



Deep Blue Sleep

Formula Monograph



Deep Blue Sleep is a targeted dietary supplement formulation designed to that help improve sleep and sleep pattern by balancing circadian rhythm and supporting neurochemicals and hormones related to sleep. **Deep Blue Sleep is a TRIAD 2 BRAIN supplement for sleep issues.**

| Supplement Facts | | | |
|--|--------------------|---------------|---|
| Serving Size: 2 Capsules Servings Per Container: 30 | | | |
| | Amount Per Serving | % Daily Value | Formula Use(s) |
| Magnesium bisglycinate chelate buffered | 100 mg | 24% | <ul style="list-style-type: none"> Co-factor involved in over 300 biochemical reactions Support sleep quantity and sleep quality Improves restless legs Calming mineral for the nervous system |
| Jujube (<i>Ziziphus jujuba</i>) fruit extract 4:1 fruit extract | 265 mg | * | <ul style="list-style-type: none"> Supports sleep quality Anxiolytic, sedative and hypnotic effects in laboratory studies Neuroprotection Increases hippocampal neurogenesis Decreases neuro-oxidative stress Supports memory and learning |
| Magnolia (<i>Magnolia officinalis</i>) bark extract Std to 98% honokiol | 100 mg | * | <ul style="list-style-type: none"> Honokiol is reported to bind to GABA_A receptors Decreases sleep latency to NREM sleep Increases NREM sleep NMDA antagonist Suppresses glial cell activation Decreases LPS induced memory deficit Antianxiety Pain modulation Endocannabinoid binding – CB1 |

| | | | |
|--------------------------------|------|---|--|
| Melatonin | 5 mg | * | <ul style="list-style-type: none"> • Natural hormone for sleep cycles • Antioxidant • Immune supportive |
| * Daily value not established. | | | • |

Recommended Uses:

Helps support the body's natural sleep cycles in order to obtain quality and restful sleep.

Recommended Dosages:

2 capsules, 1 hour before bedtime as needed.

Product Background:

Sleep is essential to a balanced metabolism. Sleep helps regulate circadian rhythms, including learning and memory, cellular repair, regulation of immunity, core body temperature, melatonin secretion by the pineal gland and plasma levels of DHEA and cortisol.¹ Sleep disorders include:

- Insomnia
- Obstructive sleep apnea
- Night-eating syndrome
- Restless leg syndrome
- Narcolepsy

Research has reported that most individuals should obtain at least 7-9 hours of quality sleep a night (Centers for Disease Control, CDC, 2011).² Less than the recommended 7-8 hours of uninterrupted sleep can lead to health consequences including:^{3,4,5,6,7,8,9}

- Increased inflammatory signaling/oxidative stress
- Increased cardiovascular disease risk, including hyperlipidemia, hypertension, endothelial dysfunction, increase mortality from CVD
- Gastrointestinal imbalances
- Increased bone loss
- Insulin resistance/type 2 diabetes
- Increase musculoskeletal aches/pains
- Neurochemical imbalances
- Weight gain/food cravings
- Immune imbalances
- Sex and thyroid hormone imbalances
- Cancer

67% of Americans experience frequent problems sleeping and 43% say lack of sleep interferes with their daily activities. Between 9-12% of the population are clinically diagnosed with insomnia.^{10,11}

Unfortunately, the pharmaceutical drug class benzodiazepines are the standard therapy for most physicians when treating insomnia, and include diazepam (Valium), lorazepam (Ativan), alprazolam (Xanax), clonazepam (Klonopin),

estazolam (ProSom) and others. However, these drugs are notorious for problems including drowsiness and a “hangover” effect, to physical and mental dependence and addiction. According to a 2016 public health study, the number of individuals using benzodiazepine drugs increased from eight million to almost 14 million between 1996 and 2013.¹²

The percentage of outpatient medical visits that led to a benzodiazepine being prescribed doubled from 2003 to 2015.¹³ There are estimates to 44% of chronic benzodiazepine users will become dependent on them, and hospital admissions for benzodiazepine misuse have tripled since 1998.¹⁴ Benzodiazepines are already being touted by researchers as the “next opioid epidemic” in the US. Efficacious alternatives to these drugs are needed.

Supporting Research:

Magnesium bisglycinate chelate

Magnesium is an essential nutrient that is a co-factor in over 200 biochemical reactions in the body. Magnesium is important in neurological health, bone health, sleep, blood glucose and insulin regulation, inflammation and cardiovascular health.

Magnesium supplementation is reported to improve sleep efficiency, sleep time and sleep onset latency, early morning awakening, and insomnia objective measures such as the concentration of serum renin, melatonin, and serum cortisol in older adults.¹⁵ A 2019 study using 60 patients with insomnia reported that use of magnesium, melatonin and vitamin B complex improved sleep significantly vs placebo over a 3 month period.¹⁶

Jujube (*Ziziphus jujube*) fruit extract and Magnolia (*Magnolia officinalis*, 98% honokiol) bark

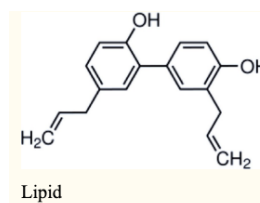
Preparations of *Magnolia officinalis* bark and *Ziziphus jujuba* seed have been traditionally used in Asia for mild anxiety, nervousness and sleep-related issues for centuries.

The fruits of *Ziziphus jujuba*, known as jujube or Chinese date, have been consumed for thousands of years particularly in Asia because of their health benefits, as both food and herbal medicine. Flavonoids, polysaccharides and triterpenic acid are the major phytochemicals in Jujube.¹⁷ Traditionally, one of the main functions of jujube is to benefit the brain by calming down the mind and improving quality of sleep. Jujube is reported to have sedative and hypnotic effects in laboratory animals.¹⁸ Jujube is reported to possess neuroprotective activities, including protecting neuronal cells against neurotoxin stress, stimulating neuronal differentiation, increasing expression of neurotrophic factors, and promoting memory and learning. Jujube is also reported to improve neurogenesis.¹⁹

Studies have reported that a proprietary combination of magnolia bark extract and jujube extract help modulate central nervous system activity, promoting muscle and overall relaxation as well as supporting optimal sleeping time.²⁰ Research has indicated that magnolia extract (specifically the phytochemical honokiol) and ziziphus have a combined calming effect in part by binding to adenosine A1, serotonin, GABA and endocannabinoid receptors.^{21,22} In addition, animal studies suggest that magnolia extract may promote positive mood and calm occasional physical and emotional stress.²³

A study involving 50 individuals indicated that a proprietary formulation of Ziziphus and Magnolia encouraged sleep and relaxation. Another study involving 45 people revealed similar results and also reported support for daytime energy levels. Moreover, combinations of Ziziphus and Magnolia have the potential to provide weight management support, based on recent research suggesting that reduced amounts of sleep are associated with increased weight. Additionally, a randomized crossover clinical trial found that unrestful sleep was associated with increased hunger and decreased levels of the satiety hormone leptin. An open-label assessment using 295 volunteers were administered a proprietary formulation of Ziziphus fruit and Magnolia bark extracts, 1 capsule nightly for 2 weeks.²⁴ Results were 86.9% of participants felt the supplement was relaxing and 82.8% felt it assisted with a restful sleep and was effective in reducing fatigue due to lack of sleep.

Our formula is improved by using 98% honokiol for the Magnolia component instead of raw magnolia bark extract. Honokiol (5,3'-diallyl-2,4'-dihydroxybiphenol) is the major phytochemical compound found in Magnolia bark, it readily crosses the blood brain barrier and is known for its antianxiety and antidepressant activity.²⁵ Honokiol is neuromodulating, by improving GABA synthesis, being a NMDA antagonist and decreasing neuroinflammation by decreasing glial cell NFκB activation and cytokine production.^{26,27} and is reported to promote NREM sleep by modulating the benzodiazepine site of the GABA_A receptor, suggesting potential applications in the treatment of insomnia, especially for patients who experience difficulty in falling and staying asleep.²⁸ Honokiol is reported in laboratory studies to promote sleep and anxiolysis as well as the benzodiazepines and without the side-effect profile of dependence, hangover and daytime drowsiness.²⁹ It is suggested that Honokiol's analgesic effects involve the inflammatory cascade, the NMDA receptor, and inhibition of inflammatory pain mediators such as glutamate and substance P.³⁰ Honokiol is also reported to bind to endocannabinoid receptors CB1.³¹



Melatonin

Melatonin is a methoxyindole hormone that is produced in the pineal gland in the brain. It is synthesized from L-tryptophan in the diet, which is converted into 5-hydroxytryptophan then into melatonin. Melatonin is reported to help regulate

sleep/wake cycles and circadian rhythms.^{32,33} Melatonin also helps improve immunity and is an antioxidant.³⁴

Melatonin levels decrease with increasing age. Other conditions that may lower melatonin levels include jet lag, night shift working, chronic stress and some medications. The following medications are reported to potentially deplete melatonin levels in the body:

- Beta-blockers
- Calcium channel blockers
- Benzodiazepines
- Estrogen-containing medications
- Hydralazine
- Loop diuretics
- Theophylline
- Antidepressants, including SSRI (Selective serotonin reuptake inhibitors)
- NSAIDs (Non-steroidal anti-inflammatory drugs)

Toxicity, Contraindications, or Side Effects:

- There are no known toxicities or side effects from taking ingredients found in ***Deep Blue Sleep***.
- Honokiol, a component of ***Deep Blue Sleep*** has been reported to be a potent inhibitor of arterial thrombosis, so it may be advisable to avoid honokiol in coagulopathic patients or in those where bleeding or hemorrhage may be of concern.³⁵
- ***Deep Blue Sleep*** may cause drowsiness, so use caution when driving an automobile or operating heavy machinery when using ***Deep Blue Sleep*** for the first time.
- If using prescription or non-prescription medications, especially for sleep and/or anxiety, use with caution.

DISCLAIMER: *This material is provided for educational and informational purposes only. This information is obtained from sources believed to be reliable, but its accuracy cannot be guaranteed. Herbs and other natural substances are powerful and can occasionally cause allergic reactions in a small percentage of the population. Licensed health care professionals should rely on sound professional judgment when recommending herbs and natural medicines to specific individuals. Individual use of herbs and natural medicines should be supervised by an appropriate health care professional. The use of any specific product should always be in accordance with the manufacturer's directions.*

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