



Supplements for Enhancing the Quality of Sleep: A Review

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Abstract

Background: *It has been observed that nowadays sleep problems are affecting an increasing number of people. Researchers from around the world are trying to find a substance that would significantly improve the lives of people struggling with sleep disorders, while being widely available and free of side effects.*

Objectives: *The purpose of this article was to summarize the benefits of using sleep supplements to improve sleep quality.*

Material and methods: *The conclusions of the article were formulated by analyzing the available literature from 2017–2024 (PubMed database). For the purpose of this paper, studies on supplements with a relatively safe use profile for any individual compared to prescription drugs were selected.*

Results: *Poor sleep quality significantly affects mental and physical health, is a risk factor for many diseases, worsens their prognosis, and impairs a person's efficiency during the day. Among the supplements used to improve the quality of nocturnal rest are melatonin, whose positive effects are found in patients who are older, herbal preparations such as valerian, saffron, cannabinoids, ashwagandha, *Melissa officinalis*, and L-theanine, which appears to be the best supplement for people suffering from mental disorders, including depression and anxiety. In addition, vitamin D and probiotics are being investigated.*

Conclusions: *Currently, there is no supplement that significantly improves the quality of sleep for every patient who has difficulty resting at night. In the coming years, there may be new reports of a substance that would be efficient and safe.*

Key words: *sleep initiation and maintenance disorders, insomnia, mental health, sleep disorders*

Introduction and purpose

Sleep significantly affects the regulation of the body's functioning, and nowadays its quality has significantly decreased. Insufficient rest can cause many physiological and behavioral problems. Poor sleep quality is a risk factor for diseases such as hypertension, cardiovascular disease, and metabolic problems [1]. Insomnia can be both an effect of mental illnesses and their cause. The main correlations are the co-presence of sleep disorders with increased anxiety, depressive states, and eating disorders [2]. All of these links can cause an increase in mortality and be a burden on both the patient and the health care system. A significant cause of the above problem may be work-related stress, negatively affecting work life. Many observations and studies show that sleep quality problems are more common among women and older people [1]. Approximately 25–30% of children also suffer from sleep disorders in various forms, in addition to an increased risk of self-harm, suicidal thoughts, and suicide [3]. Another social group that is increasingly complaining of insomnia, according to current data, are students. Recent statistics show that at least 1/3 of students are struggling with this problem, and this situation significantly affects the decline in academic performance [4]. There are various ways to treat the above ailment, such as cognitive-behavioral therapy, or pharmacotherapy, which is currently the most widely used due to its proven clinical effectiveness. The disadvantage of standard medications that relieve insomnia-related symptoms is the relatively frequent occurrence of side effects along with their addictive potential. According to recent studies, an effective alternative may be the use of sleep supplements, which have a lower incidence of side effects [5]. Prescription drugs such as benzodiazepines, barbiturates, antihistamines, and antidepressants are used to treat chronic sleep disorders, but they are associated with numerous side effects on the human body. As a result, supplements, or herbal preparations, remain an alternative for people with sleep problems [6, 7]. In addition, prescription medications should be taken strictly for a limited period of time, as some of them show addictive potential. This may be further evidence that sleep enhancement supplements may be a better option when undertaking

treatment for mild sleep disorders [8]. Nowadays, there is a growing body of research on widely available supplements designed to increase sleep efficiency and improve overall well-being [7, 9].

State of knowledge

Sleep stages

Sleep can be divided into two phases: the rapid eye movement (REM) phase and non-REM (NREM), or slow-wave sleep. The REM phase has a major role in memory consolidation, learning processes, and is characterized by decreased amplitude and increased frequency of the cortical electroencephalogram (EEG). The second stage—NREM—is important because it affects the renewal of energy, regulation of hormonal and immune functions, and during it a reduced frequency of EEG activity can be observed [10]. This phase is characterized by relative stability of autonomic functions, while the REM stage is associated with irregular breathing patterns, as well as generalized skeletal muscle atonia, changes in heart rate and blood pressure [11].

Sleep disorders

Sleep disorders are a common problem these days, as evidenced by the fact that, according to current research-based estimates, about 30% of the population faces insomnia, which is defined as difficulty sustaining sleep and falling asleep [2]. An increasingly important issue is chronic insomnia, defined as sleep problems occurring several times a week that persist for more than 3 months [12]. A significant percentage of people also struggle with excessive sleepiness, with one-third of the population experiencing “general sleep disorders”. Health care professionals should be aware of the negative consequences of poor quality nighttime rest and help patients affected by such disorders [2].

Methods used to assess sleep quality

Sleep quality is assessed using instruments that can be divided into objective ones, such as polysomnography (PSG) and actigraphy, and subjective ones, which include the Insomnia Severity Index (ISI) or Pittsburgh Sleep Quality Index (PSQI). Objective methods of assessing rest provide information on total sleep time, latency of onset or number of awakenings, and sleep efficiency. The ISI score is a valued tool for quantifying the perceived severity of insomnia, while the PSQI score is considered a reliable instrument for assessing sleep quality, which determines habitual efficiency and measures the duration of sleep [13]. The items found in the PSQI questionnaire provide information on sleep disturbance and latency, sleep medication use, daytime dysfunction, duration, subjective quality, and sleep efficiency. In interpreting the survey, it is important to remember that the higher the PSQI score, the lower the quality of rest [1]. Another subjective method of assessing nighttime rest is the Richards Campbell Sleep Questionnaire (RCSQ). It contains five components: overall sleep quality and depth, sleep latency, time spent awake, number of awakenings, and the result can range from 0 to 100 points. The more of these a patient scores, the better their sleep. The rest of patients who scored 76–100 was described as very good, and of those with scores of 1–25 as very poor [14].

Supplements to improve sleep quality

1. Melatonin

Melatonin (N-acetyl-5-methoxytryptamine) is produced endogenously by the pineal gland and released into the bloodstream during the night. Its primary function is to regulate circadian rhythms of sleep and wakefulness, but it can also activate the immune system, regulate body temperature or sexual development [1, 15]. Only 30% of the total level of the molecule in the blood occurs in the free form, unbound to proteins, and can penetrate surrounding tissues. To synthesize melatonin, pineal cells take tryptophan from the

bloodstream and metabolize it to serotonin, which, with the participation of N-acetyltransferase, is converted to N-acetylserotonin, and then methylation produces the final form of the molecule in question [15]. A randomized clinical trial (RCT) on this topic by Gandolfi et al. focused on the effect of melatonin on the sleep quality of patients in the intensive care unit. The Richards Campbell Sleep Questionnaire (RCSQ) protocol was used to assess the effect of this supplement on patients, and significant improvements were observed in the quality and depth of sleep in the melatonin-treated group compared to the placebo group [14]. The body's production of melatonin decreases with age, so the use of preparations of this compound may be beneficial in the older age group. An RCT conducted by Xu et al. aimed to determine the effectiveness of melatonin supplementation in middle-aged patients suffering from sleep disorders. The researchers showed that melatonin use improved some objective elements examined by nocturnal polysomnography, including early morning awakenings, which had the effect of improving total sleep time [16]. Recent studies also indicate that melatonin supplementation improves the quality of nocturnal rest, which can be assessed by the PSQI, and its use may be beneficial in people with sleep disorders, metabolic disorders, and respiratory diseases [1].

2. Plant substances

Ashwagandha

Ashwagandha, also known as Indian ginseng or winter cherry, is a substance that modulates the body's response to stress [17]. Recent research indicates that it can also improve the quality of nighttime rest and reduce feelings of daytime fatigue [18–20]. A meta-analysis performed by Cheah et al. analyzed five randomized clinical trials involving 400 participants. Although the effect of ashwagandha extract was small, it was shown to improve participants' overall sleep. The extract was found to have the best effects when taken at a dose of 600 mg per day for more than eight weeks, and no significant side effects were found, but the authors point out that it is worth doing studies on the safety of long-term ashwagandha intake [18]. In an RCT conducted

by Deshpande et al., participants affected by poor sleep quality were given 120 mg of ashwagandha extract for 6 weeks in a single dose per day. They observed an increase in sleep's overall quality compared to the placebo group [19]. A study conducted by Langade et al. found that ashwagandha root extract had a positive effect on sleep quality and accelerated falling asleep. The dosage regimen involved taking one capsule of the extract containing 300 mg of the substance twice a day [20]. Pandit et al. in their randomized controlled trial confirmed the efficacy of ashwagandha in alleviating anxiety and stress by using the Perceived Stress Scale (PSS), which is one of the most widely used questionnaires useful for measuring psychogenic stress. Secondary to a stressful situation, sleep and wakefulness rhythms are disrupted, so reducing tension can also help improve sleep quality [17].

Valerian (*Valeriana officinalis*)

Valerian root extract has been used to treat sleep disorders and to reduce mental tension since ancient times [6, 21]. Recent articles claim that valerian modulates the function of GABA-A receptors, reducing brain activity during sleep, and thus shows similar effects to prescription benzodiazepines. In addition, it improves the body's regenerative capacity by reducing oxidative stress. It is likely that valerian has neuroprotective effects, as it is involved in regulating the mechanisms of apoptosis and in clearing the nervous system of toxic metabolites [7]. In a randomized controlled trial conducted by Shekhar et al., participants took valerianic acid at a concentration of 2% in a dose of 200 mg one hour before going to bed at night. The authors demonstrated that the use of this substance can significantly improve overall sleep quality, increase total sleep time and efficiency, accelerate falling asleep, and reduce drowsiness and discomfort upon waking among a group of young people who have no comorbidities [6]. Studies on the effects of valerian-derived substances have shown them to be well tolerated and safe to use [6, 21].

Saffron

Saffron extract is another plant-based supplement that, according to recent studies, has a positive effect on the quality of rest in people with sleep disorders

[22–24]. The exact way saffron affects nocturnal rest is not fully understood, but studies point to its serotonergic effects, as well as its effects on the hypothalamic-pituitary-adrenal axis or neuroprotection [25]. Randomized controlled trial conducted by Pachikian et al. on people with increased anxiety examined the effect of saffron extract on sleep quality. The daily dose was 15.5 mg, and the substance was used for six weeks. The study, during which the nature of nocturnal rest was checked using actigraphy and the PSQI questionnaire, among other measures, found that saffron extract supplementation improved sleep quality and length, and accelerated falling asleep [22]. Umigai et al. in an RCT found that taking saffron-derived crocetin at a dose of 7.5 mg per day improved subjective sleep assessment parameters and accelerated recovery from exertion among people experiencing mild sleep disorders [24].

Cannabinoids

Recent medical experiments have tested the efficacy of cannabinoids in the treatment of sleep disorders and have proven that more research is needed, as current work does not conclusively confirm their significant effect on improving sleep quality [10]. Despite this, cannabidiol (CBD), which belongs to the cannabinoid group, was used by Kisiolek et al., who studied the effects of CBD administered orally at a dose of 50 mg per day for 8 weeks on sleep length and quality in a randomized controlled trial. They concluded that sleep length did not increase as a result of CBD use, but sleep quality improved instead [26]. Walsh et al. in an RCT, on the other hand, tested the efficacy of cannabinoids in the treatment of insomnia and found that taking an extract derived from them was effective in reducing the discomfort of insomnia, and did not cause serious side effects [27]. Moreover, Ried et al. in an RCT confirmed the effectiveness of medicinal cannabis oil in increasing the length and quality of sleep, as well as improving participants' daytime functioning [28].

L-Theanine

In recent years, there has been no shortage of reports on L-Theanine, a non-protein amino acid extracted from tea leaves that resembles L-glutamic acid in structure, having a positive effect on sleep [29, 30]. Despite

evidence that its effect is to improve mood, the quality of nocturnal rest, and to reduce stress disorders, the mechanism of this substance's effect on human cognitive function has not been fully elucidated [31]. Hidese et al. in a randomized trial administered L-Theanine at a dose of 200 mg per day to participants who had no significant mental health problems. Participants in the study who received the substance improved such indicators of sleep quality as speed of falling asleep, use of sleep medications, and nocturnal rest disorders in general. The researchers inferred that L-Theanine may have a positive effect on the mental health of the population, reducing feelings of stress and improving cognitive function [29]. Interestingly, new research indicates a beneficial effect of L-theanine in alleviating psychiatric disorders in people with schizophrenia, depression, generalized anxiety disorder, obsessive-compulsive disorder, attention deficit hyperactivity disorder (ADHD), and Tourette's syndrome. A potential reason for the positive effect of this substance is that it increases the secretion of neurotransmitters involved in the pathogenesis of the above diseases. L-theanine is a supplement of wide interest among people suffering from various neurotic disorders due to its relatively safe side effect profile and the possibility of obtaining it without a prescription. It provides an alternative in the treatment of various disorders, especially for long-term treatment [32].

Melissa officinalis

Melissa officinalis (MO) is a plant belonging to the Lamiaceae family, which, according to current research, has antioxidant, antidepressant, antidiabetic, anxiety-reducing, stress-reducing, and cognitive and memory-enhancing properties. Its important constituents include volatile compounds, flavonoids, phenolic acids, and triterpenoids [33–35]. Researchers report three theories of *Melissa's* effects on anxiety and sleep disorders. One describes MO's effect on lowering corticosterone, another points to its serotonergic activity, and a third suggests increasing brain levels of gamma-aminobutyric acid. In a randomized clinical trial, Haybar et al. tested the effects of MO on sleep disturbances, lowered mood states, and increased tension in patients with chronic stable angina, who are at higher risk for the above disorders. As

a result of eight weeks of *Melissa officinalis* supplementation at a dose of 3 grams per day, participants taking the described supplement experienced a significant reduction in sleep disorders, and in particular, an improvement in sleep quality, efficiency and duration of sleep [33]. An RCT by Shirazi et al. indicates that MO supplementation may help improve the quality of life of menopausal women with sleep disorders [35].

3. Vitamin D

The main tasks of vitamin D (VD) are the regulation of bone metabolism, the absorption of calcium and phosphate, and the maintenance of normal muscle function [36]. Recent studies indicate that in addition to the above-mentioned functions, vitamin D, the active form of which is 1,25-dihydroxy vitamin D3 [1,25(OH)₂D₃], has an effect on those bodily functions mediated by the central nervous system, as shown by experiments on rodents in which the active form of this vitamin was shown to stimulate glutamine and glutamate metabolism in neurons. Other studies report a potential effect of this vitamin on the expression of neurotrophic factor genes, which has the effect of stimulating neurogenesis and protecting against neurodegenerative changes. As a result, it may induce changes in behavioral and neurotransmitter function, and thus be related to abnormalities such as depression and anxiety disorders [37]. An important aspect is that VD also regulates the production of melatonin, which is responsible for circadian rhythms, so its deficiency can result in decreased melatonin production and abnormalities related to nocturnal recovery. Another potential reason for VD's association with sleep is the presence of its receptors in many areas of the brain, particularly those responsible for nocturnal resting [38]. The effectiveness of vitamin D in the treatment of sleep disorders is also confirmed by a number of studies in recent years, whose participants receiving such supplementation had better indicators of nighttime rest quality than the placebo group [39]. According to current reports, VD has an impact on regulating sleep by improving its duration and quality or speeding up falling asleep, and in particular, its deficiency can cause difficulty falling asleep and more frequent awakenings [38]. Majid et al. conducted an RCT to determine

the effect of an eight-week supplementation of vitamin D, in a dose of 50 000 units taken once every two weeks, on sleep quality in patients aged 20–50 years with sleep disorders. As a result of the therapy, falling asleep time, subjective sleep quality, particularly sleep length, improved, and the PSQI score decreased as desired. On the other hand, the above study did not suggest a significant difference in VD-supplemented patients in terms of sleep medication intake, sleep efficiency, or daytime functioning [40]. A meta-analysis by Gao et al. shows an association between the risk of sleep disorders and blood levels of VD, and suggests that VD levels below 20 ng/ml increase the risk of poor sleep quality by almost 60% [41].

4. Probiotics

The gut microbiota is defined as the totality of microorganisms including bacteria, viruses, protozoa, fungi residing in the gastrointestinal tract and their genomic elements. In recent years, there has been a growing body of literature indicating a link between the human gut microbiome and mental health, which is explained by the interrelationships within the brain-gut-microbiome axis that result from the presence of neural, hormonal, immunological, and metabolic pathways between the brain and gut. Disorders within this axis can lead to abnormal responses to stress and contribute to the development of sleep, depressive, and anxiety disorders [42–44]. Recent studies describe links between sleep and the gut microbiota, as evidenced by the fact that night shift work, circadian rhythm disturbances, or insufficient nightly rest can alter the composition of microbes in the gastrointestinal tract [43]. Probiotics contain a variety of live bacteria that colonize the host's gastrointestinal tract to regulate the balance of the intestinal microbiota, and their supplements can facilitate this process and have a therapeutic effect in disorders resulting from disruption of the bacterial environment, including problems with optimal nocturnal recovery [45]. In a randomized controlled trial, Lan et al. tested the effect of *Bifidobacterium breve* CCFM1025 on the sleep quality of participants struggling with its stress-induced disorders, who were subjected to 4-week supplementation with the probiotic. The intervention resulted in a marked improvement

in subjective sleep quality, a reduction in sleep disorders and, in particular, in the number of nocturnal awakenings, as manifested by improved PSQI scores in the study group relative to those receiving placebo [46]. Supplementation with a mixture of probiotics in a study group of elderly people with mild cognitive impairment had an equally positive effect on the PSQI [45]. Moreover, a meta-analysis by Chu et al. indicated not only an improvement in PSQI score among adults taking *Lactobacillus gasseri* CP2305, but also in at least half of the EEG scores tested [47]. An RCT by Zhu et al. found that supplementation with *Lactobacillus plantarum* JYLP-326 twice daily for 3 weeks improved sleep quality among college students, and reduced feelings of anxiety [48]. Another RCT suggesting a reduction in insomnia symptoms and an improvement in the quality of nighttime rest was conducted by Ho et al. who demonstrated the efficacy of *Lactobacillus plantarum* PS 128 in adults in the 20–40 age group. In participants using the above supplementation, the quality of deep sleep, its stability improved, and the number of awakenings during the night decreased [43].

Conclusions

Nowadays, sleep disorders are becoming increasingly common, making the topic widely discussed in public debate. Moreover, it is noteworthy that people want to increasingly deal with the problem in question on their own. In today's world, people are caught up in their daily responsibilities, lack time, and sometimes do not want to go to the doctor with their problems. The above-mentioned studies show that sleep disorder sufferers frequently choose more easily available substances that they can obtain without a prescription, and those with a low risk of side effects. The inability to get an optimal night's rest has a significant impact on people's well-being, social functioning, or work efficiency. It can also be a burden on health care systems, particularly psychiatric care, so it is worth looking for ways to improve sleep quality in the population other than the use of standard sleep aids, which have numerous side effects. In recent years, supplements aimed at reducing the discomfort associated with the described disorders have been gaining popularity. All of the substances of various origins discussed in this work have shown positive

effects in the treatment of insomnia and have been characterized by high safety of use. Despite this, there are still many unknowns about their mechanisms of action, the degree of effectiveness, but further research on them in the coming years, offers hope for an even more effective fight against sleep disorders and for improving people's quality of life.

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