagandha extracts suffer from lack of proper optimization of the extraction process, standardization of the bioactive constituents, consistency in quality, safety studies and human clinical studies. These problems have been addressed by Sensoril Ashwagandha.

Sensoril Ashwagandha uses a unique combination of leaves and roots, to deliver a comprehensive extract with increased levels of withanolide glycosides and superior performance. Sensoril is extracted using a specialized, water-based extraction process and is **standardized to three key bioactives: withanolide glycosides, oligosaccharides & withaferin A, with a patented composition** (US 7,318,938, CA2508478C). The bioactive analysis is done by HPLC /UPLC to maintain consistent quality.

Sensoril Ashwagandha is **backed by more than ten randomized, double-blind, placebo-controlled clinical studies**, done by premier research institutes in the United States as well as in India. Sensoril is GRAS affirmed, Non-GMO Project Verified, organic certified and Informed Choice certified for sports nutrition as Sensoril Sport.

These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

FROM FARM TO FINISHED INGREDIENT

Cultivation

Ashwagandha is cultivated in central and northwestern India. Ashwagandha seeds are sown under a thin covering of sand in a nursery bed before the summer-monsoon season begins around June. After around 40 days, the seedlings are transplanted to a field where they grow to their full maturity. They are harvested when the plants have developed berries and leaves are dry, about 160 to 180 days after they are sown.

Sourcing

For thousands of years, Ashwagandha has been sourced from wild plants in India. Continuing the tradition, Sensoril Ashwagandha is sourced from Madhya Pradesh in central India and the organic varieties come from certified organic farms in India. These farms provide a sustainable sourcing method that benefits local farmers, improving their livelihood and the local economy.

Quality

Quality is built into Sensoril Ashwagandha, a holistic extract, by selection of appropriate chemotype and genotype of the plant, sourcing from correct geographical area, harvesting at the correct time, using both leaves & roots and optimization of the extraction process. The bioactive level specifications are: withanolide glycosides ≥10%, oligosaccharides ≥32% and withaferin A ≤0.5%, a patented composition. Quality control testing is done by the latest analytical techniques, such as HPLC and UPLC.

Applications

Sensoril has excellent functionality in supplements, foods, beverages, and personal care products, and is particularly suited for applications in sports nutrition, stress reduction, energy, sleep, heart health, joint health and cognitive health. It can be formulated into tablets, capsules, stick packs, gummies, and sports nutrition blends.

BIOACTIVES

Withanolide glycosides are a group of naturally occurring compounds found in a variety of plants (23,24). Withanolide glycosides support a healthy immune response and have been clinically studied for reducing everyday stress (10). Withanolide glycosides have hundreds of metabolites; however, the predominant bioactives are **Withaferin A, Withaferin D and Withanone** (25-29). Withaferin A is one of the most studied withanolides, supporting heart health, brain health, and a healthy immune response. (30-35).

Extensive toxicity studies have been performed to ensure Withaferin A and other withanolides are not toxic to healthy cells when consumed at a reasonable dose (21, 36). No adverse effects were identified at doses up to 2 g/kg/day standardized to three percent Withaferin A (21).

Research has also elucidated that the Ashwagandha leaves and roots contain different concentrations of Withaferin A (22). Again, a combination of the leaf and root extract standardized to the most bioactive compounds in Ashwagandha, **(≥10% withanolide glycosides, ≥32% oligosaccharides and ≤0.5% withaferin A)**, found in clinically studied holistic Sensoril, provides diverse health benefits (37-45).

Oligosaccharides are a bioactive component from Ashwagandha that is often overlooked. Oligosaccharides are a type of carbohydrate that are critical for normal cellular function, including cell adhesion and cellular recognition (46, 47). Oligosaccharides also contribute to the soluble fiber content which supports digestion and heart health. Soluble fiber is critical for healthy digestion and may act as a prebiotic to help maintain healthy bacteria in the GI tract. Including soluble fiber as part of a healthy diet supports healthy cardiovascular function (38, 40, 41, 43, 48). **Patented Sensoril contains ≥32% Oligosaccharides.**

Standardization:

Sensoril®
Holistic Ashwagandha

Withanolide glycosides
Glycosylated Steroidal Lactones (Withanolides)
Anti-stress properties

Oligosaccharides
Act as carrier of Withanolide glycosides
Enhances bioactives

Withaferin A
Steroidal Lactone (Withanolide)
Antioxidant

These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

HEALTH BENEFITS

Recent scientific research utilizing clinically studied Sensoril has been **shown to increase muscular strength, enhance focus and reaction time, increase energy, improve sleep, support joint health and reduce everyday stress – all important factors for overall health, sports nutrition and performance** (37, 38, 39, 43, additional study pending publication). Clinically studied Sensoril clearly demonstrates the performance benefits of harnessing the power of the whole plant.

Performance

Improving performance requires a proper balance of nutrition and activity along with sleep, mental focus, recovery time, joint health and reduction of everyday stress. Clinically studied Sensoril **balances eight health benefits** that all contribute to **improved performance** (Figure 1).

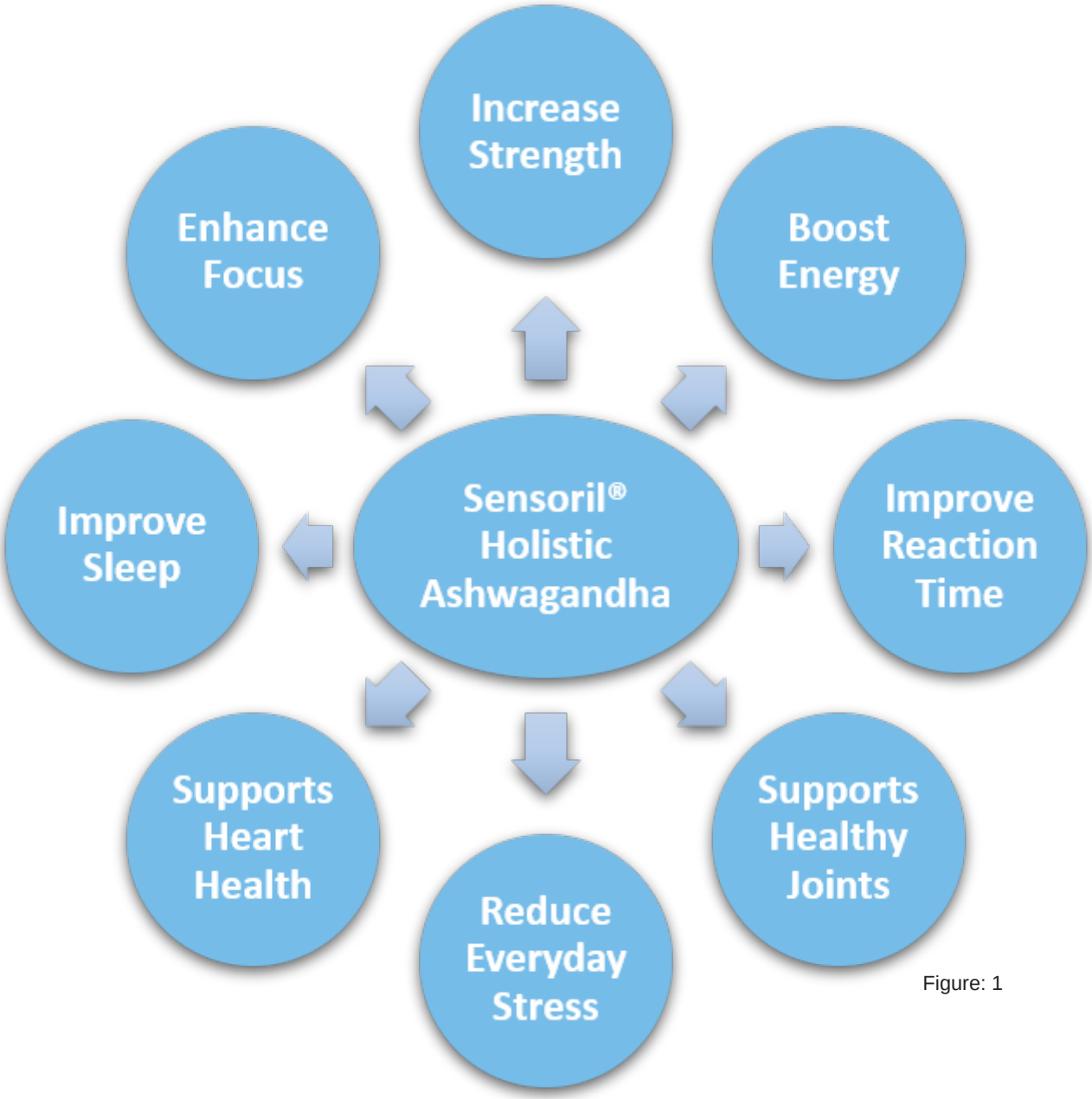


Figure: 1

Natreon Trusted Science, Naturally™

These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

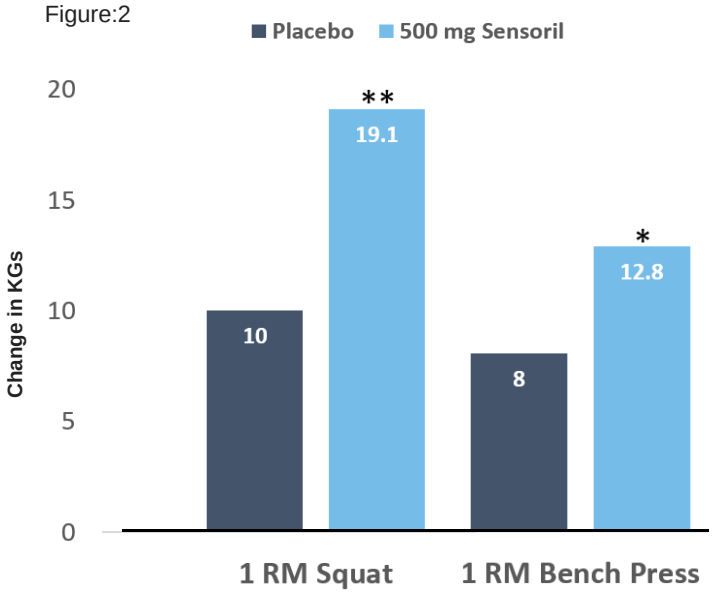
Strength

Clinically studied Sensoril significantly improves upper and lower body strength. In one study of recreationally active men, 500 mg Sensoril was administered daily for 12 weeks. The study demonstrated that **Sensoril increases 1 RM squat by 9.1 kg and 1 RM bench press by 4.8 kg compared to placebo** (Figure 2, study pending publication).

Consuming Sensoril contributes to improving overall performance by significantly increasing upper and lower body strength.

As shown in Figure 2 below, **Sensoril showed 90% improvement in 1 RM squat strength and 60% improvement in 1 RM bench press** compared to placebo.

Figure:2



**p<0.01 vs. Placebo
*p<0.05 vs. Placebo

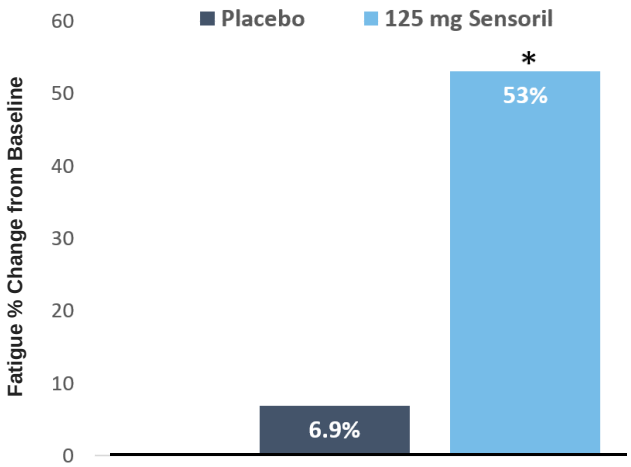
Energy

Energy is a top concern for health-conscious individuals. **Thirty percent of consumers cited energy as a top concern**, according to the Council for Responsible Nutrition's (CRN) 2016 Consumer Survey on Dietary Supplements. Balancing energy requirements is essential for peak performance. Ashwagandha has energizing properties and clinically studied Sensoril shows a **seven times greater reduction in fatigue** compared to a placebo (Figure 3) (37).

This reduction in fatigue may lead to a natural increase or balancing of energy without the highs and lows of stimulants like caffeine. Increased energy may be one mechanism for increased strength and improved performance. Sensoril's adaptogenic properties **promote an energizing response by balancing the body's natural energy requirements.**

As shown in Figure 3, **Sensoril showed a seven times greater improvement in feelings of fatigue** compared to placebo.

Figure: 3



*p<0.001 vs. Placebo

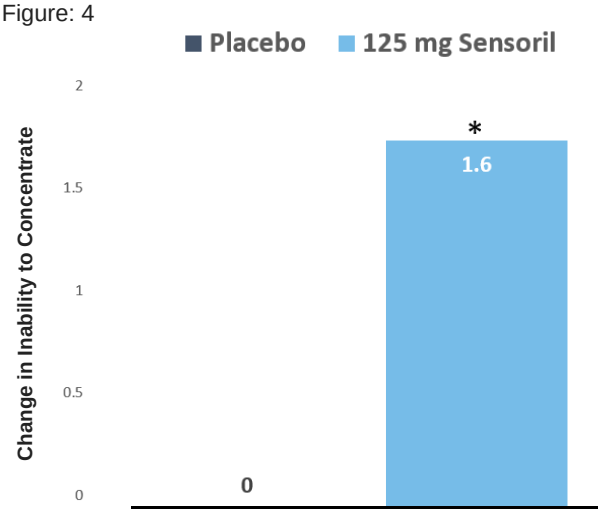
Focus & Reaction Time

Sensoril supports improved reaction time and enhanced focus. In only 2 weeks of Sensoril supplementation, subjects showed **significantly faster reaction time compared to placebo** (39).

In a separate study, subjects consuming Sensoril showed nearly **two times the ability to concentrate (focus) compared to the placebo group** (Figure 4) (37). As a unique "warming" adaptogen, Sensoril provides the ability to maintain balance in times of stress by easing the mental burden.

As shown in Figure 4, **Sensoril showed two times the ability to concentrate (focus)** compared to placebo.

Figure: 4



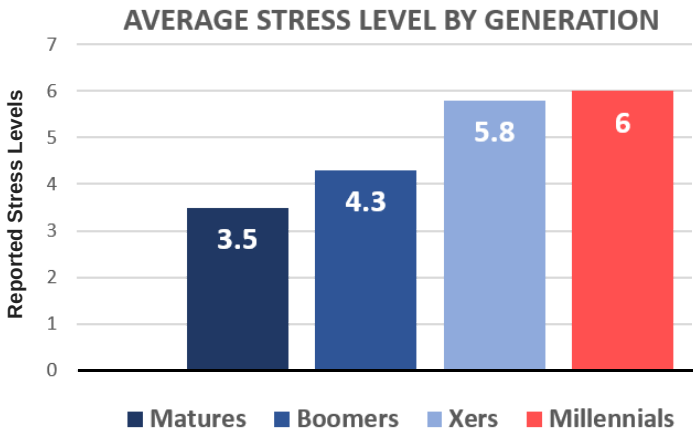
*p<0.001 vs. Placebo

Stress

In January 2017, the APA published their "Stress in America: Coping with Change" annual report based on survey results from August 2016. This eye-opening report documented the first significant uptick in stress levels in the U.S. since the survey began 10 years ago.

Although Americans' **stress levels in 2017 are on par with 2016, the nationwide stress level of 4.8 (on a 1 to 10 scale)** is still historically high. Over time, younger generations and women consistently have struggled with stress. These populations have reported higher average stress levels and been more likely than their counterparts to say that their stress has increased in the last year (Figure 5).

Figure: 5



These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

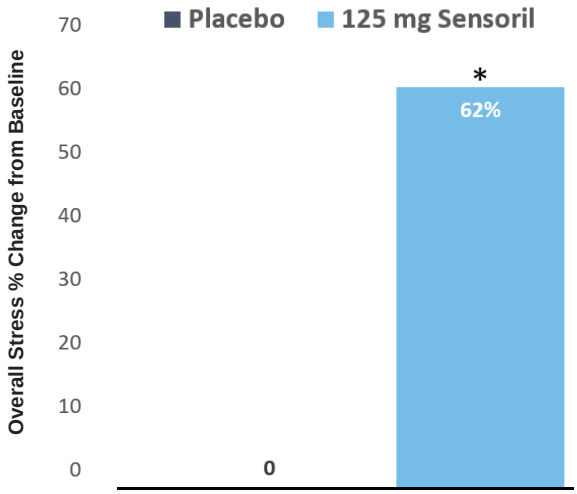
"Americans are suffering from **moderate to high stress**, **with 44%** reporting that their stress levels have increased over the past five years."

Source: American Psychology Association

Sensoril **decreases overall everyday stress by 62.2% compared to placebo** (Figure 6) using the validated modified Hamilton anxiety scale for stress (37). To further elucidate the mechanism of action, human clinical studies utilizing Sensoril demonstrate significant decreases in cortisol, a key marker of stress, (Figure 7) and CRP, a marker of the body's natural immune response compared to placebo (Figure 8).

As shown in Figure 6, **Sensoril showed a descrease in overall everyday stress by more than 60%** compared to placebo.

Figure: 6

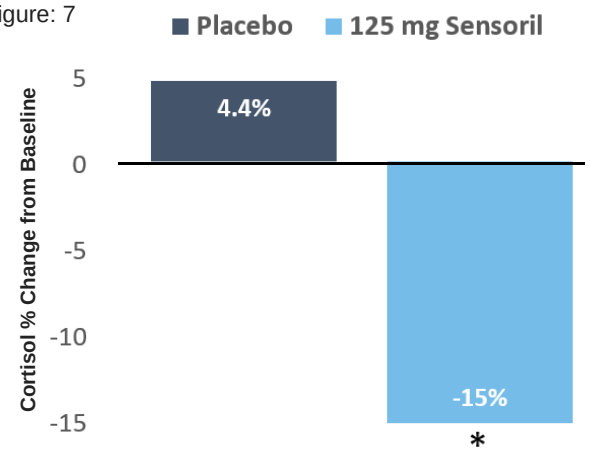


p<0.01 vs. Placebo

Two separate studies confirmed Sensoril **significantly reduced cortisol and CRP compared to placebo** (Figure 7 & 8) (37, 38). Sensoril is unique in its ability to reduce everyday stress, cortisol and CRP due to its adaptogenic properties and the neuroprotective effects of withanolide glycosides and withaferin A found in the leaves and roots of ashwagandha.

As shown in Figure 7, the **Sensoril group showed improvement in Serum Cortisol** compared to placebo.

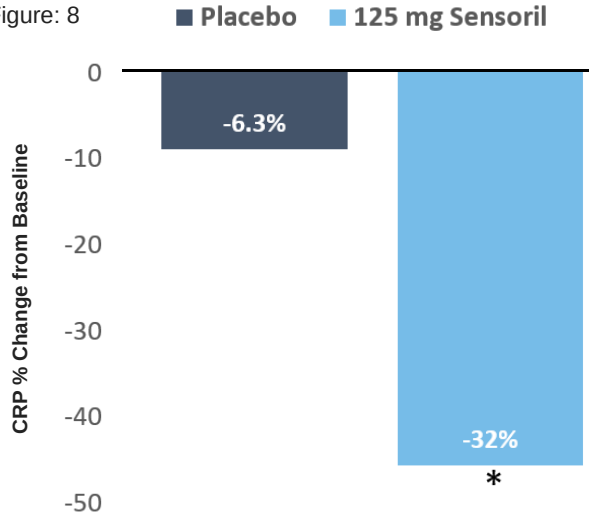
Figure: 7



*p<0.05 vs. Placebo

As shown in Figure 8, the **Sensoril group showed improvement in Serum CRP** compared to placebo.

Figure: 8



*p<0.05 vs. Placebo

Natreon Trusted Science, Naturally ™

These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

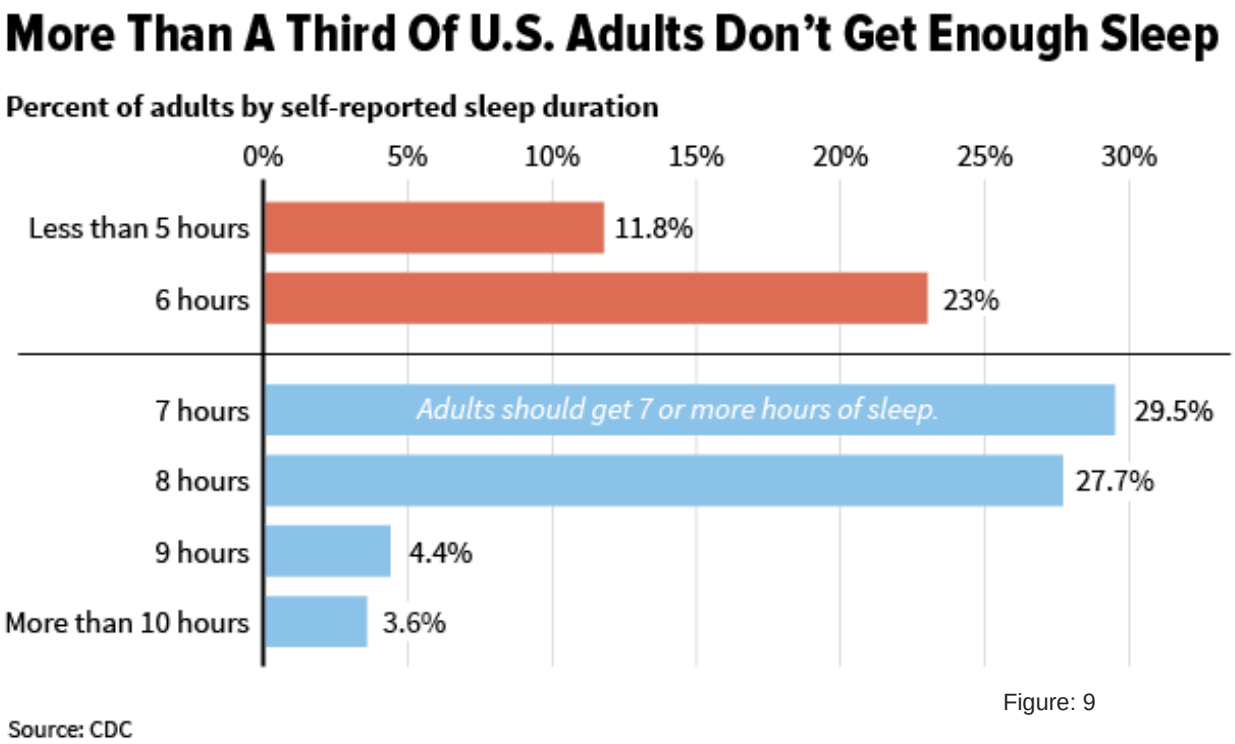


Figure: 9

Sleep

Proper recovery is essential for peak performance and the best recovery is rest achieved during a good night's sleep.

In their first study of self-reported sleep length, the U.S. Centers for Disease Control and Prevention found that **34.8% of American adults are getting less than seven hours of sleep** — the minimum length of time adults should sleep (Figure 9).

In addition to improving strength, focus, reaction time and decreasing everyday stress, Sensoril also **improves symptoms of occasional sleeplessness.**

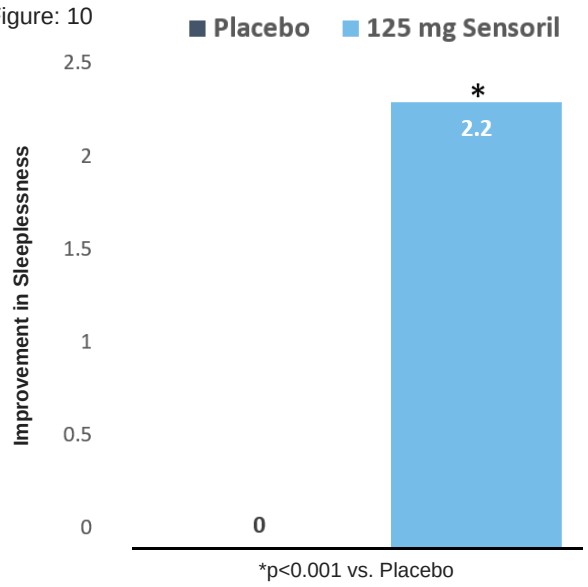
"An estimated **83.6 million** adults in the U.S. are sleep deprived."

Source: CDC

One clinical study showed that Sensoril **reduced occasional sleeplessness two times more than the placebo** (Figure 10) (37). Improving sleep is directly related to a reduction in stress and specifically a reduction in the stress hormone cortisol, which can disrupt the body's natural balance. Reducing cortisol supports healthy circadian rhythms, required for restful sleep.

As shown in Figure 10, **Sensoril showed a 70% improvement** in ability to sleep compared to baseline.

Figure: 10



Natreon Trusted Science, Naturally ™

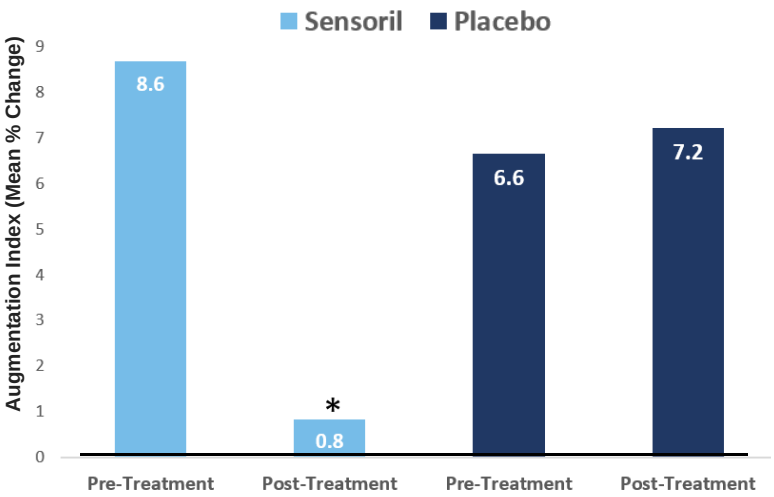
These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

Heart Health

In human clinical studies, Sensoril was shown to **promote heart health by improving endothelial function 91%** compared to placebo (Figure 11), cardiac function and supporting healthy blood pressure already within the normal range. (38, 43). These improvements in heart health are contributed to the bioactives unique to the leaves and roots in Sensoril, including withanolide glycosides and withaferin A which have cardio-protective properties and **supports a healthy immune response.**

As shown in Figure 11, **Sensoril's mean percent change in Augmentation Index (AIX) decreased significantly compared to pre-treatment.** A decrease in AIX is an indication of improved cardiovascular health.

Figure: 11



*p<0.01 vs. Placebo

Joint Health

The bioactives in Sensoril also support joint health. Determined by a validated standardized questionnaire, subjects taking Sensoril had **significant improvements in joint function along with decreased stiffness** (42). Maintaining healthy and strong joints are critical for top performance, and Sensoril supports both.

Joint Health

Blood Flow

Recovery

Natreon Trusted Science, Naturally ™

These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

REFERENCES

1. Khanna D. et al. 2007. Curr Opin Pharmacol. 7:344-351
2. Shah N. et al. 2015. PLOS One: 10: e0120554. doi: 10.1371/journal.pone.0120554
3. Singh N. et al. 2011. Afr J Tradit Complement Altern Med. 8:208-213
4. Tohda C. et al. 2000. Neuroreport. 11: 1981-1985
5. Ven Murthy MR et al. 2010. Cent Nerv Syst Agents Med Chem. 10: 238-246
6. Vyas AR & Singh SV. 2014. AAPS J.16: 1-10
7. Weiner, M.A & Weiner. J. 1994. Mill Valley, CA: Quantum Books,70–72
8. Narinderpal, K. et al. 2013. RRJBS. 2(4):6-14
9. Sunil C. Kaul, Yoshiyuki Ishida, Kazuya Tamura, Teruo Wada, Tomoko Iitsuka, Sukant Garg, Mijung Kim, Ran Gao, Shoichi Nakai, Youji Okamoto, Keiji Terao, Renu Wadhwa. PLOS ONE | DOI:10.1371/journal.pone.0166945 December 9, 2016, pp 1-15
10. Praveen Kumar, Raghavendra Singh, Arshed Nazmi, Dinesh Lakhanpal, Hardeep Kataria, and Gurcharan Kaur. BioMed Research International Volume 2014, Article ID 182029, 15 pages http://dx.doi.org/10.1155/2014/182029
11. Mahesh K. Kaushik, Sunil C. Kaul, Renu Wadhwa, Masashi Yanagisawa, Yoshihiro Urade. PLOS ONE | DOI:10.1371/journal.pone.0172508 February 16, 2017
12. Navjot Shah, Rumani Singh, Upasana Sarangi, Nishant Saxena, Anupama Chaudhary, Gurcharan Kaur, Sunil C.Kaul, Renu Wadhwa. PLOSONE|DOI:10.1371/journal.pone.0120554 March19,201
13. Renu Wadhwa, Rumani Singh1, Ran Gao, Navjot Shah, Nashi Widodo1, Tomoko Nakamoto, Yoshiyuki Ishida, Keiji Terao, Sunil C. Kaul. PLOS ONE, 2 October 2013 | Volume 8 | Issue 10 | e77189
14. Arpita Konar, Navjot Shah, Rumani Singh, Nishant Saxena, Sunil C. Kaul, Renu Wadhwa, Mahendra K. Thakur. PLOS ONE, 1 November 2011 | Volume 6 | Issue 11 | e27265
15. Hardeep Kataria, Renu Wadhwa, Sunil C. Kaul, Gurcharan Kaur. PLOS ONE, 2 May 2012 | Volume 7 | Issue 5 | e37080
16. Nashi Widodo, Didik Priyandoko, Navjot Shah, Renu Wadhwa, Sunil C. Kaul. PLOS ONE, 1 October 2010 | Volume 5 | Issue 10 | e13536
17. Shaffi Manchanda and Gurcharan Kaur. BMC Complementary and Alternative Medicine (2017) 17:136 DOI 10.1186/s12906-017-1652-0
18. Muskan Gupta and Gurcharan Kaur. Journal of Neuroinflammation (2016) 13:193 DOI 10.1186/s12974-016-0650-3
19. Hardeep Kataria, Navjot Shah, Sunil C.Kaul, Renu Wadhwa, and Gurcharan Kaur. Evidence-Based Complementary and Alternative Medicine Volume 2011, Article ID 267614, 12 pages doi:10.1093/ecam/nep188
20. Rajangam Udayakumar, Sampath Kasthurirengan, Thankaraj Salammal Mariashibu, Manoharan Rajesh, Vasudevan Ramesh Anbazhagan, Sei Chang Kim, Andy Ganapathi and Chang Won Choi. Int. J. Mol. Sci. 2009, 10, 2367-2382; doi:10.3390/ijms10052367
21. Patel, S. et al. 2016. J Ayurveda Integr Med. 7:30-37
22. Kaul, S. et al. 2016. PLOS ONE: DOI:10.1371/journal.pone.0166945
23. Glotter, E. 1991. Natural Products Report. 8(4):415
24. Kirson, I & Glotter, E. 1981. J Natural Products. 44(6):633-647
25. Deocaris CC. et al. 2008. J Transl Med. 6:14
26. Devi PU. 1996. Indian J Exp Biol. 34: 927-932
27. Kalani A. et al. 2012. BMJ Case Rep 2012
28. Kuboyama T. 2014. Biol Pharm Bull. 37:892-897
29. Sinha P & Ostrand-Rosenberg S. 2013. Cancer Immunol Immunother. 62:1663-1673
30. Grin B. et al. 2012. PLOS ONE 7: e39065. doi:10.1371/journal.pone.0039065.
31. Hahm ER. et al. 2011. PLOS ONE 6: e23354. Doi: 10.1371/journal.pone.0023354
32. Malik F. et al. 2007. Life Sci 80:1525-1538
33. Shah N. et al. 2009. Cancer Sci 100:1740-1747
34. Widodo N. et al. 2007. Clin Cancer Res 13: 2298-2306
35. Yang ES. et al. 2011. Chem Biol Interact 190:9-15
36. Budhiraja, R. et al. 2000. J Sci Ind Res. 59:904-911
37. Auddy, B. et al. 2008. J Amer Nutra Assoc. 11(1):50-56
38. Pingali U. et al. 2013. Curr Topics Nutra Res. 11(4):151-158
39. Pingali U. et al. 2014. Pharmacognosy Res. 6:12-18
40. Usharani, P. et al. 2014. Int J Ayur. Pharma. Res. 2(3):22-23
41. Usharani, P et al. 2014. Int. J Pharma. Sci Res. 5(7):2687-2697
42. Ramakanth, G. et al. 2016. J Ayurveda Integr Med. 7(3):151–157
43. Pilli, R. et al. 2016. Int J Basic & Clin Pharma. 5(3):873-878
44. K. N. Roy Chengappa, Christopher R. Bowie, Patricia J. Schlicht, David Fleet, Jaspreet S. Brar, and Ripu Jindal. Journal of Clinical Psychiatry , Vol. 74, No. 11, pp. 1076–1083, 2013
45. K. N. Roy Chengappa, Jaspreet S. Brar, Jessica M. Gannon and Patricia J. Schlicht. J Clin Psychiatry 79:5 September/October 2018
46. Feize T. 1993. Curr Opinion Struc Bio. 3(5):701-710
47. Voet D. et al. 2013. Fundamentals of Biochemistry: Life at the Molecular Level (4th ed). Hoboken, NJ: John Wiley & Sons, Inc.
48. Gupta SK. et al. 2004. Mol Cell Biochem 260: 39-47

This whitepaper is intended to provide scientific and educational information only and should not be considered medical advice. Brand manufacturers should consult with their counsel as to whether claims are properly substantiated and for appropriate structure function claims.

SUMMARY

Sensoril Ashwagandha is an adaptogen derived from a unique blend of both leaves and roots of the Withania somnifera plant, by a totally aqueous extraction process, to provide optimal efficacy and bioactive diversity. Supported by more than ten randomized, double-blind, placebo-controlled human clinical trials, Sensoril supports reducing everyday stress, cognition, cardiovascular, mental and joint health and enhancing sports performance. Sensoril has been the transparent and trusted leader in ashwagandha market with its efficacy and safety.

SENSORIL® HOLISTIC ASHWAGANDHA	
Patented Holistic Composition (Leaves & Roots)	✓
Standardized to 3 Bioactives	✓
Clinically Studied	✓
Aqueous Extract	✓
Non-GMO Project Verified	✓
Informed Choice Verified	✓
15 Year Safety Record	✓
Full Transparency	✓
Performance Benefits	✓
Organic, Vegan, GRAS Affirmed	✓

ABOUT NATREON

Natreon is a leader in nutritional ingredient innovation, quality and research. Trusted by manufacturers for over 20 years, Natreon's patented ingredients are derived from nature and founded on evidence-based Ayurveda. Committed to quality, its extracts are purified and standardized using proprietary process technology and controls that result in optimal levels of bioactive constituents. Natreon's ingredients have been tested in multiple clinical and safety studies to ensure safety, efficacy and authenticity. Natreon brings storied knowledge and expertise in botanical cultivation and extraction, and its ingredients are sustainably sourced through an integrated supply chain to ensure quality and potency. Natreon has its global headquarters in New Jersey and a state-of-the-art R&D facility in Kolkata, India. For more information, visit: https://natreoninc.com/.