



NANOEMULSIFIED

# CBD SYNERGIES-SP+

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**CBD Synergies-SP+** formula is a fast-acting blend of full spectrum hemp extract, CBG, CBN, anandamide, melatonin, GABA, 5-HTP, skullcap, and passionflower, designed to help ease tension, calm the mind, and support restorative slumber. Full spectrum hemp extract retains the non-psychoactive, Farm Bill-compliant amount of THC to enhance the effects of the other phytocannabinoids in this sleep support formula.

## EDUCATION

### THE ENDOCANNABINOID SYSTEM AND PHYTOCANNABINOIDS FOR RESTFUL SLEEP

The endocannabinoid system (ECS) is a complex network of neuromodulators and receptors that regulates many aspects of human physiology, including cognition, immune function, and inflammation.<sup>1</sup> The ECS consists of the endocannabinoids anandamide and 2-arachidonoylglycerol, their G-protein-coupled receptors, and enzymes that regulate endocannabinoid synthesis and degradation, including fatty acid amide hydrolase (FAAH). Phytocannabinoids, plant-derived cannabinoids found in the crystalline trichomes of Cannabis plants, also interact with the ECS, exerting powerful biochemical and physiological effects.

$\Delta$ 9-tetrahydrocannabinol (THC) is arguably the most well-known phytocannabinoid due to its psychoactive properties. Maintaining a small, non-psychoactive amount of THC alongside many other well-researched phytocannabinoids like cannabidiol (CBD), cannabigerol (CBG), cannabidiolic acid (CBDA), cannabinol (CBN), cannabichromene (CBC), and cannabidivarin (CBDV) can offer a more powerful therapeutic experience referred to as the 'entourage' effect.

THC interacts directly with the G-protein-coupled CB1 and CB2 receptors, CBD, and its sister phytocannabinoids indirectly influence ECS activity by enhancing endocannabinoid tone. Phytocannabinoids also interact with various non-ECS receptors, including GABA, glutamate, serotonin, and opioid receptors. The complex interactions between phytocannabinoids, the ECS, and non-ECS receptors have significant implications for many aspects of health, including sleep.

An emerging body of research indicates that the ECS influences the sleep cycle, including the duration and quality of sleep.<sup>2,3,4</sup> CBD's interactions with the ECS promote restorative non-rapid eye movement (NREM) sleep and decrease sleep latency and disturbances.<sup>5</sup> CBD does not interfere with healthy sleep-wake cycles or have "groggy" effects.<sup>6</sup> As well, a small amount of THC may gently support the sleep benefits of CBD.<sup>7</sup>



### Supplement Facts

Serving Size: 2 mL (4 Pumps)  
Servings Per Container: 25

|  | Amount<br>Per Serving | % Daily<br>Value |
|--|-----------------------|------------------|
| Full Spectrum Hemp Extracts (aerial parts)   | 18 mg                 | **               |
| Cannabidiol (CBD)  | 10 mg                 | **               |
| Cannabigerol (CBG)   | 2 mg                  | **               |
| Cannabinol (CBN)   | 2 mg                  | **               |
| Melatonin  | 0.25 mg               | **               |
| 5-HTP<br>(L-5-Hydroxytryptophan)<br>(from Griffonia simplicifolia seed extract)  | 16 mg                 | **               |
| Proprietary Blend  | 160 mg                | **               |
| GABA (gamma-aminobutyric acid), Liquid Skullcap Herb extract (Scutellaria lateriflora), Liquid Passionflower extract (Passiflora incarnata), Chamomile essential oil |                       |                  |

\*\*Daily Value not established

**Other Ingredients:** Water, glycerin, ethanol, highly purified phospholipids, tocopherols, natural citrus oils, natural mixed tocopherols, medium chain triglycerides, natural flavorings, anandamide



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## CANNABIGEROL (CBG), CANNABINOL (CBN), AND ANANDAMIDE

Cannabigerol (CBG) and cannabinol (CBN) also show promise as sleep aids. CBG offers calming effects that may prepare the mind for deep, restful sleep.<sup>8</sup> When consumed alongside other cannabinoids, CBN may induce sleepiness, further easing the body into slumber.<sup>9</sup>

Anandamide, one of the body's endocannabinoids, also appears to play a role in sleep by interacting with adenosine. Adenosine is a sleep-inducing molecule that builds up inside our bodies each day; interestingly, caffeine blocks the binding of adenosine to its receptors, which is why it induces wakefulness! Anandamide has been found to increase adenosine levels, inducing sleep. Therefore, it shows promise as a helpful sleep aid.<sup>10</sup>

## 5-HTP, MELATONIN: CIRCADIAN RHYTHM SUPPORT FOR RESTORATIVE SLEEP

The circadian rhythm is the internal set of biochemical processes within the human body that regulate many aspects of physiology, including the sleep cycle. Melatonin is a hormone released by the pineal gland in the brain that functions as an endogenous synchronizer of the circadian rhythm, stabilizing and reinforcing the sleep cycle.<sup>11</sup> Melatonin is released in response to dimming light in the evening. Several aspects of modern-day life diminish melatonin production, including evening blue light exposure, travel across time zones, and aberrant sleep schedules. Supplemental melatonin realigns melatonin rhythms, initiating sleep and increasing total sleep time. It has been found to reduce sleep latency and improve sleep quality in diverse populations, including children on the autism spectrum, healthcare professionals, shift workers, and frequent flyers.<sup>12,13</sup>

Fascinating research indicates that the endocannabinoid system, which mediates the effects of cannabinoids, also influences the circadian rhythm.<sup>14</sup> The complex interplay between these two systems suggests that simultaneously taking nutraceuticals that target both the circadian and endocannabinoid systems may lead to even greater sleep-enhancing effects.

Unfolding research indicates that serotonin is critical for the induction of sleep.<sup>15</sup> 5-Hydroxytryptophan, or 5-HTP is readily taken up by the brain and decarboxylated into serotonin with the help of vitamin B6.<sup>16</sup> Serotonin, in turn, is the precursor for melatonin, a hormone released by the brain that regulates the sleep-wake cycle.<sup>17</sup> 5-HTP thus indirectly supports melatonin production, easing the body's transition into deep sleep.

## BALANCING GABA AND GLUTAMATE NEUROTRANSMISSION

Gamma-aminobutyric acid (GABA) is the body's primary inhibitory neurotransmitter and plays a central role in sleep induction.<sup>18</sup> Its calming activity is opposed by glutamate, the body's primary excitatory neurotransmitter. A delicate balance must be achieved between GABA and glutamate to attain restful sleep.<sup>19</sup> A deficiency in GABA neuronal signaling promotes chronic hyperarousal and sleeplessness.<sup>20</sup>

## TIME-HONORED BOTANICALS FOR RESTFUL SLEEP

Skullcap (*Scutellaria lateriflora*) has been used in traditional herbal medicine for centuries to relieve tension and support relaxation.<sup>21</sup> The traditional uses of skullcap have been validated by modern-day research, indicating that the botanical balances GABA and glutamate.<sup>22</sup> Skullcap is an excellent standalone sleep aid but also synergizes well with other sleep-promoting nutraceuticals such as GABA, passionflower, and CBD.

The beautiful purple and white flowers of *Passiflora incarnata*, the passionflower vine, have been used by Native Americans and professional herbalists for centuries for their gentle sedative and anxiety-relieving properties. Passionflower potentiates GABA activity, enhancing NREM sleep. It also regulates the activity of circadian genes, normalizing the body's sleep-wake cycle.<sup>23,24,25</sup> Passionflower's calming effects are believed to be mediated by its unique flavonoids, which interact with GABA receptors.<sup>26</sup>

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