

# 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.\*

## SUPPLEMENT FACTS

Serving Size: 1 Capsule

	Amount Per Serving REGULAR	Amount Per Serving LICORICE-FREE	Servings: 90 % Daily Value†
Vitamin C (ascorbic acid)	250 mg	250 mg	278%
Vitamin B <sub>6</sub> (as pyridoxal-5'-phosphate)	25 mg	25 mg	1471%
Pantothenic acid (from calcium pantothenate)	50 mg	50 mg	1000%
Magnesium (from magnesium bisglycinate)	10 mg	19 mg	3% / 5%
Zinc (from zinc picolinate)	5 mg	5 mg	45%
Ashwagandha ( <i>Withania somnifera</i> ) root extract, 3.5% withanolides	50 mg	50 mg	**
Holy basil ( <i>Ocimum tenuiflorum</i> ) leaf extract, 10% ursolic acids	50 mg	50 mg	**
Licorice ( <i>Glycyrrhiza glabra</i> ) root extract, 10% glycyrrhizin	50 mg	—	**
Ginseng ( <i>Panax ginseng</i> ) root and leaf extract, 20% ginsenosides	50 mg	50 mg	**
Astragalus ( <i>Astragalus membranaceus</i> ) root extract, 3% astragalosides	25 mg	25 mg	**
Schisandra ( <i>Schizandra chinensis</i> ) fruit extract, 9% schizandrins	25 mg	25 mg	**
Siberian ginseng ( <i>Eleutherococcus senticosus</i> ) root extract, 0.8% eleutherosides	5 mg	5 mg	

† Percent Daily Values are based on a 2,000-calorie diet.

\*\*Daily Value not established

**Other ingredients:** Vegetable magnesium stearate, dextrin, maltodextrin, and silicon dioxide in a vegetable capsule composed of vegetable hypromellose and purified water.

**This product is non-GMO and vegan friendly.**

**Contains no:** Gluten, soy, wheat, corn protein, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

**Adrenal SAP** contains 90 capsules per bottle.

Dextrin and maltodextrin are present only in Adrenal SAP

## 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.<sup>[1]</sup>

## INDICATIONS

**Adrenal SAP:**

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

## 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.

## CAUTIONS AND WARNINGS

**WARNING:** Adrenal SAP contains licorice (*Glycyrrhiza glabra*), therefore patients with hypertension should instead use our Adrenal SAP Licorice-Free.

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

## 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.

\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Scientific Advisory Panel (SAP):  
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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).<sup>[2]</sup> 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.<sup>[3]</sup> 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.<sup>[3]</sup> 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.<sup>[3]</sup> 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.<sup>[3]</sup>

### 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.<sup>[4]</sup> 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.<sup>[5]</sup> 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,<sup>[6]</sup> 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.<sup>[6]</sup> 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 ( $\text{VO}_{2\text{max}}$ , an indicator of cardiorespiratory endurance), and reduced serum total cholesterol, LDL cholesterol, and triglyceride levels.<sup>[7]</sup> 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.<sup>[3]</sup>

#### 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.<sup>[8]</sup>

#### 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.<sup>[9]</sup> 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.<sup>[9]</sup>

#### Ashwaghandha (*Withania somnifera*)

Ashwaghandha is an adaptogen that has been used in Ayurvedic practice for more than 2500 years.<sup>[10]</sup> One of the main detrimental effects of chronic stress is immunosuppression.<sup>[11]</sup> *Withania* administered orally to chronically stressed mice significantly reversed T-cell depletion and increased the expression of  $T_H1$  cytokines.<sup>[11]</sup> 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.<sup>[10]</sup>

#### 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.<sup>[12]</sup> It has also been shown to lower serum cortisol concentrations and diminish the negative effects of noise stress in a rat model.<sup>[13]</sup>

#### Licorice (*Glycyrrhiza glabra*)

Licorice has been valued for its antimicrobial, anti-inflammatory, lipid-lowering, and antiulcerogenic 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.<sup>[14]</sup> 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.<sup>[15]</sup> In addition, *Glycyrrhiza* acts on the adrenal-pituitary-kidney axis to stimulate the release of renin and raise blood pressure.<sup>[16]</sup>

#### Schizandra (*Schizandra chinensis*)

Schizandra is an important herb in traditional Chinese medicine, and has been used as a kidney tonifier to relieve mental strain.<sup>[17]</sup> 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.<sup>[18]</sup> 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- $\alpha$ -induced apoptosis of liver cells.<sup>[19]</sup>

#### 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.<sup>[20]</sup> Supplementation of this mineral in pigs improves ability to handle long-term stress.<sup>[21]</sup>

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.<sup>[22]</sup>

#### B Vitamins

Vitamin B<sub>6</sub>, known as the “antistress vitamin,” plays a role in the production of adrenal gland hormones and is required for their proper functioning.<sup>[20]</sup>

Vitamin B<sub>9</sub> 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.<sup>[18]</sup>

#### Vitamin C (Ascorbic Acid)

Vitamin C is highly concentrated in the adrenal gland, where it functions as an antioxidant.<sup>[23]</sup> 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.<sup>[24]</sup> It has been elucidated that vitamin C acts as an auxiliary electron donor in the aldosterone formation system.<sup>[23]</sup> In a swine model, vitamin C supplementation improved coping ability in response to chronic stress.<sup>[21]</sup>

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## 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.

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Ingredient	Supporting evidence and study outcomes	Study designs; n (number of participants); dose and duration of study	Outcome measures	Safety	Evidence quality rating
<b>STRESS: Dosage Recommendation - 6 Capsules/day for About 2 Months. Additional 1 Capsule/day of Ashwagandha SAP Recommended.</b>					
Magnesium + B6 <sup>1</sup>	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 <sup>2,3,4</sup>	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	★★★★
<b>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</b>					
Ashwagandha <sup>5</sup>	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 <sup>6</sup>	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 <sup>7</sup>	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 <sup>8,9</sup>	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	★★★★
<b>IMMUNITY: Dosage Recommendation - 6 Capsules/day. Additional Astragalus SAP and Licorice Supplementation Recommended.</b>					
Zinc <sup>10</sup>	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 <sup>11</sup>	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 <sup>12</sup>	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 <sup>13,14</sup>	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.	★★★★
<b>Physical Performance: Dosage Recommendation - 6 Capsules/day. Additional Ashwagandha SAP Recommended.</b>					
Vitamin C <sup>15</sup>	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 <sup>16</sup>	Lowering of blood pressure, increase in plasma ascorbate and plasma nitric oxide concentration. Reduction in MDA and F <sub>2</sub> isoprostanes	Randomized, placebo-controlled crossover study (n=24 patients with type-2 diabetes); dose 1000 mg/day for 6 weeks	Blood pressure, MDA, F <sub>2</sub> isoprostanes and nitric oxide levels	No adverse events	★★★★
Magnesium + zinc <sup>17</sup>	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 <sup>18</sup>	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 <sup>19</sup>	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 <sup>20</sup>	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 <sup>21</sup>	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 <sup>22</sup>	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 <sup>23</sup>	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 <sup>24</sup>	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 <sup>25,26</sup>	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)**

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