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REVIEW

Androgenetic Alopecia: An Update on Pathogenesis and Pharmacological Treatment

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Abstract: Androgenetic Alopecia (AGA) is a common type of alopecia. The pathogenesis of AGA involves genetic predisposition, androgen metabolism, inflammation, fibrosis, and impaired energy metabolism. The choice of therapeutic agents for the treatment of AGA remains controversial globally, with finasteride and minoxidil being the only two widely recognized and legally approved therapeutic options. In recent years, significant progress has been made in the development of drugs targeting different pathogenic mechanisms of AGA. This article reviews the main drugs currently used for AGA treatment. By summarizing their mechanisms of action and clinical efficacy, it aims to provide a comprehensive theoretical basis and clinical reference for the treatment of AGA.

Keywords: androgenetic alopecia, pathogenesis, pharmacotherapy, research progress

Introduction

Androgenetic alopecia (AGA), as a non-cicatricial alopecia, is characterized by progressive miniaturization of hair follicles (HFs) and shortening of the hair growth cycle, and is the most common form of alopecia.[1] To understand this pathological process, it is essential to grasp the fine anatomical structure of the hair follicle (HF). From a longitudinal perspective, the HF can be divided into three key segments: the funnel, the isthmus, and the bulb. Among them, the bulb contains the matrix cells and the dermal papilla (DP), which is the core functional area of hair growth. The bulge formed by the proliferation of outer hair root sheath cells at the attachment of the arrector pili muscle in the isthmus serves as the stem cell nest and participates in HF cycle regeneration. In the cross-section, the HF is composed of inner root sheath, outer root sheath, and connective tissue sheath from inside to outside, and the inner and outer root sheaths constitute the support and guidance structure of the hair shaft. The synergistic action of these structures maintains the normal hair growth cycle: anagen, catagen, and telogen.[2]

AGA occurs in both men and women. In the male group, AGA is mainly characterized by a backward shift of the hairline on the forehead and thinning of the hair in the temporal region, called male pattern hair loss (MPHL). In contrast, in women, AGA is characterized by diffuse thinning of hair in the parietal region, but most do not involve the forehead hairline, called female pattern hair loss (FPHL).[3]

Although finasteride and minoxidil have so far only been approved by the Food and Drug Administration (FDA) for legal treatment of AGA,[4] there have been significant advances in the medical treatment of AGA in recent years. At present, the commonly used therapeutic drugs cover a variety of mechanisms of action, including improving the inhibition of androgen effect, promoting local blood circulation, reducing inflammation, delaying the fibrosis process, and regulating HF energy metabolism. These drugs provide diversified options for the treatment of AGA through multi-target intervention.

In this review, we systematically describe the main pathogenesis of AGA, including androgen metabolism, local inflammatory response, perifollicular fibrosis, and HF energy metabolism disorders. The mechanisms of action of different classes of therapeutic drugs, including antiandrogens, anti-inflammatory drugs, and vasodilators, are discussed

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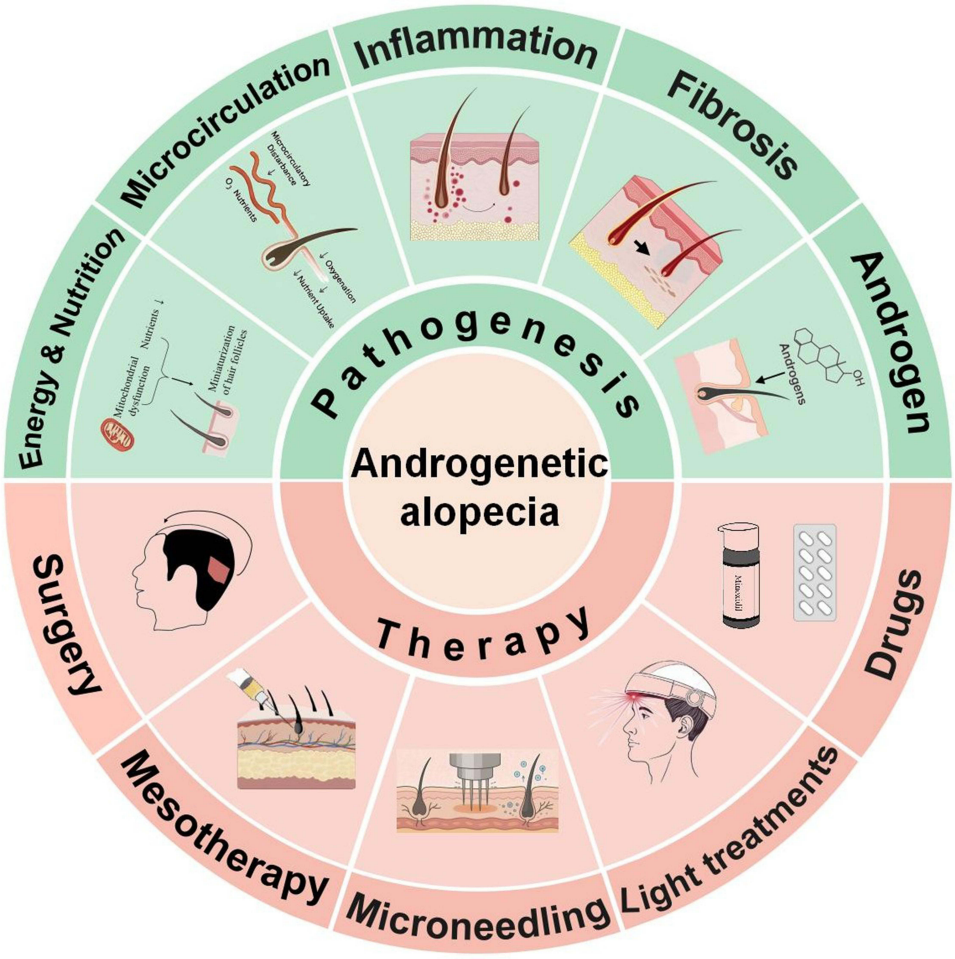

Figure 1 The pathogenesis and therapy of androgenetic alopecia.

in particular, and their clinical efficacy and potential limitations are analyzed in detail (Figure 1). For a comprehensive comparison of current treatment options, we summarize the main pharmacological therapies for AGA in Table 1, including their mechanisms of action, route and dose of administration, and adverse effects. By systematically evaluating the advantages and disadvantages of existing medical interventions, we aim to provide an evidence-based foundation for clinical decision-making and to guide the future development of optimized therapeutic strategies for AGA.

Methods

This review method involves a comprehensive literature search in the PubMed database, with a focus on the research progress in the pathogenesis and drug treatment of AGA. The search included studies published from 2005 to 2025, with inclusion criteria including clinical trials, systematic reviews, meta-analyses, and original research articles investigating the pathogenesis and treatment of AGA. Abstracts of conferences and non-peer-reviewed publications, as well as studies with insufficient sample size, lack of statistical rigor, and data redundancy or duplication, were excluded.

The Pathogenesis of Androgenetic Alopecia

The exact pathogenesis of AGA has not been fully elucidated. Previous studies on AGA mainly focused on androgen metabolism and genetic background, but recent studies have revealed the multifaceted nature of the pathogenesis of AGA, including local inflammatory response, perifollicular fibrosis, and HF energy metabolism disorders, which are also considered to be important mechanisms of AGA.[5]

Table 1 Summary of Main Current Pharmacotherapy for AGA

Treatments	Mechanism of Action	Route and Dose of Administration	Adverse Effects
Antiandrogen drugs			
Finasteride	A type II 5α-R inhibitor	Oral (1mg/day)	Sexual dysfunction, gynecomastia, and psychological symptoms
		Topical(50–200μL/day); 0.25% spray or 1% gel	Scalp pruritus, burning sensation, irritation, and contact dermatitis
Dutasteride	A type I and II 5α-*Rs* inhibitor	Oral (0.5mg/day)	Sexual dysfunction, gynecomastia, and psychological symptoms
Spironolactone	A potent ARA with mild 5α-reductase inhibitory activity	Oral (100–200mg/day)	Menstrual irregularities, dizziness or headaches, facial hirsutism, skin rashes, and hyperkalemia
		Topical (twice daily); 1% gel or 5% solution	
Flutamide	A selective ARA	Oral (62.5–250mg/day)	Potential for hepatotoxicity
Bicalutamide	A non-steroidal selective ARA	Oral (50mg/day)	Mild and transient elevated liver enzyme levels, temporary amenorrhea, endometrial hyperplasia, and migraine
Cyproterone acetate	A competitive antagonist of the nuclear androgen receptor	Oral (2mg/day); Often combined with ethinyl estradiol	Weight gain, menstrual disturbances, and breast pain
Anti-inflammatory drug			
Ketoconazole	An imidazole antifungal drug; Anti-inflammatory; Reduces testosterone synthesis	Topical (2–3 times weekly); 2% shampoo	No obvious adverse effects
Vasodilator			
Minoxidil	Induces vasodilation; Up-regulates the expression of VEGF; Anti-inflammatory and regulates the hair cycle	Oral (0.25–5mg/day)	Hypotension, fluid retention, hypertrichosis, and hypersensitivity reactions
		Topical (1mL once, twice daily); Available in 2% and 5% solutions as well as foaming agents	Hypertrichosis, scalp erythema, pruritus, irritant reactions, contact dermatitis, and application site acne and cysts
Botulinum toxin	Causes dose-dependent muscle paralysis; Improves blood supply and oxygenation in HFs	30-100 units, 1–4 treatments	Injection site reactions, temporary muscle weakness, and rare systemic effects
Energy metabolism-related drugs			
Melatonin	Improves mitochondrial dysfunction	Topical (1mL, once daily in the evening); 0.1% solution	No obvious adverse effects
Nutritional supplement			
Vitamins	Improve the microenvironment of HFs; Alleviate oxidative stress; Support the hair growth cycle	Daily as needed	No obvious adverse effects

(*Continued*)

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Table 1 (Continued).

Treatments	Mechanism of Action	Route and Dose of Administration	Adverse Effects
Trace elements	Improve the microenvironment of HFs; Alleviate oxidative stress; Support the hair growth cycle	Daily as needed	No obvious adverse effects
Other drugs			
Bimatoprost	PGE2 analogues	Topical (once daily); 0.03% solution	No obvious adverse effects
Latanoprost	PGF2α analogues	Topical (once daily); 0.1% solution	No obvious adverse effects
Cetirizine	Inhibits the release of PGD2; Stimulates the release of PGE2	Topical (1mL once, twice daily); 1% solution	No obvious adverse effects
Caffeine	Increases cAMP to promote cell proliferation and metabolism; Antioxidant	Topical (2mL once, twice daily); 0.2% solution	No obvious adverse effects
Adenosine	Increases cAMP to promote mitochondrial energy metabolism	Topical (3mL once, twice daily); 0.75% solution	No obvious adverse effects

Androgen

Androgens play a pivotal role in the pathogenesis of AGA. Recent investigations have elucidated the intricate mechanisms through which androgens regulate follicular biology via multiple molecular pathways. From a cellular signaling perspective, androgens modulate the secretion of various bioactive factors from dermal papilla cells (DPCs) through paracrine and autocrine mechanisms, thereby influencing the HF growth cycle. Specifically, androgen stimulation induces DPCs to release Dickkopf-related protein 1 (DKK-1), a molecular mediator that triggers programmed cell death in outer root sheath cells.[6] Concurrently, DPC-derived interleukin-6 (IL-6) cytokine suppresses the proliferative capacity of follicular matrix cells, while transforming growth factor-beta (TGF-β) secretion is closely associated with vascular calcification processes.[7] At the molecular level, androgens upregulate C-X-C Motif Chemokine Ligand 12 (CXCL12) chemokine expression in dermal fibroblasts, leading to a significant elevation in androgen receptor (AR) mRNA levels within DPCs, ultimately resulting in the miniaturization of human HFs in culture conditions, which is potentially linked to inflammation-mediated alopecia.[8,9] Furthermore, androgens interfere with the Wnt/β-catenin signaling pathway, inhibiting the differentiation potential of hair follicle stem cells (HFSCs), while simultaneously activating the phosphatidylinositol 3-kinase (PI3K)/AKT pathway to antagonize the cytoprotective effects of vascular endothelial growth factor (VEGF), thereby promoting HFSC apoptosis.[10] These findings provide novel insights into the molecular pathogenesis of AGA.

Microinflammation

Microinflammation plays an important role in the pathogenesis of AGA, and its role at the clinical, histological, and transcriptomic levels has been supported by several studies. Unlike cicatricial alopecia, the inflammatory response of AGA appears as a slow and subtle process, hence the name "microinflammation". This persistent microinflammatory environment is closely related to the HF miniaturization process, which is one of the core pathological features of AGA.[11] HF miniaturization is usually accompanied by the destruction of vertical muscles (arrector pili muscle) around HFs and the proliferation of sebaceous glands, which leads to increased oil secretion on the scalp surface, and often coexists with scalp inflammation such as seborrheic dermatitis, which can provide a more favorable microenvironment for the development of pro-inflammatory microorganisms.[12] Histological studies have shown the presence of lymphocyte infiltration, activated T cells, and HF mast cell degranulation in balding areas of AGA patients.[13] Activated T cells and

dendritic cells mainly infiltrate the upper region of the HF funnel, including the raised region where HFSCs are located, and are accompanied by pathological changes of perifollicular sheath fibrosis.[5] These findings suggest that chronic inflammation in the infundibular part of the HF may directly or indirectly affect the periodic regeneration function of HFSCs through the secretion of a variety of soluble factors, thereby participating in the process of HF miniaturization.[11]

Microcirculation, Energy Metabolism and Nutrition

The nutritional supply to HFs primarily depends on adequate blood perfusion, and dysfunction of the scalp microcirculation is one of the critical pathological mechanisms underlying hair loss. Impaired scalp microcirculation leads to a reduction in blood flow velocity and volume, thereby compromising the oxygenation and nutrient delivery to HFs, ultimately resulting in hair loss.[14] Studies have demonstrated that the transcutaneous oxygen pressure ($TcPO_2$) in the frontal scalp region of men with AGA is only 60% of that in healthy individuals, indicating significant microvascular abnormalities in the affected tissues of AGA patients.[15]

From a molecular perspective, androgens play a pivotal role in the dysregulation of blood perfusion in AGA. As mentioned earlier, androgen stimulation can induce DPCs to secrete TGF-β, which promotes the apoptosis of microvascular endothelial cells in the dermal papilla of balding scalp regions in AGA progression. This process leads to vascular calcification, resulting in the degeneration of the microvascular network and a reduction in blood flow. Such microcirculatory disturbances further exacerbate the ischemic and hypoxic state of the pilosebaceous unit, suppressing the activity of HFSCs and disrupting the normal hair growth cycle.[7] With the persistent reduction in local blood supply, HFs gradually enter the catagen phase, characterized by a decrease in follicle size, thinning of hair shaft diameter, and shortening of the anagen phase. Ultimately, this leads to follicular atrophy and miniaturization. Additionally, microcirculatory dysfunction can induce perifollicular fibrosis, further limiting the regenerative capacity of HFs. Therefore, improving scalp microcirculation and enhancing perifollicular microcirculation may represent a crucial therapeutic strategy for managing AGA.[15]

Mitochondrial dysfunction affects the normal physiological function of HFs mainly by interfering with the energy metabolism process of hair follicle cells. Impaired mitochondrial function leads to reduced ATP levels and increased reactive oxygen species (ROS), which can lead to oxidative damage of cellular components and ultimately trigger premature senescence or entry of HFs into the degenerative phase. In addition, excessive ROS can activate the apoptotic pathway, which further aggravates hair follicle cell death and leads to alopecia.[2]

Healthy hair growth is closely related to nutritional status, and this influence runs through all stages of the hair growth cycle. When the body has insufficient energy or specific nutrients, it will not only interfere with the normal growth cycle of hair, but also may affect the structural integrity of hair and the pigmentation process.[16] With a deeper understanding of the association between HF energy metabolism disorders and AGA, therapies that regulate mitochondrial activity and supplement key nutrients (such as vitamins and trace elements) are becoming potential auxiliary means to delay the process of hair loss.

Fibrosis

Fibrosis exhibits a significant pathophysiological correlation with AGA. Clinicopathological observations showed that about 37% of AGA patients showed significant inflammatory infiltration and fibrotic changes in the area around the atrophied HFs. Studies have revealed that the peripheral scalp muscles of AGA patients, including occipital, frontal, auricular, and temporal muscles, are often in a state of chronic and involuntary tension, which subsequently induces inflammatory responses in AGA-susceptible tissues, and persistent inflammatory cell infiltration leads to perifollicular fibrosis.[17] This fibrotic change results in impaired HF microcirculation, which is manifested by reduced local blood flow and inadequate tissue oxygen supply. This chronic hypoxic microenvironment further aggravates the hair loss process, forming a vicious cycle.[18] In addition, androgens can promote the fibrosis process in two ways: on the one hand, they increase the number of mast cells and collagen fiber synthesis; On the other hand, the production of procollagen is stimulated by up-regulating the expression of TGF-β1 in scalp fibroblasts.[5] Furthermore, the study found that fibrosis-related genes were overexpressed in AGA-affected HF bulge, and the fibrosis in the promenade region was positively correlated with AGA-affected HF miniaturization, which may directly harm the function of HFSC, lead to decreased HF regeneration ability, and accelerate the progress of AGA.[5,19]

The Pharmacotherapy of Androgenetic Alopecia

Antiandrogen Drugs

5α-Reductase Inhibitors

5α-Reductases (5α-Rs) are a group of enzymes widely present in various organs and tissues (including three isoforms: type I, II, and III), responsible for catalyzing the conversion of testosterone into dihydrotestosterone (DHT), a metabolite with significantly higher affinity for the AR. By inhibiting the activity of 5α-Rs, 5α-reductase inhibitors (5αRIs) effectively block the transformation of testosterone into DHT, thereby reducing systemic DHT levels. This mechanism has been shown to play a beneficial role in promoting hair growth.[20]

Currently, the primary 5αRIs used in the treatment of AGA include finasteride and dutasteride.[21] Finasteride selectively inhibits type II 5α-Rs, whereas dutasteride demonstrates inhibitory effects on both type I and type II isoforms. In a study conducted by Hobo et al, the concentrations of these drugs and DHT were measured in the hair of 1087 male patients with MPHL. The results revealed that finasteride and dutasteride reduced scalp DHT levels by approximately 64% and 92%, respectively.[22] Their main side effects include sexual dysfunction, gynecomastia, and psychological symptoms such as anxiety and depression.[23,24] Due to its potentially higher risk of side effects, dutasteride is generally considered a second-line treatment option.[25] Additionally, a meta-analysis by Nobari et al indicated that finasteride also exhibits efficacy in FPHL, particularly when administered at higher doses (5 mg/day) for at least one year.[26] Despite its effectiveness, finasteride has not been approved by the FDA for use in women due to its potential hormonal side effects. However, it may be considered as an off-label treatment for postmenopausal women in second-line therapy.

Oral 5αRIs are effective in the treatment of AGA, but may cause unwanted side effects, resulting in poor long-term tolerance in patients. Recent studies have explored local therapy as an alternative.[27] In the latest Phase III randomized controlled trial (RCT), topical finasteride spray (50–200μL/day) resulted in a significant increase in the change from baseline in the number of hairs in the target area at week 24 compared with placebo.[28] As compared with oral 5αRIs, topical finasteride causes few systemic side effects, such as sexual dysfunction. Most adverse effects of topical finasteride were confined to the application site, for example, scalp pruritus, burning sensation, irritation, and contact dermatitis.[29] Furthermore, combination therapy with topical minoxidil and finasteride may enhance therapeutic outcomes, offering a synergistic approach to AGA management.[30,31]

Androgen Receptor Antagonists

Androgen receptor antagonists (ARAs) play a significant role in the treatment of FPHL by competitively inhibiting the binding of DHT to AR, thereby effectively reducing sebum production and preventing follicular miniaturization.[32] Commonly used ARAs for managing AGA include spironolactone, flutamide, bicalutamide, and cyproterone acetate, among others.

Spironolactone, a potent ARA with mild 5α-reductase inhibitory activity, has emerged as the preferred off-label antiandrogen for the treatment of FPHL. Clinical studies have demonstrated that spironolactone can halt disease progression in over 90% of FPHL cases.[33] Common side effects associated with oral spironolactone include menstrual irregularities, dizziness or headaches, facial hirsutism, skin rashes, and hyperkalemia.[34] Furthermore, combination therapy with oral spironolactone and topical minoxidil has been shown to be both effective and well-tolerated in FPHL patients.[35] Topical formulations of spironolactone offer a safer alternative to oral administration and are suitable for both male and female patients. This route of administration shows promise as a viable option for individuals who exhibit suboptimal responses to minoxidil.[34]

Flutamide, as a selective ARA, has shown some efficacy in the treatment of AGA, but it is not widely used due to its potential liver toxicity. In contrast, bicalutamide, as a non-steroidal selective ARA, has shown higher affinity and better safety than flutamide. Jha et al divided 120 FPHL patients into a spironolactone group (100mg/day) and a bicalutamide group (50mg/day). The study showed that compared with the spironolactone group, the bicalutamide group showed more obvious improvement in treatment effect ($p=0.139$).[36] Common adverse reactions of bicalutamide include mild and transient elevated liver enzyme levels, temporary amenorrhea, endometrial hyperplasia, and migraine.[37] On the whole, bicalutamide not only has better efficacy in the treatment of FPHL, but also has higher safety, which may be a better treatment option than spironolactone.[36]

Cyproterone acetate is a synthetic steroid that has antiandrogenic and anti-gonadotropic effects and is a competitive antagonist of the nuclear androgen receptor (NR3C4).[38] A 12-month controlled trial comparing 2% minoxidil with cyproterone acetate for the treatment of FPHL found that minoxidil was more effective in patients with a lower body mass index (BMI) and no signs of hyperandrogenism, whereas cyproterone acetate was more effective in those with a higher BMI and hyperandrogenism.[39] Common adverse effects include weight gain, menstrual disturbances, and breast pain. Women of childbearing age need to use the drug for contraception.[40]

Anti-Inflammatory Drugs

Antifungal Drugs

Ketoconazole (KCZ), as an imidazole antifungal drug, has been widely used in the treatment of seborrheic dermatitis. In recent years, studies have found that 2% concentration of KCZ shampoo can improve hair density in AGA and the size and proportion of HFs during growth.[41] KCZ is thought to play an anti-inflammatory role by inhibiting the activity of 5-lipid oxidase and reducing the production of inflammatory mediators. Secondly, it can inhibit the steroid-producing pathway and reduce testosterone synthesis, thereby reducing the accumulation of DHT in the scalp, which has a synergistic effect with finasteride.[42] Animal experiments showed that the hair regeneration rate of the KCZ-treated group was significantly higher than that of the control group, and the ratio of bare skin area was significantly reduced. In clinical studies, an increase in hair diameter from baseline was generally observed in patients using KCZ.[41] In addition, KCZ may be more effective in AGA patients with seborrheic dermatitis due to its significant antifungal properties. Although there is limited evidence of increased hair shaft diameter and hair regeneration in human subjects following topical KCZ treatment, and even some studies failed to observe significant changes, without significant side effects, topical KCZ holds promise as a low-risk adjunct or alternative therapy for the treatment of AGA. Large-scale RCTs are also needed to further validate the efficacy of KCZ as monotherapy and adjuvant therapy for AGA.[43]

Isotretinoin

Isotretinoin, A synthetic retinoid analogue, has been widely used in the treatment of a variety of skin diseases, including acne vulgaris, psoriasis, and basal cell carcinoma.[44] Its mechanism of action is mainly through binding with retinoic acid receptors in the nucleus, thereby regulating a variety of cell activities, such as cell cycle progression, keratinocyte differentiation, apoptosis, and regulating the expression of interleukin-2 (IL-2), interferon γ (IFN-γ) and other cytokines, thus affecting the function of T cells and B lymphocytes.[45] Isotretinoin exerts anti-inflammatory effects by negatively regulating toll-like receptors 2 and 4 (TLR-2 and TLR-4) in keratinocytes, sebum cells, monocytes, and immune cells, and inhibits sebum secretion by significantly reducing the size and activity of sebum glands (up to 90%).[46]

Although studies have suggested that isotretinoin may be associated with hair loss, clinical observations suggest that only a small number of patients report hair loss as an adverse effect, and that the occurrence of hair loss is associated with age, higher cumulative doses, and longer duration of treatment.[47,48] Notably, in recent years, isotretinoin has been considered as a potential treatment option for frontal fibrotic alopecia (FFA) due to its significant anti-inflammatory and sebum-inhibiting effects.[44]

Based on its mechanism of action, we believe that in the treatment of AGA, especially in AGA patients with seborrheic dermatitis, the combination of low-dose isotretinoin therapy may have potential benefits, which can reduce the inflammatory response of balding scalp in AGA patients to a certain extent, reduce sebum secretion, and improve the scalp microenvironment, thus providing an auxiliary effect for the treatment of AGA.

Vasodilators, Energy Metabolism-Related Drugs and Nutritional Supplements

Minoxidil

Minoxidil, a potent vasodilatory agent, exerts its therapeutic effects primarily through the activation of ATP-sensitive potassium channels on vascular smooth muscle cells, thereby inducing vasodilation. Concurrently, it upregulates the expression of VEGF, which stimulates angiogenesis and subsequently enhances blood perfusion and nutrient delivery to HFs, creating a favorable microenvironment for hair growth.[24,49,50] Furthermore, minoxidil demonstrates significant anti-inflammatory properties by downregulating the expression of pro-inflammatory cytokines, including IL-2 and

prostacyclin, thereby mitigating the inflammatory cascade associated with AGA. Of particular interest is its ability to modulate the Wnt/β-catenin signaling pathway within DPCs, which not only prolongs the anagen phase of the hair cycle but also facilitates the transformation of vellus hairs into terminal hairs.[51]

Extensive clinical investigations have substantiated the remarkable efficacy of topical minoxidil in promoting hair regrowth. A 12-month longitudinal study involving 904 male patients with AGA demonstrated that 62% of participants exhibited significant improvement in scalp coverage following twice-daily application of 5% minoxidil solution, while 84.3% of the cohort reported varying degrees of new hair growth.[52] Common adverse effects include hypertrichosis, scalp erythema, pruritus, irritant reactions, contact dermatitis, and application site acne and cysts, though these typically manifest as mild, self-limiting conditions with low incidence rates.[53]

Topical minoxidil demonstrates significant efficacy in hair regrowth, with over 50% of patients showing improvement within six months, establishing it as a primary treatment for alopecia. However, its ability to completely halt hair loss progression remains limited. In recent years, the scientific community has shifted its focus toward investigating the feasibility of systemic administration routes. A comprehensive systematic review and meta-analysis conducted by Sobral et al, encompassing four clinical trials with a total cohort of 227 participants, revealed comparable therapeutic outcomes between oral and topical formulations, with no statistically significant differences in adverse event profiles.[54] The oral route, while associated with potential systemic effects such as hypotension, fluid retention, hypertrichosis, and hypersensitivity reactions, has shown favorable tolerability at lower doses (0.25–5mg). In summary, oral minoxidil can be used as an alternative for patients with intolerance or poor compliance to topical preparations, but more large-scale studies are needed to further verify it.[55]

In addition, minoxidil may cause temporary hair loss ("shedding period") in the early stage of treatment, which is common in clinical practice and often leads to anxiety or even discontinuation of treatment. The study showed that this temporary alopecia usually appeared within the first 12 weeks of treatment and lasted longer in the 2% minoxidil group than in the 5% group. Notably, after 20 weeks of treatment, hair loss was significantly lower than baseline in both groups, confirming the ability of minoxidil to prolong anagen, ultimately reducing hair loss and promoting regrowth.[56] Attempts were made to alleviate the shedding period by combining low-dose oral minoxidil with topical minoxidil, but the study by Nohria et al found that this overlapping treatment regimen did not significantly reduce the occurrence of temporary alopecia.[57] Therefore, clinicians should inform patients of this possible temporary side effect in advance to enhance treatment compliance and emphasize that long-term use can achieve the best results.

Botulinum Toxin

Botulinum toxin type A (BoNT-A) is a neurotoxin produced by Clostridium botulinum. Its mechanism of action is to inhibit the release of neurotransmitters, cause dose-dependent muscle paralysis, and induce muscle relaxation, thereby reducing the pressure on the peripheral vasculature and increasing local blood flow, thereby improving the blood supply and oxygenation of HFs. At the same time, it can inhibit the production of pro-inflammatory cytokines to reduce inflammation, further relieve vascular pressure, and enhance blood circulation.[58] Notably, BoNT-A has been found to down-regulate the expression of TGF-β1, which is a key regulator mediating androgen-dependent perifollicular fibrosis.[59–61]

Zhang et al, 's study results showed that among the 24 patients who received 50 U BoNT treatment, after 6 months of treatment, 11 patients showed significant hair regeneration (>10% from baseline), 8 patients showed slight improvement, 5 patients showed no change, and no patients had adverse reactions.[62] A randomized open-label trial conducted by Zhou et al in 63 AGA patients compared the effects of BoNT-A alone with BoNT-A in combination with finasteride, confirming that BoNT-A is a safe and effective treatment option for AGA and is more effective when combined with finasteride.[63] Overall, BoNT-A showed positive therapeutic effects in promoting hair growth and improving AGA, and could serve as a potential treatment option for patients with different types of hair loss.[64]

Melatonin

As a substance with significant antioxidant and DNA repair functions, melatonin can reduce HF damage by improving mitochondrial dysfunction.[2,65] A controlled clinical study conducted by Fischer's group confirmed the favorable efficacy of topical melatonin formulations for FPHL: AGA patients in the experimental group showed a significant increase in

growth phase hair in the occipital region (+8.7%), compared with only 3.9% in the control group.[66] Based on the existing research evidence, melatonin has shown potential application value in delaying hair aging and treating early AGA, providing a new treatment option for male and female patients with alopecia.

Nutritional Supplements

Nutritional supplements such as vitamins and trace elements may play an indirect role in the adjuvant treatment of AGA by improving the microenvironment of HFs, alleviating oxidative stress, and supporting the hair growth cycle. For example, vitamin D may regulate the HF cycle, while B vitamins such as folic acid and biotin, which act as catalysts in the process of nucleic acid synthesis and amino acid metabolism, may participate in the pathogenesis of AGA by regulating DPC proliferation.[67,68] Elements such as iron, zinc, copper, and selenium play key roles in immune regulation, inflammation control, and antioxidant defense.[69] Most clinical data support the association between the deficiency of these vitamins and trace elements and AGA.[70–72] Although clinical studies have shown that these nutritional supplements are helpful in correcting AGA in the deficient state, their efficacy alone is limited, and they usually need to be used in combination with mainstream treatments (such as minoxidil and finasteride).[73] In the future, more well-designed studies with large samples are needed to clarify the best intervention timing, dosage, and combination strategy of various nutrients in the prevention and treatment of AGA.

Antifibrotic Drugs

In the current clinical treatment of AGA, there is a lack of drugs specifically targeting the fibrosis process, and most treatment options mainly work through indirect pathways. Taking BoNT-A as an example, it can effectively relieve perivascular pressure and promote local blood circulation by inducing scalp muscle relaxation, thereby delaying the progression of fibrosis. In the field of anti-fibrosis drug research and development, pirfenidone, as a TGF-β inhibitor, has been approved by the European Union EMA (2011) and the United States FDA (2014) for the treatment of idiopathic pulmonary fibrosis.[74] Its mechanism involves the regulation of TGF-β1/TAK1/MKK3/p38 MAPK signaling cascade, which inhibits pro-inflammatory cytokines and fibrosis factors, and then significantly inhibits the proliferation and collagen synthesis of fibroblasts.[75] Although the drug is currently mainly used in pulmonary fibrosis, its potential value in the treatment of AGA deserves further exploration.

Other Drugs

Prostaglandins

The growth of hair is significantly regulated by prostaglandin (PG). The study found that in the hair loss area of AGA patients, the expression levels of prostaglandin E2 (PGE2) and prostaglandin F2α (PGF2α) were significantly reduced, while the level of prostaglandin D2 (PGD2) was significantly increased.[76,77] Specifically, PGD2 negatively affects HF growth by inhibiting hair growth through multiple mechanisms, including promoting AR expression, activating AKT signaling, and inhibiting Wnt signaling. In contrast, PGE2 and PGF2α promote the transition of HFs from resting to growth, thereby stimulating hair growth.[78] These findings reveal the complex role of prostaglandins in the regulation of hair growth and provide a theoretical basis for the development of new hair loss treatment strategies.

Prostaglandin analogues, such as bimatoprost (PGE2 analogues) and latanoprost (PGF2α analogues), have shown promising applications in the treatment of AGA. Bimatoprost was approved by the FDA in 2008 for the treatment of low eyelashes due to its significant hair growth-promoting effect.[79]

Studies have shown that bimatoprost can promote the synthesis of hair in scalp HFs and effectively stimulate fur regeneration in mice in animal experiments.[79] Subedi's team further found that 5% of bimatoprost applied topically in AGA mouse models was more effective than minoxidil at the same concentration, with a lower incidence of adverse reactions.[80] In clinical studies, prostaglandin analogues have also shown significant therapeutic effects. An RCT in men with mild AGA showed that after 24 weeks of treatment with 0.1% latanoprost, both terminal and vellus hair density in the treated area increased significantly from baseline values and from placebo groups.[81]

Cetirizine is a second-generation histamine H1 receptor antagonist, but it also inhibits the release of PGD2 and stimulates the release of PGE2.[82] In a triple-blind randomized clinical trial conducted by Alavi et al, 60 patients with

FPHL were randomly assigned to receive 1% cetirizine local treatment or 2% minoxidil local treatment. After 6 months of treatment, hair diameter and density improved in both groups, but the improvement was more significant in the minoxidil group. Although less effective than minoxidil, topical cetirizine treatment can still bring good results in patients with FPHL.[83] Studies by Mostafa et al showed that cetirizine was equally effective against MPHL, with no adverse effects reported.[82]

Overall, prostaglandins have shown superior efficacy to placebos in the treatment of hair loss and have a high safety profile, making them a topical treatment option for AGA, especially for patients who have not responded well to other treatments. Nevertheless, determining the optimal dose of prostaglandins for AGA treatment still requires further research.

Caffeine

As the most widely used central nervous stimulant in the world, caffeine has shown a unique mechanism of action in the field of hair biology. Studies have shown that caffeine, as a phosphodiesterase inhibitor, can interact with the adenosine pathway to increase intracellular cyclic adenosine monophosphate (cAMP) levels, thereby up-regulating cell signaling pathways that promote cell proliferation and metabolic activity in HF. At the same time, caffeine has antioxidant properties that prevent degeneration processes in cells.[84] In addition, some studies have found that caffeine can not only up-regulate the expression level of insulin-like growth factor 1 (IGF-1), but also inhibit the expression of TGF-β1 mediated by DHT, which provides a theoretical basis for its application in the treatment of hair loss.[85,86]

In an in vitro study, Fischer's team conducted an in-depth analysis of scalp samples from AGA patients using an organ culture model and found that 5μg/mL testosterone significantly inhibited HF growth, while 0.001–0.005% caffeine effectively reversed this inhibition.[87] Further studies have found that caffeine has excellent transdermal absorption properties, can penetrate deep into the HF in a few minutes, and can maintain a residence time of more than 48h after repeated cleaning, which provides a pharmacokinetic basis for its local application.[88]

In clinical studies, a multicenter non-inferior study (n=210) conducted by Dhurat et al compared the efficacy of caffeine topical solution with 5% minoxidil solution for MPHL. The results showed that the two treatment regimens had a comparable clinical effect in improving the proportion of HFs in the growing phase (p=0.574), suggesting that topical preparations of caffeine may be a potential alternative to minoxidil.[89] These findings provide strong evidence-based medical evidence for the use of caffeine in the field of hair loss treatment.

Adenosine

Adenosine is a purine nucleoside produced by dephosphorylation of adenosine monophosphate (AMP), which plays a key role in tissue protection and repair.[90] Its mechanism of action is mainly through activating the adenosine receptor signaling pathway, increasing the level of intracellular cAMP, and then promoting the cAMP-mediated mitochondrial energy metabolism. In addition, adenosine activates the Wnt/β-catenin signaling pathway by regulating the activity of glycogen synthetase kinase 3β (Gsk3β) in human DPC.[91] Together, these findings reveal the multiple mechanisms of action of adenosine in regulating the biological processes of HFs.

Several studies have shown that adenosine has a significant effect in promoting hair growth. Kim et al found through in vitro culture of human HFs that adenosine not only extends the growth period of hair, but also increases the density and thickness of hair and reduces the ratio of fine hair to terminal hair.[90] In addition, some researchers have found that adenosine can effectively promote hair growth and increase hair density in the growth phase of Japanese AGA patients.[92] In addition, when comparing the efficacy of topical 5% minoxidil and 0.75% adenosine solution in the treatment of AGA, adenosine was not found to be statistically significantly better than minoxidil. However, patients are more satisfied with adenosine, mainly because it prevents hair loss more quickly and promotes new growth.[93] Still, these findings need to be validated and explored in depth with larger sample sizes or further studies with different drug dosages.

JAK Inhibitors

JAK inhibitors can inhibit the production of inflammation-related cytokines by targeting the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway. Therefore, they have shown remarkable therapeutic effects in the treatment of alopecia areata (AA) and scarring alopecia.[94] At present, scholars are also exploring whether JAK inhibitors can be used for the treatment of AGA. Meephansan et al found that topical application of tofacitinib (a kind

of JAK inhibitor) promoted hair growth more than minoxidil in C57BL/6 mice ($P < 0.001$), possibly by increasing VEGF levels and reducing inflammation, suggesting that tofacitinib may be a potential treatment option for AGA.[95] However, Yale et al reported four cases of AGA-like alopecia after regrowth of hair in patients with AA treated with JAK inhibitors.[96] Fiore et al further observed 14 patients with AA and found that although JAK inhibitors improved the symptoms of AA, there was no change in the alopecia grade of AGA, suggesting that JAK inhibitors may have limited efficacy in AGA.[97] In conclusion, the role of JAK inhibitors in the treatment of AGA still needs to be verified by more studies.

Combination Therapies

Compared with single therapy, combination therapy has shown more significant therapeutic advantages in the clinical intervention of AGA, so its clinical application is increasingly widespread. Chen et al used a network meta-analysis to confirm that combination strategies, including the combination of local and systemic agents and the synergy of medical and adjuvant therapy, were the most effective of all interventions. In terms of mechanism of action, combination therapy can significantly improve the therapeutic effect through multi-target synergy, while avoiding the increase in the incidence of adverse reactions.[98]

The meta-analysis of 5 RCTs by Chen et al showed that finasteride combined with minoxidil was more effective than a single drug and had similar safety.[99] Hamza et al divided 60 AGA patients into three groups: 5% minoxidil group, 1% spironolactone group, and combination treatment group. The results showed that 90% of patients in the minoxidil group improved, 80% of patients in the spironolactone group responded, and all patients (100%) in the combination group had a clinical response, confirming the synergistic effect of the combination drugs.[100] Bazargan et al further compared the efficacy of different combination regimens for FPHL. In this study, 60 female AGA patients were treated for 16 weeks, and it was found that minoxidil combined with spironolactone was better than minoxidil combined with finasteride in terms of doctors' satisfaction, hair density, and hair loss improvement, suggesting that spironolactone may be more suitable for female patients.[101]

Hassan et al compared vitamin D therapy alone with vitamin D plus minoxidil and showed that the combination group was superior to the monotherapy group in both clinical assessments and dermoscopic evaluation.[102] In addition, other combined treatment strategies, such as drugs (minoxidil/finasteride, etc.) combined with low-intensity laser therapy (LLLT), microneedles, platelet-rich plasma (PRP), or hair transplantation surgery, have shown more significant advantages than single treatment.

Conclusion

The pathogenesis of AGA is complex, involving multiple physiological and pathological processes. This review of different classes of drugs reveals the diversity and pertinence of current treatment strategies. Conventionally approved AGA therapies (topical minoxidil and oral finasteride) have limited efficacy and individual variation. In recent years, studies on oral minoxidil and topical finasteride have gradually increased and shown certain efficacy. In particular, a novel formulation of topical finasteride has passed phase III clinical trials and is on the market, providing patients with a more convenient and potentially less side-effect treatment option. In addition, other drugs such as spironolactone, adenosine, caffeine, and prostaglandins have also been proven to be effective, further enriching the treatment options. Adjunctive therapies such as anti-inflammatory drugs, melatonin, and nutritional supplements can improve the microenvironment of HFs and delay the process of hair loss through multi-target effects. In terms of local treatment, emerging therapies such as botulinum toxin type A injection and PRP have also shown potential, especially when combined with conventional drugs, which may achieve better efficacy.

However, there are still some limitations of current treatment regimens, for example, the safety of long-term use, patient compliance, and durability of efficacy have not been fully resolved. Future research directions should focus on the development of new drugs, optimization of combination treatment strategies, and exploration of precision treatment models based on individualized medicine, to achieve the goal of more efficient and safer AGA treatment.

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Disclosure

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References

1. Li H, Cai H, Li P, Zeng Y, Zhang Y. Assessing causality between androgenetic alopecia with depression: a bidirectional mendelian randomization study. *Clin Cosmet Invest Dermatol*. 2025;18:445–451. doi:10.2147/CCID.S501182
2. ru DT, Jie LY, yu JS, et al. Progress on mitochondria and hair follicle development in androgenetic alopecia: relationships and therapeutic perspectives. *Stem Cell Res Ther*. 2025;16:44. doi:10.1186/s13287-025-04182-z
3. Corrêa AC, Machado CJ, Carneiro SCS. Split-scalp pilot study to evaluate effectiveness of minoxidil 0,5% MMP® versus topical minoxidil 5% in the treatment of female pattern hair loss. *Arch Dermatol Res*. 2024;316(6):313. doi:10.1007/s00403-024-03053-6
4. Rosenthal A, Conde G, Greco JF, Gharavi NM. Management of androgenic alopecia: a systematic review of the literature. *J Cosmet Laser Ther*. 2024;26(1–4):1–16. doi:10.1080/14764172.2024.2362126
5. Xiao Y, Zhang Y, Deng S, Yang X, Yao X. Immune and non-immune interactions in the pathogenesis of androgenetic alopecia. *Clin Rev Allergy Immunol*. 2025;68(1):22. doi:10.1007/s12016-025-09034-5
6. Zhang Y, Huang J, Fu D, et al. Transcriptome analysis reveals an inhibitory effect of dihydrotestosterone-treated 2D- and 3D-cultured dermal papilla cells on hair follicle growth. *Front Cell Dev Biol*. 2021;9:724310. doi:10.3389/fcell.2021.724310
7. Deng Z, Chen M, Liu F, et al. Androgen receptor-mediated paracrine signaling induces regression of blood vessels in the dermal papilla in androgenetic alopecia. *J Invest Dermatol*. 2022;142(8):2088–2099.e9. doi:10.1016/j.jid.2022.01.003
8. Zheng M, An S, Park IG, et al. Differential expression of CXCL12 in human and mouse hair: androgens induce CXCL12 in human dermal papilla and dermal sheath cup. *Int J Mol Sci*. 2024;26(1):95. doi:10.3390/ijms26010095
9. Zheng M, Kim MH, Park SG, Kim WS, Oh SH, Sung JH. CXCL12 neutralizing antibody promotes hair growth in androgenic alopecia and alopecia areata. *Int J Mol Sci*. 2024;25(3):1705. doi:10.3390/ijms25031705
10. Zhang X, Zhou D, Ma T, Liu Q. Vascular endothelial growth factor protects CD200-rich and CD34-positive hair follicle stem cells against androgen-induced apoptosis through the phosphoinositide 3-kinase/akt pathway in patients with androgenic alopecia. *Dermatol Surg*. 2020;46(3):358–368. doi:10.1097/DSS.0000000000002091
11. Cuevas-Diaz Duran R, Martinez-Ledesma E, Garcia-Garcia M, et al. The biology and genomics of human hair follicles: a focus on androgenetic alopecia. *Int J Mol Sci*. 2024;25(5):2542. doi:10.3390/ijms25052542
12. Torkamani N, Rufaut NW, Jones L, Sinclair R. Destruction of the arrector pili muscle and fat infiltration in androgenic alopecia. *Br J Dermatol*. 2014;170(6):1291–1298. doi:10.1111/bjd.12921
13. Bsy H, Exp H, Chu CW, et al. Microbiome in the hair follicle of androgenetic alopecia patients. *PLoS One*. 2019;14(5):e0216330. doi:10.1371/journal.pone.0216330
14. Grada A, Issa N. Boosting skin microcirculation for androgenetic alopecia: does it work? *J Invest Dermatol*. 2025;2025:S0022–202X
15. English RS. A hypothetical pathogenesis model for androgenic alopecia: clarifying the dihydrotestosterone paradox and rate-limiting recovery factors. *Med Hypotheses*. 2018;111:73–81. doi:10.1016/j.mehy.2017.12.027
16. Wróblewska-Kończalik K, Pawlaczyk M, Kolasiński J, et al. Non-cicatricial alopecia and its association with anthropometric measurements and nutritional laboratory markers. *Life*. 2024;14(5):609. doi:10.3390/life14050609
17. Naik PP. Utilities of botulinum toxins in dermatology and cosmetology. *Clin Cosmet Invest Dermatol*. 2021;14:1319–1330. doi:10.2147/CCID.S332247
18. Upadhyay DK, Sharma A, Sarma GS, Gupta GD, Rai VK. Mechanism of androgenic alopecia: addressing speculations through empirical evidences. *Dermatol Ther*. 2019;32(6):e13120. doi:10.1111/dth.13120
19. Li K, Liu F, Sun Y, et al. Association of fibrosis in the bulge portion with hair follicle miniaturization in androgenetic alopecia. *J Am Acad Dermatol*. 2022;86(1):213–215. doi:10.1016/j.jaad.2021.01.078
20. Keerti A, Madke B, Keerti A, Lopez MJC, Lirio FS. Topical finasteride: a comprehensive review of androgenetic alopecia management for men and women. *Cureus*. 2023;15(9):e44949. doi:10.7759/cureus.44949
21. Lama SBC, Pérez-González LA, Kosoglu MA, Dennis R, Ortega-Quijano D. Physical treatments and therapies for androgenetic alopecia. *J Clin Med*. 2024;13(15):4534. doi:10.3390/jcm13154534
22. Hobo Y, Nishikawa J, Taniguchi Asai N, et al. Evaluation of the therapeutic effects of Aga drugs by measuring finasteride, dutasteride, and dihydrotestosterone in hair. *Clin Chim Acta Int J Clin Chem*. 2023;547:117456. doi:10.1016/j.cca.2023.117456
23. Lauck KC, Limmer A, Harris P, Kivelevitch D. Sexual dysfunction with 5-alpha-reductase inhibitor therapy for androgenetic alopecia: a global propensity score matched retrospective cohort study. *J Am Acad Dermatol*. 2024;91(1):163–166. doi:10.1016/j.jaad.2024.03.019
24. Kaiser M, Abdin R, Gaumond SI, Issa NT, Jimenez JJ. Treatment of androgenetic alopecia: current guidance and unmet needs. *Clin Cosmet Invest Dermatol*. 2023;16:1387–1406. doi:10.2147/CCID.S385861
25. Courtney A, Triwongwarant D, Chim I, Eisman S, Sinclair R. Evaluating 5 alpha reductase inhibitors for the treatment of male androgenic alopecia. *Expert Opin Pharmacother*. 2023;24(18):1919–1922. doi:10.1080/14656566.2023.2280630
26. Nobari NN, Roohaninasab M, Sadeghzadeh-Bazargan A, et al. A systematic review of clinical trials using single or combination therapy of oral or topical finasteride for women in reproductive age and postmenopausal women with hormonal and nonhormonal androgenetic alopecia. *Adv Clin Exp Med*. 2023;32(7):813–823. doi:10.17219/acem/157990

27. Escamilla-Cruz M, Magaña M, Escandón-Perez S, Bello-Chavolla OY. Use of 5-alpha reductase inhibitors in dermatology: a narrative review. *Dermatol Ther*. 2023;13(8):1721–1731. doi:10.1007/s13555-023-00974-4
28. Zhou C, Yang B, Zeng H, et al. Efficacy and safety of topical finasteride spray solution in the treatment of Chinese men with androgenetic alopecia: a Phase III, multicenter, randomized, double-blind, placebo-controlled study. *Chin Med J*. 2025;2025:10–97
29. Gupta AK, Talukder M. Topical finasteride for male and female pattern hair loss: is it a safe and effective alternative? *J Cosmet Dermatol*. 2022;21(5):1841–1848. doi:10.1111/jocd.14895
30. Abeck F, Hansen I, Kött J, et al. Patient-reported outcomes of topical finasteride/minoxidil treatment for male androgenetic alopecia: a retrospective study using telemedical data. *J Cosmet Dermatol*. 2024;23(9):2956–2963. doi:10.1111/jocd.16360
31. Asad N, Naseer M, Ghafoor R. Efficacy of topical finasteride 0.25% with minoxidil 5% versus topical minoxidil 5% alone in treatment of male pattern androgenic alopecia. *J Drugs Dermatol*. 2024;23(11):1003–1008. doi:10.36849/JDD.7826
32. Luo X, Ni X, Zhi J, Jiang X, Bai R. Small molecule agents against alopecia: potential targets and related pathways. *Eur J Med Chem*. 2024;276:116666. doi:10.1016/j.ejmech.2024.116666
33. Rathnayake D, Sinclair R. Innovative use of spironolactone as an antiandrogen in the treatment of female pattern hair loss. *Dermatol Clin*. 2010;28(3):611–618. doi:10.1016/j.det.2010.03.011
34. Wang C, Du Y, Bi L, Lin X, Zhao M, Fan W. The efficacy and safety of oral and topical spironolactone in androgenetic alopecia treatment: a systematic review. *Clin Cosmet Invest Dermatol*. 2023;16:603–612. doi:10.2147/CCID.S398950
35. James JF, Jamerson TA, Aguh C. Efficacy and safety profile of oral spironolactone use for androgenic alopecia: a systematic review. *J Am Acad Dermatol*. 2022;86(2):425–429. doi:10.1016/j.jaad.2021.07.048
36. Jha AK, Zeeshan MD, Singh A, Singh AK. Efficacy and safety of spironolactone versus bicalutamide in female pattern hair loss: a retrospective comparative study. *Australas J Dermatol*. 2024;65(5):437–443. doi:10.1111/ajd.14306
37. Fernandez-Nieto D, Saceda-Corralo D, Jimenez-Cauhe J, et al. Bicalutamide: a potential new oral antiandrogenic drug for female pattern hair loss. *J Am Acad Dermatol*. 2020;83(5):e355–e356. doi:10.1016/j.jaad.2020.04.054
38. Müller Ramos P, Melo DF, Radwanski H, de Almeida RFC, Miot HA. Female-pattern hair loss: therapeutic update. *An Bras Dermatol*. 2023;98(4):506–519. doi:10.1016/j.abd.2022.09.006
39. Vexiau P, Chaspoux C, Boudou P, et al. Effects of minoxidil 2% vs. cyproterone acetate treatment on female androgenetic alopecia: a controlled, 12-month randomized trial. *Br J Dermatol*. 2002;146(6):992–999. doi:10.1046/j.1365-2133.2002.04798.x
40. Levy LL, Emer JJ. Female pattern alopecia: current perspectives. *Int J Women's Health*. 2013;5:541–556.
41. Fields JR, Vonu PM, Monir RL, Schoch JJ. Topical ketoconazole for the treatment of androgenetic alopecia: a systematic review. *Dermatol Ther*. 2020;33(1):e13202. doi:10.1111/dth.13202
42. Pozo-Pérez L, Tornero-Esteban P, López-Bran E. Clinical and preclinical approach in Aga treatment: a review of current and new therapies in the regenerative field. *Stem Cell Res Ther*. 2024;15(1):260.
43. Manabe M, Tsuboi R, Itami S, et al. Guidelines for the diagnosis and treatment of male-pattern and female-pattern hair loss, 2017 version. *J Dermatol*. 2018;45(9):1031–1043. doi:10.1111/1346-8138.14470
44. Shahpar A, Nezhad NZ, Sahaf AS, Ahramiyanpour N. A review of isotretinoin in the treatment of frontal fibrosing alopecia. *J Cosmet Dermatol*. 2024;23(6):1956–1963. doi:10.1111/jocd.16245
45. Chu S, Michelle L, Ekelem C, Sung CT, Rojek N, Mesinkovska NA. Oral isotretinoin for the treatment of dermatologic conditions other than acne: a systematic review and discussion of future directions. *Arch Dermatol Res*. 2021;313(6):391–430. doi:10.1007/s00403-020-02152-4
46. Bagatin E, Costa CS, da RMAD, et al. Consensus on the use of oral isotretinoin in dermatology - brazilian society of dermatology. *An Bras Dermatol*. 2020;95 Suppl 1(Suppl 1):19–38. doi:10.1016/j.abd.2020.09.001
47. Tran PT, Evron E, Goh C. Characteristics of patients with hair loss after isotretinoin treatment: a retrospective review study. *Int J Trichol*. 2022;14(4):125–127. doi:10.4103/ijt.ijt_80_20
48. Aksac SE, Bilgili SG, Yavuz GO, Yavuz IH, Aksac M, Karadag AS. Evaluation of biophysical skin parameters and hair changes in patients with acne vulgaris treated with isotretinoin, and the effect of biotin use on these parameters. *Int J Dermatol*. 2021;60(8):980–985. doi:10.1111/ijd.15485
49. Zeltzer AA, Keren A, Paus R, Gilhar A. Topical minoxidil rejuvenates hair follicles from men with androgenetic alopecia in vivo. *Acta Dermato-Venereologica*. 2024;104:24213. doi:10.2340/actadv.v104.24213
50. Gupta AK, Talukder M, Venkataraman M, Bamimore MA. Minoxidil: a comprehensive review. *J DermatolTreat*. 2022;33(4):1896–1906. doi:10.1080/09546634.2021.1945527
51. Shen Y, Zhu Y, Zhang L, et al. New target for minoxidil in the treatment of androgenetic alopecia. *Drug Des Devel Ther*. 2023;17:2537–2547. doi:10.2147/DDDT.S427612
52. Nestor MS, Ablon G, Gade A, Han H, Fischer DL. Treatment options for androgenetic alopecia: efficacy, side effects, compliance, financial considerations, and ethics. *J Cosmet Dermatol*. 2021;20(12):3759–3781. doi:10.1111/jocd.14537
53. Li Y, Liu B, Wu W, Li J. Assessing the safety of topical minoxidil through disproportionality analysis of FAERS reports. *Expert Opin Drug Saf*. 2025;2025:1–8.
54. Sobral MVS, Moreira JL de ML, Rodrigues LK, et al. Efficacy and safety of oral minoxidil versus topical solution in androgenetic alopecia: a meta-analysis of randomized clinical trials. *Int J Dermatol*. 2025;64(3):479–84.
55. Gupta AK, Taylor D, Ravi SP, Wang T, Talukder M. A bibliometric analysis of alternative drug therapy options in the treatment of androgenetic alopecia. *J Cosmet Dermatol*. 2024;23(10):3287–3294. doi:10.1111/jocd.16427
56. Bi L, Kan H, Wang J, et al. Whether the transient hair shedding phase exist after minoxidil treatment and does it predict treatment efficacy? A retrospective study in androgenetic alopecia patients. *J Dermatol Treat*. 2025;36(1):2480739. doi:10.1080/09546634.2025.2480739
57. Nohria A, Desai D, Sikora M, Mandal S, Shapiro J, Lo Sicco K. Combating "dread shed": the impact of overlapping topical and oral minoxidil on temporary hair shedding during oral minoxidil initiation. *JAAD Int*. 2024;15:220–224. doi:10.1016/j.jdin.2024.03.005
58. Perez SM, AlSalman SA, Nguyen B, Tosti A. Botulinum toxin in the treatment of hair and scalp disorders: current evidence and clinical applications. *Toxins*. 2025;17(4):163. doi:10.3390/toxins17040163
59. Martina E, Diotallevi F, Radi G, Campanati A, Offidani A. Therapeutic use of botulinum neurotoxins in dermatology: systematic review. *Toxins*. 2021;13(2):120. doi:10.3390/toxins13020120

60. Shon U, Kim MH, Lee DY, Kim SH, Park BC. The effect of intradermal botulinum toxin on androgenetic alopecia and its possible mechanism. *J Am Acad Dermatol*. 2020;83(6):1838–1839. doi:10.1016/j.jaad.2020.04.082
61. English RS, Ruiz S. Use of botulinum toxin for androgenic alopecia: a systematic review. *Skin Appendage Disord*. 2022;8(2):93–100. doi:10.1159/000518574
62. Zhang L, Yu Q, Wang Y, Shi Y, Ma Y, Li X. A small dose of botulinum toxin a is effective for treating androgenetic alopecia in Chinese patients. *Dermatol Ther*. 2019;32(4):e12785.
63. Zhou Y, Yu S, Zhao J, Feng X, Zhang M, Zhao Z. Effectiveness and safety of botulinum toxin type a in the treatment of androgenetic alopecia. *Biomed Res Int*. 2020;2020:1501893. doi:10.1155/2020/1501893
64. Hussein RS, Dayel SB, Abahussein O. Botulinum toxin a for hair loss treatment: a systematic review of efficacy, safety, and future directions. *JPRAS Open*. 2023;38:296–304. doi:10.1016/j.jpra.2023.09.006
65. Xu D, Liu L, Zhao Y, et al. Melatonin protects mouse testes from palmitic acid-induced lipotoxicity by attenuating oxidative stress and DNA damage in a SIRT1-dependent manner. *J Pineal Res*. 2020;69(4):e12690. doi:10.1111/jpi.12690
66. Greco G, Di Lorenzo R, Ricci L, Di Serio T, Vardaro E, Laneri S. Clinical studies using topical melatonin. *Int J Mol Sci*. 2024;25(10):5167. doi:10.3390/ijms25105167
67. Martin-Biggers J, Barbosa Bueno de Campos ME. A randomized, placebo-controlled clinical study evaluating a dietary supplement for hair growth. *J Clin Aesthet Dermatol*. 2024;17(11):34–38.
68. Zubair Z, Kantamaneni K, Jalla K, et al. Prevalence of low serum vitamin D levels in patients presenting with androgenetic alopecia: a review. *Cureus*. 2021;13(12):e20431. doi:10.7759/cureus.20431
69. Wang R, Lin J, Liu Q, Wu W, Wu J, Liu X. Micronutrients and androgenetic alopecia: a systematic review. *Mol Nutr Food Res*. 2024;68(22):e2400652. doi:10.1002/mnfr.202400652
70. Öner Ü, Akdeniz N. Nonscarring scalp alopecia: which laboratory analysis should we perform on whom? *Turk J Med Sci*. 2022;52(1):188–194. doi:10.3906/sag-2106-28
71. Chen Y, Dong X, Wang Y, Li Y, Xiong L, Li L. Serum 25 hydroxyvitamin D in non-scarring alopecia: a systematic review and meta-analysis. *J Cosmet Dermatol*. 2024;23(4):1131–1140. doi:10.1111/jocd.16093
72. Chang HC, Chang YS. Association between serum zinc levels and androgenetic alopecia: a systematic review and meta-analysis. *J Cosmet Dermatol*. 2022;21(4):1774–1777. doi:10.1111/jocd.14564
73. Marotta JC, Patel G, Carvalho M, Blakeney S. Clinical efficacy of a topical compounded formulation in Male androgenetic alopecia: minoxidil 10%, finasteride 0.1%, biotin 0.2%, and caffeine citrate 0.05% hydroalcoholic solution. *Int J Pharm Compd*. 2020;24(1):69–76.
74. Giulianelli G, Cocconcelli E, Fiorentù G, Bernardinello N, Balestro E, Spagnolo P. Idiopathic pulmonary fibrosis, today and tomorrow: certainties and new therapeutic horizons. *Pulm Ther*. 2025;11:195–234. doi:10.1007/s41030-025-00296-0
75. Sung JS, Ko IG, Hwang L, et al. Pirfenidone alleviates against fine particulate matter-induced pulmonary fibrosis modulating via TGF-β1/TAK1/MKK3/p38 MAPK signaling pathway in rats. *Biomedicines*. 2025;13(4):989. doi:10.3390/biomedicines13040989
76. Shin DW. The physiological and pharmacological roles of prostaglandins in hair growth. *Korean J Physiol Pharmacol off J Korean Physiol Soc Korean Soc Pharmacol*. 2022;26(6):405–413. doi:10.4196/kjpp.2022.26.6.405
77. Chovarda E, Lazaridou E, Vakirlis E, Sotiriou E, Ioannides D. The role of prostaglandins in androgenetic alopecia. *Int J Dermatol*. 2021;60(6):730–735. doi:10.1111/ijd.15378
78. Ryu YC, Park J, Kim YR, et al. CXXC5 mediates DHT-induced androgenetic alopecia via PGD2. *Cells*. 2023;12(4):555. doi:10.3390/cells12040555
79. Khidhir KG, Woodward DF, Farjo NP, et al. The prostamide-related glaucoma therapy, bimatoprost, offers a novel approach for treating scalp alopecias. *FASEB J off Publ Fed Am Soc Exp Biol*. 2013;27(2):557–567. doi:10.1096/fj.12-218156
80. Subedi L, Pandey P, Shim JH, et al. Preparation of topical bimatoprost with enhanced skin infiltration and in vivo hair regrowth efficacy in androgenic alopecia. *Drug Deliv*. 2022;29(1):328–341. doi:10.1080/10717544.2022.2027046
81. Blume-Peytavi U, Lönnfors S, Hillmann K, Garcia Bartels N. A randomized double-blind placebo-controlled pilot study to assess the efficacy of a 24-week topical treatment by latanoprost 0.1% on hair growth and pigmentation in healthy volunteers with androgenetic alopecia. *J Am Acad Dermatol*. 2012;66(5):794–800. doi:10.1016/j.jaad.2011.05.026
82. Hossein Mostafa D, Samadi A, Niknam S, Nasrollahi SA, Firooz A, Guishard A. Efficacy of cetirizine 1% versus minoxidil 5% topical solution in the treatment of male alopecia: a randomized, single-blind controlled study. *J Pharm Pharm Sci*. 2021;24:191–199. doi:10.18433/jpps31456
83. Alavi SMK, Layegh P, Vahabi-Amlashi S, Sabeti V, Forouzanfar M, Darchini-Maragheh E. Therapeutic effects of topical cetirizine in the treatment of female pattern hair loss: a randomized controlled noninferiority trial. *Expert Rev Clin Pharmacol*. 2023;16(10):1009–1015. doi:10.1080/17512433.2023.2243813
84. Szendzielorz E, Spiewak R. Caffeine as an active ingredient in cosmetic preparations against hair loss: a systematic review of available clinical evidence. *Health Care*. 2025;13(4):395.
85. Szendzielorz E, Spiewak R. Caffeine as an active molecule in cosmetic products for hair loss: its mechanisms of action in the context of hair physiology and pathology. *Molecules*. 2025;30(1):167. doi:10.3390/molecules30010167
86. Völker JM, Koch N, Becker M, Klenk A. Caffeine and its pharmacological benefits in the management of androgenetic alopecia: a review. *Skin Pharmacol Physiol*. 2020;33(3):93–109. doi:10.1159/000508228
87. Fischer TW, Hipler UC, Elsner P. Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro. *Int J Dermatol*. 2007;46(1):27–35. doi:10.1111/j.1365-4632.2007.03119.x
88. Trauer S, Patzelt A, Otberg N, et al. Permeation of topically applied caffeine through human skin--a comparison of in vivo and in vitro data. *Br J Clin Pharmacol*. 2009;68(2):181–186. doi:10.1111/j.1365-2125.2009.03463.x
89. Dhurat R, Chitallia J, May TW, et al. An open-label randomized multicenter study assessing the noninferiority of a caffeine-based topical liquid 0.2% versus minoxidil 5% solution in Male androgenetic alopecia. *Skin Pharmacol Physiol*. 2017;30(6):298–305. doi:10.1159/000481141
90. Kim J, Young SJ, Choi YH, et al. Hair thickness growth effect of adenosine complex in Male-/female-patterned hair loss via inhibition of androgen receptor signaling. *Int J Mol Sci*. 2024;25(12):6534. doi:10.3390/ijms25126534
91. Kim J, Shin JY, Choi YH, Kang NG, Lee S. Anti-hair loss effect of adenosine is exerted by cAMP mediated wnt/β-catenin pathway stimulation via modulation of Gsk3β activity in cultured human dermal papilla cells. *Molecules*. 2022;27(7):2184. doi:10.3390/molecules27072184

92. Watanabe Y, Nagashima T, Hanzawa N, et al. Topical adenosine increases thick hair ratio in japanese men with androgenetic alopecia. *Int J Cosmet Sci*. 2015;37(6):579–587. doi:10.1111/ics.12235
93. Faghihi G, Iraji F, Rajaee Harandi M, Nilforoushzadeh MA, Askari G. Comparison of the efficacy of topical minoxidil 5% and adenosine 0.75% solutions on Male androgenetic alopecia and measuring patient satisfaction rate. *Acta Dermatovenerol Croat: ADC*. 2013;21(3):155–159.
94. Yan T, Wang T, Tang M, Liu N. Comparative efficacy and safety of JAK inhibitors in the treatment of moderate-to-severe alopecia areata: a systematic review and network meta-analysis. *Front Pharmacol*. 2024;15:1372810. doi:10.3389/fphar.2024.1372810
95. Meephansan J, Thummakriengkrai J, Ponnikorn S, Yingmema W, Deenonpoe R, Suchonwanit P. Efficacy of topical tofacitinib in promoting hair growth in non-scarring alopecia: possible mechanism via VEGF induction. *Arch Dermatol Res*. 2017;309(9):729–738. doi:10.1007/s00403-017-1777-5
96. Yale K, Pourang A, Plikus MV, Mesinkovska NA. At the crossroads of 2 alopecias: androgenetic alopecia pattern of hair regrowth in patients with alopecia areata treated with oral janus kinase inhibitors. *JAAD Case Rep*. 2020;6(5):444–446. doi:10.1016/j.jdcr.2020.02.026
97. Casale F, Yale K, Mesinkovska NA. Are janus kinase (JAK) inhibitors beneficial in the treatment of androgenic alopecia? *Int J Dermatol*. 2022;61(11):e457–e458. doi:10.1111/ijd.15946
98. Chen D, Yang X, Liu X, et al. Efficacy comparison of monotherapies and combination therapies for androgenetic alopecia: a Bayesian network meta-analysis. *Dermatol Ther*. 2022;35(3):e15262. doi:10.1111/dth.15262
99. Chen L, Zhang J, Wang L, Wang H, Chen B. The efficacy and safety of finasteride combined with topical minoxidil for androgenetic alopecia: a systematic review and meta-analysis. *Aesthetic Plast Surg*. 2020;44(3):962–970. doi:10.1007/s00266-020-01621-5
100. Abdel-Raouf H, Aly UF, Medhat W, Ahmed SS, Abdel-Aziz RTA. A novel topical combination of minoxidil and spironolactone for androgenetic alopecia: clinical, histopathological, and physicochemical study. *Dermatol Ther*. 2021;34(1):e14678. doi:10.1111/dth.14678
101. Sadeghzadeh Bazargan A, Tavana Z, Dehghani A, et al. The efficacy of the combination of topical minoxidil and oral spironolactone compared with the combination of topical minoxidil and oral finasteride in women with androgenic alopecia, female and male hair loss patterns: a blinded randomized clinical trial. *J Cosmet Dermatol*. 2024;23(2):543–551. doi:10.1111/jocd.15979
102. Hassan GFR, Sadoma MET, Elbatsh MM, Ibrahim ZA. Treatment with oral vitamin D alone, topical minoxidil, or combination of both in patients with female pattern hair loss: a comparative clinical and dermoscopic study. *J Cosmet Dermatol*. 2022;21(9):3917–3924. doi:10.1111/jocd.14743