

Adrenal SAP

Science-based nutrients for adrenal gland support

Stress is an unavoidable force to which humans are constantly exposed in both short-term bursts and over extended periods of time. The body's ability to withstand the damaging effects of stress is mediated primarily by the adrenal (aka suprarenal) glands: small, triangular glands located on top of the kidneys, that secrete hormones involved in blood-pressure regulation, reproduction, and the stress response. Excessive and prolonged mental and physical stress can lead to adrenal insufficiency and associated symptomatic manifestations including fatigue, immunosuppression, and impaired blood-sugar and blood-pressure control. **Adrenal SAP** is a combination of vitamins, minerals and adaptogenic herbs that support and strengthen the adrenal glands to improve adrenal function.

ACTIVE INGREDIENTS

Each non-GMO vegetable capsule contains:

	REGULAR	LICORICE-FREE
Vitamin C (ascorbic acid)	250 mg	250 mg
Vitamin B ₅ (calcium pantothenate)	50 mg	50 mg
Magnesium (from magnesium bisglycinate).	10 mg	19 mg
Vitamin B ₆ (pyridoxal-5'-phosphate)	25 mg	25 mg
Zinc (from zinc picolinate).	5 mg	5 mg
Schisandra (<i>Schizandra chinensis</i>) fruit extract, 9% schizandrins	25 mg	25 mg
Astragalus (<i>Astragalus membranaceus</i>) root extract, 3% astragalosides	25 mg	25 mg
Holy basil (<i>Ocimum tenuiflorum</i>) leaf extract	50 mg	50 mg
Panax ginseng (<i>Panax ginseng</i>) root extract, 20% ginsenosides	50 mg	50 mg
Siberian ginseng (<i>Eleutherococcus senticosus</i>) root extract, 0.8% eleutherosides.	5 mg	5 mg
Licorice (<i>Glycyrrhiza glabra</i>) root extract, 10% glycyrrhizin.	50 mg	—
Ashwagandha (<i>Withania somnifera</i>) root extract, 3.5% withanolides	50 mg	50 mg

Other ingredients: Microcrystalline cellulose, vegetable magnesium stearate and silicon dioxide in a capsule composed of vegetable carbohydrate gum and purified water.

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

Adrenal SAP contains 90 capsules per bottle.

DIRECTIONS FOR USE

Adults: 1 capsule two or three times daily. Take with food. If you are taking other medications, take this product a few hours before or after them.

INDICATIONS

Adrenal SAP can:

- Help promote adrenal function through the combination of its key nutritional and botanical components.
- Help improve energy levels and foster mental and physical performance.
- Be used to enhance memory and improve mood balance.
- Help promote immune function and increase the ability to withstand the effects of acute and chronic stress.

CAUTIONS AND WARNINGS

Adrenal SAP contains licorice (*Glycyrrhiza glabra*),^[1] therefore patients with hypertension should instead use our **Adrenal SAP Licorice-Free**.

If you are pregnant or breast-feeding, consult your healthcare practitioner before taking this product.

INCREASED BIOAVAILABILITY

The botanicals in **Adrenal SAP** are ethanol-extracted for standardized isolation of active constituents.

Adrenal SAP is supplied in a vegetable capsule for easy digestion.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Adrenal SAP** lot numbers have been tested by an ISO 17025-accredited third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP):
adding nutraceutical research
to achieve optimum health



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THE ADRENAL GLAND AND ITS ROLE IN THE BODY

The adrenal glands produce hormones involved in mediating the stress response (epinephrine, norepinephrine, and cortisol), immunity (cortisol), reproduction (including estrogen and testosterone), and blood pressure control (aldosterone).^[2] They are a key component of the hypothalamic-pituitary-adrenal (HPA) axis, a complex hormone feedback system between the brain and the adrenal glands that controls the stress response and regulates many body processes including digestion, the immune system, mood and emotions, sexuality, and energy storage and expenditure.^[3] The adrenal glands are also involved in the sympatho-adrenal axis, secreting acetylcholine in response to acute stressors to initiate the sympathetic "fight or flight response."

ADAPTOGENIC HERBS INCREASE THE BODY'S ABILITY TO WITHSTAND ACUTE AND CHRONIC STRESS

An adaptogen is defined as a substance that increases bodily resistance to noxious agents or factors, has a normalizing influence on a pathological state, and increases the ability of an organism to adapt to and avoid damage from environmental factors.^[3] The beneficial effects of multidose administration of adaptogens are mainly associated with their effects on the HPA axis via balancing the releases of adrenaline, corticosteroids, and nitric oxide.^[3] Conversely, a single dose can mediate the sympatho-adrenal system, providing a rapid response to control the acute reaction to a stressor by dampening the spike in catecholamines, neuropeptides, ATP, nitric oxide, and eicosanoids.^[3]

ADRENAL FATIGUE

Dysfunction of the HPA axis has been shown to produce clinical symptoms of profound fatigue, unrefreshing sleep, postexertional malaise, headaches, and impaired memory and concentration.^[4] A study demonstrated that chronic unpredictable stress (CUS) results in significant depletion of dopamine (DA), noradrenaline (NA), and 5-hydroxytryptophan (5-HTP) in the hippocampus, in contrast to the sharp increase of these monoamines that occurs when subjected to an acute stressor.^[5] The paradoxical decrease in monoamine level in CUS can partly be explained on the basis of increased stress sensitization and their preferential and higher utilization during severe stressful conditions,^[6] and supports the theory that long-term stress causes eventual "burnout" of the adrenal gland.

BOTANICAL AND NUTRITIONAL SUPPORT FOR ADRENAL FUNCTION

Siberian ginseng (*Eleutherococcus senticosus*)

Eleutherococcus has historically been used as a tonic during periods of recovery from surgery and convalescence, and recent research has demonstrated that it increases aerobic metabolism of tissues to facilitate tissue repair.^[6] A study of 50 volunteers of both sexes was conducted to examine the effects of an *Eleutherococcus* extract on immune function and physical fitness. After 30 days of supplementation, researchers documented an increased rate of blastic transformation of lymphocytes, greater maximal oxygen uptake ($VO_{2\max}$, an indicator of cardiorespiratory endurance), and reduced serum total cholesterol, LDL cholesterol, and triglyceride levels.^[7] Even a single dose of this herb results in increased mental performance and physical working capacity, without any of the side effects commonly associated with pharmacological stimulants including addiction, tolerance, abuse potential, disordered sleep, and rebound hypersomnolence.^[3]

Panax ginseng (*Panax quinquefolium*)

Panax species have had widespread use as a general tonic in Southern Asia for more than 5000 years, and are believed to promote health and longevity. Recent research shows that the ginsenosides in this herb are effective in normalizing the negative effects seen with chronic stress in mice: elevated plasma cortisol, increased levels of the proinflammatory cytokines IL2 and IL6, and depletion of noradrenaline, dopamine, and 5-hydroxytryptophan in the hippocampus.^[8]

Astragalus (*Astragalus membranaceus*)

Astragalus is a well-known herb in traditional Chinese medicine, and the saponins from this plant demonstrate significant lymphocyte proliferation and immunostimulatory activities.^[9] In a study on diabetic mice, the polysaccharides were shown to enhance the adaptive capacity of the hepatic endoplasmic reticulum, improving insulin sensitivity, and lowering blood glucose.^[9]

Ashwaghandha (*Withania somnifera*)

Ashwaghandha is an adaptogen that has been used in Ayurvedic practice for more than 2500 years.^[10] One of the main detrimental effects of chronic stress is immunosuppression.^[11] *Withania* administered orally to chronically stressed mice significantly reversed T-cell depletion and increased the expression of T_{H1} cytokines.^[11] In a rat model of long-term stress, an extract of this herb attenuated symptoms of glucose intolerance, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression, and mental depression that were seen in control animals.^[10]

Holy Basil (*Ocimum sanctum*)

Holy basil is another important herb in Ayurvedic medicine, and research has shown that it possesses antioxidant, antimicrobial, anti-inflammatory, anthelmintic and radioprotective activities.^[12] It has also been shown to lower serum cortisol concentrations and diminish the negative effects of noise stress in a rat model.^[13]

Licorice (*Glycyrrhiza glabra*)

Licorice has been valued for its antimicrobial, anti-inflammatory, lipid-lowering, and antitumorogenic effects. Seven-day supplementation at a dose of 150 mg/kg in mice was shown to enhance memory and learning capacity and significantly reverse pharmacologically induced amnesia.^[14] This herb has also demonstrated antidepressant effects in mice, comparable to treatment with imipramine (15 mg/kg i.p.) and fluoxetine (20 mg/kg i.p.) via an increase in norepinephrine and dopamine.^[15] In addition, *Glycyrrhiza* acts on the adrenal-pituitary-kidney axis to stimulate the release of renin and raise blood pressure.^[16]

Schizandra (*Schizandra chinensis*)

Schizandra is an important herb in traditional Chinese medicine, and has been used as a kidney tonifier to relieve mental strain.^[17] In a double-blind, placebo-controlled study of athletes, an extract of schizandra supplemented prior to heavy physical exercise significantly increased performance, and prevented the rise in salivary nitric oxide and cortisol that was observed in the placebo group.^[18] This herb has also been shown to be hepatoprotective in mice via enhancement of mitochondrial glutathione status and induction of heat shock proteins which protects against TNF- α -induced apoptosis of liver cells.^[19]

Trace Minerals: Magnesium and Zinc

Magnesium is an especially important cofactor in energy production, and has important roles in pH balance and body temperature homeostasis.^[20] Supplementation of this mineral in pigs improves ability to handle long-term stress.^[21]

Zinc is highly concentrated in the adrenal glands and has structural, enzymatic and regulatory actions. It is required for adrenal hormone production and is depleted during periods of stress.^[22]

B Vitamins

Vitamin B₆, known as the "antistress vitamin," plays a role in the production of adrenal gland hormones and is required for their proper functioning.^[20]

Vitamin B₉ is involved in more bodily functions than almost any other single nutrient. It is required for normal nervous system function, in the synthesis of RNA and DNA, and aids in maintaining sodium and potassium balance.^[18]

Vitamin C (Ascorbic Acid)

Vitamin C is highly concentrated in the adrenal gland, where it functions as an antioxidant.^[23] It is released in response to adrenocorticotrophic hormone (ACTH), which is then followed by a decrease in adrenal cholesterol levels, suggesting the role of ascorbate in steroidogenesis.^[24] It has been elucidated that vitamin C acts as an auxiliary electron donor in the aldosterone formation system.^[23] In a swine model, vitamin C supplementation improved coping ability in response to chronic stress.^[21]

REFERENCES

1. Sigurjonsdottir, H.A., et al. "Is blood pressure commonly raised by moderate consumption of liquorice?." *Journal of Human Hypertension* Vol. 9, No. 5 (1995): 345-348.
2. Meletis, C.D. and W.A. Centrone. "Adrenal fatigue: Enhancing quality of life for patients with a functional disorder." *Alternative and Complementary Therapies* Vol. 8, No. 5 (2002): 267-272.
3. Panossian, A. and H. Wagner. "Stimulating effect of adaptogens: an overview with particular reference to their efficacy following single dose administration." *Phytotherapy Research* Vol. 19, No. 10 (2005): 819-838.
4. Van Den Eede, F., et al. "Hypothalamic-pituitary-adrenal axis function in chronic fatigue syndrome." *Neuropsychobiology* Vol. 55, No. 2 (2007): 112-120.
5. Rasheed, N., et al. "Involvement of monoamines and proinflammatory cytokines in mediating the anti-stress effects of *Panax quinquefolium*." *Journal of Ethnopharmacology* Vol. 117, No. 2 (2008): 257-262.
6. Bleakney, T.L. "Deconstructing an adaptogen: *Eleutherococcus senticosus*." *Holistic Nursing Practice* Vol. 22, No. 4 (2008): 220-224.
7. Szolomicki, J., et al. "The influence of active components of *Eleutherococcus senticosus* on cellular defence and physical fitness in man." *Phytotherapy Research* Vol. 14, No. 1 (2000): 30-35.
8. Ragupathi, G., et al. "Evaluation of widely consumed botanicals as immunological adjuvants." *Vaccine* Vol. 26, No. 37 (2008): 4860-4865.
9. Mao, X., et al. "Astragalus polysaccharide reduces hepatic endoplasmic reticulum stress and restores glucose homeostasis in a diabetic KKAY mouse model." *Acta Pharmacologica Sinica* Vol. 28, No. 12 (2007): 1947-1956.
10. Bhattacharya, S. and A. Muruganandam. "Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress." *Pharmacology, Biochemistry, and Behavior* Vol. 75, No. 3 (2003): 547-555.
11. Khan, B., et al. "Augmentation and proliferation of T lymphocytes and Th-1 cytokines by *Withania somnifera* in stressed mice." *International Immunopharmacology* Vol. 6, No. 9 (2006): 1394-1403.
12. Gupta, P., et al. "Constituents of *Ocimum sanctum* with antistress activity." *Journal of Natural Products* Vol. 70, No. 9 (2007): 1410-1416.
13. Cohen, M.M. "Tulsi—*Ocimum sanctum*: A herb for all reasons." *Journal of Ayurveda and Integrative Medicine* Vol. 5, No. 4 (2014): 251-259.
14. Dhingra, D., M. Parle, and S. Kulkarni. "Memory enhancing activity of *Glycyrrhiza glabra* in mice." *Journal of Ethnopharmacology* Vol. 91, No. 2-3 (2004): 361-365.
15. Dhingra, D. and A. Sharma. "Antidepressant-like activity of *Glycyrrhiza glabra* L. in mouse models of immobility tests." *Progress in Neuro-Psychopharmacol & Biological Psychiatry* Vol. 30, No. 3 (2006): 449-454.
16. Al-Qarawi, A.A., et al. "Licorice (*Glycyrrhiza glabra*) and the adrenal-kidney-pituitary axis in rats." *Food Chemical Toxicology* Vol. 40, No. 10 (2002): 1525-1527.
17. Lai, Q., et al. "Pharmacokinetic and nephroprotective benefits of using *Schizandra chinensis* extracts in a cyclosporine A-based immune-suppressive regime." *Drug Design, Development and Therapy* Vol. 9 (2015): 4997-5018.
18. Panossian, A. and G. Wikman. "Pharmacology of *Schizandra chinensis* Bail: An overview of Russian research and uses in medicine." *Journal of Ethnopharmacology* Vol. 118, No. 2 (2008): 183-212.
19. Tang, M., P. Chiu, and K. Ko. "Hepatoprotective action of schizandrin B against carbon tetrachloride toxicity was mediated by both enhancement of mitochondrial glutathione status and induction of heat shock proteins in mice." *Biofactors* Vol. 19, No. 1-2 (2003): 33-42.
20. Balch, P. *Prescription for nutritional healing*, Fourth Ed. New York, NY, USA: Penguin Group, 2006.
21. Peeters, E., et al. "Influence of supplemental magnesium, tryptophan, vitamin C, and vitamin E on stress responses of pigs to vibration." *Journal of Animal Science* Vol. 83, No. 7 (2005): 1568-1580.
22. King, J.C. and C.L. Keen. "Zinc" in *Modern Nutrition in Health and Disease*, Ninth Ed. Shils, M.E., J.A. Olson, M. Shike, and A.C. Ross, eds. Baltimore, MD, USA: Williams & Wilkins, (1999): pp. 223-240.
23. Mitani, F., et al. "Ascorbate stimulates monoxygenase-dependent steroidogenesis in adrenal zona glomerulosa." *Biochemical and Biophysical Research Communications* Vol. 338, No. 1 (2005): 483-490.
24. Padayatty, S., et al. "Human adrenal glands secrete vitamin C in response to adrenocorticotrophic hormone." *The American Journal of Clinical Nutrition* Vol. 86, No. 1 (2007): 145-149.

INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc) assessed and have been rated using a 5 star ★ rating classification.

Ingredient	Supporting evidence and study outcomes	Study designs; n (number of participants); dose and duration of study	Outcome measures	Safety	Evidence quality rating
STRESS: Dosage Recommendation - 6 Capsules/day for About 2 Months. Additional 1 Capsule/day of Ashwagandha SAP Recommended.					
Magnesium + B6 ¹	Reduction in stress with magnesium, magnesium + B6 proved to be better for higher stress levels.	Randomized, single-blind clinical trial (n=264), dose 300 mg elemental magnesium + 30 mg vitamin B6 for 8 weeks	Depression anxiety stress scale-42, stress subscale score, serum magnesium concentration.	Mild diarrhea, 1 participant had severe gastroenteritis.	★★★
Ashwagandha ^{2,3,4}	Improvement in stress, food cravings and serum cortisol, body weight, body mass index. Reduction in anxiety, depression, cortisol and DHEA-S levels. Improved mental health, concentration, social functioning, vitality, overall quality of life	3 Randomized, double-blind, placebo-controlled studies (n=187), dose 600 mg/day (extract containing 5% withanolides) for 8-12 weeks or 240 mg/day for 60 days	Stress Scale, Food Cravings Questionnaire, Oxford Happiness Questionnaire, serum cortisol, body weight, body mass index. Hamilton Anxiety Rating Scale, Depression scale, Neck Anxiety Inventory, Fatigue Symptom Inventory, dehydroepiandrosterone-sulphate (DHEA-S), testosterone	No adverse events	★★★★
MENTAL HEALTH, MEMORY, AND COGNITION: Dosage Recommendation - 3-4 Capsules/day for About 2 Months. Additional 1 Capsule/day of Ashwagandha SAP, Siberian Ginseng Supplementation Recommended					
Ashwagandha ⁵	Improved immediate and general memory, executive function, sustained attention, information processing speed	Randomized, double-blind, placebo-controlled study (n=50); 600 mg/day (extract containing 5% withanolides) for 8 weeks	Wechsler Memory Scale III, Erikson Flanker task, Wisconsin Card Sort test, Trial-Making test part A, Mackworth Clock test.	No adverse events	★★★★
Licorice ⁶	Improved daily activities, tremors, motor and rigidity scores.	Randomized, double-blind, placebo-controlled study (n=39 Parkinson's disease patients); 136 mg/day for 6 months (with 8.9% glycyrrhizin)	Parkinson's rating scale, blood pressure, glucose, sodium and potassium levels, quality of life, dizziness.	Mild adverse effects of nausea, diarrhea and urticaria in 3 patients	★★★★
Siberian ginseng ⁷	Improvement of social functioning and some aspects of mental health at 4 weeks.	Randomized, double-blind, placebo-controlled trial (n=20); dose 300 mg/day for 8 weeks (non-standardized extract)	Evaluation of health-related quality of life aspects	No adverse events	★★★★
Panax ginseng ^{8,9}	Increase in mental Numerical Rating Scale scores, Visual Analog Scale scores, reduced MDA and reactive oxygen species, anti-fatigue effects. Improvement in cognition of Alzheimer patients with 4.5 g dose.	Randomized, double-blind, placebo-controlled trial (n=90); dose 1-2 g/day for 4 weeks- mental score. Open label study (n=97); dose 4.5 g/day for 12 weeks (low potency extract, ~0.2% ginsenosides, second study 8.19% ginsenosides)	Fatigue severity - Numerical Rating Scale, Visual Analogue Scale, reactive oxygen species, malondialdehyde (MDA), glutathione, glutathione reductase activity. Cognitive performance and Alzheimer disease assessment.	Rash and pruritis in 1 subject. No other adverse events.	★★★★
IMMUNITY: Dosage Recommendation - 6 Capsules/day. Additional Astragalus SAP and Licorice Supplementation Recommended.					
Zinc ¹⁰	Reduction in C-reactive protein (CRP), hs-CRP, neutrophils. Increase in CD3 and CD4 levels.	35 randomized controlled trials (n=1995); dose >50 mg/day for >8 weeks optimal for increasing CD3 level especially. <15 mg/day does not have an effect on immunity	Biomarkers of immunity	No adverse events	★★★★★
Licorice ¹¹	Increase in <i>H. pylori</i> eradication with licorice treatment	1 randomized, double-blind, placebo-controlled clinical trial (n=120) dose 760 mg/day for 2 weeks with conventional <i>H. pylori</i> treatment (non-standardized extract)	<i>H. pylori</i> eradication assessment	No adverse events	★★★★
Holy basil ¹²	Reduction in interferon-γ, interleukin-4, and percentage of T-helper cells and NK-cells.	Randomized, double-blind, placebo-controlled crossover trial (n=22); dose 300 mg/day for 4 weeks (non-standardized extract)	Levels of Th1 and Th2 cytokines (interferon-γ and interleukin-4), T-helper cells, T-cytotoxic cells, B-cells, NK-cells	No adverse events	★★★★
Astragalus ^{13,14}	Restoration of immunological balance in stress induced in athletes. Reduction in IL-8, IL-1β, IL-32 and TNF-α. Improved expiratory rate and force.	1 randomized, double-blind, placebo-controlled trial (n=18 athletes); dose 1 g/day for 6 weeks, 1 randomized trial (n=82 cardiac patients) dose 30 mg/day for 14 days (0.5% 3-hydroxy 7-methoxy isoflavonoids, second study non-standardized extract)	Rowing performance, interleukin and interferon biomarkers, lymphocytes and killer cell levels. Pulmonary function, cytokine and immunocyte levels.	Mild diarrhea and abdominal distension in 2 patients.	★★★★
Physical Performance: Dosage Recommendation - 6 Capsules/day. Additional Ashwagandha SAP Recommended.					
Vitamin C ¹⁵	Reduced lipid peroxidation, interleukin-6 post exercise	18 randomized controlled trials (n=313); dose >500 mg/day. Acute effect, 40 min post ingestion observed, long-term supplementation did not change outcome compared to acute.	Oxidative stress and inflammation markers.	No adverse events	★★★★★

Vitamin C ¹⁶	Lowering of blood pressure, increase in plasma ascorbate and plasma nitric oxide concentration. Reduction in MDA and F ₂ -isoprostanes	Randomized, placebo-controlled crossover study (n=24 patients with type-2 diabetes); dose 1000 mg/day for 6 weeks	Blood pressure, MDA, F ₂ -isoprostanes and nitric oxide levels	No adverse events	★★★★
Magnesium + zinc ¹⁷	Reduction in fasting plasma glucose, insulin, C-reactive protein increase in HDL, total nitrite, total antioxidant capacity. Reduced symptoms of depression and anxiety.	Randomized, double-blind, placebo-controlled trial (n=60 patients of type-2 diabetes and coronary heart disease); dose 250 mg/day magnesium oxide + 30 mg elemental zinc, duration 12 weeks	Glycemic control, serum lipids, biomarkers of oxidative stress and inflammation.	No adverse events	★★★★★
Magnesium ¹⁸	Higher BMI and CRP with low dietary magnesium. Magnesium supplementation-decreased CRP	Randomized, placebo-controlled trial (n=100); dose 320 mg magnesium as magnesium citrate for 7 weeks.	BMI, diet, blood and urine biochemical markers, sleep quality.	No adverse events.	★★★
Zinc ¹⁹	Reduced MDA levels, increased serum total antioxidant capacity, glutathione levels	10 randomized, double-blind, placebo-controlled trials (n=721); dose avg. of 7 studies - 54 mg/day elemental zinc, avg. 15 weeks	Biomarkers of oxidative stress in oxidative stress-related diseases.	No significant adverse events reported	★★★★★
Ashwagandha ²⁰	Increased muscle strength and size, reduced exercise-induced muscle damage, increased testosterone, decreased body fat percentage	Randomized, placebo controlled, double-blind (n=57); 600 mg/day (extract containing 5% withanolides) for 8 weeks	Muscle strength (1 repetition maximum), testosterone serum levels, muscle size, body fat percentage, muscle recovery.	No adverse events	★★★★
Siberian ginseng ²¹	Reduced LDL and LDL/HDL ratio, DNA damage.	Randomized trial (n=40); dose 3000 mg/day for 6 months. (non-standardized extract)	Total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, MDA, lymphocyte DNA damage	No adverse events	★★★
Siberian ginseng ²²	Reduction in edema of the lower limbs 2-4 hours after treatment.	Randomized, crossover trial (n=50); dose 100 mg/day, acute study, effect observed after 6 hours. (standardization information not available)	Edema in lower limbs (by checking volume of lower limbs at 0,2,4,6 hours after ingestion).	No adverse events	★★★
Siberian ginseng ²³	Improved endurance time, heart rate. Reduced glucose and plasma-free fatty acids.	Randomized, double-blind, placebo controlled and crossover design (n=9); dose 800 mg/day for 8 weeks (standardization information not available)	Cycling - Endurance time, heart rate, glucose, plasma-free fatty acids.	No adverse events	★★★
Panax ginseng ²⁴	Improvement in exercise endurance	5 randomized controlled trials (n=90); dose about 200 mg of panax ginseng with 5-10 mg of ginsenosides/day (1 trial administered 1350 mg/day of panax ginseng extract). Duration- 21-30 days, or acute use.	Exercise endurance, acute and over a period of 1 month.	No adverse events	★★★★
Schizandra ^{25,26}	Increase in muscle strength, decrease in lactate levels. In obese women - reduction in waist circumference, fat mass, glucose, triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), modified gut microbiota.	2 randomized, double-blind, placebo-controlled trial (n=45 adult women); dose 1000 mg/day for 12 weeks, (n=28 obese women) dose 6.7 g/day for 12 weeks (~0.5% of schizandrins, second study used non-standardized extract)	Quadriceps muscle strength, physical function, lactate. Blood, fecal sampling, body weight, fat mass, glucose, lipid biomarkers, AST, ALT, gut microbiota.	No adverse events	★★★★

★**Safety data: Daily dose recommended by Health Canada (for adults):**

Vitamin C - 2000 mg

Vitamin B5 - 500 mg

Magnesium - 500 mg

Vitamin B6 - 100 mg (dose exceeded with 5 capsules, please observe for lack of muscle coordination (ataxia), skin lesions, photosensitivity, and gastrointestinal symptoms.

Zinc - 25 mg (for zinc from zinc picolinate source, do not use if you are pregnant or breastfeeding, dose should not exceed 25 mg/day. Zinc supplementation can cause copper deficiency)

REFERENCES

- Pouteau E, Kabir-Ahmadi M, Noah L, Mazur A, Dye L, Hellhammer J, Pickering G, Dubray C. Superiority of magnesium and vitamin B6 over magnesium alone on severe stress in healthy adults with low magnesemia: A randomized, single-blind clinical trial. *PLoS One*. 2018 Dec 18;13(12):e0208454
- Choudhary D, et al. Body weight management in adults under chronic stress through treatment with ashwagandha root extract: a double blind, randomized, placebo controlled trial. *J Evid Based Complementary Altern Med*. 2017 Jan;22(1):96-106.
- Lopresti AL, Smith SJ, Malvi H, Kodgule R. An investigation into the stress-relieving and pharmacological actions of an ashwagandha (*Withania somnifera*) extract: A randomized, double-blind, placebo-controlled study. *Medicine (Baltimore)*. 2019 Sep;98(37):e17186.
- Cooley K, et al. Naturopathic care for anxiety: a randomized controlled trial ISRCTN78958974. *PLoS One*. 2009 Aug;4(8):e6628.
- Choudhary D, Bhattacharya S, Bose S. Efficacy and Safety of Ashwagandha (*Withania somnifera* (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions. *J Diet Suppl*. 2017 Nov 2;14(6):599-612.
- Petramfar P, Hajari F, Yousefi G, Azadi S, Hamed A. Efficacy of oral administration of licorice as an adjunct therapy on improving the symptoms of patients with Parkinson's disease. A randomized double blinded clinical trial. *J Ethnopharmacol*. 2020 Jan 30;247:112226.
- Cicero AF, Derosa G, Brilante R, Bernardi R, Nascetti S, Gaddi A. Effects of Siberian ginseng (*Eleutherococcus senticosus* maxim.) on elderly quality of life: a randomized clinical trial. *Arch Gerontol Geriatr Suppl*. 2004;9:69-73.
- Kim HG, Cho JH, Yoo SR, Lee JS, Han JM, Lee NH, Ahn YC, Son CG. Antifatigue effects of Panax ginseng CA. Meyer: a randomised, double-blind, placebo-controlled trial. *PLoS One*. 2013 Apr 17;8(4):e61271.
- Lee ST, Chu K, Sim JY, Heo JH, Kim M. Panax ginseng enhances cognitive performance in Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2008 Jul-Sep;22(3):222-6.
- Jafari A, Noormohammadi Z, Askari M, Daneshzad E. Zinc supplementation and immune factors in adults: a systematic review and meta-analysis of randomized clinical trials. *Crit Rev Food Sci Nutr*. 2022;62(11):3023-3041.
- Hajjaghahmohammadi AA, Zargar A, Oveis S, Samimi R, Reisian S. To evaluate of the effect of adding licorice to the standard treatment regimen of *Helicobacter pylori*. *Braz J Infect Dis*. 2016 Nov-Dec;20(6):534-538.
- Mondal S, Varma S, Bamola VD, Naik SN, Mirdha BR, Padhi MM, Mehta N, Mahapatra SC. Double-blinded randomized controlled trial for immunomodulatory effects of Tulsi (*Ocimum sanctum* Linn.) leaf extract on healthy volunteers. *J Ethnopharmacol*. 2011 Jul 14;136(3):452-6.
- Lator E, Arlet J, Lator EE, Juszkiewicz A, Luczkowska K, Marcinkiewicz A, Basta P, Trzeciak J, Machaliński B, Skarpańska-Stejneger A. Standardized astragalus extract for attenuation of the immunosuppression induced by strenuous physical exercise: randomized controlled trial. *J Int Soc Sports Nutr*. 2021 Jul 16;18(1):57.
- Jiang D, Wang X, Su Q, Jiang S, Yuan F, Zhang C, Gong F, Dong Q, Shi J, Chen B. Milkvech root improves immune function in patients with acute exacerbation of COPD. *Biomed Mater Eng*. 2015;26 Suppl 1:S2113-21.
- Righi NC, Schuch FB, De Nardi AT, Pippi CM, de Almeida Righi G, Puntel GO, da Silva AMV, Signori LU. Effects of vitamin C on oxidative stress, inflammation, muscle soreness, and strength following acute exercise: meta-analyses of randomized clinical trials. *Eur J Nutr*. 2020 Oct;59(7):2827-2839.
- Boonthongkaew C, Tong-Un T, Kanpetta Y, Chaungchot N, Leelayuwat C, Leelayuwat N. Vitamin C supplementation improves blood pressure and oxidative stress after acute exercise in patients with poorly controlled type 2 diabetes mellitus: A randomized, placebo-controlled, cross-over study. *Chin J Physiol*. 2021 Jan-Feb;64(1):16-23.
- Hamedifard Z, Farrokhan A, Reiner Z, Bahmani F, Asemi Z, Ghotbi M, Taghizadeh M. The effects of combined magnesium and zinc supplementation on metabolic status in patients with type 2 diabetes mellitus and coronary heart disease. *Lipids Health Dis*. 2020 May 28;19(1):112.
- Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. *Magn Res*. 2010 Dec;23(4):158-68.
- Mousavi SM, Hajshafiee M, Clark CCT, Borges do Nascimento IJ, Milajerd A, Amini MR, Esmailzadeh A. Clinical effectiveness of zinc supplementation on the biomarkers of oxidative stress: A systematic review and meta-analysis of randomized controlled trials. *Pharmacol Res*. 2020 Nov;161:105166.
- Wakhede S, et al. Examining the effect of *Withania somnifera* supplementation on muscle strength and recovery: a randomized controlled trial. *J Int Soc Sports Nutr*. 2015 Nov;25:12-43.
- Lee YJ, Chung HY, Kwak HK, Yoon S. The effects of A. *senticosus* supplementation on serum lipid profiles, biomarkers of oxidative stress, and lymphocyte DNA damage in postmenopausal women. *Biochem Biophys Res Commun*. 2008 Oct 10;375(1):44-8.
- Fukada K, Kajiya-Sawane M, Matsumoto Y, Hasegawa T, Fukaya Y, Kajiya K. Antiedema effects of Siberian ginseng in humans and its molecular mechanism of lymphatic vascular function in vitro. *Nutr Res*. 2016 Jul;36(7):689-95.
- Kuo J, Chen KW, Cheng IS, Tsai PH, Lu YJ, Lee NY. The effect of eight weeks of supplementation with *Eleutherococcus senticosus* on endurance capacity and metabolism in human. *Chin J Physiol*. 2010 Apr 30;53(2):105-11.
- Ikeuchi S, Minamide M, Nakamura T, Konishi M, Kamioka H. Exploratory Systematic Review and Meta-Analysis of *Panax* Genus Plant Ingestion Evaluation in Exercise Endurance. *Nutrients*. 2022 Mar 11;14(6):1185.
- Park J, Han S, Park H. Effect of *Schizandra chinensis* Extract Supplementation on Quadriceps Muscle Strength and Fatigue in Adult Women: A Randomized, Double-Blind, Placebo-Controlled Trial. *Int J Environ Res Public Health*. 2020 Apr 4;17(7):2475.
- Song MY, Wang JH, Eom T, Kim H. *Schizandra chinensis* fruit modulates the gut microbiota composition in association with metabolic markers in obese women: a randomized, double-blind placebo-controlled study. *Nutr Res*. 2015 Aug;35(8):655-63.