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Melatonin for hair regrowth: Preclinical insights, current evidence, and future perspectives

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ABSTRACT

Melatonin, a neurohormone regulating circadian rhythms, also plays a role in hair follicle physiology through its antioxidant and anti-inflammatory effects. This scoping review aimed to assess preclinical and clinical evidence supporting melatonin as a therapeutic option for alopecia. A systematic search of MEDLINE, Scopus, and DOAJ identified studies on androgenetic alopecia, telogen effluvium, and diffuse hair loss. Preclinical findings suggest melatonin promotes follicular stem cell proliferation, modulates signaling pathways, and protects against damage. Clinical trials indicate that topical melatonin increases hair density, prolongs the anagen phase, and reduces hair shedding with minimal adverse effects. While current evidence supports its potential, variability in study design highlights the need for standardized clinical trials.

Keywords: alopecia, hair follicle, hair regeneration, melatonin, oxidative stress, signal transduction

INTRODUCTION

Melatonin is primarily known for its role in the regulation of circadian rhythms. This hormone is produced primarily by the pineal gland in response to darkness and helps to synchronize the body's internal clock with the external environment [1, 2]. However, melatonin is also synthesized in peripheral tissues, including the skin and hair follicles (HFs) [3]. It plays a direct role in HF development and supports hair growth by promoting the anagen phase of the hair growth cycle. Human scalp HFs in the anagen phase are important sites for extra-pineal melatonin synthesis, suggesting potential autocrine and paracrine regulatory mechanisms [4].

Melatonin has effects on various receptors, genes, and biological pathways during hair growth. Melatonin receptor 1 (MT1 or MTNRa) and melatonin receptor 2 (MT2 or MTNRb) are G protein-coupled membrane-bound melatonin receptors. MT1 is expressed in multiple layers of the epidermis and within HFs, whereas MT2 is localized in the inner root sheath of these structures. These receptors play a role in pigmentation and growth [5]. A human hair culture model demonstrated that melatonin exerts bimodal effects on hair shaft elongation, stimulating growth at 30 μM, while inhibiting it at millimolar concentrations [6]. Moreover, melatonin inhibits the expression of retinoic acid receptor-related orphan receptor alpha (RORα) in hair follicle stem cells (HFSC). This nuclear receptor is involved in regulating HF cycling and growth, suggesting that the compound may influence stem cell maintenance and hair growth by modulating RORα expression [4, 7]. Additionally, melatonin upregulates genes in the WNT/β-catenin signaling pathway, which is essential for hair regeneration and follicle development. It also enhances the expression of key genes associated with hair growth, including alkaline phosphatase, bone morphogenetic protein 2, versican, and wingless-int 5A [8]. Furthermore, it indirectly regulates FOXC1, a gene that is crucial for maintaining HFSC quiescence. FOXC1 activation is essential for self-renewal and re-entry into the cell cycle, ensuring the preservation of stem cell reservoirs and preventing premature activation [9]. This hormone modulates several biological pathways that are essential for HF development and function. For instance, it activates the WNT/β-catenin signaling pathway, which is crucial for hair proliferation and differentiation of follicle cells [8, 10]. In addition, it stimulates the AKT-GSK3β-β-catenin pathway, leading to the stabilization of β-catenin, which is a key factor in promoting hair growth [8].

In addition to its receptor-mediated effects, melatonin is a potent antioxidant and DNA repair inducer that protects the anagen hair bulb against oxidative stress. Furthermore, it counteracts the effects of testosterone and dihydrotestosterone, both of which contribute to androgenetic alopecia (AGA), reinforcing its potential as a therapeutic option for hair loss [11]. This protective role against oxidative stress is crucial, because oxidative stress can lead to HF damage and loss. Additionally, melatonin promotes the translocation of the transcription factor NRF2 from the cytosol into the nucleus, resulting in increased gene expression of phase-2 antioxidative enzymes, including γ-glutamylcysteine synthetase (γ-GCS), heme oxygenase-1 (HO-1), and NADPH:quinone dehydrogenase-1 (NQO1). This process strengthens the antioxidant capacity of the keratinocytes [12].

Building on the potential of melatonin demonstrated in preclinical studies, attention has increasingly been paid to the clinical application of melatonin as a hair loss treatment. Preclinical findings have suggested that melatonin supports hair growth through its roles in hair cycle regulation, antioxidative protection, and hormone modulation. These mechanisms and promising preclinical findings have led to clinical investigations assessing the efficacy of melatonin in various hair loss conditions, including AGA and telogen effluvium. In this review, we evaluate the available clinical studies that have explored the therapeutic use of melatonin for hair loss and assess its effectiveness, safety profile, and potential advantages over conventional treatments. Additionally, we analyzed the possible mechanisms by which melatonin regulates hair growth and hair loss. By synthesizing the current evidence, we aimed to provide insights into the clinical relevance of melatonin and its potential applications prior to clinical implementation.

MATERIALS AND METHODS

Search Strategy & Study Selection

A scoping review was conducted based on literature searches of MEDLINE, Scopus, Cochrane, and DOAJ electronic databases to identify studies examining the effects of melatonin treatment on hair loss and the related mechanisms, for the period from 2004 to 2025. The search strategy included the keywords “melatonin,” “hair loss,” “alopecia,” and “hair growth,” combined using Boolean operators (e.g., “melatonin AND (hair loss OR alopecia OR hair growth)”). Studies investigating the role of melatonin in HF biology, signaling pathways, and potential therapeutic applications were included. Gray literature, including conference proceedings, theses, and clinical trial registries, were excluded. Duplicate records were removed using automated software and manual screening to ensure the inclusion of unique studies.

The review adhered to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) for scoping reviews guidelines to maintain methodological rigor and transparency [13], as shown in **Figure 1**.

Eligibility Criteria

Studies were included if they were randomized controlled trials (RCTs), cohort studies, or case-control studies that evaluated melatonin as a treatment for hair loss or investigated the mechanisms related to its role in HF biology. Only studies conducted on human participants with hair loss conditions, such as AGA or telogen effluvium, were considered for therapeutic evaluation, with primary outcomes including hair density, hair diameter, and patient-reported improvements in hair growth. Preclinical studies were included if they provided mechanistic insights into the effects of melatonin on HF function, signaling pathways, or cellular interactions relevant to hair regrowth. Reports were excluded if they were related to animal or in vitro research studies without translational relevance, did not assess melatonin as a therapeutic intervention or biological regulator, or lacked primary data, e.g., review articles, editorials, or conference abstracts. Additionally, studies with insufficient methodological details and those lacking quantitative outcomes were excluded.

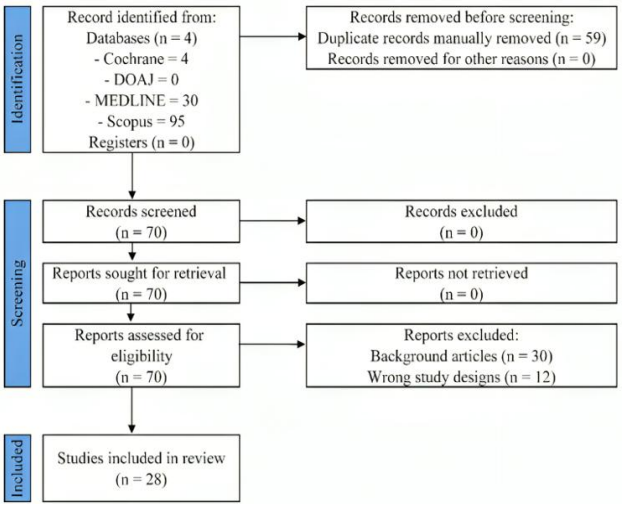

Figure 1. PRISMA flow diagram of study selection (Source: Authors’ own elaboration)

Screening & Data Extraction

The screening process, which focused on titles, abstracts, and full texts, was conducted independently by 2 reviewers using predefined eligibility criteria. During data extraction, we concentrated on critical variables, such as study design, sample size, melatonin dosage, treatment duration, and both primary and secondary outcomes for clinical studies. Data were extracted using a standardized form, capturing information on study characteristics, interventions, outcomes, and results. For mechanistic studies, we extracted further details regarding the experimental models, signaling pathways, and molecular or cellular effects of melatonin on HF biology. Any discrepancies that arose in study selection or data extraction were resolved by discussion to consensus between the 2 reviewers.

RESULTS

Preclinical studies in rodents, cashmere goats, and ex vivo human HF models have demonstrated the physiological effects of melatonin on HF function via multiple mechanisms. Twenty-two studies were reviewed, including 15 studies in cashmere goats, 5 studies in rodent models, 1 study using an ex vivo human HF organ culture model, and 1 study in human dermal papilla cells. The detailed mechanistic effects of melatonin are summarized in **Table 1**.

Melatonin plays a key role in HF regulation by interacting with follicular receptors (MT1, MT2, and RORα) and influencing hormonal sensitivity and androgen-related follicular responses [14-18]. It also modulates gene expression pathways [19-21], particularly those related to the WNT/β-catenin signaling pathway, which supports HFSC viability, dermal papilla cell proliferation, and follicular development [8, 10, 22, 23]. Additionally, melatonin helps to regulate the hair growth cycle, prolonging the anagen phase, delaying catagen transition, and contributing to seasonal hair growth adaptation [7, 14, 16, 21, 22-31]. Beyond its role in follicular signaling, melatonin also influences metabolic and molecular processes by regulating lipid, amino acid, and nucleotide metabolism and modulating FOXO signaling, which is essential for cellular homeostasis and follicular function [20, 29, 32].

Table 1. Possible mechanisms by which melatonin affects hair growth and regulates hair loss

Primary physiological effects	Mechanistic insights	References
Receptor interaction and hormonal modulation	Interacts with follicular melatonin receptors (MT1, MT2, and RORα), modulating androgenic effects and influencing follicle sensitivity to hormonal changes.	[14-18]
Gene and pathway regulation	Regulates WNT signaling, keratin genes (KRT and KRTAP), and other essential genes for follicle growth and maintenance.	[19-21]
WNT/β-catenin pathway activation	Upregulates WNT10b, β-catenin, and other key regulators of follicle morphogenesis, enhances dermal papilla cell proliferation, and accelerates transition from the telogen to the anagen phase.	[8, 10, 22, 23]
Enhancement of HFSC viability and proliferation	Promotes HFSC viability, proliferation, and cyclin expression, while modulating ROR and FOXC1 transcription to balance activation and regeneration.	[7, 24, 25]
Stimulation of HF growth	Enhances secondary HF development, increases the number of active secondary HFs, and promotes follicle morphogenesis.	[7, 16, 22, 23, 25-28]
Hair cycle modulation	Prolongs the anagen phase, delays catagen transition, and modulates seasonal hair growth cycles, affecting cashmere production and fiber elongation in goats.	[14, 21, 29-31]
Metabolic and molecular impacts	Influences lipid, amino acid, nucleotide metabolism, and FOXO signaling, supporting follicle development and function.	[20, 29, 32]
Stem cell protection and maintenance	Protects HFSCs from oxidative stress, chemotherapy-induced apoptosis, and excessive activation, ensuring long-term follicle regeneration.	[14, 24, 26]
Antioxidant and anti-aging properties	Activates KEAP1–NRF2 and NF-κB pathways, reducing oxidative stress and delaying follicular aging, while preserving hair quality.	[16, 26, 27]

Note. β-Catenin: Beta-catenin (a key component of the WNT signaling pathway); FOXO: Forkhead box O (a transcription factor involved in cellular metabolism and longevity); KEAP1-NRF2: Kelch-like ECH-associated protein 1-nuclear factor erythroid 2-related factor 2 (an antioxidant regulatory pathway); KRT: Keratin; KRTAP: Keratin-associated protein; MT1 & MT2: Melatonin receptors 1 and 2, respectively; NF-κB: Nuclear factor kappa B (a transcription factor regulating inflammation and stress responses); ROR: Retinoic acid-related orphan receptor; & WNT: Wingless-related integration site signaling pathway

It also supports stem cell maintenance and protection by reducing oxidative stress, mitigating chemotherapy-induced follicular damage, and preventing excessive HFSC activation [14, 24, 26]. Moreover, its antioxidant and anti-aging properties are mediated through activation of the KEAP1-NRF2 and NF-κB pathways, which help to preserve follicular integrity and hair quality [16, 26, 27].

Notably, melatonin exhibits dose-dependent effects, where low doses enhance follicular activity, whereas higher doses help to maintain stem cell reserves by preventing excessive activation [7]. In ex vivo human HF models, melatonin protected against chemotherapy-induced follicular damage and modulated androgen-related follicular responses [24].

A total of six clinical publications were reviewed to examine the effects of melatonin on hair growth and related disorders, as summarized in **Table 2**.

Table 2. Clinical trials investigating the effects of melatonin on hair growth and hair disorders

R	D & P	FUD	Intervention	Main findings
[33]	RCT, 40 males of AGA	3-month treatment, evaluated at week 16	Group I (n = 20): Topical melatonin solution & Group II (n = 20): Topical melatonin NLCs (formula NLC2)	**Primary outcomes:** (1) Improvement scores: 100% of patients in group II showed improvement compared to 40% in group I ($p < 0.05$); (2) Hair-pull test: Group II demonstrated a significantly greater reduction in hair loss compared to group I ($p < 0.05$); (3) Hair shaft thickness: Group II showed a significantly greater increase than group I ($p < 0.05$): Group I: 48.54 ± 4.67 μm to 51.54 ± 3.90 μm & Group II: 44.98 ± 3.60 μm to 83.25 ± 7.39 μm; & (4) Dermoscopic examination: Group II exhibited a significantly greater increase in hair density and shaft diameter, along with a greater reduction in yellow dots, than that in group I ($p < 0.05$). **Adverse reactions:** No side effects were reported in either group, confirming the safety of and patient compliance with both treatments.
[34]	RCT, 40 males with AGA	3-month treatment, evaluated at week 16	Patients were divided into 2 groups (n = 20 each): Group I: Melatonin solution & Group II: Melatonin aspasomal formula A3	**Primary outcomes:** (1) Improvement grade assessed by investigators: Group I: 8 patients (40%) showed improvement & Group II: All 20 patients (100%) showed improvement; (2) Hair-pull test: Group I: Pulled hairs reduced from 7.9 ± 0.96 to 6.6 ± 0.82 & Group II: Pulled hairs reduced from 7.9 ± 0.78 to 3.3 ± 1.38; (3) Hair diameter: Group I: Increased from 48.55 ± 4.68 μm to 51.54 ± 3.90 μm & Group II: Increased from 48.78 ± 5.85 μm to 66.44 ± 3.66 μm; & (4) Dermoscopic improvement: Group I: 3 patients (15%) showed improvement & Group II: 12 patients (60%) showed improvement **Adverse reactions**: No side effects were reported in either group, demonstrating the safety and patient compliance of both treatments.
[35]	An open-label, evaluator-blinded, prospective, proof-of-concept study on the efficacy and safety of Forti5® in managing AGA, involving 10 participants (6 males, 4 females)	24 weeks	Two tablets of Forti5® daily for 24 weeks, containing green tea extract, omega-3 and omega-6 fatty acids, cholecalciferol, melatonin, beta-sitosterol, and soy isoflavones	**Primary outcomes:** (1) HMI: Mean increase of 9.5% (+4.5 HMI, $p = 0.003$); (2) Terminal hair count: Mean increase of 5.9% (+4.2 terminal hairs, $p = 0.014$); & (3) Investigator global photography assessment: 80% (8/10) showed improvement after 24 weeks (mean change +1.4) with 40% (4/10) showing moderate improvement and 10% (1/10) showing marked improvement. **Adverse reactions:** Well-tolerated with no major side effects reported. However, no specific statistical data on adverse reactions were provided.

Table 2 (Continued). Clinical trials investigating the effects of melatonin on hair growth and hair disorders

R	D & P	FUD	Intervention	Main findings
[36]	A double-blind RCT including 40 females with diffuse alopecia (n = 28) or AGA (n = 12)	6 months	Participants applied either a 0.1% melatonin-alcohol solution or a placebo (alcohol solution) topically once daily in the evening for 6 months (1 mL per day, administered in 8 sprays)	**Primary outcomes:** (1) AGA (n = 12): The melatonin group showed a significant increase in anagen hair rate in occipital trichograms compared to placebo (odds ratio 1.90, 95% CI 1.22-2.96, p = 0.012) & (2) Diffuse alopecia (n = 28): The melatonin group demonstrated a significant increase in anagen hair rate in frontal trichograms compared to placebo (odds ratio 1.41, 95% CI 1.05-1.90, p = 0.046). **Adverse reactions:** No explicit adverse reactions were reported. However, plasma melatonin levels increased in the treatment group but remained within the physiological night peak of ≤ 250 pg/mL, suggesting minimal systemic absorption.
[37]	An open-label prospective study including 31 males with AGA (Hamilton's scale II-III)	6 months	Daily application of 0.1 mg melatonin hydro-alcoholic lotion on the scalp	**Primary outcomes:** (1) Hair count increased on the parietal area (142.13 ± 45.94 to 152.6 ± 38.98) and decreased on the frontal area (153.47 ± 56.89 to 133.21 ± 31.30), both non-significant (p > 0.05) & (2) In 51.7% of patients who improved, hair density significantly increased (119.4 ± 40.1 to 156.3 ± 29.0 hairs/cm^2; p = 0.007). And physician evaluation showed 62% of patients improved. **Adverse reactions:** (1) Tolerance was excellent in 28 out of 29 patients who completed the trial & (2) One patient reported an adverse reaction, which was pruritus.
[38]	Study 1: Pharmacokinetic study (double-blind, placebo-controlled crossover) involving 8 females	14 days	Topical 0.0033% melatonin solution, applied to the scalp each evening	**Primary outcome:** Maximum serum melatonin concentration was 83.4 pg/mL (melatonin group) vs. 71.2 pg/mL (placebo group). **Adverse reactions:** No significant changes in laboratory tests, circulatory parameters, or central nervous system effects. Some reports of moderate headache and gastrointestinal issues, but the incidence was the same in both groups.
	Study 2: Open-label observational study involving 30 patients (15 males, 15 females)	90 days	Topical 0.0033% melatonin solution, applied to the scalp each evening	**Primary outcome:** Significant reduction in alopecia severity at 30 and 90 days (p < 0.001). **Adverse reactions:** No specific data reported.
	Study 3: Open-label, clinically controlled study using TrichoScan, involving 35 males	6 months	Topical 0.0033% melatonin solution, applied to the scalp each evening	**Primary outcomes:** (1) Hair count increased by 29.2% in 3 months and 42.7% in 6 months (p < 0.001) & (2) Hair density increased by 29.1% in 3 months and 40.9% in 6 months (p < 0.001). **Adverse reactions:** Good tolerability reported, but no specific statistical data provided.
	Study 4: Observational study conducted at hair salons with 60 patients (40 males, 20 females)	90 days	Topical 0.0033% melatonin solution, applied to the scalp each evening	**Primary outcomes:** (1) Significant improvement in hair texture (p = 0.002 for females, p < 0.001 for males) & (2) Significant reduction in hair loss (p < 0.001for females, p < 0.001 for males). **Adverse reactions:** 4 patients experienced mild side effects (temporary reddening, sensitivity, itching, or burning), but none discontinued treatment.
	Study 5: Multicenter study with 1,891 patients (901 males, 990 females)	90 days	Topical 0.0033% melatonin solution, applied to the scalp each evening	**Primary outcomes:** (1) Patients with severe/moderate hair loss decreased from 61.6% to 7.8% after 90 days (p < 0.001) & (2) Patients with no hair loss increased from 12.2% to 61.5% after 90 days (p < 0.001). **Adverse reactions:** (1) 88.0% of investigators and 82.7% of patients reported good tolerability & (2) 2.0% of investigators and 3.0% of patients rated the treatment as poorly tolerated.

Collectively, these publications reported on ten individual studies, comprising three RCTs, five open-label studies (evaluator-blinded), one pharmacokinetic study, and one multicenter observational study. The sample sizes ranged from 8 to 1891, encompassing small pilot studies to large multicenter trials, with follow-up durations varying from 14 days to 6 months.

Efficacy of Melatonin in AGA

Four studies focused on the efficacy of melatonin in individuals with AGA. The studies in [33, 34] conducted 2 RCTs to evaluate different melatonin formulations in 40 male participants. Both studies reported a significant reduction in hair shedding and an increase in hair diameter. Notably, the melatonin aspasomal formula group achieved a remarkable 100% improvement rate, as compared to only 40% in the group using the standard melatonin solution. An open-label study was conducted using Forti5, a supplement that included melatonin and other compounds, in 10 participants with AGA [35]. After 24 weeks, significant increases were recorded in the hair mass index (HMI) and terminal hair count (p = 0.003 and p = 0.014, respectively), with 80% of participants showing overall improvement. It was conducted a double-blind RCT involving 40 females with either diffuse alopecia or AGA [36]. It was found that the use of topical melatonin significantly increased the rate of hair in the anagen phase, as compared to that achieved with placebo, in both conditions (AGA: odds ratio [OR] 1.90, 95% confidence interval [CI] 1.22-2.96, p = 0.012; diffuse alopecia: OR 1.41, 95% CI 1.05-1.90, p = 0.046) However, it was reported less promising results in their open-label study involving 31 males with early-stage AGA who applied 0.1 mg melatonin lotion daily for six months [37]. Although overall hair counts did not change significantly, 51.7% of participants

showed a significant increase in hair density ($p = 0.007$), and physician assessments indicated improvement in 62% of cases.

Impact on Telogen Effluvium and Diffuse Hair Loss

Melatonin treatment has also been examined for its effects on telogen effluvium and diffuse hair loss. A large multicenter study in [38] involving 1,891 participants reported a significant reduction in hair shedding. The proportion of patients with severe or moderate hair loss decreased dramatically from 61.6% to 7.8% after 90 days of topical melatonin application ($p < 0.001$). Over this period, the number of participants without hair loss increased from 12.2% to 61.5% ($p < 0.001$). Additionally, a 6-month TrichoScan study involving 35 males reported a 42.7% increase in hair count ($p < 0.001$), whereas a separate 90-day observational study conducted in hair salons, involving 60 individuals, found significant improvements in hair texture and a reduction in hair loss ($p < 0.001$).

Pharmacokinetics and Mechanistic Insights

A pharmacokinetic study in [38] examined application of a topical melatonin solution (0.0033%) in 8 females over a period of 14 days. Although the maximum serum melatonin concentration increased slightly, it remained within the physiological peak typically observed at night, indicating minimal systemic absorption. Mechanistically, melatonin modulates HF cycling, exerts antioxidant effects, and counteracts androgenic effects, thereby supporting its role in promoting hair growth.

Safety and Tolerability

Overall, the reviewed studies highlighted a favorable safety profile for melatonin-based treatments, with no serious adverse events reported. While a few participants experienced mild, transient side effects, such as scalp redness, itching, or burning, these did not lead to discontinuation of treatment in any participant.

DISCUSSION

The findings of the reviewed studies indicate that melatonin is effective in promoting hair growth and reducing hair shedding, particularly in individuals with AGA or telogen effluvium. RCTs demonstrated significant improvements in hair density, hair count, and prolongation of the anagen phase [33, 34, 36]. Some studies have reported better results using advanced melatonin formulations, such as aspasomal or nanostructured lipid carriers (NLCs) [33, 34]. Observational studies and open-label trials further support these findings, with large-scale studies showing decreased hair shedding and increased hair thickness over treatment periods ranging from 90 days to 6 months [38]. Although RCTs provide stronger evidence due to their controlled designs and objective outcome assessments, observational studies offer valuable real-world insights into patient adherence to and long-term effects of treatment. However, despite the overall positive trend, 1 RCT reported no significant improvement in hair count following melatonin treatment, highlighting the need for further investigation into the potential variability in the treatment response [37]. In addition to their efficacy, melatonin-based treatments exhibited a favorable safety profile across all reviewed studies. No serious adverse effects were reported, and mild side effects, such as transient scalp irritation, redness, or itching, were infrequent and did not lead to treatment discontinuation. Pharmacokinetic studies have shown minimal systemic absorption with serum melatonin levels remaining within physiological ranges, suggesting a low risk of systemic hormone disruption.

When comparing the effects of melatonin with those of conventional therapy, such as minoxidil, it was reported that topical minoxidil significantly increased mean hair diameter, from 18.89-19.30 μm to 20.80-21.61 μm, after 6 months of treatment [39]. Similarly, oral minoxidil led to an increase in mean hair diameter, from 17.75-18.21 μm to 19.67-20.30 μm, at the 6-month follow-up. It was further shown the effectiveness of minoxidil in increasing hair thickness [40]. They found that topical minoxidil significantly increased mean hair diameter from 43 ± 4 μm to 47 ± 4 μm after 9 months, while oral minoxidil led to an increase from 44 ± 3 μm to 48 ± 3 μm over the same period. These positive effects were consistent with the reported benefits of melatonin in the promotion of hair growth. However, direct comparisons between minoxidil and melatonin remain limited because existing studies differ in baseline hair loss severity, study populations, and outcome measures. Given these variations, head-to-head trials are necessary to determine the relative efficacy and potential complementary effects, particularly under different hair loss conditions and treatment protocols.

This review has some limitations that must be addressed to understand the findings fully. First, the inclusion criteria were limited to studies published in English, which may have excluded valuable studies published in other languages. Second, most studies have primarily focused on AGA and telogen effluvium. This narrow focus reduces the applicability of the findings to other important forms of hair loss, such as alopecia areata, chemotherapy-induced alopecia, and various scarring alopecias, such as frontal fibrosing alopecia. Third, due to heterogeneity in the study designs, such as RCTs with and without controls, observational studies, and varying outcome measures, conducting a meta-analysis would face significant challenges. The absence of randomization in observational studies introduces selection bias, confounding factors, and variability in patient characteristics, making it difficult to draw robust conclusions when these studies are pooled with controlled trials [41]. Additionally, differences in follow-up duration can lead to time-related biases, where longer studies may appear to show greater effects, simply because of their duration, rather than because of the actual efficacy of the intervention [42]. Finally, the lack of long-term safety data regarding melatonin use for hair growth remains a critical gap. Therefore, future studies should explore its sustained efficacy and potential adverse effects beyond the treatment periods evaluated in existing research. Addressing these limitations is essential for advancing our understanding of the role of melatonin in hair restoration.

Larger and long-term RCTs are necessary to establish the durability and clinical utility of melatonin for hair regrowth. Those future studies should also include more specific outcome measures, such as hair density and hair diameter, to better assess efficacy. Studies with follow-up periods of more than 6 months would provide insight into whether the effects of melatonin persist over time or whether continuous application is required to sustain the benefits. To understand the effectiveness of melatonin, direct comparisons between melatonin and the standard treatments with minoxidil and finasteride are needed. Combination therapies, such as melatonin combined with minoxidil, platelet-rich plasma, or

low-level laser therapy, could be explored. This provides exciting possibilities for improving hair regrowth. Another important direction for future research is to identify biomarkers or genetic factors that can help determine which individuals are most likely to benefit from melatonin therapy. Given the mixed findings of clinical trials, personalized treatment approaches based on individual genetic or biochemical profiles may be required to optimize the results. Furthermore, future studies should examine the potential applications of melatonin beyond AGA and telogen effluvium, particularly in conditions such as alopecia areata, frontal fibrosing alopecia, and chemotherapy-induced alopecia, in which oxidative stress and immune dysregulation play significant roles. Further research is needed to compare the effectiveness and safety of topical and oral melatonin in hair regrowth. Future studies should investigate whether oral melatonin works as well as, or even better than topical formulations, while ensuring that its long-term use is safe. By addressing these knowledge gaps, future studies can better define the role of melatonin in the treatment of hair disorders and guide its clinical application in a broader range of patients.

CONCLUSIONS

Melatonin supports hair growth via several mechanisms. It interacts with follicular receptors to regulate androgenic effects and follicular sensitivity to hormonal changes. It modulates expression of genes, particularly those involved in WNT signaling and keratin production, promoting proliferation of dermal papilla cells, and facilitating the transition to the anagen phase. Additionally, it enhances HFSC viability, extends the growth phase, delays shedding, and protects against oxidative stress, thereby supporting overall hair health. Clinical trials have suggested that topical melatonin is a well-tolerated treatment that improves hair density, reduces shedding, and prolongs the anagen phase. Advanced formulations, such as aspasomal formulations and NLCs show superior efficacy to standard solutions; however, evidence for the use of oral supplementation remains unclear. However, the limitations of studies to date include small sample sizes, short follow-up periods, and inconsistent assessment methods. Larger, long-term, placebo-controlled trials are required to compare formulations, determine optimal dosing, standardize evaluations, and assess the long-term safety of using melatonin to treat hair loss.

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Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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