# Botanical and Nutritional Compounds to Optimize Neurocognitive Health

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### Introduction

Adaptogenic botanicals, an elite group of herbs, promote natural, healthy function and replenish depleted energy reserves that are essential for cognition, positive mood and restorative sleep. Chronic stress, whether environmental, internal or social, has significant impact on our emotional and mental health because of its adverse effect on the neuroendocrine system. Botanical medicines offer a profound alternative or adjunct to pharmaceutical medicines, especially when used in combination with nutrients and natural compounds to support foundational issues and optimize healthy function of cognition and mood. This paper reviews the role of botanicals combined with natural compounds in restoring neurocognitive and emotional health by supporting the root issue: *normalizing neuroendocrine function*.

As we integrate knowledge about the neuroendocrine system with knowledge regarding actions of nutrients and botanicals, we can tailor use of these natural compounds to support our individual patients and clients, each of whom is biochemically, emotionally, mentally and spiritually unique.

#### Mood and Sleep Disorders

Mood disorders, such as depression and anxiety, are those which persistently affect a person's emotional state (mood) and adversely influence their daily life. Anxiety and depression are often concurrent with impaired sleep and cognitive function. These conditions may be triggered by a variety of factors including nutritional, psychological, biochemical, emotional, environmental, social and spiritual. Genetic tendencies and brain disease are also factors. While most of us experience some degree of anxiety, depression or insomnia in our lives, for some these are chronic and even debilitating conditions. Cognitive, mood and sleep disorders affect many people, adversely influencing their ability to lead vibrant, healthy lives and to respond appropriately to the many challenges of life.

In 2012, according to the National Institute of Mental Health (NIMH), major depression is one of the most common mental disorders in the United States,<sup>1</sup> with incidence of about 6.9% of adults. Women are 70% more likely to experience depression.<sup>2</sup> Findings show that eleven percent of Americans, aged 12 years and over, take antidepressant medication. Twenty-three percent of women age 40 to 49 take antidepressants, more than in other age groups.<sup>3</sup>

According to the NIMH, 40 million adults, or about 18.1%, of adults in America, suffer from some type of anxiety. This is almost three times the incidence of depression. Women are 60% more likely than men to experience some form of anxiety.<sup>4</sup> Anxiety disorders are common in Western countries, ranging between 13.6% and 28.8% of the population. Three out of four people with chronic anxiety experience one or more other mental disorders during their lifetime.<sup>5</sup>

Many suffer with generalized anxiety disorder, which includes chronic worriers or those who experience lowlevel chronic anxiety with an inability to relax. Additionally, people with chronic anxiety experience trouble with their sleep cycle or ability to experience a deep, restorative sleep. Inadequate sleep adversely affects mood, anxiety and the ability to function well at work and socially. This is reported to be an issue for onethird of Americans.<sup>6</sup>



#### Cognition

The healthy adult brain has about 100 billion neurons, which branch and extend to form multiple connections with other neurons. Chemical compounds called neurotransmitters flow across connective junctures, or synapses, acting as chemical switches or signals that activate or inhibit chemical responses. There are about 100 trillion synapses in the adult brain, which facilitate signals that create, maintain and change memories, thoughts, emotions, motor skills and a multitude of other functions.<sup>7</sup>

As the aging population increases, cognitive disorders are of growing concern. This includes the whole spectrum from occasional mild memory loss to major neurocognitive disorders, such as Parkinson's, Alzheimer's and other forms of dementia. Alzheimer's and Parkinson's disease are the most common neurological conditions that develop with aging. Incidence of dementia and Alzheimer's (the most common form of dementia) increases with age. In 2014, incidence for those 65 to 74 years old was 15%, for those 75 to 84 years was 44%, while for those 85+ years, incidence was 38%. One in nine people age 65 and older have some form of Alzheimer's.<sup>7</sup>

### Role of Botanical and Nutritional Compounds

Antidepressants and anti-anxiety medications are essential for those with serious conditions and biochemical imbalances. But for many people these medications have intolerable side-effects or offer no relief from their symptoms. Botanical and nutritional compounds play a supportive and sometimes central role in providing tangible relief in those with mild to moderate conditions. In more serious and chronic conditions, botanical and nutritional compounds physiological functions at the cellular and neuroendocrine level. Botanicals and natural compounds work on multiple levels to support and modulate healthy function and halt disease progression without side-effects.

With long-term pharmaceutical medication, over time, the brain changes and adjusts its output of neurotransmitters. This is known as brain plasticity. Over time, drugs lose efficacy and people often end up, for example, on as many as three antidepressants, along with other medications. Stopping any or all of the medications becomes a huge issue, and is sometimes impossible, because the withdrawal symptoms are very intense. In some cases, brain function adjusts so much to medications that there is no going back.

Pharmaceutical drugs focus on symptom suppression. Botanicals, nutrients and natural compounds address the root cause of dysfunction, help restore normal levels of neurotransmitters and harmonize the interface between the hormonal, immune and nervous systems.

### Stress Response and Neurocognitive Function

Our bodies operate on a foundation of simple biochemical reactions, which either "turn on" (stimulate or arouse) or "turn off" (inhibit or dampen) specific responses. This simple on-off process, occurring constantly in the cellular, nervous and endocrine systems, creates an ongoing, ever-changing concert of complex biochemical actions and interactions that maintains our homeostasis on a daily basis. For example, glutamate, an excitatory compound, stimulates brain activity while GABA, known as a calming compound is inhibitory – it calms neural activity. Elevated glutamate, due to increased or chronic sympathetic nervous system activation, can be a root cause of serotonin and GABA imbalance and ultimately cause depletion of those beneficial compounds.



This ongoing process of arousal and inhibition of the organism constitutes our interaction with our internal and external environment. These responses occur across multiple systems in concert to support the ongoing ability of the organism to function optimally. Allostasis refers to this adaptive response of our body's internal systems to seen and unseen factors - the constant adjusting of our internal functions to maintain homeostasis and health. The continual process of maintaining stability through change describes the body's ability to adapt. When the stress load exceeds the body's ability to adapt, it is referred to as allostatic overload.



Common signs include cognitive impairment, depression, fatigue, anxiety and disruption of the sleep cycle.

When you add to this the factors of a person's energy, perception, outlook on life, attitude, and emotional capacity this begins to include a fuller perspective of the adaptive capacity of a person. Mentally and emotionally, individuals respond to challenges, or stressors, according to their temperament, past experience,

genetic and familial tendencies, level of maturity and complex physiological responses that can be learned or genetic.

Good health can be measured by our ability to adapt to the constant changes and challenges of life. Stress is a fact of life, as we are constantly faced with challenges in our interaction with self, others and environment. When stress is due to a happy event such as the birth of a child or moving to a wonderful new home, it is referred to as eustress, or "good stress" and still requires a multitude of adaptive changes.

The constant production and relay of



neurotransmitters, hormones and cell-signaling adjusts our physiological and cellular functions to support us in our daily activities as we respond to the moment-to-moment changes, decisions, challenges and stresses we continually face. Our emotions and attitudes influence the release of specific neurotransmitters and hormones. With chronic stress, whether internal, environmental or social, our energy reserves are taxed. Our emotions, attitudes and mental faculties are adversely affected due to the influence of the stress hormones that keep us in the fight-or-flight mode, promoting anxiety, depression and cognitive impairment.

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#### Stress Response: Arousal and Resolution

The initial stress response involves the release of epinephrine and cortisol to increase alertness and ready the physiological response for fight-or-flight. This can contribute to increased heart rate, feeling panicky or anxious and negatively affect mental cognition and memory. Arousal systems include noradrenergic, serotonergic, histaminergic, cholinergic, and glutamatergic. Though these are not necessarily activated all at once, various systems become activated and work in concert, depending on the individual.

Immune responses and digestive function are down-regulated as the body enters the arousal phase. Prolonged stress results in the release of inflammatory cytokines. These generate free radicals, causing cellular damage and immune dysfunction. With prolonged stress, whether real or perceptual, the physiology remains on constant alert due to over-activity of the arousal systems. This leads to depletion of vital energy reserves, with concomitant fatigue and a host of other issues.

#### Hans Selye's General Adaptation Syndrome (GAS)

Hans Selye, a pioneer in the field of stress research, describes the stress response as the general adaptation syndrome (GAS), which has three phases. Each phase involves a different level of response to the stress that correlates with a specific physiological response.

Phase One is the alarm phase, where the body is aroused to threat and mounts its response. The hypothalamus signals the pituitary gland to secrete ACTH (adrenocorticotrophic hormone) which stimulates release of corticosteroids from the adrenal cortex. As the adrenal medulla releases adrenaline (epinephrine), this activates the sympathetic nervous system and classic fight-or-flight response – shunting energy and blood supply away from the core and into the musculoskeletal system. Basic functions are put on hold, such as digestion, cellular healing and repair, along with the relaxation response that allows for sleep and restoration.

In Phase Two, as the stressors continue over time, the body adapts its functions to deal with the ongoing stress. Cortisol levels may remain elevated over time instead of their normal, fluctuating rhythm. Endocrine, immune and central nervous system responses are engaged and interact in such a way as to prioritize the continued response to stress.

With time and other factors, the person's system becomes depleted of vital energy and energy reserves and cannot continue on the draining path of adaptation. Thus, Phase Three is that of exhaustion. Something in the system gives and a person may experience sleep, mood or immune system disorders, nervous system dysfunction, hyper- or hypo-activity and either a simple illness such as a flu or a serious illness due to internal depletion.

### Stress Resolution: Healing and Repair

Ideally, once the challenge or stress has been resolved and the threat has passed the system relaxes, discharging the excitatory response, and returns to normal function. When a person is exhausted, with depleted reserves from a prolonged stress response, their nervous system is stuck in the sympathetic mode (fight-or-flight). As a person is able to relax into a parasympathetic state, where healing and repair can take place, they are able to respond to the real or perceived stressors in a more positive manner and potentially find resolution.



The conundrum is that stress drains the vital and bioenergetic energy necessary for relaxation and healing and individuals are caught in a vicious cycle. Botanical medicines are invaluable agents to restore vital energy, enhance recovery and address the root causes of the body-mind's capacity to respond to stress. Botanicals and nutrients support production of the calming neurotransmitters and enhance overall restorative function. This allows the person to regain their natural allostatic and circadian rhythms, thus supporting wellness at all levels.

### Circadian (Biological) Rhythms

The body's basic biorhythm, based on cycles of activity and rest, is correlated with our circadian cycle. In the neuroendocrine system and brain, this is a basic binary rhythm, with certain chemicals inducing arousal or activity and other chemicals exerting inhibitory or relaxing response. These basic "on" and "off" signals run constantly and occur as a complex series of interactions at the biochemical level that keep all systems running smoothly through periods of activity and relaxation.

Circadian biorhythms are natural biological processes common to all living organisms attuned to cycles of night/day. Our natural Circadian cycle of wakefulness and rest, synchronized with day (light) and night (dark), is regulated by the SCN (suprachiasmatic nuclei) in the hypothalamus. The SCN are responsive to light and dark via the optic nerve. The SCN signals other brain and endocrine systems influencing hormones, body temperature and other functions. As morning light enters the eyes, it stimulates the SCN which sends signals causing a rise in body temperature. It also causes release of cortisol and other hormones. At night, with onset of darkness, melatonin is released. Elevated levels of melatonin help promote deep, restorative sleep.

These embedded biological rhythms are synchronized with rhythms of the planet and with physiological energy cycles inherent in the cells of our body. Circadian rhythms are processes that help coordinate various physiological systems. Our natural, endogenous circadian rhythms serve to optimize our well-being and modulate homeostasis in the brain, nervous system, tissues, organs and cells. Holistic therapies restore these natural biorhythms which are foundational to health and vitality.

#### Healing Response and Restorative Sleep

It is essential to initiate the healing response and restore vital function to resolve impaired or prolonged stress response. Evoking the healing response facilitates restorative processes at all levels. This includes addressing physiological, nutritional, emotional/mental, spiritual and lifestyle issues.

Sleep disturbance is consistently a risk factor for development of and recovery from mental/emotional disorders. It is a clinical factor in chronic arousal conditions such as PTSD (post-traumatic stress disorder), attention disorders, dementia, Alzheimer's, anxiety and depression. Lack of sleep or other interruption of the normal, restorative sleep cycle furthers the maladaptive stress response. It triggers mood disorders including anxiety, depression, and disrupts cognitive function.

We spend an average of about 30% of our lives sleeping and if our normal, personal circadian rhythm and sleep cycle is disrupted, a myriad array of health issues can ensue. Our metabolism, hormonal levels, cellular healing and repair, nervous system response and other functions perform in a specific chronobiological rhythm. Cortisol levels tend to rise in the early morning and dip in the evening before sleep. Our body typically cools during the very early morning hours and warms as we prepare to get up. Night shift workers or those whose work shifts are constantly changing from day to night shifts are found to be at greater risk



for immune system issues and even certain kinds of cancer because with a disrupted sleep pattern, natural physiological processes cannot function optimally.

Foundational to any healing process is the ability to sleep well, which is also a key indicator of physical, cognitive and mental health. Sleep, of course, has a profoundly restorative function. Sleep is characterized by quiescence and reduced responsiveness. It has a restorative effect that optimizes neurocognitive, emotional and physiological functions during our waking time.

Additionally, researchers find that sleep has transformative effects – promoting lasting changes in the brain, enhancing brain function and exerting a positive influence of learning and memory.<sup>8</sup> Studies find that cognitive and emotional memories of events are processed and organized during sleep. Sleep is a state of rest but not of inactivity. There is a lot of neurological activity with neurons firing during the nighttime as the brain and nervous system work to integrate our experiences. Researchers find that sleep is a highly-organized, cyclic process with specific states and transitions.<sup>8</sup> Both sleep and wakefulness are regulated by interacting homeostatic and circadian processes.

### **Therapeutic Approaches**

#### Adaptogenic Herbs

Adaptogens are the elite class of herbs essential for restoring the foundation of well-being, normalizing function and fueling the vital and reserve energy so the body has the ability to heal and repair. Adaptogens,

a group of unique botanicals, are particularly suited to addressing the multitude of issues due to exhaustion and depletion of reserves from a prolonged stress response. They engage the body's healing response by normalizing function, enhancing repair mechanisms and promoting restorative sleep.

Normalizing function (whether hypo- or hyper-) involves mechanisms such as lowering corticosteroid levels, which allows the neuroendocrine system to return to a balanced rhythm of activity and repose.

When a person is in a state of exhaustion, they literally have no energy, from the cellular level

up, with which to engage in the healing process. They are too exhausted to relax, just as tired little children get wired and won't sleep. As the person's energy reserves are restored and their stress response calms, they are able to return to a normal rhythm of activity and relaxation. Nighttime sleep is when the body does restorative and healing work at the cellular, organ, energetic and other levels of the system.

Adaptogenic herbs were first researched and designated as such by Russian scientists. They were looking for non-toxic herbs to enhance physical stamina, performance and endurance in Russian athletes, cosmonauts





and factory workers during prolonged stress, workload and athletic performance. They searched amongst botanical compounds with long histories of safe use in humans as an alternative to pharmaceutical compounds that have adverse side-effects offering short-term benefits with long-term adverse effects on wellbeing.

The simplest definition of adaptogens is any compound that (1) acts in a nonspecific manner to strengthen physiological adaptation, (2) exerts a normalizing action upon physiological responses, and (3) has a restorative effect on the organ and energy systems, enhancing optimal function – all with no side effects and while bringing the system as a whole back into its natural state of harmony.

This approach to healing has been utilized for thousands of years by ancient medicines, such as Ayurvedic and Chinese, along with the more modern Vitalist herbal tradition. Each of these traditions recognizes that there is a vital life force or energy that drives the neuroendocrine, cellular and other systems of the body. This vital life force is known in ancient traditions around the world as Prana (Ayurveda), Qi (Chinese Medicine), Ki (Kiatsu in Japan) and a multitude of other names. In these age-old medical traditions, specific herbs are recognized, classified and used according to their ability to nourish and support this vital life force in its very specific manifestations, and in relation to specific organ systems and functions.

#### **Combining Herbs and Formulations**

In most herbal traditions, herbs are combined together for synergistic effects, similarly to how a group of people with varying skills and abilities working together accomplish much more than one person working alone. Modern clinicians use botanicals, nutrients and natural compounds in various combinations for optimal benefits. Since most people present with complex issues, herbs are combined that work in concert to support multiple systems. Just like a race car at the track, where many aides run out at the pit stop to change the tires, fuel the tank, change the oil, and support the driver, so does combinations of herbs support the system as a whole through their combined individual actions.

Combination formulas offer enhanced effectiveness especially for the variety of complex issues that clinicians are faced with today in their clients. By utilizing several combination formulas together, a skilled clinician can provide a concert of beneficial botanicals and nutrients to support the healing path of their clients without side effects. Over time, as the person improves, some foundational formulas may be retained for long-term use, while other formulas may be rotated in and out while following the healing needs of the person's individual situation.

#### Adaptogenic Herbal Formulations are Foundational

Adaptogens play the primary role in any formula and are accompanied by herbs that play supportive though essential roles. The primary formula must consist of adaptogenic botanicals to support the body's vital and

reserve energy, restore normal function and enhance relaxation of the nervous system.

Adaptogenic, restorative herbs greatly enhance physiological response to other botanical or nutritional compounds. Adaptogenic herbs and formulations are foundational, working to support the system as a whole.

#### Key actions of adaptogenic herbs and formulas:

- calm the stress response
- normalize function
- replenish vital energy
- promote restorative sleep



For long-term recovery and to support healing from the maladaptive and exhaustion phases of the stress response, it is essential to provide foundational adaptogens along with adjunctive botanical and nutritional compounds appropriate for the individual according to their specific needs.

#### Supportive, Adjunct Compounds and Formulations

Supportive herbs, nutrients and natural compounds are used to focus therapeutic support in a particular area, such as cardiovascular or neurocognitive. These play a supportive and/or adjunct role in the overall therapeutic treatment.

Often nutritive or other natural compounds enhance formulations through their calming, supportive or nourishing functions. B-complex vitamins support a multitude of metabolic pathways and enhance healthy neurotransmitter function. Herbs high in flavonoids and other such compounds provide raw materials for healing and repair in cells, vascular tissue and organ function and can provide antiinflammatory and anti-oxidative benefits. Carnitine supports mitochondrial function and energy metabolism at the cellular level.

#### Examples of adjunct compounds for neurocognitive health include:

- nutrients such as B-complex or others
- plant compounds such as • flavonoids
- beneficial natural compounds such as acetyl-L-carnitine
- botanicals chosen by action, such as nervines

For cognitive and mood issues, many nervine herbs both nourish and calm the nervous system. Which of the hundreds of nervine herbs is chosen depends on the person and their needs. There is also a host of nutritional, herbal and other natural compounds to consider. Many of these are discussed later in this paper.

Combination botanical formulas provide foundational support. Such formulas combine adaptogenic herbs with organ- and system-specific botanicals and nutrients. When higher doses of individual nutrients are desired, these can be integrated into the overall program tailored for the individual. For example, glycine is a key nutrient to modulate anxiety. It can be especially beneficial when taken at night before bed, often combined with the glycinate form of magnesium. Therapeutic dose of glycine for this purpose is usually between 150mg to 300mg before bed. A formula containing glycine combined with supportive herbs and nutrients can enhance beneficial results. If additional amounts of glycine are desired, it can be used singly to meet the desired dosage.

A formula containing a number of compounds can provide a synergistic blend that is greater than one compound given alone, even at a higher dose. But individual response can differ, and some may benefit with additional amounts of specific compounds or botanicals. This is one way that protocols can be tailored for specific needs.

#### Holistic Treatment Approach

A holistic treatment is an integrative approach designed to address individual needs. Chosen therapies may be adjunctive to pharmaceutical approaches but will always address physiological, emotional/mental and spiritual dimensions of the person along with appropriate lifestyle, nutritional and botanical support. The primary therapeutic goal is to calm the stress response and restore

#### The holistic treatment approach:

- Lifestyle changes
- Integrative natural therapies
- Nutritional foundation
- Botanical medicine adaptogenic formulas



normal function as much as possible. This requires nourishing and supportive measures. Botanical and nutritional therapy should include an abundance of adaptogenic herbs combined with supportive herbs chosen for the individual needs. Adaptogenic formulas are primary to utilize at every stage of treatment.

#### Foundational Treatment: Calm Stress Response, Restore Normal Function

Lifestyle changes are an essential foundation to any holistic treatment. There are many multidisciplinary body-mind, spiritual, psycho-spiritual and other approaches that support healing from prolonged stress and trauma. These tools help us to learn more successful strategies to dealing with life's challenge. Lifestyle approaches could include therapy (from cognitive to trauma therapy), mindfulness methods, meditation, relaxation techniques and Qi Gong or Tai Chi. Beneficial integrative therapies for mood disorders along with sleep and cognitive issues include acupuncture, Jin Shin Jyutsu, cranio-sacral therapy, therapeutic massage and somato-emotional approaches.

Dietary counseling is needed to identify and eliminate any allergens or stressors. It is essential to support healthy digestive function and gut flora. A diet appropriate for the person with ample protein, fresh, organic foods, healthy beverage choices and an abundance of nutrient-dense vegetables provides essential nourishment. Providing support with specific natural compounds or nutrients enhances the nutritional foundation of the individual.

The essential cornerstone of any holistic protocol is a combination formula consisting of restorative, adaptogenic botanicals appropriate for the individual needs. Adaptogenic herbs support strength, stamina, stressrelief; enhance vitality and resilience; modulate HPA axis response to stress and help restore depleted systems.

Another advantage of adaptogens is that this class of herbs restores vital energy. Yet, they are in no sense stimulants. Stimulants cause further exhaustion to an already depleted system since they tax the nervous

| Adaptogenic Plants & Main Active Compounds |   |  |
|--|---|--|
| Adaptogenic Plant                          | Main Compound                               |  |
| Panax ginseng (ginseng) & Panax q.         | Ginsenosides                                |  |
| Withania somniferum (ashwagandha)          | Withanolides                                |  |
| Eleutherococcus senticosus                 | Eleutherosides                              |  |
| Astragalus membranaceus                    | Astragalosides                              |  |
| <i>Ocimum sanctum</i> (holy basil)         | Triterpenic acids                           |  |
| <b>Rhodiola rosea</b> (rose crown)         | Flavonoids                                  |  |
| Schisandra chinensis (5 spice)             | Lignans                                     |  |
| <b>Oplopanax</b> (Devil's club)            | Saponins                                    |  |
| Cordyceps sinensis                         | Cordycepic acid, also rich in<br>Vanadium," |  |

system, the adrenals and further exacerbate the stress response.

Adaptogenic botanicals normalize function, modulate the HPA axis and support the relaxation response. They are the optimal choice for deep restorative work at all systemic levels: cellular, tissue, organ, immune, energetic and neuroendocrine. Adaptogenic botanicals exert normalizing function, perform restorative work and supply raw materials that the body can utilize for the healing process.

#### Therapeutic Focus: Supportive Adjunct Compounds

Adjunct formulas and compounds are chosen to support the areas of greatest need, depending on how the person is manifesting stress overload. It is essential to assess both the areas of strength (resilience) and weakness (from depletion to exhaustion). When reserves are depleted, cognitive function is impaired, resulting in further stress and decreased ability to make wise, adaptive choices. This could be a short-term impairment, as in intense, stressful situations or a more serious impairment as in the various neurological diseases such as Parkinson's, Alzheimer's or dementia which have more far-reaching and complex causes. In either case, the principle is the same – to supply restorative and supportive botanicals and nutrients that support neuroendocrine function and harmonization. It is also essential to increase the ability of the organism to cope with and adapt to stress, supporting resilience and vitality.

For neurocognitive syndromes the most important areas of focus are to promote restorative sleep, enhance cognitive function and support positive mood and outlook.

#### Method: Pathways to Accomplish Therapeutic Focus

- 1. Restore and revitalize with adaptogenic botanicals
- 2. Nourish and calm with botanical nervines and natural compounds
- 3. Modulate neuroendocrine function, nourish beneficial neurotransmitter production with botanicals and natural compounds
- 4. Support cerebral and nervous system and modulate neurological activity with botanicals and natural compounds

#### **Combination Formulas**

A foundational combination formula should include supportive botanicals for the nervous system to enhance restorative sleep, to calm the mood disorders of anxiety and depression and to optimize cognitive function. For all neurocognitive issues we want to be sure to supply restorative adaptogenic botanicals, calm the nervous system, replenish depleted neurotransmitters and normalize cortisol levels.

When the neuroendocrine system is maintained in a stressful sympathetic mode it can be difficult to remain positive in outlook. Emotions such as anxiety or depression can settle in. For some people the causes are endogenous and pharmaceutical medication is invaluable, because botanical and natural compounds will often not be powerful enough. But for a large percentage of people,

#### Best results are obtained by:

- utilizing adaptogenic formulations as part of every protocol
- using several compatible adaptogenic formulations together
- including formulations with a specific restorative focus
- adding single agents as necessary for desired dosage
- using formulations that combine botanicals, natural compounds and nutrients

pharmaceuticals cause unwanted side-effects, mask their feelings and cause intense discomfort or anxiety. For such people and to support those who are undergoing or healing from stress, botanical medicines combined with specific nutrients and natural compounds can be supportive in their healing process.



### Herbs for Neurocognitive Health

#### Foundational Adaptogenic Herbs

**Therapeutic Principles:** Calm stress response; restore normal function; enhance recovery **Method:** Restore and vitalize with adaptogenic herbs

#### Eleuthero (*Eleutherococcus senticosus*)

This is the premier adaptogenic herb, first researched by Russian scientist Dr. Nikolai Lazarev in the late 1940s, which led him to coin the term "adaptogen". Later, Israel I. Brekhman MD, used the remarkable properties of Eleuthero to define the parameters of adaptogenic herbs. While initially marketed as Siberian Ginseng in the 1970s, it is only a distant relative of the true Ginsengs. A member of the Araliaceae family, Russian Eleuthero (grown in northern and eastern Russia) is considered the most potent, containing the largest amount of the bioactive compounds.



Eleutherococcus senticosus

One of these, Eleutheroside B, is the key compound found to play a significant role in the anti-stress and anabolic activity of Eleuthero.<sup>9-12</sup>

More than any adaptogenic botanical, Eleuthero normalizes function, increases biological resistance and normalizes individual physiological responses. It enhances energy, optimizes endocrine function and supports adrenal gland function when the body is challenged by stress.<sup>13</sup> Offering anabolic activity, it enhances physical energy and endurance, mental acuity and work capacity.

#### Schisandra (Schisandra chinensis)

Schisandra has been used for thousands of years in China, Russia and Tibet. Hunters in the Siberian wild used the dried berries to provide energy, stave off exhaustion and improve night vision on long treks. Known as "Five Flavor Fruit" in Chinese medicine, while it is revered as a tonic that benefits all five energetic/organ systems, it was used specifically to nourish the Lungs, enhance Liver function and benefit the eyes. Modern research reports its ability to increase mitochondrial glutathione redox status.<sup>14-16</sup> It is also found to protect the liver and DNA from damage due to chemicals such as carbon tetrachloride.<sup>14,15</sup>

#### Rhodiola (Rhodiola rosea)

Known as Golden or Artic root, Rhodiola was used in Tibetan medicine to promote circulation and prevent hypertension. Valued for its ability to enhance mental and physical performance and stamina, it nourishes the central nervous system, improves resistance to stress and helps eliminate fatigue. Rhodiola enhances HPA (hypothalamic-pituitary-adrenal) axis response to stress. It is found to help reduce stress-induced depression and decrease anxiety, likely through its harmonizing actions on the neuroendocrine system.



#### American Ginseng (Panax quinquefolius)

American Ginseng is prized for its deeply nourishing properties, which allows for deep, restorative tonification without any of the "heating" effects seen with Red or Korean Ginsengs. American Ginseng is particularly revered as a lung tonic and is specific as a restorative for those suffering with exhaustion from overwork.

#### Ashwaganda (Withania somnifera)

Ashwaganda is a powerful herb revered as a restorative tonic in Ayurvedic medicine. Traditionally it was believed to confer the vigor, virility, and strength of a stallion. It modulates the HPA axis with a normalizing rather than stimulating effect on the nervous system. With anabolic activity, Ashwaganda nourishes those in a weakened physical or mental condition.

Ashwaganda is also found to enhance cognitive function. Studies demonstrate that Ashwaganda offers significant brain- and neuro-protective qualities. One study found 80% reduction in cell degeneration in the brain of stressed animals.<sup>17</sup> Another discussed the ability of an isolate of Ashwaganda to positively influence regeneration of neuritis and synapses in damaged neurons and neural circuits – vital components of the nervous system and brain.<sup>18,19</sup> Ashwaganda may be protective of brain cells and healthy brain function against degenerative brain conditions.<sup>20</sup> It was reported to increase acetylcholine receptor activity which may partially explain its ability to enhance cognition and memory.<sup>21</sup>

#### Reishi (Ganoderma lucidum)

Reishi, historically known as a longevity herb and elixir of immortality, is often portrayed in Chinese art in the hands of Taoist sages. It was used in Chinese medicine for over 2,000 years especially to nourish and restore the deep reserve energy. Its active constituents include polysaccharides, triterpenoids and plant sterols, offering an immune-modulating effect. It also supports restorative sleep and modulates homeostasis.

Reishi (Ganoderma lucidum)

#### Cordyceps (Cordyceps sinensis)

Ancient and modern Chinese herbalists highly value Cordyceps as a tonic for the respiratory system and to support reserve energy, overall vitality and stamina. Cordyceps first gained international attention when it was discovered that Chinese Olympic athletes included Cordyceps as part of their daily herbal training formula. Studies confirm that Cordyceps increases endurance, vigor and athletic performance.<sup>22-24</sup>





#### **Restorative Botanicals and Nutrients**

Overview of Therapeutic Principles:

- a. Calm anxiety and promote restorative sleep
- b. Harmonize neuroendocrine system; alleviate depression
- c. Support and enhance cognitive function
- a. **Therapeutic Principles:** Calm anxiety; promote restorative sleep **Method:** Nourish and calm with botanical nervines and natural compounds

Anxiety is a response that involves activation of the sympathetic nervous system with varying degrees of feelings of fear, apprehension and accompanying physiological distress that varies from person-to-person. The classic response is tightness in the chest or increased heart rate. Some experience tightness in the belly or stomach. Some report pain or discomfort in their lower back around the kidney area. It is useful to ask each person how they experience anxiety and to have them describe where in their body they feel the sensations they describe. Physical sensations that correlate with anxiety can vary widely from person to person, though the underlying physiological response of sympathetic nervous system arousal that characterize anxiety is always similar in the cascade of biochemical events.

The stress response system involves complex interactions and feedback loops between the nervous, endocrine and immune systems. The body relies on the restful, restorative phase of nighttime sleep to counterbalance our daily activity. If the nervous system is unable to discharge stress and endocrine levels of corticosteroids and other compounds remain unbalanced, the system remains on a low or high state of alert and a person experiences sleep issues. They may find themselves unable to sleep, unable to get to sleep or unable to sleep deeply. This often leads to further anxiety.

Our natural sleep cycle is disrupted by factors such as work, social and family events, travel, medications, diet, lifestyle and lack of sufficient exercise. Many factors influence our ability to sleep well including emotions, trauma, pain, excess exercise, nutrition and lifestyle. Anxiety or inability to sleep can be a temporary situation such as when travelling, moving to a new home and other factors. With prolonged anxiety, cortisol levels may be chronically elevated with resultant inability of the nervous system to relax. When cortisol levels spike in the evening and at night, instead of dropping to allow for rest and sleep, our natural circadian biorhythms that are naturally synchronized with the cycles of day (light) and night (dark) are altered. With prolonged stress response the cortisol levels and rhythm are imbalanced, causing disturbance in the normal sleep/wake cycle along with anxiety.

#### Nervines

Nervines are a broad group of herbs that help calm and restore balance to the nervous system. Some nervine herbs are nutritive and restorative, such as Milky Oats (*Avena sativa*), which is also a restorative tonic for the adrenal axis. Others calm the nervous system on a spectrum from gently calming to strongly sedating. Gently calming nerviness such as Passion Flower (*Passiflora incarnata*), Lemon Balm (*Melissa officinalis*) and Chamomile (*Anthemis nobilis*), are excellent for children and for sensitive adults. More strongly sedating nerviness, such as Kava Root (*Piper methysticum*) are useful to dampen an overreactive nervous system.



#### Glycine

Glycine is a nonessential amino acid and neurotransmitter that is metabolized in the brain. It inhibits release of norepinephrine and exerts a calming influence. For this reason is found to modulate anxiety. Receptors for glycine are found throughout the vertebral central nervous system, in the brain stem and in the spinal cord and throughout the tissues. Highest concentrations of glycine are found in the thalamus, amygdala, substantia nigra and other areas.<sup>25</sup> GABA receptors, melatonin, serotonin and dopamine play a big part in controlling mood, circadian rhythm, sleep duration and depth. Glycine is a precursor to GABA.

**Passion Flower** (*Passiflora incarnata*), **Skullcap** (*Scutellaria lateriflora*), **Wild Oats** (*Avena sativa*) The combination of these three herbs is a time-revered, classic nervine formula to calm the nervous system, induce relaxation and promote a restful sleep. The Eclectic physicians used this formula for those suffering from mental worry and overwork. These herbs are very gentle and effective for all types of people to help calm an overactive mental, emotional and nervous system.

Passion flower was an Eclectic remedy for stress, nervousness and insomnia, especially in conditions of mental overwork or worry. Skullcap was used by Native Americans and Eclectic physicians to ease stress and anxiety. The Eclectics used it to calm restlessness along with irritability or excitability of the nervous system. The milky seed of Wild Oats is known both as a restorative tonic for the nerves and as a restorative tonic to calm and nourish the adrenal gland system.

#### Zizyphus Seed (Zizyphus spinosa)

Zizyphus Seed is one of the most powerful herbs in the Chinese materia medica to promote relaxation, allowing the mind to calm and the person to experience a naturally deep, restorative sleep through the night. Used successfully for those with past or present traumatic stress, it is very nourishing and gentle with no side-effects.

#### Kava (Piper methysticum)

Kava is widely known in the South Pacific for over 3,000 years as both a medicine and as a ceremonial beverage. It is said that in Fiji, when it seemed the men might be getting ready to fight, someone would suggest a kava ceremony. This brought everyone together and the kava drink calmed and grounded the overexpressive energy. It is known for its ability to calm anxiety and will help ground the energy when in an overactive state, to allow for rest. Fishermen and laborers in ancient Hawai'i drank kava tea at the end of a long day of hard, manual work to relax their muscles and help them sleep well.



Kava (Piper methysticum)

#### Lavender (Lavandula angustifolia) flowers and Lemon Balm (Melissa officinalis)

These traditional nervine tonics calm the nervous system and enhance relaxation. Lavender flowers have a long history of being used as a treatment for anxiety and depression. Known to the lift the spirits, it can be used as an herbal decoction or as an essential oil in aromatherapy. Lemon Balm is a gentle calmative that also calms digestive upset due to overactivity of the nervous system.



#### L-theanine

L-theanine is an amino acid found in tea leaves (*Camellia sinensis*), which have a 5,000 year history as a beverage and medicine in the Chinese culture. In Chinese, Japanese and other Asian cultures there are special tea drinking ceremonies, but even in daily use, tea is revered for its ability to promote calmness and clarity.

L-theanine is found to stimulate the production of alpha brain waves and is a precursor of GABA, helping to promote the relaxation response. Originally discovered in green tea, it is found in both black and green tea. Studies confirm that it calms nervous agitation, improves mental clarity, acuity and performance and aids mental concentration. L-theanine antagonizes glutamate receptors and increases brain GABA levels. It is also found to be neuroprotective with antioxidant properties.<sup>26</sup>

b. **Therapeutic Principles:** Harmonize neuroendocrine system; alleviate depression **Method:** Modulate neuroendocrine function; nourish beneficial neurotransmitter production with botanicals and natural compounds

#### Vitamins B6, B12 and Folate

These members of the vitamin B-complex are especially protective and nourishing for the nervous system. They play a key role in metabolic (energy-production) pathways at the cellular level. Some members of the B-complex act as precursors for calming neurotransmitters. B-complex vitamins act as co-factors that support enzymes reactions facilitating numerous biochemical responses. They also play a vital role in healthy function of the liver's methylation system, supporting healthy liver clearance and metabolic function. Studies indicate that elevated homocysteine results from inadequate folate, Vitamin B12 and B6 intake, and correlates with cognitive impairment.<sup>27</sup>

Vitamin B6 is an essential co-factor for the formation of neurotransmitters. Serum B12 and folate are found to support cognition and functional ability<sup>28</sup> and low vitamin B12 levels could be a contributing factor to neuron atrophy and cognitive decline.<sup>29</sup>

#### St. John's Wort (Hypericum perforatum)

Traditionally used for depressive disorders, this herb exerts a beneficial effect on the nervous system. Hypericum extract has been widely studied as a treatment for depression and at doses of 300 to 900 mg is shown to be significantly more effective than placebo and well-tolerated in cases of mild to moderate depression.<sup>30</sup>

#### Muira Puama (Ptychopetalum olacoides)



St. John's Wort (Hypericum perforatum)

Muira Puama is highly regarded as a nerve tonic in the Amazon where it is traditionally used to treat those with lack of motivation and fatigue. Extract of Muira Puama is reported to exert a modulating effect on the HPA axis.<sup>31</sup>



#### Albizia (Albizia julibrissin)

The flowers and bark of the mimosa tree, *Albizia julbrissin*, are among the most valued Chinese botanicals used to relieve stress, insomnia and depression. Studies find that Albizia bark extract enhances neurotransmitter regulation with positive effects on mood.<sup>32-34</sup>

#### L-Tryptophan

This essential amino acid, obtained from food, is the precursor to serotonin and melatonin, which play key roles in regulating mood, appetite and balanced circadian rhythms. Tryptophan is a precursor to serotonin, a key neurotransmitter that influences mood, sleep, metabolism, appetite and sexuality. Serotonin also modulates anger and aggression. Supplementation of tryptophan is found to be beneficial in the management of neuropsychiatric disorders.<sup>35</sup>

#### N-Acetyl-L-Tyrosine

L-tyrosine is precursor to catecholamines influencing synthesis of dopamine, epinephrine and norepinephrine and can support replenishment of catecholamnes when they are depleted due to stress. Some studies suggest that L-tyrosine helps improve cognitive function and memory while under stress.<sup>36</sup> Tyrosine is also essential for the formation of thyroid hormone. Practitioners often use the N-Acetyl-L-Tyrosine which is 20 times as water-soluble as tyrosine and hence better absorbed through the digestive tract.

#### L-Theanine

L-theanine is found to stimulate the production of alpha brain waves and is a precursor of GABA, helping to promote the relaxation response. Studies done with neurons in cell culture linked theanine to significant reversal of glutamate-induced neurotoxicity, a major cause of degenerative brain conditions. Theanine is also shown to be neuroprotective.<sup>37</sup>

c. Therapeutic Principle: Support and enhance cognitive function Method: Support cerebral and nervous system; modulate neurological activity with botanicals and natural compounds

Healthy cognitive ability and function is essential for daily work, self-care and social interaction and is the foundation for healthy mental, emotional and spiritual life. Supporting neurocognitive health can be accomplished with use of botanical adaptogenic compounds combined with nutrients known to enhance cognition and brain function.

There are a variety of botanicals that support cognitive function, are neuroprotective, and encourage healthy cerebral blood flow and oxygenation. Many herbs and natural compounds also modulate inflammatory response in the brain and modulate neurological activity. Additionally, these herbs and nutrients enhance mental and emotional recovery after stress, whether the stress is physical (such as endurance sports), mental (as in long work hours with intensive mental projects) or emotional – where emotional stress, anxiety and lack of sleep can adversely affect mental cognition.



#### Bacopa (Bacopa monnieri)

Bacopa, used for centuries in Ayurvedic medicine, is recognized for its benefits to enhance memory and learning and as a sedative. It is rich in steroidal saponins that help modulate the HPA axis and protect the hippocampus, a key area of the brain. It supports GABA production, which has a calming effect on the brain, enhancing the ability to concentrate and retain information. Considered both neuroprotective and nootropic (enhancing cognition and memory), it could potentially be beneficial for those with memory loss.<sup>38</sup>

#### Ginkgo (Ginkgo biloba)

With a history of medicinal use dating back to 2800 BC, Ginkgo was traditionally used to relieve cough and asthma. Modern research has focused on Ginkgo's unique ability to increase cerebral blood and oxygen flow and to protect and enhance brain health. Studies report that Ginkgo extract is a powerful antioxidant with anti-inflammatory and neuroprotective qualities.<sup>39</sup> Ginkgo is found to protect brain cells during a stroke.<sup>40</sup> A study with mice found Ginkgo helped reduce copper-induced neurotoxicity in Parkinson's by reducing overall copper content.<sup>41</sup>



Ginkgo biloba

#### Rosemary (Rosmarinus officinalis)

Traditional European herbalists called Rosemary the "Herb of Remembrance". They valued it as a tonic for the heart, brain and nervous system. It was found to increase circulation, mental outlook and vitality. Rosemary has also been used to calm anxiety, alleviate tension and depression and help promote sleep. It contains numerous antioxidant compounds that are neuroprotective, hepatoprotective and anti-inflammatory.

#### Gotu Kola (*Centella asiatica*)

Gotu Kola is highly esteemed as a powerful restorative tonic, known as Rasayana, in Ayurvedic medicine. For thousands of years, Gotu Kola has been recognized as a brain tonic and used to improve memory, cognition and brain function. In modern times, Gotu Kola is found to increase brain levels of GABA, thus inhibiting the uptake of glutamate by the brain.<sup>42</sup> A recent study found that one of the main triterpenes in Gotu Kola dramatically reduced the build-up of amyloid plaque.<sup>43</sup> It is also found to be beneficial in cases of cereberal ischemia.<sup>44</sup>

#### Chinese Salvia (Salvia miltiorrhiza)

Known as Dan Shen in Chinese medicine, it is one of the "shen" or spirit herbs that can be used safely long-term with multiple benefits. Traditionally used to nourish the blood and invigorate blood circulation it is also valued as a restorative tonic. One of its constituents, salvianic acid, is being researched for neuroprotective and antioxidant activity. Another constituent, salvianolic acid, shows protective effect on brain injury, is found to improve brain mitochondria,<sup>45</sup> and to enhance cognitive performance.<sup>46</sup>

#### Acetyl L-Carnitine

Acetyl L-carnitine, a derivative of the amino acid L-carnitine, has specific influence on brain and cognitive function. Studies find acetyl L-carnitine effective to support brain health and optimize cognition especially during age-related cognitive decline but also in Alzheimer's disease. It is found to



enhance neuronal function and to help stabilize the mitochondrial membrane of neurons.<sup>47</sup>

#### Polygala tenuifolia

This herb has been used in Chinese medicine to help calm the "shen" or spirit (mind) and nourish the heart. Recent studies indicate that Polygala root extracts supports cognition and memory and exerts neuroprotective effects.<sup>48</sup>

#### Phosphatidylserine

A key component of cellular and neuronal membranes, phosphatidylserine is essential nutrient for brain function. This phospholipid promotes membrane fluidity and enhances glucose metabolism in the brain. Clinical studies demonstrate its ability to improve learning and memory-related tasks.<sup>49</sup> Phosphatidylserine is known for its ability to reduce cortisol levels and can be used in the evening to help promote a restorative sleep, especially when combined with supportive herbs.

#### Vinpocetine

Vinpocetine is a semisynthetic derivative alkaloid from the Periwinkle plant (*Vinca minor*). Studies show that it enhances cerebral blood flow.<sup>50</sup> Found to be neuroprotective, providing antiinflammatory and antioxidant activity, vinpocetine could be useful to support recovery from cerebrovascular conditions.<sup>51,52</sup>

#### Huperzine A

Huperzine A is extracted from *Huperzia serrata*, a club moss. Modern research is focusing on the ability of Huperzine A to enhance memory and support cognitive function.<sup>53,54</sup> It also demonstrates neuroprotective qualities.

### Conclusion: Adaptogenic Botanicals Optimize Neurocognitive Health

Since adaptogenic botanicals work in a non-specific manner, they work on the system as a whole while modulating the neuroendocrine and immune system function and response. Adaptogenic botanicals enhance a resilient stress response and the capacity to achieve the best therapeutic benefits from any integrative protocol. Use of botanical and nutritional medicines to support and balance hormonal and neurotransmitter responses and to calm and nourish the nervous system offer a foundational approach to any integrative program. This is central to address issues such as cognitive health, mood and a restorative sleep cycle to enhance optimal well-being.

For more information, please contact Linda Jo Strouse at Natura Health Products. Call 1-888-628-8720, ext. 308 or email lindajo@naturahealthproducts.com.



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