

Excessive chronic stress is recognized as a causal or exacerbating factor in chronic non-communicable illness. It is increasingly acknowledged that chronic stress can no longer be assessed solely through measurement of cortisol levels. In contrast, research indicates that as chronic stress leads to a state of adrenocortical exhaustion or "burnout," a compensatory adrenal response may occur in the form of increased sympathetic, catecholamine activity.¹ Because of this increasingly common phenomenon, which is associated with such conditions as post-traumatic stress disorder and classic fibromyalgia,²-6 it is clinically prudent to employ formulations that not only optimize cortisol balance but correct catecholamine imbalances as well, particularly when sympathetic responses appear to be excessive.

CatecholaCalm™ is specifically designed to address this unique but increasingly prevalent set of adrenal hormone and neurotransmitter imbalances (often referred to as the "wired and tired" individual). The product accomplishes this by providing adaptogenic, nervine and adrenal tonic herbs for relaxation along with nutrients designed to help with adaptation to stress and optimization of adrenal gland health. The specific focus is on both cortisol and catecholamine balance. Elevated catecholamines and especially cortisol can affect serum blood glucose and insulin levels, thereby contributing to the development of metabolic syndrome and type 2 diabetes, both of which have reached overwhelming prevalence.<sup>7,8</sup>

#### **BOTANICAL HIGHLIGHTS**

#### **Ashwagandha** (Withania somnifera)

This adaptogenic herb has a long history of use as a nerve tonic in Ayurvedic medicine. It has been demonstrated to have a sparing effect on stress-induced cortisol depletion and to promote relaxation. "Somnifera" in the botanical nomenclature of this herb is derived from the word somnolence, meaning rest and sleep. Thus, ashwagandha is considered a relaxing adaptogen.

## **Valerian root** (*Valeriana officinalis*)

This herb has demonstrated sedative effects due to its ability to induce the release of GABA from brain tissue and also to inhibit the degradation of GABA.10 Valerian and its primary active component, valerenic acid, have anxiolytic and sedative effects also through GABAergic mechanisms. Human trials have validated the use of valerian for anxiety, insomnia and restlessness, which may be beneficial for those whose mental and emotional distress interfere with restful sleep.<sup>11-13</sup> This herb may work through effects on benzodiazepine receptors but without the undesirable side-effects of such drugs. Researchers evaluating the effect of valerian on insomnia and anxiety wrote that valerian may be useful in weaning patients with insomnia off of benzodiazepines and similar potential has been observed for passion flower extract.<sup>13,14</sup>

#### **Passion flower** (*Passiflora incarnate*)

Human and animal studies support the use of passion flower for improving anxiety, agitation and nervousness.<sup>15</sup> Like valerian, this botanical may also be helpful for individuals with insomnia.<sup>16</sup> It has been suggested that apigenin, a constituent of passion flower, binds to central benzodiazepine receptors, possibly causing anxiolytic effects without impairing memory or motor skills.<sup>17</sup> Passion flower exerts anxiolytic activity also via GABAergic mechanisms and may help attenuate benzodiazepine dependence.<sup>14,18-20</sup>

#### Lemon balm (Melissa officinalis)

This herb has been suggested to improve calmness via the inhibitory action of GABA, similar to benzodiazepines but without the overt side-effects of these medications.<sup>21</sup> In vitro studies indicate that lemon balm extract substantially inhibits GABA transaminase (GABA-T), the enzyme that degrades GABA, which may be the basis for its calming effects.<sup>22,23</sup>

#### Additional ingredients documented to optimize mood and stress physiology:

**L-Theanine** has been demonstrated in human studies to significantly reduce cortisol response and subjective stress response to cognitive stressors and to suppress the stimulatory effect of caffeine. Theanine crosses the blood brain barrier and is known to block the binding of glutamic acid to glutamate receptors in the brain "and has been considered to cause anti-stress effects by inhibiting cortical neuron excitation." Studies in healthy adults show that L-theanine reduces anxiety and attenuates blood pressure increases under conditions of physical or psychological stress, and animal studies suggest that L-theanine increases brain levels of serotonin, dopamine and GABA. Human EEG studies show "L-theanine significantly increases activity in the alpha

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frequency band which indicates that it relaxes the mind without inducing drowsiness,"28 making it a valuable tool for relieving feelings of anxiety or stress while not negatively impacting alertness and focus.

**Phosphatidylserine (PS)** has been demonstrated to decrease reactivity of the pituitary-adrenal axis to stress and control cortisol release. <sup>30,31</sup> Healthy male subjects given PS and phosphatidic acid (a precursor to PS) showed normalized levels of ACTH and cortisol compared to placebo. <sup>32</sup> This result was seen in subjects defined as "chronically high-stressed" but not in those with lower stress levels. This finding confirmed those of an earlier study in which PS (combined with omega-3 fats) was found to favorably affect the stress response in a group of healthy men with high chronic stress compared to those with lower regular stress levels. <sup>33</sup> It may be that lower-stress individuals have less exaggerated stress responses to begin with and would therefore benefit less from substances that target a lowering of cortisol. The PS used in this formula is derived from sunflower lecithin and is soy-free.

**Taurine**, along with GABA, is recognized to be a major inhibitory neurotransmitter, specifically acting as a modulator of GABAergic function.<sup>34</sup> Animal models show that taurine administration leads to reductions in anxiety and fear-like behaviors as well as a dampening of the cortisol response following acute stress.<sup>35</sup> Research in rodents indicates taurine has an anti-depressant effect via modulation of the HPA axis, and that in depressive rats taurine attenuates decreases in serotonin, dopamine, noradrenaline and brain-derived neurotrophic factor whereas it attenuates the increase in glutamate and corticosterone.<sup>36</sup>

**Magnesium (as di-magnesium malate)** has a general calming effect and may help reduce irritability under stress. Given that patients who are experiencing elevated catecholamines are often insulin resistant<sup>37</sup> and that insulin resistance impairs cellular uptake of magnesium,<sup>38</sup> it is recommended to use highly absorbable chelated forms of magnesium such as malate or glycinate. Concerning catecholamine metabolism, magnesium has been demonstrated to suppress the release of catecholamines by the heart, which is an indirect index of sympathetic efferent neuronal activity.<sup>38</sup>

**Thiamine (vitamin B1)** is the core component of thiamin pyrophosphate (TPP), a coenzyme required for catabolism of the branched chain amino acids, which are nitrogen sources for the synthesis of GABA and glutamate.<sup>39</sup> Research indicates that thiamine deficiency causes oxidative and endoplasmic reticulum stress and autophagy associated with various neurodegenerative disorders.<sup>40</sup>

**Vitamin B12 (as methylcobalamin)** is a cofactor for or is otherwise involved in catecholamine degradation as well as synthesis of epinephrine from norepinephrine and also plays a role in myelin synthesis, making it crucial for healthy nervous system function.<sup>41</sup> B12 deficiency, including subclinical insufficiency, may be associated with agitation, irritability, impaired concentration and focus, and feelings of panic such as those that might occur under prolonged psychological stress.<sup>42</sup>

**Vitamin B6 (as pyridoxal-5-phosphate)** is a cofactor for the enzyme aromatic L-amino acid decarboxylase, required for the synthesis of serotonin and dopamine. It is also involved in the synthesis of GABA and norepinephrine.<sup>43</sup>

**Vitamin C** has been found to reduce the oxidation rate of catecholamines and is also required for synthesis of catecholamines and cortisol.<sup>44</sup> The fatigue associated with vitamin C deficiency has many putative causes, one of which may be decreased synthesis of norepinephrine.<sup>45</sup>

CatecholaCalm $^{\text{TM}}$  also includes pantothenic acid and riboflavin (vitamin B2, as riboflavin 5-phosphate), which play critical roles as enzyme cofactors in the production of stress hormones.

### **BENEFITS:**

- · Promotes healthy cortisol & catecholamine levels
- Supports neurotransmitter synthesis
- Promotes calm & relaxation without inducing drowsiness
- Supports healthy adrenal gland function
- Helps reduce adverse effects of chronic stress
- · Supports GABA activity for mental calm

#### Medicinal Ingredients (per capsule):

Taurine	100 mg
L-Theanine	66.67 mg
Ashwagandha (Withania somnifera-Root) (1.5% Withanolides 5:1)	33.33 mg
Lemon balm (Melissa officinalis-Herb) (3% Rosmarinic acid 5:1)	33.33 mg
Passionflower (Passiflora incarnata-Flower, Herb) (3.5% Bioflavonoids 6:1)	33.33 mg
Valerian ( <i>Valeriana officinalis</i> -Root) (0.8% Valerenic acid 8:1)	33.33 mg
Vitamin C	
Magnesium (Dimagnesium malate)	25 mg
Pantothenic acid (Calcium d-pantothenate)	16.67 mg
PhosphatidylserinePhosphatidylserine	16.67 mg
Thiamine (Thiamine hydrochloride)	16.67 mg
Riboflavin (Riboflavin 5'-phosphate sodium)	3.33 mg
Vitamin B6 (Pyridoxal 5-phosphate)	1.67 mg
Vitamin B12 (Methylcobalamin)	0.67 mg

**Non-Medicinal Ingredients:** Hypromellose, magnesium stearate (vegetable source), microcrystalline cellulose. **Recommended Dose:** Adults: Take 3 capsules per day, or as directed by your health care practitioner. Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage. Any product containing botanical substances has the potential for causing individual sensitivities. Individual monitoring, including liver function tests, may be appropriate.

# **CatecholaCalm™**

Natural support to help promote calmness and relaxation

CatecholaCalm™ contains a blend of vitamins, minerals and adaptogenic herbs designed to support a healthy response to stress. The most well-known stress chemicals in the body are cortisol and the catecholamines — specifically, epinephrine (adrenaline) and norepinephrine. CatecholaCalm™ is formulated to help balance the levels of these chemicals and to support overall health. The mind-body connection is a powerful system; proper levels of stress chemicals help to support healthy blood sugar and insulin levels, body weight, the immune system and a positive mental outlook.

# **Highlights**

- Vitamin C and the B vitamin family: Help support steady energy levels. When the body is under occasional stress, it can get "revved up" and burn through nutrients quickly, so it is important to maintain sufficient levels of these valuable vitamins. Vitamin B12 helps support proper levels of catecholamines. Vitamins C and B5 (pantothenic acid) are important for healthy adrenal gland function the adrenals being the primary glands responsible for producing the stress response.
- **Phosphatidylserine (PS):** Nutrient that promotes healthy hormone levels by helping to normalize cortisol levels when the body is under occasional stress. The PS in this product is soy-free and is derived from sunflower lecithin.
- **Ashwagandha:** An adaptogenic herb with a long history in Ayurvedic medicine for aiding a healthy stress response. "Adaptogenic" herbs are given this name because they help the body "adapt" to stress, assisting the body in optimizing levels of hormones and neurotransmitters.
- **Magnesium:** One of the body's most important minerals; aids in muscle relaxation and therefore may help with occasional simple nervous tension and may offer a calming effect for both body and mind.
- **Valerian, lemon balm and passion flower:** Herbs that promote relaxation, in part by supporting the production of GABA, a calming neurotransmitter that helps balance the stress catecholamines.

**Recommended Dose:** Take three capsules per day, or as directed by your health care practitioner. Consumption with alcohol or other medications with sedative properties is not recommended. **Does not contain gluten.** 

