

LONGEVITY ELITE™

Longevity Elite[™] is our master adaptogen and hormone tonic, containing a harmonious blend of adaptogenic herbs, phytochemicals, and the hormone precursor pregnenolone, designed to provide maximal support for hormonal balance and longevity. Adaptogenic herbs act as powerful allies to the HPA axis, the body's primary stress-response system, while also offering protective support to cardiovascular, neurocognitive, and immune function. The optimization of each of these systems facilitates healthy aging and youthful vitality across the lifespan.

THE HPA AXIS AND LONGEVITY: WHAT'S THE CONNECTION?

Supplement Facts

Serving Size: 5 mL (1 tsp.) Amount % Daily Servings Per Container: 20 Per Serving Value

Pregnenolone	10mg	**
Astragaloside IV extract (Astragalus membranaceus root)	10mg	**
Cycloastragenol extract (Astragalus membranaceus root)	10mg	**

Proprietary Blend: 1000mg
He Shou Wu (Fo-ti) root extract
(Polygonum multiflorum), Zhi Gan Cao root extract
(Chinese honey-prepared licorice) (Glycyrrhiza

uralensis), GS15-4° Fermented Korean Panax Ginseng extract, Ginseng Plus° Panax Notoginseng root extract, Ashwagandha root extract (Withania somnifera)

**Daily Value not established

Other Ingredients: Glycerin, water, ethanol, tocofersolan, phospholipids (from purified sunflower seed lecithin), medium chain triglycerides, natural citrus oil, natural mixed tocopherols, natural cinnamon bark oil

The hypothalamic-pituitary-adrenal axis, or the HPA axis, is an elegant network of endocrine glands, hormones, and neurons that regulates the body's stress response, metabolism, libido, immune system, and energy levels. It consists of three organs that function synchronously – the hypothalamus, the pituitary gland, and the adrenal glands. This ancient physiological "axis" allowed our hunter-gatherer ancestors to respond adeptly to acute stressors, such as being chased by a lion on the African savannah and return seamlessly back to a "rest and digest" state once the stressor had passed.

However, in the modern industrialized world, most people contend with chronic stress rather than acute stress. Unfortunately, the HPA axis is not evolutionarily designed to handle chronic stressors. A chronically stressed body pumps out high levels of cortisol, a critical stress hormone that literally accelerates aging on a cellular level. Sustained high cortisol levels disrupt blood sugar control, wreaking havoc on metabolic health.¹ Elevated cortisol ages the hippocampus, a critical part of the brain involved in memory and cognitive function.² Cortisol dysregulation also impacts levels of crucial sex hormones, catabolizes vital skeletal muscle, and compromises immune function.³, ⁴ HPA axis dysfunction, with its turbulent effects on cortisol, thus directly impacts our longevity.⁵

The HPA axis influences six primary physiological systems involved in aging, including:

- Glycemic control: Blood glucose dysregulation plays a central role in the aging process by triggering insulin resistance, oxidative stress, and inflammation. Blood glucose levels are, in turn, significantly impacted by hormones intrinsic to the HPA axis, including cortisol and DHEA. Optimization of HPA axis function has been found to improve glycemic control.
- Neurocognitive function: Feeling "less sharp" is considered a normal aspect
 of aging, but it's not inevitable. However, without a well-functioning HPA axis,
 cognitive function can significantly decline with age. Higher blood glucose levels are a risk factor for cognitive decline;
 while the mechanisms behind this connection have yet to be fully elucidated, high blood glucose may trigger oxidative
 stress in the brain, damaging neurons.

BENEFITS & APPLICATIONS:

- Provides comprehensive support for longevity and healthspan
 - AMPK activation
 - Sirtuin activation
 - Telomere support
 - Modulation of cellular senescence
 - HPA Axis support
- Supports hormonal balance
- Enhances stress resilience
- Enhances energy levels and vitality
- Promotes healthy brain aging
- Promotes healthy cardiovascular function
- Supports healthy immune activity

- · Cardiovascular health: Heart disease and atherosclerosis are manifestations of biological aging or aging that occurs as the body gradually accumulates damage to cells and tissues; this process is distinct from chronological aging, defined as one's age in years. Chronic stress increases the release of epinephrine and norepinephrine neurochemicals that raise blood pressure. Elevated blood pressure, in turn, damages the vascular endothelium, precipitating cardiovascular disease. Optimization of HPA axis function can thus improve cardiovascular health.
- Sex hormone status: Hyperactivation of the HPA axis changes the expression of genes involved in sex hormone synthesis and can lead to declines or imbalances in estrogen, progesterone, testosterone, and DHEA, the body's most important sex hormones. Suboptimal levels of these hormones adversely contribute to low vitality during the aging process.
- · Immune function and inflammation: A chronically activated stress response adversely impacts the body's antiinflammatory responses, leading to chronic inflammation. Chronic inflammation, in turn, drives a loss of Th1 status,
 increasing the body's vulnerability to infection. This chain of events is one reason why chronic stress contributes to aging
 and a reduced ability to fight off pathogens. Chronic stress can also dampen total cortisol production; insufficient levels of
 cortisol, particularly first thing in the morning, impairs immune surveillance and allows dysfunctional autoreactive immune
 cells to escape destruction. Over time, this dysfunctional process may lead to the onset of autoimmunity.8
- Telomere biology: Cortisol levels are closely related to the length of telomeres, regions of repetitive nucleotide sequences (nucleotides are the building blocks of DNA) found at the end of each chromosome in the body. Telomeres protect the chromosome from damage and serve as a "buffer," safeguarding the chromosome during the cell replication process. However, telomeres are also shortened with each round of chromosome replication, contributing to the aging process.9 By balancing HPA axis function, we may be able to attenuate telomere shortening, thus addressing a critical node in the aging process.

OPTIMIZE LONGEVITY WITH PREGNENOLONE & TIME-HONORED ADAPTOGENIC HERBS

The HPA axis has far-reaching effects on numerous drivers of aging. Through strategic supplementation with the "mother hormone," pregnenolone, and adaptogens, we can support healthy HPA function and longevity. Adaptogens are plants and plant extracts that fortify the body against the effects of physiological, mental, and emotional stress. They boost stress resilience by inducing a mild stress response when consumed; this process, referred to as "hormesis," allows our bodies to become more vigorous and vital. Pregnenolone complements the activity of adaptogens by acting as a steroidal precursor to our essential HPA axis and sex hormones.

PREGNENOLONE

Each of the body's steroid hormones, including cortisol, estrogen, progesterone, testosterone, and DHEA, is biosynthesized from an endogenous steroid precursor, pregnenolone. Pregnenolone helps maintain a normal balance between the body's stress and sex hormones. It is synthesized in various tissues, including the brain, adrenal glands, skin, testicles, ovaries, and retina.

BUSTING THE MYTH OF THE "PREGNENOLONE STEAL"

Chronic stress was previously thought to deplete pregnenolone through a process referred to as the "pregnenolone steal." The pregnenolone steal concept posits that when stress is high, the body shunts pregnenolone down a path that culminates in cortisol production, leaving less pregnenolone available to create anti-inflammatory DHEA and vital sex hormones. However, we now understand that there is no single pool of pregnenolone available for all steroid hormone synthesis. Thus, demand for the production of cortisol in the adrenal cortex will not necessarily drain pregnenolone available for estrogen, progesterone, or testosterone production. The downregulated production of sex hormones in response to stress is more a factor of processes such as feedback inhibition, receptor signaling, and gene expression that ultimately influence hormone production.

Supplying the body with pregnenolone supports healthy HPA axis function and aging by facilitating the balanced production of ALL steroid hormones. Pregnenolone is a neuroactive steroid that influences memory processes and healthy brain aging. Pregnenolone supplementation may enhance DHEA production; DHEA is an anti-inflammatory hormone that improves blood glucose balance, cardiovascular health, brain function, and sexual function. DHEA levels peak between the ages of 25 and 30 and decline from there. DHEA levels are also downregulated by chronic stress. Conversely, robust levels of DHEA support healthy aging. [11]

ASTRAGALOSIDE IV AND CYCLOASTRAGENOL

Astragalus membranaceous is a revered herb in the Traditional Chinese Medicine botanical compendium. It contains two primary phytochemicals, Astragaloside IV and Cycloastragenol, that promote telomerase activity, maintaining and even restoring telomere length to inhibit aging at the cellular level and support overall physical vitality.

Astragaloside IV supports telomerase expression in critical immune cell populations and may stave off the decline in immune function that occurs with age.¹² Cycloastragenol supports telomerase expression in neuronal cells, supporting neuronal integrity.¹³ Through their regenerative effects on telomeres, astragalosides may restore tissue and organ function compromised by telomere shortening.

In preclinical research, whole extracts of Astragalus membranaceous have also been found to dampen the adverse effects of chronic stress on learning and memory processes, suggesting a role for this botanical in the maintenance of cognitive integrity during times of stress.¹⁴ It also regulates immune function, including increasing the proliferation of B and T lymphocytes and regulating the expression of pro-inflammatory cytokines.¹⁵ Because immune function tends to decline with age, Astragalus may represent a useful therapeutic tool for regulating and optimizing the aging immune system.

GS15-4° FERMENTED KOREAN PANAX GINSENG EXTRACT

In Traditional Chinese Medicine, Panax ginseng is a fundamental tonic used to tone the vital energy, or qi, of all bodily organs. In the USSR, Panax ginseng was introduced as an adaptogen, a substance that induces a mild stress response, thereby upregulating the body's own resilience to stress. Since its early inception as a tonifying, fortifying herb, Panax ginseng has remained a central herb for regulating the stress response and enhancing whole-body health.

Today, we know that ginseng is rich in primary bioactive constituents called ginsenosides. Ginsenosides have a four-ring, cholesterol-like skeleton, which appears to endow them with unique steroid hormone-like properties. More than 100 different ginsenosides have been isolated and identified in Panax ginseng; these ginsenosides may account for ginseng's powerful impacts on hormonal balance, libido, cognition, metabolic health, and overall vitality. Ginseng also contains polysaccharides, fatty acids, and other bioactive compounds that interact with our biology.

Research indicates that ginseng mitigates stress-induced gene expression and dampens the effects of chronic stress on the hippocampus, a critical portion of the brain that is impacted during aging and implicated in cognitive decline.^{17, 18} Ginseng also enhances nitric oxide production for healthy cardiovascular aging. Ginsenosides also improve glycemic control, bolster levels of DHEA, the body's crucial anti-aging hormone, and upregulate AMPK, a critical cellular energy sensor intrinsically involved in the aging process.^{19, 20}

Ginseng may alleviate menopausal symptoms by exerting beneficial estrogenic effects through interactions with estrogen receptor-alpha (ERa) and estrogen receptor-beta (ERB).¹⁶ Steep declines in ovarian estrogen production and reduced estrogen signaling at the cellular level in the brain, bones, and reproductive tissues may contribute to common menopause symptoms such as vaginal dryness, loss of bone density, brain fog, and weight gain. Supplementation with ginseng stimulates estrogenic activity and may counteract health declines associated with reduced estrogen levels.²¹ Interestingly, activation of ERa and ERB by ginseng occurs in a tissue- and organ-specific manner, such that the plant's constituents modulate estrogen receptor activity in healthy tissues, but do not promote proliferative estrogen signaling by binding to cell receptors in estrogen-sensitive cancerous tissues.^{22, 23}

GINSENG PLUS® PANAX NOTOGINSENG

Panax notoginseng comes from the same plant genus as Panax ginseng but offers different benefits for healthy aging. Panax notoginseng contains phytochemicals called ginsenosides that modulate cellular senescence, the process by which somatic cells stop dividing and instead become stagnant secretors of pro-inflammatory compounds that ultimately exacerbate inflammation and damage neighboring cells. Senescent cells are implicated in many of the adverse changes associated with aging, including chronic inflammation and declines in immune function. By cleaning up senescent cells, Panax notoginseng supports an internal environment more conducive to healthy aging.²⁴

Panax ginseng also protects the vascular system during the aging process, maintaining healthy microcirculation, decreasing blood pressure, and inhibiting the accumulation of misfolded proteins in the central nervous system, an insidious process implicated in brain aging. In preclinical studies, Panax notoginseng has been found to increase stress resistance and slow the accumulation of age-related biological damage, including free radical damage, in model organisms.²⁵

HE SHOU WU

He shou wu, also known as "tuber fleece flower," is a revered botanical in the Traditional Chinese Medicine herbal compendium. Modern-day scientific research indicates that this time-honored longevity herb impacts multiple pathways involved in the HPA axis and biological aging process. A compound found in He Shou Wu called 2,3,5,4'-tetrahydroxystilbene-2-O-ß-d-glucoside (TSG) has been found to inhibit acetylcholinesterase activity and exert antioxidant activity in the brain, thus inhibiting brain aging. ²⁶

Immune system activity declines with age, rendering the body more susceptible to infection. He Shou Wu's polysaccharides and anthraquinone glycosides modulate the immune system, improving natural killer cell activity and macrophage phagocytosis, thereby enhancing the body's frontline defenses against invading microbes. These changes may bolster the aging immune system, promoting more youthful immune activity.

ASHWAGANDHA

Ashwagandha is primarily a strengthening tonic in Indian Ayurvedic medicine, lauded as a "Rasayana," or rejuvenator. Ashwagandha phytochemicals, including the sitoindosides VII-X and Withaferin-A, have been shown to exert anti-stress activity by influencing the HPA axis and heat shock proteins (HSPs), critical mediators of the stress response that are also intrinsically involved in aging.^{27, 28} Ashwagandha improves mental alertness and sleep quality in aged individuals and bolsters DHEA-S and testosterone in aging males.^{29, 30}

ZHI GAN CAO

Zhi Gan Cao is a Chinese honey-prepared licorice long used in Traditional Chinese Medicine to tonify Spleen-Qi, which correlates with the digestive system and aspects of the circulatory system. This gentle tonic harmonizes with the effects of the more stimulating herbs in our formula, such as Panax Ginseng.

Licorice root contains a phytochemical called glycyrrhetinic acid that inhibits an enzyme called 11ß hydroxysteroid dehydrogenase, which is involved in the deactivation of cortisol into cortisone. By balancing active cortisol and inactivated cortisone, licorice root helps to maintain HPA axis balance from the top down.³¹

Quicksilver Delivery Systems® improves upon liposomal and emulsification technology with smaller, more stable particles made from the highest-grade ingredients available. In addition to exceptional absorption rates, these tiny liposomal and nanoemulsified particles increase diffusion across mucous membranes, enhance lymphatic circulation of nutrients and support cellular delivery.

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