

Supporting Adrenal Function with Adaptogenic Herbs

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ABSTRACT

Adaptogens are plant derived compounds that normalize endocrine function and promote adaptation to environmental stress. Adaptogenic herbs modulate stress responses, enhancing energy production and sleep quality and improving immune function. Eleuthero Root (*Eleutherococcus*), Holy Basil (*Ocimum*), and Rhodiola (*Rhodiola*) have been used for the treatment of stress, fatigue, sleep disturbances, elevated cortisol levels, adrenal deficiency, low DHEAS and alterations in DHEAS/cortisol ratio, chronic infection, impaired memory, and exercise intolerance. Adaptogens have been used as single agents or in combination with other plant-derived products such as *Panax quinquefolius*, *Withania somnifera*, *Glycyrrhiza* spp, *Schisandra chinensis*, and *Gynostemma pentaphyllum*. Other herbs that have shown efficacy as adjuncts to adaptogens include *Scutellaria lateriflora*, *Matricaria recutita*, *Tilia* spp, *Hypericum perforatum* and *Melissa officinalis*, which are known for their calming effect on the nervous system. Eleuthero root and rhodiola have been associated with anxiety and insomnia, although these effects have not been validated in clinical studies. Adverse effects of *Eleutherococcus* such as increased blood pressure in hypertensive patients and heart palpitations have occurred as a result of inappropriate dosing. Overall, adaptogenic herbs are safe and no known drug interactions exist with the exception of a few cases of accidental misidentification of the herb, and their broad range of beneficial effects supports their development as valuable agents for the treatment of a variety of conditions.

Keywords: Adaptogen, Stress, Adrenal function

CLINICAL IMPLICATIONS

Adaptogens are a category of herbs that may increase an organism's ability to adapt to its environment¹. It is possible that adaptogenic herbs can prevent, treat, and enable people to recover from the effects of acute or long-term stress.

KEY HERBS DISCUSSED

Eleuthero Root (*Eleutherococcus*), Holy Basil (*Ocimum*), and Rhodiola (*Rhodiola*)

PRIMARY INDICATIONS

Stress, fatigue, poor sleep, elevated cortisol, adrenal deficiency, low DHEAS, altered DHEAS/cortisol ratio, chronic infections, impaired memory and mental function, exercise intolerance, easy exhaustion with moderate exertion.

ADJUNCTIVE OR STAND-ALONE TREATMENT

The herbs discussed in this review may be used either as an adjunctive or a stand-alone treatment for the above indications.

DOSE OF BIOACTIVE CONSTITUENTS

Eleuthero Root (*Eleutherococcus*) (whole plant extracts) 80-900 mg per day; containing a minimum of 4 mg eleutherosides daily

Holy Basil (*Ocimum*) (whole plant extracts) 80-900 mg per day

Rhodeola (*Rhodeola*) 300 mg BID, containing a minimum of 1 mg Salidroside Glycosides

SYNERGISTIC HERBAL FORMULA

Eleuthero root (*Eleutherococcus*), Sarsaparilla (*Smilax*), Rhodeola (*Rhodiola*), Holy Basil (Tulsi), other herbs to consider are *Panax quinquefolius*, *Withania somnifera*, *Glycyrrhiza* spp, *Schisandra chinensis*, *Gynostemma pentaphyllum*. Nervine (calming) herbs such as *Scutellaria lateriflora*, *Matricaria recutita*, *Tilia* spp, *Hypericum perforatum*, and *Melissa officinalis* are also useful adjuncts to adaptogens.

SIDE EFFECTS (AND CAUTIONS)

The key herbs discussed can be safely used when used appropriately. A few cases of drug interaction have been mistakenly blamed with Eleuthero Root as the herb was accidentally misidentified as the toxic herb *Periploca*.

UNSUBSTANTIATED THEORETICAL CONCERNS

Although some *Eleutherococcus* users report symptoms of stimulation, anxiety and insomnia, it has not been validated in clinical studies. There has been some concern that *Eleutherococcus* may increase blood pressure in hypertensive patients, or promote heart palpitations—side effects suggested to occur with excessive and inappropriate dosing^{2,3}. Clinical studies have not substantiated any of these theoretical concerns. *Rhodiola* may also be stimulating and theoretically promote anxiety, heart palpitations, and insomnia.

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DISCUSSION

Adaptogens are herbs capable of restoring normal tone and function to the HPA (Hypothalamic/ pituitary/adrenal) axis and SAS (sympatho-adrenal system), and therefore to the entire body. Adaptogens are considered safe agents that normalize endocrine function through numerous broad and non-specific actions, and increase overall resistance to stressors. Because of this rather vague description, the term “adaptogen” has not been widely adopted in mainstream Western medicine.² Nevertheless, adaptogenic herbs possess some unique actions on the adrenal system that tend to promote resistance to the negative effects of stress on the body.

The adrenal glands underlie much of the body’s response to external and internal stressors. Likewise, stress is a primary contributor to adrenal/HPA axis dysfunction. Adaptogenic herbs may improve resistance to stress as well as prevent some of the more common symptoms of stress (*e.g.*, poor concentration, sleep disturbance, fatigue, decreased immune response, and decreased resistance to infections). Adaptogenic herbs modulate stress responses, prevent down-regulation of the adrenal glands, enhance energy production and sleep quality, and improve immune function.¹ This review will elucidate current research on the use adaptogenic herbs for the adrenal axis, and general human health and well-being.

THE HPA AXIS AND ADRENAL GLAND HEALTH

The HPA axis encompasses the synergism and feedback between adrenal hormones, and hormones released by the hypothalamus and pituitary gland. The hypothalamus and pituitary gland are greatly affected by stress, and the emotional state of the individual person. The effect of the HPA axis on the emotional state was first described in the field of psychology, where biochemical adaptations noted from long-term stress and overwork led to sleep disturbances, irritability, and exhaustion. One portion of the HPA axis activated by stress is known as SAS. Psychological and physical challenges cause acute stress responses involving brain neurotransmitters that in turn affect the release of corticotro-

pins and other hormones from the pituitary gland and hypothalamus. The pituitary and hypothalamic hormones subsequently act on the adrenal glands. Long-term stimulation of the adrenal glands leads to adrenal gland dysfunction.⁴⁻⁶ the glands become hypertrophic, less responsive, or erratically responsive as evidenced by abnormal cortisol release, ACTH response, and altered DHEA to cortisol ratios (as well as other hormonal regulation disturbances). Chronic stress and the resultant increase in cortisol are known to suppress normal white blood cell activity, which subsequently is associated with altered cytokines and a greater incidence of inflammatory and allergic responses. Impairment and disturbance in the HPA axis is also associated with reproductive and metabolic dysfunctions, as well as altered psychological presentations (*e.g.*, anxiety and depression).

THE HPA AXIS AND ADAPTOGENIC HERBS

Adaptogenic herbs act on the HPA axis⁷, and may improve reproductive hormone regulation and exert anti-allergy and immune supportive effects; they may also enhance mood and mental stamina. *Eleutherococcus senticosus*, *Rhodiola rosea*, and *Ocimum sanctum* are well-studied adaptogenic herbs; all of these may be recommended for individuals who suffer from weakness and debilitation. Adaptogen herbs may be appropriate for use by the elderly and other individuals with fatigue and poor stress response, as well as for use by healthy persons, who wish to improve energy, stamina, and concentration. These herbs offer adrenal support mechanisms that improve the release of ACTH from the pituitary, CRH from the hypothalamus, and optimize adrenal gland responsiveness. These herbs also improve adrenal response to stress and physical challenges, and normalize some of the neurotransmitters involved in the HPA axis.

Hsp70 is a molecular chaperone sometimes referred to as a stress sensor; it helps the body to repair damaged proteins that arise from chronic stress and inflammation. Hsp70 inhibits the expression of NO (nitric oxide) synthase II genes and interacts with glucocorticoid receptors directly and via kinase

enzymes, thus affecting the levels of circulating cortisol and NO. Prevention of the stress-induced increase in NO (and the associated decrease in ATP production) results in increased performance and endurance; *Eleutherococcus*, *Schisandra*, and *Rhodiola* help the body elaborate specific heat shock proteins (Hsp).^{1,8} In addition, adaptogen herbs have also demonstrated significant antioxidant effects in humans. Reducing oxidative stress in the body with adaptogen herbs may improve overall health and well-being.⁹

Eleutherococcus senticosus

Eleutherococcus (Siberian ginseng) is a member of the *Araliaceae* family and a commonly used adaptogen. Not only is this herb commonly used in Russia (where the first studies were conducted in the 1950s), but in North America and throughout the world. Native to Siberia and the northern regions of Russia, the Korean peninsula, and the northeast region of China, *Eleutherococcus* has *Panax ginseng*-like effects. Interestingly, in Greek,



Eleutherococcus senticosus of the *Araliaceae* family
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the word *Eleutheros* means 'free', and the word *kokkos* means 'seed'. Meanwhile, *Eleutherococcus* is known as *Acanthopanax senticosus* in China, and some research studies and texts still use this older nomenclature for this herb.

Beginning in the 1950s, the scientific literature on *Eleutherococcus* reported that it improved stress tolerance and energy, increased resistance to infection, and acted as an adrenal tonic.¹⁰ *Eleutherococcus* has demonstrated stress-relieving effects on the HPA axis, reducing excessive corticotropin release and optimizing adrenal response.^{11,12} *Eleutherococcus* may act directly on the hypothalamus to regulate hormones, including mineralocorticoids, glucocorticoids, and reproductive hormones. Syringin, lignans, and sesamin found in this plant have been shown to exert immune-enhancing effects.¹³

Eleutherococcus contains coumarins, steroidal glycosides, and a group of polysaccharides, eleutherosides A, B, C, D, and E, which have significant immune-stimulating properties.¹⁴ Among the specific conditions where *Eleutherococcus* has shown possible effects are in treating immune depression (*i.e.*, compromise), head colds, influenza, bronchitis, respiratory allergies, atherosclerosis, rheumatic valve lesions, arrhythmias, arthritis, chemotherapy side effects, and altitude sickness, as well as for general weakness, fatigue, stress intolerance, and nervous debilities.¹⁵⁻¹⁸ Some of the anti-allergy and anti-inflammatory responses may relate to inhibition of nitric oxide synthase and cyclooxygenase during macrophage activation.¹⁹

Numerous studies have demonstrated the ability of *Eleutherococcus* to enhance physical stamina in athletes and also inhabitants of high altitudes. The herb may increase oxygen consumption and utilization and increases overall work performance,²⁰ though this effect is not seen in all studies.^{21,22} The mechanisms identified include improved physical stamina via adrenal responses as well as improved glucose uptake/metabolism in muscle cells and prevention of nitrogen depletion.²³ Positive effects on fibrinogen and blood coagulation have been demonstrated and proposed as another mechanism of enhanced exercise performance.²⁴ *Eleutherococcus* has been shown to improve general mental function, well-being and quality of life in the elderly.³ *Eleutherococcus* is reported to affect

noradrenalin responses in the brain in a manner that helps to blunt the stress response. Specifically, the paraventricular and supra optic nuclei (regions of the brain found to be integral to stress responses) are affected.²⁵

Ocimum sanctum

Ocimum sanctum (Holy Basil or *tulsi*) is a plant species from India. *Ocimum* is in the *Lamiaceae* (mint) family and has been used traditionally in the treatment of diabetes, stress, ulcers and inflammation. Agrawal and colleagues showed its ability to reduce fasting and postprandial blood glucose levels in humans.²⁶ *Ocimum sanctum* also has anti-inflammatory properties. *Ocimum* has been found to promote glutathione transferase, reductase, and peroxidase enzymes as well as promote superoxide dismutase^{27,28} *Ocimum* contains common anti-inflammatory flavonoids such as apigenin, luteolin, and one unique to *Ocimum* (called *ocimarin*). Other constituents include ocimumosides and cerebro-sides. Oil extracted from the seeds can reduce



Ocimum sanctum (Holy Basil or *tulsi*)
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inflammation by lipoxygenase inhibition and histamine antagonism²⁹ and can help to heal ulcers.³⁰ In addition to its antioxidant properties, modern research has shown *Ocimum* to be radioprotective, anticarcinogenic²⁷ and cardioprotective.³¹ The ocimumosides in *Ocimum* have anti-stress effects in that they help to normalize hyperglycemia, corticosterones, and adrenal hypertrophy from chronic stress.³² *Ocimum* has been shown to reduce serum cortisol and glucose.³³

Numerous effects on the brain, neurotransmission, and stress response have been demonstrated by *Ocimum*. Ethanol extracts of *Ocimum* tend to blunt the stress response in animals regardless of the experimental protocol. The plant extract reduced behavioral and neurochemical responses to stress in the swimming endurance test³⁴ and gravitation, restraint stress,³⁵ and noise stress.^{36,37} In fact, noise pollution has been shown to be a real and significant stress causing changes in the central nervous system's neurotransmitter balance and activity. Exposure to constant, irritating noise can lead to increased dopamine and serotonin in the brain, with a simultaneous reduction in acetylcholine and an increase in acetylcholinesterase, presumably as a stress response to the noise irritation. Response to a noise stimulus may be used as a research tool to evaluate the effects of stress-alleviating herbs and medications. *Ocimum* has been shown to prevent the above changes in brain neurotransmitters suggesting an anti-stress effect directly within the central nervous system.^{38,39} Animal studies have demonstrated a dopaminergic activity that promoted a calming and mood stabilizing activity.⁴⁰ One study found enhancement of GABA neurotransmission enabled *Ocimum* to exert a normalizing effect on immune modulation.⁴¹

Like other adaptogens, *Ocimum* has been shown to prevent both humoral and cell-mediated responses associated with stress, and researchers point to calming mechanisms as underlying contributors. These calming effects may also extend to the vasculature as *Ocimum* has been shown to be both vasodilating and hypotensive.⁴² It has demonstrated positive effects on cognitive ability and has possible application for dementia⁴³ while animal studies have shown anticonvulsant affects.⁴⁴ All of the above demonstrate the plant's adaptogen normalizing effects on the brain and neurotransmission.

Rhodiola rosea

Rhodiola rosea (Rose Root or Golden Root) is a member of the *Crassulaceae* family. It is a widely used adaptogen and anti-stress herb for mood disorders, fatigue, and adrenal weakness. This plant is native to Russia, where most of the initial scientific and clinical research was conducted. *Rhodiola* contains rosavin, rosarin, rosin, tyrosol and salidroside, and these are often used as markers to standardize *Rhodiola* extracts. The herb's main use is as an adaptogen for mood disorders, sleep difficulties, irritability, fatigue, poor concentration, headaches, vascular stress, and generalized deficiency states.⁴⁵ *Rhodiola* elevates serotonin levels in the central nervous system in animal models of depression and hippocampal suppression.⁴⁶ *Rhodiola* is believed to exert antidepressant, anti-anxiety and adaptogenic effects.⁴⁷

Cardiac complaints that arise from stress (such as hypertension and arrhythmias) may respond to *Rhodiola* therapy.⁴⁸ As with other adaptogenic herbs, its cardio-protection may minimize ischemic injury.¹⁷ ⁴⁹ Antiarrhythmic effects are due to its ability to block excessive epinephrine-driven stimulation and activation of opiate pathways in the central nervous system.⁵⁰

In a rat model of acute stress, *Rhodiola* prevented changes in behavior, immunity and hormonal regulation to the same degree as fluoxetine.⁵¹ Certain stress-inducing paradigms can cause reproducible effects on serotonin, cell proliferation, and differentiation in the central nervous system. *Rhodiola* increased serotonin and had a normalizing effect on hippocampal stem cells and related structures of the brain in studies, restoring them to levels seen in non-stressed control animals.⁵² One research study in humans found *Rhodiola* supplementation improved energy and promoted mental focus and concentration in chronic fatigue syndrome (CFS) patients while normalizing their cortisol levels.⁵³

ADAPTOGEN HERBS FOR GENERAL HEALTH

The three herbs described in this review—*Eleutherococcus*, *Ocimum*, and *Rhodiola*—all fit the classic definition of an adaptogen due to their influence on overall health via a variety of non-specific, broad-scope, normalizing mechanisms. By exerting an effect on the HPA axis, hormonal regulation, and a mitigation of the harmful effects of stress, these three adaptogenic herbs can improve energy, reduce stress symptoms, and improve hormonal balance and general well-being. Allergies, inflammation, nervousness, mood disorders, and poor physical stamina are among the many conditions that may respond to adaptogen therapy. Enhanced immune response, resistance to infection, and improved concentration are also among the more common benefits associated with the use of adaptogenic herbs.

DISCLOSURE OF INTERESTS

Dr. Saunders reports personal fees related to employment or seeing patients from CCM, the Dundas Naturopathic Centre, and from Beaumont Health Systems, Troy Hospital, MI, outside the submitted work. Dr. Winston reports personal fees from Herbalist & Alchemist, Inc, outside the submitted work. Dr. Stansbury has nothing to disclose.

REVIEW ESSAY

Many nutrients and herbs that have not been the subject of randomized controlled studies are used regularly by clinicians. They have also been used traditionally for hundreds, sometimes thousands of years. Review Essays contain the opinions of professionals and experts in the fields of nutritional and botanical medicine on how to most effectively use herbs and nutrients in clinical practice. The dosages recommended are based on clinical experience. Side effects that are described in "Unsubstantiated Theoretical Concerns" have not been seen in clinical practice or clinical studies but are speculative based on, for example, possible mechanisms of action.

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