

# EndoAxis

## Formula 19

### EXHAUSTED PHASE

Adaptogenic blend for adrenal support.

### AT A GLANCE

Chronic stress and adrenal dysfunction are prevalent issues in today's fast-paced society, leading to a range of health problems, including anxiety, depression, and fatigue.

Adrenal dysfunction can manifest in several stages, depending on the underlying cause and severity of the condition. In a healthy individual, our hypothalamus will generate CRH in response to a stress signal. CRH triggers our pituitary to generate ACTH. ACTH acts as a “knock” on the adrenal glands, triggering production within the adrenal cortex to produce DHEA (from the zona reticularis), Cortisol (from the zona fasciculata) and Aldosterone (from the zona glomerulosa). ACTH also triggers production of Norepinephrine from the adrenal medulla.

Cortisol metabolism reflects the total daily tissue exposure to, and clearance of, free cortisol over the collection window. This formulation targets low overall cortisol production, confirmed by truly low free and metabolized cortisol output.

Recall, true adrenal insufficiency, a condition called Addison's Disease, is quite rare, affecting about 1 in 100,000 people. However, with chronic stress over time, it has been demonstrated that the hypothalamus will start to decrease CRH pulsations, reducing ACTH activity, and subsequently lowering cortisol production when stress is experienced.[1] This is a more common phenomenon, and can impact overall health and vitality. This formulation utilizes herbs and minerals that target overall adrenal health, optimize the HPA stress response at the level of the hypothalamic-pituitary axis, and restore mitochondrial activity to support production of cortisol and an appropriate response to stress.

### Meet Optimize

Products blended to support alignment to our HPA axis. Optimizing our circadian activity and adrenal balance.



Scan to view all formulas.



### KEY BENEFITS



Focused on restoring HPA communication and a healthy stress response



Herbs targeting cortisol production and energy response in the body



Nutrients formulated to help optimize mitochondrial activity and energy expenditure

## FORMULA ANALYSIS

### *Schisandra chinensis*

*Schisandra sinensis* contains a rich array of phytochemicals, including lignans, schisandrins and deoxyschisandrin compounds. These bioactive constituents contribute to the plant's adaptogenic and health-promoting properties. Schisandra modulates the hypothalamuspituitary-adrenal (HPA) axis, the primary stress-response system in the body.[2] Additionally, its antioxidant properties may protect against the detrimental effects of chronic stress and oxidative damage. Furthermore, Schisandra's ability to enhance mitochondrial function may contribute to improved energy levels and overall vitality. Several clinical studies have explored the effects of Schisandra sinensis on stress reduction and adrenal health. These studies have demonstrated promising results, including improvements in stress resilience, reduced cortisol levels, and enhanced physical and mental performance.[3]

### *Glycyrrhiza glabra*

*Glycyrrhiza glabra* (licorice) is used classically as an adrenal adaptogen targeting free cortisol in circulation. Licorice has been investigated for its ability to modulate cortisol levels through several mechanisms including inhibition of 11 $\beta$ -hydroxysteroid dehydrogenase type 2 (11 $\beta$ -HSD2). This enzyme converts cortisol to its inactive form, cortisone, in specific tissues. Glycyrrhiza glabra compounds, particularly glycyrrhetic acid, inhibit 11 $\beta$ -HSD2 activity, leading to increased cortisol levels maintained in free circulation[4]. Licorice also demonstrates several anti-inflammatory and antioxidant properties, including inhibition of pro-inflammatory cytokines, such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6, as well as inhibition of the NF- $\kappa$ B pathway[5], a central regulator of inflammatory responses. Licorice contains flavonoids and polyphenols that possess antioxidant properties[6], helping to reduce oxidative stress and inflammation that can be drivers of elevated cortisol metabolism.

### Ubiquinol

Ubiquinol plays a crucial role in supporting adrenal health and stress management. Its antioxidant activity and involvement in the electron transport chain contribute to mitochondrial health during times of stress. It is an essential component of ATP production through the respiratory chain in the mitochondria, a function that is particularly important during times of stress, when energy demands are high.[7]

### Carnitine blend

Carnitine plays a pivotal role in mitochondrial function by facilitating the transport of long-chain fatty acids into the mitochondria for  $\beta$ -oxidation. This process is essential for energy production, making carnitine a key player in maintaining mitochondrial health, while acetyl-L-carnitine has been shown to enhance the synthesis of acetyl-CoA, a key molecule in energy production.[8] The combination of L-carnitine with acetyl-L-carnitine may improve adrenal health and stress response through their effects on the hypothalamic-pituitary-adrenal (HPA) axis. A study by Vermeulen et al. found that supplementation with L-carnitine improved HPA axis function, specifically in patients with chronic fatigue syndrome.[9] Moreover, carnitine has been found to have antioxidant properties, protecting mitochondria from oxidative damage when exposed to chronic stress.[10]

## FORMULATION COMPLEMENTS

This product can be complemented well by an Adrenal Glandular or compounded hydrocortisone, if that fits with your therapeutic concerns.

## SUPPLEMENT FACTS

Serving Size 3 Capsules  
Servings Per Container 60

Amount Per Serving		% Daily Value
Vitamin C (as calcium ascorbate)	150 mg	167%
Thiamin (as thiamin hydrochloride, thiamin pyrophosphate)	25 mg	2083%
Riboflavin (as riboflavin 5-phosphate)	10 mg	769%
Niacin (as niacinamide)	50 mg NE	313%
Vitamin B <sub>6</sub> (as pyridoxal 5-phosphate)	5 mg	294%
Vitamin B <sub>12</sub> (as 50% hydroxocobalamine and 50% adenosylcobalamine)	125 mcg	5208%
Biotin	250 mcg	833%
Pantothenic Acid (Vitamin B <sub>5</sub> ) (as Calcium d-Pantothenate)	15 mg	300%
Selenium (as L-Selenomethionine)	100 mcg	182%
Eleuthero ( <i>Eleutherococcus senticosus</i> ) (root) extract	300 mg	†
L-Carnitine Tartrate	250 mg	†
Schisandra ( <i>Schisandra chinensis</i> ) (fruit) extract 10:1	250 mg	†
N-acetyl L-tyrosine	150 mg	†
Acetyl-L-Carnitine (as acetyl-L-carnitine HCl)	125 mg	†
Alpha Lipoic Acid	100 mg	†
Ubiquinol (Kaneka Ubiquinol® †) active form of CoEnzymeQ10	50 mg	†
Licorice ( <i>Glycyrrhiza glabra</i> ) (root) extract (standardized to 20% Glycyrrhizic Acid)	50 mg	†

† Daily Value not established

**Other ingredients:** Gelatin capsule, microcrystalline cellulose, vegetable stearate and silicon dioxide.

## SUGGESTED USE

Take 3 capsules 2 times per day with a meal or as directed by your healthcare practitioner.

**NOTE:** Take 3 caps upon waking to optimize cortisol output. Take an additional 3 caps between 11am-3pm to continue adrenal support throughout the afternoon. Avoid use after 3 pm as it may be too stimulating.

**CAUTION:** Do not use if pregnant or nursing. Consult your physician before use if you have a medical condition, or taking any medication. Do not use product if the safety seal is broken or damaged. Keep out of reach of children.

## MADE WITHOUT

Wheat, gluten, corn, yeast, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, artificial colors, artificial sweeteners, or preservatives.

## REFERENCES

1. Kvetnanský R, Pacák K, Fukuhara K, Viskupic E, Hiremagalur B, Nankova B, Goldstein DS, Sabban EL, Kopin IJ. Sympathoadrenal system in stress. Interaction with the hypothalamic-pituitary-adrenocortical system. *Ann N Y Acad Sci.* 1995 Dec 29;771:131-58.
2. Su D, Luo J, Ge J, Liu Y, Jin C, Xu P, Zhang R, Zhu G, Yang M, Ai Z, Song Y. Raw and Wine Processed Schisandra chinensis Regulate NREM-Sleep and Alleviate Cardiovascular Dysfunction Associated with Insomnia by Modulating HPA Axis. *Planta Med.* 2022 Nov;88(14):1311-1324.
3. Esmaealzadeh N, Iranpanah A, Sarris J, Rahimi R. A literature review of the studies concerning selected plant-derived adaptogens and their general function in body with a focus on animal studies. *Phytomedicine.* 2022 Oct;105:154354.
4. Chapman K, Holmes M, Seckl J. 11 $\beta$ -hydroxysteroid dehydrogenases: intracellular gate-keepers of tissue glucocorticoid action. *Physiol Rev.* 2013 Jul;93(3):1139-206.
5. Liu W, Huang S, Li Y, Li Y, Li D, Wu P, Wang Q, Zheng X, Zhang K. Glycyrrhizic acid from licorice down-regulates inflammatory responses via blocking MAPK and PI3K/Aktdependent NF- $\kappa$ B signalling pathways in TPA-induced skin inflammation. *Medchemcomm.* 2018 Jul 19;9(9):1502-1510.
6. Wahab S, Annadurai S, Abullais SS, Das G, Ahmad W, Ahmad MF, Kandasamy G, Vasudevan R, Ali MS, Amir M. Glycyrrhiza glabra (Licorice): A Comprehensive Review on Its Phytochemistry, Biological Activities, Clinical Evidence and Toxicology. *Plants (Basel).* 2021 Dec 14;10(12):2751.
7. Gutierrez-Mariscal FM, Arenas-de Larriva AP, Limia-Perez L, Romero-Cabrera JL, Yubero-Serrano EM, López-Miranda J. Coenzyme Q10 Supplementation for the Reduction of Oxidative Stress: Clinical Implications in the Treatment of Chronic Diseases. *Int J Mol Sci.* 2020 Oct 23;21(21):7870.
8. Alhasaniah AH. L-carnitine: Nutrition, pathology, and health benefits. *Saudi J Biol Sci.* 2023 Feb;30(2):103555.
9. Vermeulen RC, Scholte HR. Exploratory open label, randomized study of acetyl- and propionylcarnitine in chronic fatigue syndrome. *Psychosom Med.* 2004 Mar-9 Apr;66(2):276-82.
10. Fathizadeh H, Milajerdi A, Reiner Ž, Amirani E, Asemi Z, Mansournia MA, Hallajzadeh J. The effects of L-carnitine supplementation on indicators of inflammation and oxidative stress: a systematic review and meta-analysis of randomized controlled trials. *J Diabetes Metab Disord.* 2020 Sep 15;19(2):1879-1894.

\*These statements have not been evaluated by the Food & Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.