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"ROLE OF BIOACTIVE COMPOUNDS IN REGULATING SLEEP": MECHANISM AND CLINICAL EVIDANCE

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ABSTRACT

Sleep is a vital physiological process essential for cognitive performance, metabolic regulation, and overall health. Increasing evidence indicates that various bioactive compounds—including polyphenols, alkaloids, terpenes, amino acid derivatives, and melatonin-like substances—can modulate sleep quality and duration through multiple biochemical pathways. These compounds act primarily by influencing neurotransmitter systems (such as GABAergic, serotonergic, and dopaminergic pathways), oxidative stress, inflammatory mediators, and circadian rhythm regulators. For instance, compounds like L-theanine, resveratrol, curcumin, and caffeic acid derivatives exhibit anxiolytic and sedative properties by enhancing GABA activity or melatonin synthesis. Clinical and preclinical studies suggest that dietary intake or supplementation of these bioactives can improve sleep latency, efficiency, and total sleep time, particularly in individuals experiencing insomnia or stress-related sleep disturbances. However, variations in dosage, bioavailability, and individual metabolic responses remain challenges in establishing standardized therapeutic applications.

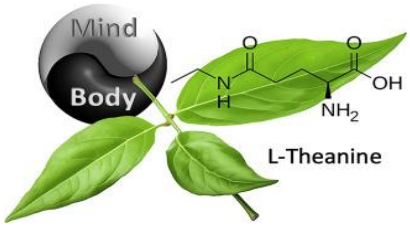
KEYWORDS: sleep quality, melatonin, l – theanine, anxiety reduction, relaxation.

INTRODUCTION

Insomnia is trouble falling or staying a sleep, or poor-quality sleep, despite having the chance to rest, leading to daytime problems. Causes include medications and health issues. Doctors assess sleep history, habits, medical background, and tests to find possible causes and create a personalized treatment plan for better sleep.[1]

Melatonin is a natural hormone made in the brain that helps regulate the sleep-wake cycle. It is often taken as an over-the counter supplement by people who struggle to fall or stay asleep. Available as tablets, capsules, gummies, or liquids, melatonin works by signalling darkness to the body, helping prepare for sleep.[1] It is produced in the pineal gland, starting from the amino acid tryptophan, which is converted through several steps into melatonin. Levels naturally rise in the evening, stay high overnight, and drop in the morning with daylight. This hormone mainly acts as a sleep regulator, supporting healthy circadian rhythms.[8]

L-theanine is a natural amino acid found in tea leaves, often promoted as a supplement for relaxation and brain health. It is absorbed well and can reach the brain, where it may increase alpha waves linked to calmness and focus. Some studies suggest it helps reduce stress, improve sleep, and enhance attention, especially when combined with caffeine. Animal studies also show possible brain-protective effects. However, results in humans are mixed, and strong clinical evidence is lacking. While considered safe, the health claims are not fully proven. More well-designed studies are needed before recommending high-dose L theanine use widely.[5]



OBJECTIVES

1. Promotes deep relaxation.
2. Improves sleep quality.
3. Supports falling asleep.
4. Reduces insomnia and restlessness.

1. HERBS USED FOR ENHANCING SLEEP

1.1 Ashwagandha

Ashwagandha is mainly used for sleep support to help the body relax and reduce stress. It lowers cortisol levels, which makes it easier to calm the mind before bedtime. It helps people fall asleep faster and improves overall sleep quality. Ashwagandha also reduces nighttime awakenings, allowing for deeper and more restful sleep. It works by supporting the nervous system and promoting relaxation. Some studies show it increases total sleep time and sleep efficiency.[3]

Biological Source: Ashwagandha consists of the dried roots and leaves of withania somnifera (L.) Dunal, belonging to the family Solanaceae.

Chemical Constituent: Alkaloids – about 0.13%, Steroidal Lactones (Withanolides & Withaferins), Saponins, Strach, Reducing sugar.

Main Constituent

Withanolides**:** Modulate GABAergic signaling, promoting relaxation and reducing neuronal excitability. Exhibit anti-stress and anxiolytic effects by normalizing cortisol levels.

Alkaloids**:** It have sedative and anxiolytic actions, supporting the calming effect of ashwagandha. They contribute to neuroprotective and mild hypnotic properties.

1.2 Tart cherries

Cherries, especially tart cherries, are often used in sleep support gummies because they are a natural source of melatonin, the hormone that regulates the sleep–wake cycle. Eating cherries or their extracts can help improve sleep duration and quality. They also contain antioxidants like anthocyanins, which reduce inflammation and may support relaxation at night. Cherries help in reducing sleep latency, meaning they make it easier to fall asleep faster. Regular intake has been linked to deeper and more restorative sleep.[6]

Biological Source: Tart Cherries consist of the fruits of prunus cerasus L., belonging to the family Rosaceae.

Chemical Constituent: melatonin, Phenolic compounds (Anthocyanins, Flavonols, Phenolic acids), Vitamins & Minerals.

Main Constituent

Tart cherries are rich in melatonin, the key ingredient in sleep-support that regulates circadian rhythm and improves sleep quality. They also contain anthocyanins and phenolic compounds, which provide antioxidant and anti-inflammatory benefits. Together, these compounds promote natural relaxation, reduce oxidative stress, and support restful, restorative sleep without synthetic additives.

1.3 Chamomile

Chamomile is widely used for sleep support because of its natural calming and soothing effects. It contains a compound called apigenin, which binds to brain receptors and helps reduce anxiety, making it easier to relax before bedtime. Chamomile promotes faster sleep onset and improves overall sleep quality by reducing restlessness. It also supports deeper and more restful sleep, so you wake up feeling refreshed.

Biological Source: Chamomile consists of the dried flower heads of L. (syn.), belonging to the family Asteraceae (Compositae).

Chemical Constituent: Flavonoids, Terpenoids, cumarins, phenolic acid.

Main Constituent

Flavonoids: Apigenin is the principal flavonoid responsible for chamomile's sedative and anxiolytic effects. It binds to benzodiazepine receptors on the GABA complex, promoting relaxation and sleep induction. Flavonoids also possess antioxidant and anti-inflammatory effects, which support healthy sleep by reducing oxidative stress and anxiety.

1.4 TULSI

Tulsi also known as Holy Basil, plays an important role in sleep support due to its powerful adaptogenic and calming properties. It helps the body manage stress by regulating cortisol levels, thereby reducing anxiety and promoting mental relaxation, which are essential for sound sleep. The bioactive compounds in Tulsi, such as eugenol and rosmarinic acid, exert a soothing effect on the nervous system, helping to calm the mind and prepare the body for rest. Additionally, its antioxidant and detoxifying effects help combat oxidative stress, improving overall health and supporting better sleep quality. By maintaining hormonal balance and promoting relaxation naturally, Tulsi serves as a safe and effective herbal ingredient for enhancing sleep without causing dependence or drowsiness, making it a valuable component.[2]

Biological Source: Tulsi consists of the dried or fresh leaves of Ocimum sanctum L., belonging to the family Lamiaceae.

Chemical Constituent: Volatile Oils (Essential Oils), Eugenol, Phenolic Compounds, Rosmarinic acid, Tannins, Saponins.

Main constituent

Eugenol: It has mild sedative and claming effects on the nervous system which helps to reduce stress and anxiety. This promoting relaxation which indirectly improves sleep quality.

1.5 TEA LEAVES

Tea leaves, particularly those from herbal or decaffeinated varieties such as green tea, chamomile tea, or valerian-infused tea extracts, play a beneficial role in sleep support. They contain natural compounds like L-theanine, a calming amino acid that promotes relaxation by reducing stress and anxiety without causing drowsiness. L-theanine works by increasing levels of neurotransmitters such as serotonin, dopamine, and GABA, which help regulate mood and improve sleep quality. Additionally, herbal tea extracts provide antioxidant and anti-inflammatory effects that support overall well-being and help the body unwind before bedtime.[5][9]

Biological Source: The biological source of tea leaves is the plant Camellia sinensis (L.) Kuntze, which belongs to the family Theaceae.

Chemical Constituent: Alkaloids, Amino acid (l – theanine), volatile oil.

Main Ingredient

Amino acid (l -theanine): The main sleep-promoting compound in tea leaves is L-theanine, a natural amino acid that helps the brain relax by boosting calming neurotransmitters. It supports better sleep and enhances the effects of melatonin or herbal extracts on sleep support.

MECHANISM OF ACTION

The overall mechanism for sleep support containing Ashwagandha, Tulsi, Tea Leaves, Stevia, Tart Cherries, Chamomile, and Passion Flower, works through a synergistic, multi-pathway action on the brain and body to promote natural and restful sleep. These herbal ingredients primarily act by reducing stress and anxiety, balancing neurotransmitters, and regulating the sleep–wake cycle. Adaptogens like Ashwagandha and Tulsi lower cortisol (stress hormone) levels and calm the nervous system. Tea leaves, Chamomile, and Passion Flower enhance the activity of GABA (gamma-aminobutyric acid), a key inhibitory neurotransmitter that decreases nerve excitability and induces relaxation. Tart cherries naturally boost melatonin levels, signaling the body to prepare for sleep and improving sleep duration and quality. Stevia supports this formulation by maintaining a sugar-free balance, preventing glucose spikes that can disrupt sleep. Overall, the gummies act by reducing stress, calming the mind, balancing sleep hormones, and enhancing relaxation, leading to deep, refreshing, and natural sleep without dependency.[7][10]

CONCLUSION

Sleep regulation is a complex physiological process influenced by numerous neural, hormonal, and metabolic pathways. Increasing evidence demonstrates that bioactive compounds derived from plants and natural sources play a significant role in modulating these pathways to promote healthy sleep. Compounds such as withanolides (Ashwagandha), apigenin (Chamomile), L-theanine (Green tea), melatonin (plants and foods), and various polyphenols and terpenes exert their effects primarily through GABAergic activation, serotonergic modulation, melatonin pathway regulation, and stress hormone balance.[4]

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