# THE BIG CHILL GUM

# INTRODUCTION

The Big Chill chewing gum has a special blend of ingredients that help give your brain a boost of energy while improving cognition, performance and focus. It also aids in relaxation, avoiding the harmful effects that chronic stress and anxiety can cause to your overall health and wellbeing, all while maintaining an alert calmness.

Stress can cause the release of hormones, such as cortisol, that can alter the structure of important connections in the brain over long periods of time.\* The level of serotonin in the brain also decreases in response to stress. Serotonin is important for mood, symptoms of depression and anxiety as well as cognition and memory.\*

Persistent stress and anxiety can lead to memory impairments. The size of certain structures in the brain, such as the hippocampus, can have a negative effect on both younger and older individuals.\* The hippocampus in particular, is the structure in the brain where memories are formed, organized, and stored. Stress and anxiety hinder this structure from functioning properly and this leads to problems with processing, retaining, and recalling information.\*

# THE BIG CHILL INGREDIENTS

### Zembrin™

Zembrin<sup>™</sup> is the first patented, standardized and clinically studied extract of the South African plant Sceletium tortuosum. Zembrin<sup>™</sup> is a highly effective, fast acting, mood-lifting and anxiety reducing indigenous plant extract. It boosts mood and relieves stress without stimulants while improving cognitive function, reducing symptoms associated with stress and anxiety, as well as increasing processing speed and concentration.

#### L-Theanine

L-Theanine is a unique amino acid found almost exclusively in green tea that exerts beneficial effects on brain metabolism. L-Theanine enhances both dopamine and serotonin production which improves mood, increases satiety and alpha brain activity thus enhancing mental performances while maintaining a calm and relaxed state.

## Crocus Sativus (Saffron Extract)

Crocus Sativus from the saffron flower acts via the reuptake inhibition of dopamine, glutamate, norepinephrine and serotonin. It improves memory, inhibits neuronal degeneration, has antioxidative properties, reduces signs of depression, and inhibits the formation of insoluble amyloids. Crocus Sativus is also known to reduce appetite, cravings and compulsive snacking due to improved emotional behavior.

# MECHANISMS OF ACTION

### Zembrin ™

Zembrin<sup>™</sup> is a patented extract of Sceletium Tortuosum, which is grown in South Africa. Zembrin<sup>™</sup> extract enhances cognition and regulates mood symptoms (reducing stress symptoms and anxiety) thru its dual PDE4 and 5-HT reuptake inhibition.\*

Studies have shown that Sceletium tortuosum acts on the CNS neurons to block the reuptake of serotonin, resulting in increased serotonin concentrations in the synaptic cleft. This increased concentration maintains a higher level of occupied serotonin receptors in the post-synaptic neuron, resulting in an increased serotonergic activity in the anxiety neural circuit. This is the same mechanism of action of the pharmaceutically available SSRI's prescribed by physicians to treat anxiety and depression.\* Zembrin<sup>TM</sup> also has been shown to have phosphodiesterase E4 (PDE4) inhibition effects. Some researches have postulated this combined SSRI/PDE4 inhibitor action may be more effective in treating anxiety and depression.\*

#### L-Theanine

L-Theanine is an amino acid and a glutamic acid analog primarily found in tea. It's known to improve brain activity, increase mood and enhance cognitive performance. It exhibits anxiolytic effect by regulating levels of dopamine and serotonin by blocking the effects of glutamate at the NMDA Receptor. \* It is also known to enhance alpha waves in the brain. Increased alpha wave levels reflect calm, but alert brain states required to focus and complete complex tasks.

L-Theanine also decreases stress related food cravings through moderating effects on stress levels and has an appetite-suppressing effect that is mediated through the inhibition of cerebral cortical excitability; which is stimulated by reducing orexinergic (appetite stimulating) neurons in the hypothalamus.\* The molecular properties of L-Theanine allow it to cross the blood-brain barrier and influence brain activity.\* It has been shown to promote quicker reaction time, faster numeric calculations, improve working memory reaction time and improve sentence verification accuracy in several clinical studies.\*

## Crocus Sativus (Saffron Extract)

Crocus Sativus has been historically known for improving symptoms in mood disorders. It is theorized that the clinical effects are due to the reuptake inhibition of dopamine, norepinephrine and serotonin by crocin and safranal, the two major components in Crocus Sativus.\* As a serotonin reuptake inhibitor, safranal increases serotonin concentrations in the synapses, which correspondingly increases the propagation signals that influence satiety and mood. Any metabolic or physiological state, which contributes to a depletion of serotonin such as stress, depression or other mood changes, can trigger cravings for increased carbohydrate intake to improve mood. Serotonin deficiency has been linked to stress-induced carbohydrate cravings.\*

# CLINICAL INDICATIONS

#### Zembrin™

In a double-blind, placebo-controlled, cross over designed study that included 16 healthy subjects, the effects of Zembrin<sup>TM</sup> were studied on anxiety related activity in the amygdala and connected anxiety neural circuitry.\* Subjects were administered either Zembrin<sup>TM</sup> 25 mg or placebo prior to undergoing a fMRI to evaluate CNS neuronal activity during a stressful, emotional task. The fMRI findings provided evidence amygdala activity was elevated during fearful presentations and this activity was attenuated after a single dose of Zembrin<sup>TM</sup>.\* The research also reported that neuronal activity levels in the amygdala and hypothalamus were clearly linked during the tasks. In this study Zembrin<sup>TM</sup> was confirmed to be a potent PDE4) inhibitor as well. PDE4 inhibition potentiates the effects of serotonin and has independent anxiolytic effects on the subcortical anxiety neural circuitry.\* The authors postulate that this dual serotonin-PDF4 activity may function better than the SSRI individual effect on anxiety and depression. The authors also concluded that these results demonstrate that Zembrin<sup>TM</sup> treats the hyperactivity in the neural circuitry.

## L-Theanine

L-Theanine is shown to have significant beneficial effects on anxiety, mood, and concentration. Individuals taking supplemental L-Theanine show improvements in mental and emotional health.

In one key study, students with high school levels of anxiety manifested the classical signs including tachycardia, impaired concentration, and slower reaction time. One group of students administered L-Theanine were found to have slower heart rates, improved attention and reaction times compared to a control group of anxious students that were administered a placebo. L-Theanine also did not have the side effects of drowsiness, slowed reflexes or diminished concentration common among anti-anxiety prescribed medication.\*

An additional study assessing the effect of L-Theanine on cognitive tasks, reported that the administration of L-Theanine resulted in a significantly improved general state of mental alertness, due to the increase in alpha wave levels.\*

#### Crocus Sativus

Crocin is the main chemical compound identified in saffron, whose scientific name is Crocus sativus. It has been used over the years in folk medicine as an antispasmodic, gingival sedative, nerve sedative, carminative, and expectorant stimulant. \* It has been reported that saffron active constituents have anticonvulsant, antidepressant, anti-inflammatory effects, and also improve learning and memory.\* Crocin is the actual active component involved in both the improvement of learning and memory and preventing effects of long term potentiation blocked by ethanol\* and its potential in the treatment of neurodegenerative diseases like AD.\* In animal models, the effectiveness of crocin has been shown in antagonizing the cognitive deficits caused by neurotoxic agents like streptozocin.\* Crocin improved cognition as evaluated by means of ADAS-Cog and CDR-SB in subjects with mild to moderate AD.\* In a recent in vivo study, it has been demonstrated that crocin significantly modulates the levels of oxidative markers in the hippocampus, abolishing the deleterious effects of chronic stress on learning and memory.\*

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