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Propolis extract: antioxidant effects and potential implications for human health in sleep

Tamirys Caroline Silva SOUZA[1], Suelaine Barbosa de OLIVEIRA[1], Laudelina Ferreira de ANDRADE[1], Patrícia Soares ROCHA[1], Karla Sabrina Magalhães Andrade PADILHA[1], João Gabriel Silva SOUZA[2], Charles Martins AGUILAR[1], Caroline Honaiser LESCANO[3,4], Dario Alves de OLIVEIRA[5], Igor Viana BRANDI[1,5], Ivan Pires de OLIVEIRA[1]*

Abstract

Propolis is a natural product produced by bees from plant exudates found around hives, serving as a protective barrier against microorganisms and environmental factors. Its therapeutic use dates back to ancient civilizations, and in recent decades, propolis extract has gained increasing scientific attention due to its chemical diversity and wide range of biological effects, particularly as a remedy for various diseases, which highlight its therapeutic potential and applicability in different health-related areas. Despite the growing scientific interest in the bioactive properties of propolis extract, most investigations have focused on its antioxidant, anti-inflammatory, and antimicrobial effects, with a scarcity of systematized evidence regarding its direct influence on sleep quality in adults. Considering the clinical and social relevance of sleep disorders—associated with increased oxidative stress and a higher risk of metabolic, cardiovascular, and neurodegenerative diseases—a critical and comprehensive analysis of the literature is necessary. This study aims to gather and evaluate the available evidence on the combined effects of a healthy diet and propolis extract on sleep quality, offering an innovative and complementary perspective compared with previously published works.

Keywords: propolis extract; healthy diet; antioxidants; sleep.

Practical Application: Propolis extract contains therapeutic properties, including several bioactive compounds such as flavonoids and phenolic acids, known for their antioxidant, neuroprotective, and immunomodulatory effects, which may contribute to reducing oxidative stress and, consequently, sleep benefits..

1 INTRODUCTION

Propolis is a natural product produced by bees from plant exudates growing around hives, serving as a protective barrier against microorganisms and adverse environmental factors (Bankova et al., 2018; Freitas et al., 2019). Its therapeutic use dates back to ancient civilizations, and in recent decades, propolis extract has attracted increasing scientific interest due to its chemical diversity and broad spectrum of biological effects, particularly as a remedy for various diseases (Hossain et al., 2022).

The chemical composition of propolis is highly variable and depends on factors such as local flora, bee species, and climatic conditions. Propolis exhibits antioxidant, antimicrobial, anti-inflammatory, immunomodulatory, and hepatoprotective properties, which reinforce its therapeutic potential and applicability in different health-related areas (Anjum et al., 2019). Recent studies have also explored its relationship with the regulation of physiological processes, including cellular repair mechanisms, energy metabolism, and even the modulation of sleep through interactions with melatonin, although these investigations remain incipient (Matias et al., 2025).

Its main constituents include flavonoids, phenolic acids, terpenoids, aromatic aldehydes, and esters, which confer functional and pharmacological properties to the extract (Pobiega et al., 2019). This diversity highlights the importance of chemical characterization to establish correlations between the phytochemical profile and the biological activities attributed to propolis (Figure 1).

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[1]*Universidade Federal de Minas Gerais, Institute of Agricultural Sciences, Applied Molecular Systems Research Group, Montes Claros, Minas Gerais, Brazil.*
[2]*Universidade de Guarulhos, Dental Research Division, Guarulhos, São Paulo, Brazil.*
[3]*Universidade Federal do Amazonas, Institute of Biological Sciences, Manaus, Amazonas, Brazil.*
[4]*Universidade Federal de Mato Grosso do Sul, Faculdade de Ciências Farmacêuticas, Alimentos e Nutrição, Campo Grande, Mato Grosso do Sul, Brazil.*
[5]*Universidade Estadual de Montes Claros, PhD Program in Biotechnology, Montes Claros, Minas Gerais, Brazil.*
*Corresponding author: ivan.pires.oliveira@gmail.com
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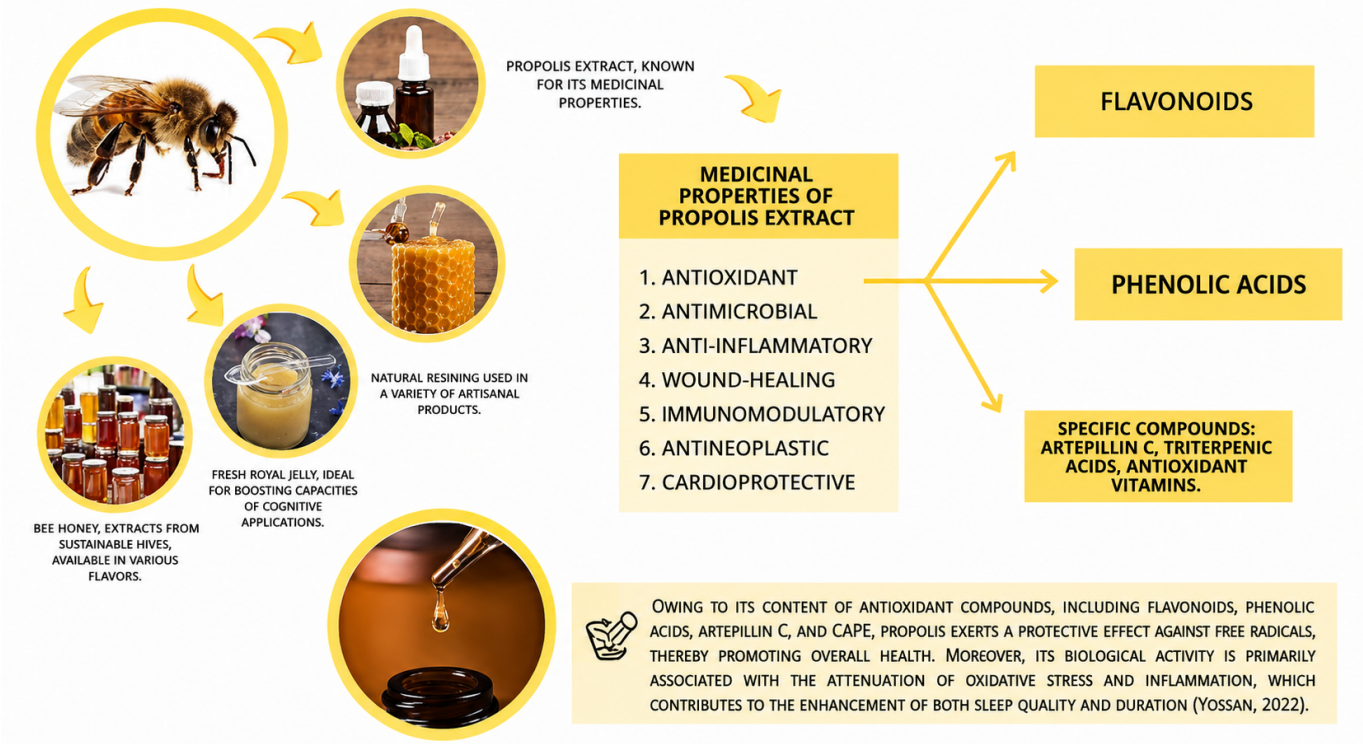

Figure 1. Bee products and properties of propolis extract, rich in flavonoids and phenolic acids, with antioxidants, antimicrobial, anti-inflammatory, immunomodulatory, and cardioprotective actions.

Among these activities, the antioxidant effect is the most widely documented. Phenolic compounds present in propolis extract act by neutralizing reactive oxygen species (ROS) and reactive nitrogen species, thereby contributing to the reduction of oxidative stress—a condition associated with the development of chronic diseases such as cancer, diabetes, cardiovascular disorders, and neurodegenerative diseases (Pasupuleti et al., 2017). In vitro assays, including 2,2-Diphenyl-1-picrylhydrazyl (DPPH), 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), Ferric Reducing Antioxidant Power (FRAP), and nitric oxide (NO), have been extensively employed to evaluate the antioxidant capacity of propolis, confirming its relevance as a bioactive agent (De-Melo et al., 2014).

Despite the growing scientific interest in the bioactive properties of propolis extract, most investigations have focused on its antioxidant, anti-inflammatory, and antimicrobial effects, while systematized evidence regarding its direct influence on sleep quality in adults remains scarce. Previous reviews have primarily addressed propolis in the context of chronic disease prevention and oxidative stress modulation, without exploring, in an integrated manner, the interaction between a healthy diet, oral supplementation with propolis extract, and sleep-related outcomes. Given the clinical and social relevance of sleep disorders—closely associated with increased oxidative stress and a higher risk of metabolic, cardiovascular, and neurodegenerative conditions—a critical and comprehensive analysis of the literature is warranted.

Therefore, this systematic and integrative review is justified by its aim to fill this gap, gathering and evaluating the available evidence on the combined effects of healthy diet and propolis extract supplementation on improving sleep quality in adults, thus offering an innovative and complementary perspective compared with previously published studies.

1.1. Relevance of the work

Propolis is extensively used across different cultures, with numerous health benefits and therapeutic properties documented in scientific literature. Although there has been growing interest in the bioactive properties of propolis extract, most studies have primarily focused on its antioxidant, anti-inflammatory, and antimicrobial effects. However, there is a lack of comprehensive evidence examining its direct impact on sleep quality in adults. Given the clinical and societal significance of sleep disorders—often linked to increased oxidative stress and a higher risk of metabolic, cardiovascular, and neurodegenerative conditions—a thorough and critical review of the existing literature is essential. This review aims to assess the available evidence on the combined effects of a healthy diet and propolis extract on sleep quality, offering an update and complementary perspective in comparison to previously published works.

2 METHODOLOGY

This study is a systematic review of the literature conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The search was performed in the databases PubMed, Scopus, Web of Science, Embase, and SciELO, using terms related to propolis extract,

antioxidant effects, and potential implications for human sleep health, combined with the Boolean operators "AND" and "OR." Studies published between 2000 and 2025, in Portuguese or English, addressing the topic and available in full text, were included. Exclusion criteria comprised duplicate records, case reports, opinion articles, or studies with irrelevant data.

The selection process was carried out in two stages:

- Screening of titles and abstracts to identify potentially eligible studies;
- Full-text reading to confirm eligibility, with disagreements resolved by consensus.

Extracted data included: author, year, country, study design, population, intervention/exposure, outcomes, and main findings. Data synthesis was performed qualitatively, grouping similar results by thematic category, with the support of tables and figures when appropriate. After applying the inclusion and exclusion criteria, 70 studies were included in the review, as illustrated in the flowchart below (Figure 2).

3 PROPOLIS: COMPOSITION, ORIGINS, USES, AND GLOBAL COMMERCIALIZATION

The modern definition considers propolis as a complex beekeeping product whose composition varies according to local flora and environmental conditions (Barreto et al., 2020). Its basic composition includes plant resins (50–60%), waxes (30–40%), essential oils, pollen, flavonoids, and phenolic acids, which confer different therapeutic properties, such as antimicrobial, anti-inflammatory, and antioxidant activities (Almeida et al., 2002) (Figure 3). The botanical and geographical origin plays a decisive role in the chemical composition of propolis. In Brazil, different types of propolis are particularly noteworthy, such as:

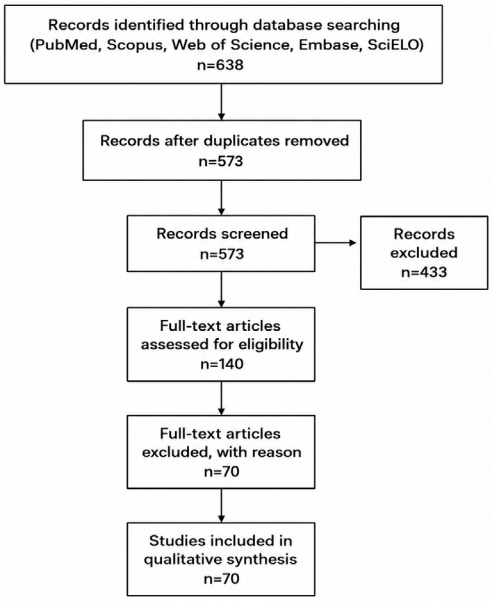

Figure 2. Methodological flowchart of the systematic and integrative review on the effects of healthy eating and oral supplementation with propolis extract on sleep quality in adults, including search strategy, inclusion criteria, study selection, and data analysis.

- Green propolis, derived mainly from *Baccharis dracunculifolia*, is rich in artepillin C and prenylated flavonoids.
- Red propolis, associated with exudates of *Dalbergia ecastaphyllum*, with a high content of isoflavonoids.
- Brown propolis, obtained from various plant sources, with a more heterogeneous composition (Barreto et al., 2020).

On the international stage, botanical diversity results in propolis with unique chemical profiles, such as Eastern European propolis, which is rich in flavonoids, and propolis from Japan and China, with higher concentrations of specific phenolic compounds. In this context, propolis exhibits a wide range of therapeutic and nutritional applications. Clinical and experimental studies demonstrate its potential in the prevention and treatment of respiratory infections, modulation of immune responses, and protection against oxidative stress (Sforcin & Bankova, 2011). Beyond its medicinal use, propolis is incorporated into cosmetics, pharmaceutical formulations, dietary supplements, and veterinary products.

The global propolis market has experienced continuous growth, driven by the increasing demand for natural products and dietary supplements. Asia, particularly China and Japan, is estimated to represent one of the largest consumer markets, followed by Europe and North America (Zabaiou et al., 2017). In Brazil, the propolis market is highly significant, not only due to diversified production but also because of exports, with green propolis being one of the main Brazilian bee products traded internationally. Brazil stands out as a world leader in green propolis production, owing to the abundant presence of *Baccharis dracunculifolia*, becoming both a scientific and commercial reference (Barreto et al., 2020). Brazilian propolis is considered a high-quality product, with certifications that enhance its competitiveness in the global market.

The use of propolis is widespread, encompassing traditional medicine, dentistry, cosmetics, and the pharmaceutical industry. Its global commercialization has grown significantly, with Brazil, China, and Russia standing out as leading producers and exporters (Barreto et al., 2020).

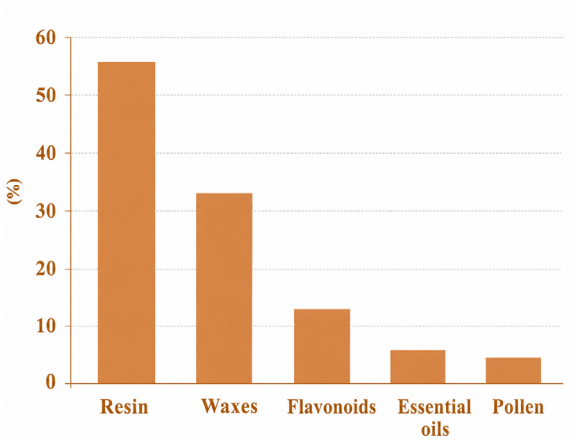

Figure 3. Approximate chemical composition of Brazilian propolis according to data from recent literature (Barreto et al., 2020).

4 METHODS FOR CHARACTERIZATION AND QUALITY CONTROL OF PROPOLIS

The characterization of propolis involves physicochemical, phytochemical, and microbiological analyses (Table 1) to ensure its quality and authenticity. Techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry are widely used to identify and quantify bioactive compounds, including flavonoids and phenolic acids.

Brazilian studies have demonstrated the efficacy of these approaches. Green propolis derived from *Baccharis dracunculifolia* and identified high levels of artepillin C, caffeic acid, and prenylated flavonoids, highlighting the unique chemical profile of this variety. Similarly, Salatino et al. (2005) confirmed that botanical diversity directly influences composition, indicating marked differences between green, red, and brown propolis in Brazil. In other counties, Ahn et al. (2007) employed HPLC to quantify flavonoids in Chinese and Japanese propolis, revealing high concentrations of pinocembrin and galangin, which are associated with strong antioxidant activity.

Table 1. Some methods of analysis and quality control of propolis.

Method	Objective	Main compounds analyzed	References
HPLC	Quantification	Flavonoids, phenolic acids	Woźniak et al. (2023)
Mass spectrometry	Structural identification	Various bioactive compounds	Bankova et al. (2018)
Colorimetric assays	Determination of total flavonoids/ phenols	Total flavonoids, total phenols	Bouchelaghem et al. (2022); Matsushita et al. (2024)
Microbiological analysis	Contamination assessment	Bacteria, fungi	Eryilmaz et al. (2026)

HPLC: high-performance liquid chromatography.

In addition to chemical parameters, Sforcin and Bankova (2011) emphasized the importance of microbiological assessment, as propolis exhibits antimicrobial activity against Gram-positive bacteria and fungi, supporting its use in both therapeutic applications and food preservation.

Quality control is essential to ensure the safety and efficacy of the product. Parameters such as total flavonoid content, antioxidant activity, presence of microbiological contaminants, and heavy metals are routinely monitored. Standardization of extracts, such as Brazilian green propolis, is based on specific chemical markers, including artepillin C, to ensure batch-to-batch consistency (Barreto et al., 2020). Additionally, sensory analysis and evaluation of physicochemical stability during storage are fundamental to determine the shelf life and therapeutic effectiveness of propolis.

5 BIOLOGICAL ACTIVITIES OF PROPOLIS

Propolis exhibits a wide range of biological activities and has been extensively studied for its therapeutic properties. Among these, it modulates inflammatory pathways, such as the inhibition of Nuclear Factor kappa B (NF-κB), Factor Nuclear kappa B, and caspases, thereby reducing pro-inflammatory cytokines (Almeida et al., 2002); induces apoptosis in tumor cells and inhibits angiogenesis (Hossain et al., 2022); influences the central nervous system, promoting sedative effects; and neutralizes free radicals, protecting cells against oxidative damage (Figure 4).

5.1 Anti-inflammatory activity

Phenolic compounds in propolis modulate different inflammatory signaling pathways, notably through the inhibition of the NF-κB pathway, which is responsible for the transcription

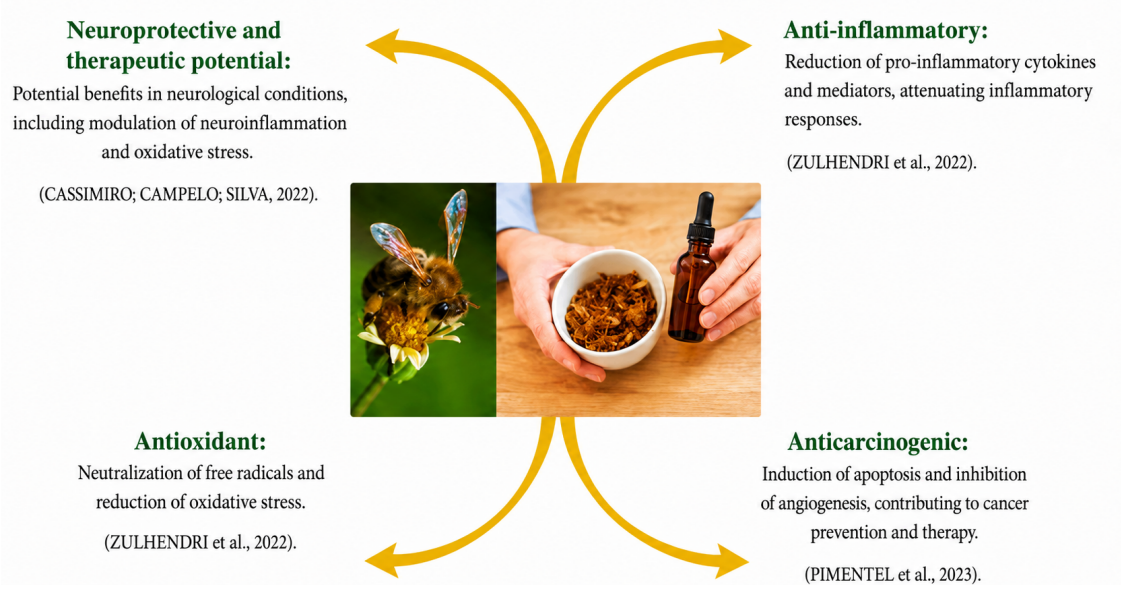

Figure 4. Biological activities of propolis and main mechanisms of action.

of pro-inflammatory genes, and the negative regulation of caspases involved in the activation of the inflammatory response (Almeida et al., 2002).

In vitro studies: CAPE, isolated from propolis, suppressed the production of tumor necrosis factor alpha-α, interleukin 1 beta, and interleukin 6 in lipopolysaccharide-stimulated macrophage cultures (Orsi et al., 2000).

In vivo studies: In a murine inflammation model, propolis administration reduced edema and cellular infiltration, confirming its anti-inflammatory effects (Sforcin & Bankova, 2011).

5.2 Antitumor activity

Several compounds in propolis, such as flavonoids and CAPE, have been shown to induce apoptosis in tumor cells through the activation of the mitochondrial intrinsic pathway and the inhibition of anti-apoptotic proteins (Bcl-2) (Altabbal et al., 2023).

In vitro studies: In breast cancer cell lines (Michigan Cancer Foundation-7 [MCF-7]), CAPE induced apoptosis and caused cell cycle arrest in the G0/G1 phase (Natarajan et al., 1996).

In vivo studies: Mice bearing tumors treated with propolis exhibited a significant reduction in tumor growth and angiogenesis, mediated by the inhibition of vascular endothelial growth factor (Altabbal et al., 2023).

5.3 Effects on the Central Nervous System

Propolis influences neurotransmission by modulating GABAergic and serotonergic receptors, contributing to sedative and anxiolytic effects.

In vitro studies: Ethanol extracts of propolis demonstrated the ability to enhance Gamma-Aminobutyric Acid (GABA)-A receptor activity, a mechanism similar to that of benzodiazepines (Savage et al., 2018).

In vivo studies: In animal models, propolis administration reduced locomotor activity and increased pentobarbital-induced sleep duration, suggesting a central sedative effect (Savage et al., 2018).

5.4 Antioxidant activity

Propolis is rich in flavonoids and phenolic acids capable of neutralizing ROS, acting as free radical scavengers and modulators of antioxidant enzyme activity (superoxide dismutase [SOD], catalase [CAT], glutathione peroxidase [GPx]). In vitro studies: Propolis extracts exhibited high free radical scavenging capacity in DPPH and ABTS assays, as well as inhibition of lipid peroxidation in cellular membranes (Kurek-Górecka et al., 2014). In vivo studies: In rats subjected to induced oxidative stress, supplementation with propolis significantly increased the activity of SOD and CAT, while reducing malondialdehyde levels, a marker of lipid peroxidation (Kumazawa et al., 2004).

These biological activities make propolis a promising candidate for the development of natural and complementary therapies. Biotechnology has enabled the creation of innovative propolis-based products (Figure 5). Among these formulations, incorporation into lipidic or polymeric systems improves the solubility and bioavailability of bioactive compounds (Hoain et al., 2022); creams and lotions utilize propolis for its antimicrobial and anti-inflammatory properties (Barreto et al., 2020); combination with conventional drugs enhances therapeutic effects in respiratory infections and inflammatory diseases (Almeida et al., 2002); and capsules and liquid extracts support immune function and promote overall health (Altabbal et al., 2023). These innovations expand the applicability of propolis in modern medicine and the pharmaceutical industry.

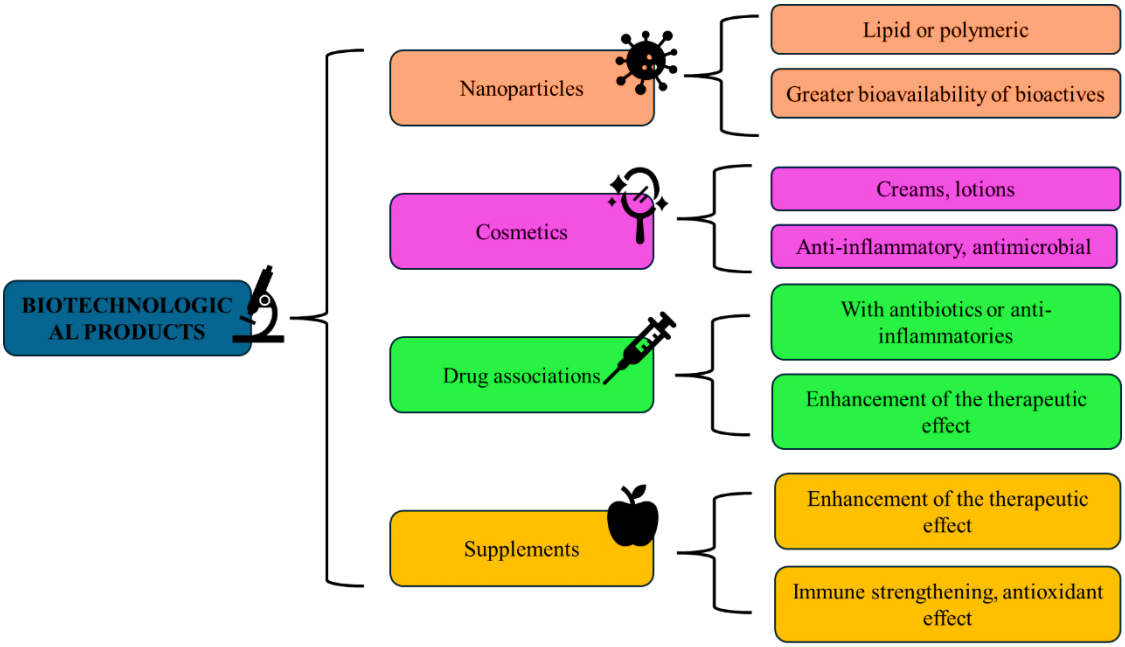

Figure 5. Main biotechnological products derived from propolis (Barreto et al., 2020).

6 RELATIONSHIP BETWEEN PROPOLIS, DIET, AND SLEEP

Sleep quality is closely related to nutritional factors and the balance of oxidative stress in the body. Bioactive compounds present in propolis exhibit antioxidant and anti-inflammatory effects, which may contribute to the regulation of neurotransmitters involved in the sleep-wake cycle, such as GABA and serotonin (Almeida et al., 2002). When combined with a healthy diet rich in fruits, vegetables, and antioxidant nutrients, supplementation with propolis may enhance the reduction of free radicals and pro-inflammatory cytokines, promoting a physiological environment favorable for the induction and maintenance of restorative sleep. Experimental studies suggest that this combination not only improves oxidative stress markers but may also modulate sleep parameters in animal models, indicating a potential synergistic effect between a balanced diet and propolis supplementation in promoting sleep health (Kurek-Górecka et al., 2014).

Sleep is an essential physiological process for mental and physical health, being directly related to immunity, memory consolidation, metabolic balance, and overall well-being. Insomnia, in turn, is one of the most prevalent sleep disorders in the adult population and is characterized by difficulty initiating or maintaining sleep, early awakenings, or non-restorative sleep, resulting in daytime impairments such as fatigue, irritability, and cognitive difficulties (American Academy of Sleep Medicine, 2014).

Diet plays a key role in the regulation of the sleep-wake cycle, influencing both the duration and quality of sleep. Diets characterized by high consumption of fruits, vegetables, whole grains, fish, and olive oil, such as the Mediterranean diet, have been effectively associated with reduced insomnia and improved sleep quality, possibly due to their anti-inflammatory and antioxidant effects (Godos et al., 2019).

Treatment for insomnia can be divided into conventional and non-conventional approaches, which can be used alone or in combination. Conventional methods primarily include the use of sedatives and hypnotics, such as benzodiazepines and melatonin receptor agonists, as well as cognitive-behavioral therapy for insomnia, considered the gold standard due to its sustained efficacy and absence of significant adverse effects (Riemann et al., 2017).

In this context, non-conventional treatments gain prominence, including herbal medicines, meditation techniques, supplementation with melatonin or propolis extract, acupuncture, and lifestyle modifications, particularly in diet. These natural and integrative approaches have demonstrated potential to improve sleep quality with a lower risk of adverse effects, being particularly relevant in mild to moderate cases and in patients seeking alternatives to pharmacotherapy (Ferracioli-Oda et al., 2013).

Recent scientific studies suggest that oxidative stress and chronic inflammatory processes are associated with poor sleep quality and insomnia (Lee et al., 2019). In this context, bioactive compounds in propolis—particularly flavonoids and phenolic acids—may exert neuroprotective and anxiolytic effects, promoting relaxation and sleep induction (Gholami et al., 2022).

Melatonin is an endogenous hormone primarily synthesized by the pineal gland from tryptophan, with its secretion regulated by the light-dark cycle. Its main function is related to circadian rhythm regulation, acting as a synchronizer of the sleep-wake cycle. Melatonin production increases significantly during the night, signaling to the body that it is time to sleep, thereby contributing to sleep induction and maintenance. Disruptions in melatonin secretion patterns, such as those caused by exposure to artificial light at night or alterations in the biological clock, are frequently associated with insomnia, jet lag, and other sleep disorders (Sack et al., 2007).

Exogenous melatonin supplementation has been widely studied as a non-sedative therapeutic strategy, demonstrating efficacy in reducing sleep latency and improving sleep quality, particularly in populations with naturally reduced production, such as older adults and individuals with circadian sleep disorders (Ferracioli-Oda et al., 2013). Due to its safety profile and low toxicity, melatonin is considered a viable and promising option for managing sleep-related disorders.

The combination of propolis and melatonin has been gaining attention in the scientific literature as a promising approach to improving sleep quality, due to the potential synergy between their mechanisms of action. Melatonin directly regulates the circadian cycle and induces sleep, while propolis extract possesses antioxidant and anti-inflammatory properties that may modulate neurophysiological pathways associated with oxidative stress and neuroinflammation—factors known to be linked to sleep disturbances (Bouchelaghem et al., 2022). Table 2 summarizes the comparative mechanisms and effects of propolis, melatonin, and their synergistic association on sleep and related parameters.

Experimental evidence suggests that propolis may enhance the effects of melatonin by improving mitochondrial function and reducing the activation of inflammatory cytokines in the central nervous system, creating a neurochemical environment more conducive to restorative sleep (Gholami et al., 2022). Additionally, both substances exhibit mild anxiolytic effects, which may facilitate natural and safe sleep induction, particularly in individuals with mild insomnia or stress-related sleep disturbances.

7 LIMITATIONS OF CURRENT STUDIES

Despite advances in research on healthy diets and propolis in the context of sleep and oxidative stress, several limitations in current studies restrict the robustness of conclusions. Studies vary widely in protocols, including different doses, forms, and durations of interventions, as well as in the definition of what constitutes a healthy diet. This heterogeneity complicates comparisons and meta-analytic syntheses (Bahari, et al., 2025; Kimball et al., 2008).

Many studies evaluate short-term effects, which prevents assessment of long-term benefits or adverse effects—essential considerations for interventions involving dietary changes and chronic supplement use (Kimball, et al., 2008). In addition, numerous clinical trials involve a limited number of participants, reducing statistical power and limiting the generalizability of results to broader populations (Alvarenga et al., 2021).

Table 2. Comparison of mechanisms and effects of propolis, melatonin, and their synergistic association on sleep and related parameters.

Category	Propolis – Antioxidant, anti-inflammatory, and neuroprotective action	Melatonin – Regulation of circadian rhythm via MT1 and MT2 receptors	Association – Synergistic modulation of the neuroendocrine axis and reduction of oxidative stress
Sleep induction	Reduces anxiety and neuronal excitation	Reduces sleep latency, induces drowsiness	Faster improvement in sleep onset quality
Sleep maintenance	Protects neurons against stress and inflammation	Maintains nocturnal hormone levels	Promotes continuous and deep sleep
Antioxidant effects	Strong – via flavonoids and phenolic compounds	Indirect – via increased antioxidant enzymes	Combined protection against oxidative damage
Mood regulation	Anxiolytic and adaptogenic effect	Mild mood modulator	Reduces anxiety related to insomnia
Safety and toxicity	Natural and safe, minimal side effects	Well tolerated, low toxicity at therapeutic doses	Combined use may reduce drug requirements
Benefited populations	People with stress, anxiety, mild sleep disorders	Elderly, shift workers, jet lag, primary insomnia	Populations with multiple insomnia-related factors

Source: Prepared by the author, based on Altabbal et al. (2023); Bahari et al. (2025); Bouchelaghem et al. (2022); Woźniak et al. (2022); Gholami et al. (2022); Ferracioli-Oda et al. (2013); Lee et al. (2019).

8 CONCLUSIONS

Propolis is a unique natural remedy, used since antiquity in traditional medicine, whose pharmacological properties are continually being updated. This review indicates that both a healthy diet and supplementation with propolis extract show promising effects in improving sleep quality and reducing oxidative stress.

The available scientific literature confirms the efficacy of propolis and its bioactive components. However, a major challenge in studying the therapeutic applications of propolis lies in its variable composition, which depends on regional flora, harvest season, climatic conditions, environmental pollution, and the inclusion of contaminant waxes, among other factors. This variability complicates the standardization of propolis for medicinal use. The studies analyzed demonstrate that balanced dietary patterns, rich in bioactive compounds, combined with the antioxidant, regulatory, immunomodulatory, and anti-inflammatory properties of propolis, synergistically contribute to overall physiological balance and the promotion of sleep health.

Thus, it can be concluded that the combination of healthy nutritional interventions and natural propolis supplementation may represent an effective complementary approach for managing sleep disorders and mitigating oxidative stress. Nevertheless, further research is needed to validate these strategies across different populations and clinical contexts, ensuring safety, efficacy, and practical applicability.

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