

Calm Sleep SAP

Science-based sleep support

Sleep is a crucial cornerstone of health that can be disrupted due to various circumstances such as travel, work stress, and disease states. Improvement of sleep duration, sleep quality, and reduction of anxiety are key factors for a better quality of life. Ingredients such as tryptophan, melatonin, passionflower, and L-theanine are clinically proven natural therapeutic agents that can improve sleep quality. Additionally, recent studies have successfully shown that passionflower, chamomile, and L-theanine can reduce levels of anxiety and stress by decreasing not only perceived stress and anxiety but also reducing heart rate and immunoglobulin levels. Although studies are preliminary, jujube and notoginseng extracts have been long used in traditional Chinese medicine effectively for their calmative and sedative properties. **Calm Sleep SAP** provides optimum dosages of these ingredients that help with sleep quality and daily stress and anxiety, while also helping with occasional life events such as travel, jet lag, shift work, or otherwise altered sleep schedule.

Calm Sleep SAP provides a safe dose of key nutraceuticals and botanicals for better sleep quality and relaxation.

ACTIVE INGREDIENTS

Each vegetable capsule contains

L-Tryptophan	200 mg
Chamomile (<i>Matricaria chamomilla</i>) flower extract	150 mg
Passionflower (<i>Passiflora incarnata</i>) herb top extract	120 mg
L-theanine	100 mg
Notoginseng (<i>Panax notoginseng</i>) root extract (25% saponins)	50 mg
Jujube (<i>Ziziphus jujuba</i> var <i>spinosa</i>) 8:1 seed extract	30 mg
Melatonin	1.5 mg

Other ingredients: Vegetable magnesium stearate and silicon dioxide in a capsule composed of vegetable carbohydrate gum and purified water.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, artificial flavour and colour, or sugar.

This product is non-GMO and vegan friendly.

Calm Sleep SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: See indication-specific dosages outlined in the indication-specific dosage table (available as an additional resource material)

Adults: All uses except jet lag: Take 1 capsule once a day, at or before bedtime. Jet lag: Take 1 capsule once a day at bedtime, while travelling, and at destination, until adapted to the new time zone or daily pattern.

The directions and dosage provided in this document are based on the research studies and the study population studied. It is suggested that the dosage, timing, and duration of use be personalized for each patient by the healthcare practitioner based on the patient's medical history, symptoms, concomitant medications, and responsiveness to the dosage for effectiveness.

INDICATIONS

Calm Sleep SAP can help:

- Relieve restlessness and nervousness, especially during times of mental stress.
- Reset the body's sleep-wake cycle (circadian rhythm) and increase total sleep time with people suffering from sleep restriction or altered sleep schedule.
- Reduce daytime fatigue and sleep disturbance especially for people travelling over two or more time zones.

CAUTIONS AND WARNINGS

(These are generic Health Canada Warnings)

Avoid taking with alcohol or products that cause drowsiness. Consult your healthcare practitioner if sleeplessness persists for more than 4 weeks (chronic insomnia) and prior to use if you are taking seizure, blood pressure and immunosuppressive medications, or medications to affect mental state or increase sedation, steroids or blood thinners, or if you have cardiovascular, immune, liver or chronic kidney disease, hormonal or seizure disorders, asthma, depression, diabetes, low blood sugar, or migraine, or if symptoms persist or worsen. If you experience any of the following symptoms within a few hours after taking this product, discontinue use and consult a healthcare practitioner: changes in mental state such as restlessness or confusion, increased heart rate, enlarged pupils, loss of muscle coordination, sweating, shivering, and/or gastrointestinal symptoms such as nausea, vomiting, diarrhea.

CONTRAINDICATIONS

Do not drive or use machinery for 5 hours after taking melatonin. Do not use this product if you are pregnant or breastfeeding or if you are taking drugs/supplements with serotonergic activity such as carbidopa, selective serotonin reuptake inhibitors (SSRIs), serotonin modulators, L-tryptophan, S-adenosylmethionine (SAME), St. John's wort, antidepressants, pain killers, over-the-counter cough and cold medication containing dextromethorphan, anti-nausea medication, and anti-migraine medication.

KNOWN ADVERSE REACTIONS

Some people may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle, or are involved in activities requiring mental alertness. Stop use if hypersensitivity/allergy occurs, or if you experience headache, confusion, or nausea.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Calm Sleep SAP** lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP):
adding nutraceutical research
to achieve optimum health



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The American Academy of Sleep Medicine defines insomnia as “difficulty with sleep initiation, duration, consolidation or quality that occurs despite adequate opportunity for sleep, and that results in some form of daytime impairment”. [1] Impaired sleep can occur due to a variety of reasons such as travel, jet lag, altered routines, shift work, or stressful life situations. Impaired sleep can contribute to an increased risk of metabolic disorders such as obesity, cardiovascular diseases, and diabetes, in addition to posing a risk to public health due to industrial and traffic accidents occurring from lack of rest. [2,3] Good quality sleep is essential to prevent cognitive dysfunction and maintain a healthy mood balance. [3] Use of conventional sleep medications such as barbiturates and benzodiazepines is fraught with issues such as side effects and addiction. [4] Alternative plant-based or naturally derived therapies have been used in traditional medicine to improve sleep quality. Recent clinical trials have tested these ingredients to establish and verify a safe and efficacious dose.

L-Tryptophan

Tryptophan is an essential amino acid found in protein-rich foods such as milk. Several clinical trials have studied the impact of tryptophan supplementation on sleep latency and quality. A meta-analysis of 21 randomized controlled trials (n=522) showed that a dose of about 1 g of tryptophan for an average of 5.5 days can significantly decrease wake time after onset of sleep. [5] In addition to improvement of sleep quality, tryptophan has been studied for its ability to reduce fatigue and increase endurance. In a randomized controlled trial (n=20), administration of 600 mg/day of tryptophan for 4 days reduced fatigue, increased power output, and increased the distance covered in last 20 minutes of workout. [6] These results were observed in another randomized double-blind placebo-controlled trial (n=12), where a dose of 800 mg 24 hours before workout reduced exercise fatigue and increased total exercise time. [7]

Chamomile (*Matricaria chamomilla*)

Chamomile has been famously used in traditional medicine for its anxiolytic, calmative, and sedative properties. Generally safe to take, the bioactive apigenin in chamomile binds to benzodiazepine sites in the central nervous system, providing a tranquilizing effect. [8] A systematic review and meta-analysis of 12 randomized controlled trials (n=965) showed that an average dose of 931 mg/day for 7.5 weeks can improve sleep quality and symptoms of generalized anxiety disorders, as observed in 9 clinical trials. Although mild adverse events were observed in 3 of these trials, chamomile is considered overall safe for consumption. [9]

Passionflower (*Passiflora incarnata*)

Passiflora incarnata, commonly known as passionflower, is another plant-based treatment that has been used for a long time for insomnia and anxiety. A double-blind, randomized study (n=41) showed that a dose of 60 mg/day for 2 weeks can significantly increase total sleep time and improve sleep efficiency and wake after sleep onset. [10] The main benefits of passionflower have been seen in its anxiolytic effects. A double-blind randomized crossover trial (n=40) showed that supplementation of 260 mg of passionflower extract 30 minutes before surgery had an anxiolytic effect similar to that of conventional anxiolytic drug midazolam. [11] Anxiety was also lowered in patients receiving spinal anesthesia with administration of 700 mg 30 minutes prior to surgery, as demonstrated in a randomized double-blind placebo-controlled trial with 60 participants. [12] Interestingly, passionflower with acute use appears to alleviate anxiety without inducing sedation. A double-blind placebo-controlled (n=60) study showed that a dose of 500 mg prior to surgery lowered anxiety scores but did not increase sedation in ambulatory surgery patients. [13]

L-theanine

L-theanine is an amino acid commonly found in green tea (*Camellia sinensis*) and is known for its relaxation properties. A randomized double-blind crossover trial has shown reduced sleep latency, disturbance, and use of other sleep medication with the administration of 200 mg/day of L-theanine in 30 participants for 4 weeks. The study also found an improvement in cognition and verbal fluency. [14] L-theanine is well known for management of anxiety and stress. A randomized controlled trial (n=60) showed that a dose of 400 mg/day of L-theanine along with an anti-psychotic protocol for 8 weeks improved symptoms of anxiety, schizophrenia, and general psychopathology. [15] These anxiolytic effects are comparable with common anxiolytic medications such as alprazolam, where similar anxiety reducing effects were observed with 200 mg of L-theanine compared with 1 mg of alprazolam, in a randomized, double-blind placebo-controlled trial with 16 participants. [16] The effects of L-theanine on stress have been observed in another trial (n=12) where acute supplementation with 200 mg/day of L-theanine reduced heart rate, immunoglobulin levels, showed potential inhibition of cortical neuron excitation, and overall anti-stress effects. [17]

Notoginseng (*Panax notoginseng*)

Panax notoginseng has been used in traditional Chinese medicine to treat circulatory disorders such as stroke, ischemia, and other cardiovascular diseases. Recent studies point to the possibility that *P. notoginseng* may help with cognitive impairment occurring from sleep deprivation. [18] Containing over 70 saponins, bioactivity of *P. notoginseng* has been attributed to its triterpenoidal saponins. [19]

Melatonin

Melatonin is a naturally occurring hormone released by the pineal gland that helps regulate the circadian rhythm. Supplementation with melatonin can help regulate a disturbed sleep schedule. A systematic review and meta-analysis of 23 randomized, controlled trials (n=1965) showed that an average dose of 4.3 mg/day for about 9 weeks can significantly improve sleep quality in patients with respiratory, metabolic, and sleep disorders. [20]

Jujube (*Ziziphus jujuba* var *spinosa*)

Commonly known as spine date seeds or jujube seeds, the *Ziziphus jujuba* plant is relatively new to the clinical research sphere but has been used in traditional Chinese and Korean medicine for the treatment of insomnia since ancient times. [21] When 500 mg of jujube seed powder was administered to postmenopausal women for 21 days, there appeared to be an improvement in sleep quality scores. Sleep quality scores improved in the placebo group as well, but the intervention group showed a higher degree of improvement. [22] Although research into the clinical efficacy of these seeds is still in its preliminary stages, the data looks promising. Administration of these seeds has been associated with an altered intestinal flora and metabolic profiles, with an improvement in symptoms of insomnia in rats. [23] The seed extract may have the potential to improve symptoms of Alzheimer's disease. [24] Further research is warranted to help understand and corroborate these benefits.

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INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc) assessed and have been rated using a 5 star ★ rating classification.

Ingredient	Supporting evidence and study outcomes	Study design; n (number of participants); dose and duration of study	Outcome measures	Safety (adverse events and product safety)	Evidence quality rating
Sleep quality - Dosage recommendation: 2-3 capsules/day. Additional L-tryptophan supplementation recommended					
Tryptophan ¹	Shortened wake time after onset of sleep, better results with ≥1 g compared to < 1g dose	21 randomized, controlled trials (n=522), dose ≥1 g / day recommended, avg. duration 5.5 nights	Sleep quality outcomes - sleep latency, total sleep time, sleep efficiency, rapid and non-rapid eye movement	No adverse events	★★★★★
Passionflower ²	Significant increase in total sleep time. Non-significant, but improvement in sleep efficiency and wake after sleep onset	Randomized, double blind, placebo-controlled trial (n=41), dose 60 mg/ day of extract for 2 weeks	Overnight polysomnography, sleep diaries, Insomnia Severity Index, Pittsburgh Sleep Quality Index	No adverse events	★★★★★
Melatonin ³	Improvement in sleep quality in patients with respiratory, metabolic and sleep disorders	23 randomized, controlled trials (n= 1965), dose avg. 4.3 mg/ day for avg. duration 9 weeks	Pittsburgh Sleep Quality Index	No adverse events	★★★★★
L-theanine ⁴	Reduced scores for sleep latency, disturbance, and use of sleep medication. Improved cognition, verbal fluency and executive function	Randomized, placebo-controlled, crossover, and double-blind (n=30), dose 200 mg/day for 4 weeks	Self-rating depression scale, state-trait anxiety inventory-trait, Pittsburgh sleep quality index	No adverse events	★★★★
Jujube seeds ⁵	Reduced scores of sleep quality in both groups, but higher reduction in intervention group	Randomized, double-blind placebo-controlled trial on (n=106) postmenopausal women, dose 500 mg/day of seed powder for 21 days	Pittsburgh sleep quality index (PSQI)	No adverse events	★★★★

Anxiety and Stress - Dosage recommendation: 3-4 capsules/day. Additional chamomile supplementation recommended

Passionflower ⁶	Anxiolytic effect similar to midazolam observed	Randomized, double-blind, crossover trial (n=40), dose 260 mg 30 minutes before surgery, compared with 15 mg of midazolam (acute use)	Questionnaires, heart rate, blood pressure, oxygen saturation	Mild adverse effects such as drowsiness, muscle relaxation with both treatments	★★★★★
Passionflower ⁷	Lower increase in anxiety prior to spinal anesthesia administration	Prospective, randomized, double-blind and placebo-controlled trial (n= 60), dose 700 mg 30 minutes prior to procedure (acute use)	Hemodynamic parameters, State-Trait Anxiety Inventory, sedation score, psychomotor function test	No adverse effects	★★★★★

Passionflower ⁸	Lower numerical rating scale anxiety scores. Passionflower reduced anxiety without increase in sedation	Double-blind, placebo-controlled study (n=60), dose 500 mg/day prior to surgery (acute use)	Numerical rating scale for anxiety and sedation, psychomotor function (trieger dot test and digit-symbol substitution test)	No adverse events	★★★★
Chamomile ⁹	Improvement in generalized anxiety disorders and sleep quality	12 randomized, controlled trials (n=965), dose avg. 931 mg/day from 9 trials for avg. duration of 7.5 weeks	Hamilton anxiety scale, Hospital anxiety-depression scale, Patient health questionnaire, Pittsburgh sleep quality index, postpartum sleep quality scale, clinical global impressions scale	Mild adverse events in 3 trials	★★★★
L-theanine ¹⁰	Improvement in symptoms of anxiety, schizophrenia severity, and scores of general psychopathology	Randomized, double-blind, placebo-controlled trial (n=60), 400 mg L-theanine + anti-psychotic protocol for 8 weeks	Positive and Negative Syndrome Scale, Hamilton Anxiety Rating Scale, the Cambridge Neuropsychological Test Automated Battery for neurocognitive functioning	No adverse events	★★★★
L-theanine ¹¹	Anti-stress effects pertaining to - Reduced heart rate, immunoglobulin levels, potential inhibition of cortical neuron excitation	Randomized, double-blind, placebo-controlled, crossover acute study (n=12), 200 mg L-theanine given at start and middle of stress task	Arithmetic task performed, Perceived stress and visual analog scale, State-Trait Anxiety Inventory (STAI), electrocardiogram, salivary secretory immunoglobulin A (s-IgA) levels	No adverse events	★★★
L-theanine ¹²	Mild anxiolytic effects in resting state, comparable or more than anxiolytic effects of alprazolam	Randomized, double-blind, placebo-controlled (n=16), 200 mg L-theanine, acute effects compared to 1 mg alprazolam	Visual analog mood scale, state-trait anxiety inventory, Beck depression inventory-II, Beck anxiety inventory	No adverse events	★★★

Safety data: Maximum daily dose recommended by Health Canada (for adults):

- Tryptophan - 220 mg/day
- Passionflower - 8 g dried herb top/day
- L-theanine - 250 mg/day
- Melatonin - 10 mg/day

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