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Research Article

# Modern approaches to the treatment of androgenetic alopecia and alopecia areata

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## Abstract

**Introduction**: Alopecia, whether as an independent pathological condition or as a manifestation of other diseases, is a pressing medical and social issue. Hair loss can lead to serious psychological problems and significantly reduce people's quality of life.

**Materials and Methods**: In preparing this article, we reviewed over 120 scientific papers on the PubMed, Scopus, and Web of Science platforms using the keywords "alopecia", "androgenetic alopecia", and "alopecia areata".

**Results and Discussion**: The review revealed that a wide variety of pharmacological, instrumental, and invasive treatments for both androgenetic alopecia and alopecia areata currently exist, targeting various components of its pathogenesis: minoxidil, 5-alpha reductase inhibitors, therapeutic antibodies, anti-inflammatory and immunosuppressive drugs, Janus kinase inhibitors, growth factor therapy, plasma therapy, microneedling, laser therapy, and surgical treatments. Furthermore, numerous scientific studies were identified aimed at developing new and improving existing therapeutic strategies, including gene therapy, stem cell therapy, high-tech nanoparticles, and many others.

**Conclusion**: The need to halt the progression of alopecia and achieve optimal hair restoration to improve patients' quality of life dictates the need for effective treatment approaches for various types of alopecia in modern medicine. Given that current therapeutic methods, despite their diversity, do not always achieve the expected effect, further in-depth research into the etiology, pathogenesis, clinical presentation, and diagnostic criteria of this dermatological disease is required to develop more effective treatment strategies.

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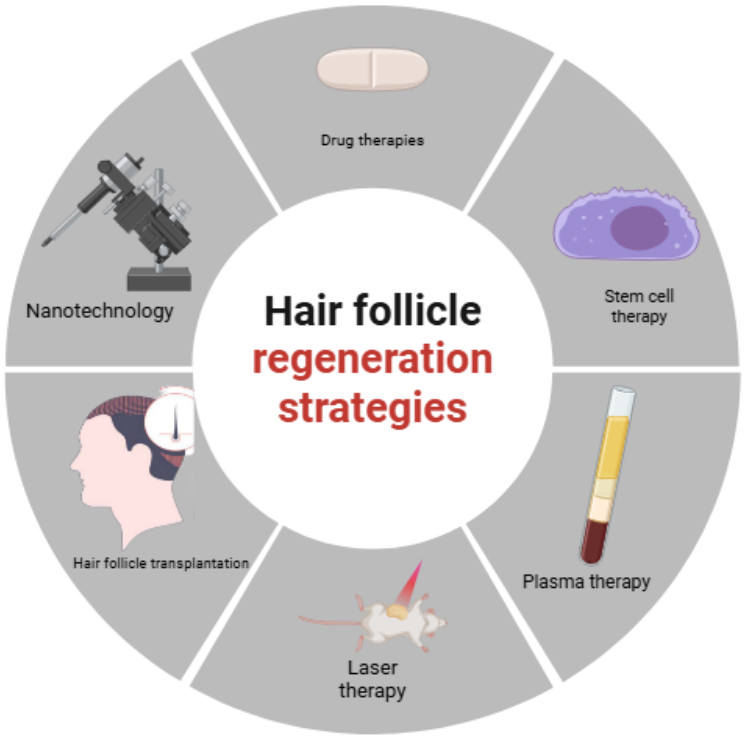
## Graphical Abstract




## Keywords

androgenetic alopecia; alopecia areata; treatment strategies

## Introduction

In recent decades, there has been a steady increase in the incidence of various hair loss manifestations caused by lifestyle changes, the impact of stress and poor diet, environmental pollution, and the increasing incidence of chronic diseases (Prie at al. 2016; Almohanna et al. 2019; Shi et al. 2023). Hair loss often causes psychological distress, decreased self-confidence, and difficulties in socialization, turning the issue of alopecia into a complex problem affecting not only health but also social aspects of life. Moreover, hair loss manifestations can be a symptom of more serious diseases or an undesirable effect of treatment (Mistry and Sibbald 2025). Despite significant advances in research into the causes of hair loss and the development of treatments, much remains unclear about the origins of the disease, its dynamics, and effective treatment methods. Thus, the importance of studying new treatment methods is dictated by the need to organize modern information on the factors of occurrence, pathogenesis and diagnosis, as well as the development of innovative, reliable and safe therapeutic approaches.

## Materials and Methods

In preparing this article, we reviewed 128 scientific papers on the treatment of alopecia. The review included the most relevant fundamental, clinical, preclinical, and review articles published between 2016 and 2025, as well as older, more seminal studies. The search was conducted using the keywords “alopecia”, “androgenetic alopecia”, and “alopecia areata”.

All materials used were obtained from the following databases: PubMed (https://pubmed.ncbi.nlm.nih.gov/); Scopus (https://www.scopus.com/); and Web of Science (https://www.webofknowledge.com).

# Results and Discussion

The two most common forms of alopecia are androgenetic alopecia (AGA) and alopecia areata (AA). The pathogenesis of AGA involves androgen-dependent involution of hair follicles. Although this mechanism is not fully understood, the greatest significance is attributed to the genetically determined hypersensitivity of hair follicles to dihydrotestosterone. Therefore, the most effective treatments for AGA are antiandrogen medications and agents that block the interaction of dihydrotestosterone with the hair follicle. AA is caused by autoimmune damage to hair follicles without scarring, so anti-inflammatory and immunosuppressive medications are most effective in treating these patients (figure 1). However, there are also more universal methods for correcting alopecia, aimed at strengthening and enlarging follicles, prolonging the hair growth phase, or promoting the formation of new follicles. These methods include minoxidil, laser therapy, plasma therapy and hair transplantation (Correia et al. 2023).

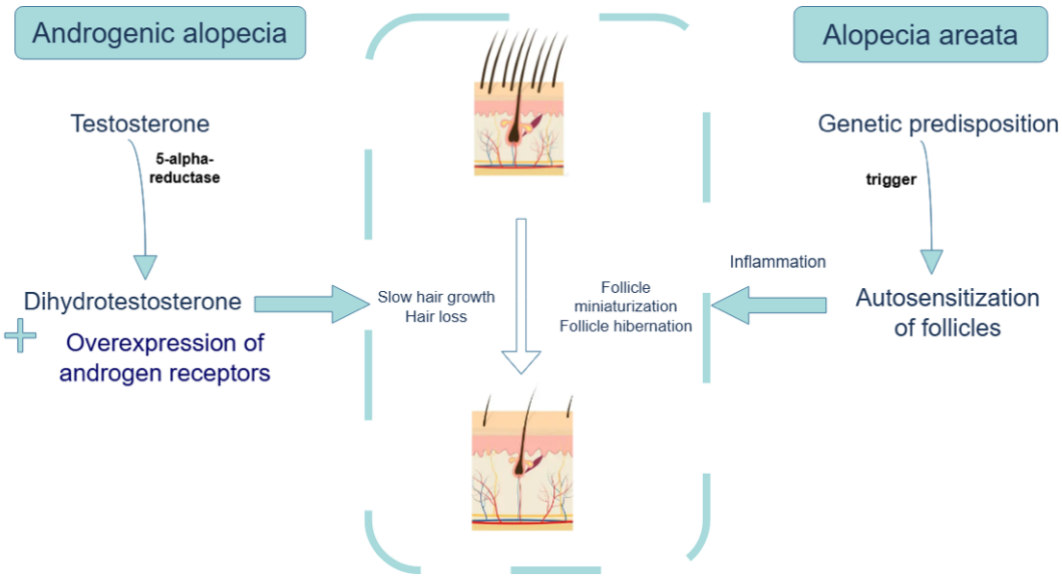



**Figure 1.** The main stages of the pathogenesis of androgenic and alopecia areata.

### Minoxidil

Minoxidil is currently the most popular drug for the treatment of alopecia. Minoxidil is a pyrimidine derivative (2,4-diamino-6-piperidinopyrimidine-3-oxide) and was originally developed as a systemic antihypertensive agent (Dargie et al. 1977). Minoxidil promotes peripheral vasodilation through the activation of ATP-dependent potassium channels. Early studies have shown a link between minoxidil use and the expression of various growth factors in the hair follicle area, such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and insulin-like growth factor (IGF-1), which promoted cell growth in the hair follicles and initiated the anagen phase (Lachgar et al. 1998). At the beginning of the 21$^{st}$ century, it was discovered that the effect of minoxidil was due not only to the nonspecific effect of increasing follicle blood flow but also to its specific effect on keratinocytes. Thus, the use of minoxidil at a concentration of 1 μmol in a hair papilla cell culture increased the expression of the protective anti-apoptotic proteins ERK by 351%, Akt – by 257%, and Bcl-2 – by 150% (Han et al. 2004). At the same time, the expression of the pro-apoptotic protein Bax decreased by 50%. Due to these hypertrichotic properties, 2% and 5% minoxidil solutions quickly became the most important and widely used topical therapy among dermatologists for AGA (Kanti et al. 2018). More recent studies have shown that the effect of topical minoxidil is also observed in AA, although to a lesser extent. The best results in hair restoration are observed in the early stages of hair loss, with the first noticeable improvements appearing after 4–6 months, and stabilization of hair growth occurring after approximately a year, provided minoxidil is used regularly (DeVillez et al. 1994; Pazoki-Toroudi et al. 2012; Kanti et al. 2015; Randolph and Tosti 2021).

Moreover, a 2018 study showed that oral minoxidil in combination with spironolactone helped reduce the severity of alopecia by 1.3 points on the Sinclair scale in women aged 18 to 80 years. However, this form of minoxidil administration is limited by more serious side effects, such as hypertrichosis and cardiovascular disorders (Sinclair 2018). In June 2024, a blinded,

placebo-controlled, randomized clinical trial at a clinic in Brazil showed that oral minoxidil 5 mg once daily for 24 weeks showed no benefit over topical minoxidil 5% twice daily in men with androgenetic alopecia (Penha et al. 2024).

Using minoxidil in combination with other treatments may also improve hair growth. For example, a study of combined unilateral subcutaneous botulinum toxin injections for the treatment of androgenetic alopecia showed that after 3 and 6 months of treatment, hair density increased in all patients compared to baseline. Furthermore, hair growth was found to be denser on the side of the scalp where botulinum toxin A was injected than on the opposite, control side. After completing the 6-month course, the combined use of botulinum toxin A with finasteride and minoxidil resulted in improvement in 77.5% of patients, with no serious side effects reported (Tian et al. 2022).

**5-alpha reductase inhibitors**

Another drug popular in the US and Europe for the treatment of AGA is finasteride. Its mechanism of action is through the inhibition of 5-alpha reductase type II, which blocks the conversion of testosterone to dihydrotestosterone, thus reducing androgen-mediated follicular miniaturization (Goren et al. 2019; Dhurat et al. 2020). Finasteride can be applied topically as a spray or gel, or taken orally as tablets. A 2021 randomized controlled clinical trial shows that topical finasteride produces a significant increase in hair count compared to placebo and is well tolerated. The mechanism of action is similar to oral finasteride, but systemic absorption of the drug is significantly reduced, resulting in less effect on serum dihydrotestosterone concentrations (Piraccini et al. 2021). Another multicenter, randomized, double-blind, placebo-controlled phase III study in China showed that topical finasteride spray promoted hair growth and demonstrated good safety and tolerability over a 24-week treatment course (Zhou et al. 2025). Also, daily oral administration of 1 mg of finasteride can significantly reduce the severity of AGA in men aged 20 to 60 years over 10 years (Rossi et al. 2011). It should be noted that, although topical finasteride is somewhat effective in men (Piraccini et al. 2021), similar therapy has no significant effect on female AGA (Rossi et al. 2020).

A drug related to finasteride for the treatment of alopecia areata is dutasteride, which inhibits 5-alpha reductase, but not only type II but also type I. This effect further dissociates the androgen-mediated mechanism of alopecia areata pathogenesis (Seo et al. 2024). Data from a 2022 meta-review suggests that, over a 24-week period, 0.5 mg of dutasteride per day has the best effect on hair regrowth compared to finasteride and minoxidil. (Gupta et al. 2022).

However, it should be noted that the use of 5-alpha-reductase inhibitors has serious side effects in the form of sexual dysfunction, changes in libido, erectile dysfunction, ejaculatory dysfunction and gynecomastia (Herz-Ruelas et al. 2020).

**Antiandrogen drugs**

Antiandrogen medications are also effective in the treatment of AGA. One such drug is flutamide, used for prostate cancer. Several studies have shown that daily intake of 250 mg of flutamide significantly reduces the severity of alopecia in women, even in cases of resistance to minoxidil and spironolactone (Carmina and Lobo 2003; Yazdabadi and Sinclair 2011). In addition to flutamide, antiandrogen drugs include cyproterone acetate, which blocks gonadotropin-releasing hormones and androgen receptors. Its hypertrichotic effect in women with AGA was identified as early as 1989 (Peereboom-Wynia et al. 1989). A later 12-month study showed that in women with evidence of hyperandrogenism, oral cyproterone was more effective than topical 2% minoxidil (Vexiau et al. 2002).

The topical antiandrogen drug clascoterone deserves special mention. Initially tested as an acne treatment, this drug was found to have significant hypertrichosis as a side effect, making it a potential topical treatment for AGA (Hebert et al. 2020).

**Therapeutic antibodies**

Therapeutic antibodies (TAs) represent a promising approach to treating AGA, offering an alternative to existing treatments such as minoxidil and finasteride. Due to their large molecular structure, TAs administered subcutaneously persist in the body for more than two weeks, allowing for monthly or even less frequent injections. However, developing TAs for the treatment of AGA is challenging, as they must specifically interact with androgens, interfering with the pathogenesis of AGA, and act in the extracellular space or on the surface of cells associated with hair follicles. Monoclonal antibodies to prolactin, interleukin-6, CXCL12, and DKK1 have already been developed and studied. All of these agents, through their receptors in the follicle or parafollicular space, potentiate the involution of the follicular-seborrheic complex and also increase the risk of conditions such as psoriasis and acne. Accordingly, antibody-

mediated inhibition of such agents may positively impact hair growth. It should be noted that most TAs intended for the treatment of AGA are in the early stages of clinical and preclinical trials, and further development of therapeutic monoclonal antibodies, as well as the validation and refinement of new targets, are required for the full implementation of this treatment option for AGA (Jin et al. 2024).

**Anti-inflammatory and immunosuppressive drugs**

Due to the predominantly autoimmune pathogenesis of AA, drugs capable of locally or systemically suppressing the inflammatory process are actively used for its treatment. Thus, since the beginning of the 21st century, topical corticosteroids have become the first-line drug for the treatment of AA, demonstrating the restoration of up to 70% of hair cover within 3 months (Das et al. 2010). In severe, total, and rapidly progressing variants of AA, systemic oral corticosteroids can be used at dosages of 0.5–1 mg/kg/day or in a wide variety of pulse therapy. However, this method is very limited by the pronounced side effects of glucocorticosteroids (Majid et al. 2009; Ait Ourhroui et al. 2010; Gupta et al. 2019). In this regard, methods for increasing the effectiveness of glucocorticosteroids in AA continue to be studied. Thus, a recent study shows that topical latanoprost potentiates the therapeutic effect of topical betamethasone in the treatment of GA. Therefore, latanoprost can be recommended as a safe and effective adjuvant therapy, enhancing the efficacy of existing treatment regimens without additional side effects (Ghassemi et al. 2022).

Anthralin is also a topical treatment for alopecia areata. Due to its immunosuppressive and anti-inflammatory effects (inhibition of tumor necrosis factors), this drug promotes hair follicle restoration in patients with alopecia. For example, in a study by Tang et al. (2004), topical application of 0.2% anthralin resulted in hair restoration in 64% of mice with a model of alopecia areata.

In addition to glucocorticosteroids, other oral medications with immunosuppressive and cytostatic effects can be used as systemic therapy for GA. These medications include azathioprine (1 mg/kg/d), cyclosporine (3-5 mg/kg/d), methotrexate (0.2-0.4 mg/kg/d), and sulfasalazine (500-3000 mg/d). The effectiveness of this therapy in various studies for different medications varies from 43 to 66%, and it is also associated with systemic side effects (Saoji et al. 2019; Husein-ElAhmed and Steinhoff 2022; Phan et al. 2019; Otberg 2011).

Another group of drugs that disrupt the immune pathogenesis of AA are contact sensitizers. These include dinitrochlorobenzene, diphenylcyclopropenone, and squaraic acid dibutyl ester. The pharmacological mechanism of action of these substances has not been fully determined, but their use significantly reduces lymphocytic infiltration of the hair follicle and perifollicular dermis in patients with AA. Contact sensitizers are applied topically with increasing dosage and prior sensitization (Malhotra and Madke 2023). In a 2019 article, diphenylcyclopropenone monotherapy resulted in complete hair regrowth in 62.5% of patients with AA (Ibrahim et al. 2019).

**Janus kinase inhibitors**

Another promising avenue for the treatment of AA is inhibition of the JAK-STAT pathway. The Janus kinase family, or JAK kinases in combination with the signal transducer and activator of transcription (STAT) family, have a significant impact on the development of innate and adaptive immunity. Disruptions in these systems lead to various congenital autoimmune diseases (Schwartz et al. 2016). In AA, in particular, the JAK-STAT pathway activates CD8+ T cells and NK cells, which are the main damaging agents in autoimmune damage to hair follicle cells (Xing et al. 2014). Thus, pharmacological inhibition of this pathway has a beneficial effect on hair growth in patients with AA (Phan and Sebaratnam 2019). The main drugs in this group are the oral forms of tofacitinib and baricitinib (Triyangkulsri and Suchonwanit 2018; Olamiju et al. 2019). A new drug in this group, currently in clinical trials, is ritlecitinib (Blair 2023). The increased selectivity of JAK kinase inhibitors significantly reduces the severity of their side effects (Cohen et al. 2017; King et al. 2024; Mesinkovska et al. 2024).

The efficacy of baricitinib has been repeatedly confirmed in placebo-controlled, randomized trials in which adult patients with significant hair loss (more than 50%) were treated with baricitinib for 36 weeks (Ko et al. 2023). Results from the study by Kwon et al. (2023) showed that 40.9% of patients receiving 4 mg daily and 21.2% of patients receiving 2 mg daily experienced less than 20% hair loss. The most common adverse events were upper respiratory tract infections, headache, nasopharyngitis, acne, urinary tract infections, increased creatine phosphokinase, and COVID-19. Long-term use of baricitinib has demonstrated continued hair regrowth in adults with severe alopecia areata and was not associated with additional adverse events.

Brepocitinib, another drug from the JAK kinase inhibitor class, reduces the expression of inflammatory biomarkers and decreases clinical disease severity when administered daily at 45 mg for 24 weeks, while maintaining a favorable safety profile (David et al. 2025). Multiple systemic studies have found no association between long-term use of JAK kinase inhibitors and an increased risk of death (Ingrassia et al. 2024). Other studies also support the promise of this treatment option (Gonzalez et al. 2025).

**Mesotherapy**

Mesotherapy is an intradermal technique that involves introducing small concentrations of active substances into specific areas of the affected scalp. A study by Melo et al. (2020) reported a case in which hair density significantly increased after 20 sessions using a mixture of 1 mL minoxidil 0.5%, 1 mL finasteride 0.05%, 2 mL biotin 5 mg/mL, and 2 mL D-panthenol 50 mg/mL. Mesotherapy with natural ingredients has been shown to be effective as an adjunct to minoxidil and finasteride therapy (Tian et al. 2022). Although this procedure is considered minimally invasive, potential side effects include burning, skin redness, headaches, subcutaneous necrosis, scalp abscesses, and swelling (Melo et al. 2022).

Local injections of 5-alpha reductase inhibitors should be highlighted as a separate mesotherapy option. Saceda-Corralo et al. (2022) demonstrated in their study that local injections of dutasteride can be effective in patients with AGA, although a positive response to this therapy was observed in only 15.9% of subjects. Later studies also noted a reduced effectiveness of mesotherapy with 0.5 mg dutasteride per day compared to the classical form of use in a similar dosage (Gupta et al. 2025). Nevertheless, the virtually complete absence of side effects characteristic of dutasteride makes this use of 5-alpha-reductase inhibitors quite promising.

**Growth factors**

To date, numerous factors influencing hair follicle growth are known, including the mechanisms that initiate this process and the regulators of transitions between growth stages. Several theories have been proposed to study the cyclical nature of hair growth, such as the epithelial theory, which attributes a key role to cells located in the follicular bulge region (Joulai Veijouye et al. 2017). Paracrine effects also have an impact. Epithelial cells of the inner root sheath produce fibroblast growth factors 1 and 22, transforming growth factor (TGFa), SHH signaling molecules, ß-catenin, and others (Nozdrin and Gorpinich 2007). Also noteworthy is the influence of VEGF, a marker of angiogenesis, on the hair cycle stages. It stimulates hair follicles by improving the supply of nutrients to hair follicles and increasing follicle diameter (Ozeki and Tabata 2003). Growth factors such as VEGF and IGF-1, when used as drugs, have significant potential for stimulating hair growth and treating alopecia. For example, Yano et al. (2001) found a clear correlation between perifollicular dermal vascularization, VEGF mRNA expression, and follicle proliferation in the anagen phase. Furthermore, their study demonstrated that the use of anti-VEGF antibodies significantly suppresses hair growth, while overexpression of the VEGF gene, conversely, stimulates it. In a subsequent study, 2 mcg recombinant human VEGF administered subcutaneously to mice in the form of a collagen gel demonstrated its effectiveness. As early as 10 days after injection, statistically significant increases in dermal vascularization, hair follicle area, and hair length were observed (Ozeki and Tabata 2002).

It has been known for over 25 years that VEGF receptors are found not only in endothelial cells, but also directly in hair follicles, sebaceous glands, hair papilla cells, and other mesenchymal cells (fibroblasts of the fibrous sheath and dermal fibroblasts), and increase the area of hair follicles (Gnann et al. 2013; Kostina et al. 2025), and IGF-1 regulates key processes of cellular activity during hair formation (Lachgar et al. 1996; Kozlowska et al. 1998b; Kozlowska et al. 1998a; Castro et al. 2012). Moreover, VEGFR-2 is the main receptor for VEGF and mediates most of its functional effects in both endothelial and non-endothelial cells (Terman et al. 1992; Millauer et al. 1993). Subsequently, Wu et al. (2014) revealed pronounced expression of VEGFR-2 in the cells of the outer hair sheath and hair papilla. Moreover, in their work, they showed that VEGF potentiates the proliferation and migration of stem cells of the outer hair sheath into the hair matrix area, while the use of anti-VEGFR-2 antibodies, on the contrary, disrupted this process.

Growth factors can be used in combination with conventional alopecia treatments. For example, the use of basic fibroblast growth factor (bFGF) and 5% minoxidil in the early stages of AGA in men provides better treatment outcomes and higher patient satisfaction compared to the use of 5% minoxidil alone. These results were obtained in a 2022 study, which, to evaluate the effectiveness of various approaches to treating androgenetic alopecia in men, randomly divided 80 patients with Hamilton grade II–IV alopecia into two groups of 40 people. The first group received standard treatment – 1 mL of topical minoxidil twice daily. The second group received combination treatment: 1 mL of topical minoxidil twice daily and 3,500 IU bFGF. Hair

condition was assessed using global photography before treatment, as well as after 3 and 6 months (Liu et al. 2022).

### Platelet-rich plasma

Another treatment for AGA registered in the Russian Federation is local injections of platelet-rich plasma (PRP) (Clinical Guidelines 2025). The procedure involves drawing up to 30 mL of blood from the patient, centrifuging it, separating it into fractions, and injecting 4-8 mL of the platelet-rich fraction into the target area. The resulting mixture, containing multiple growth factors (EGV, VEGF, EGF, IGF, TGF, etc.), potentiates proliferation and regeneration in the injection site (Dhillon et al. 2012), which promotes hair follicle restoration and activation of the anagen phase. A 2018 review article found that PRP had a significant therapeutic effect in 10 out of 12 studies on both male and female pattern alopecia (Cervantes et al. 2018). n a more recent article from 2022, researchers conclude that the use of PRP is a promising area of treatment for various types of alopecia, both as monotherapy and as part of a comprehensive treatment; it also notes that PRP has significantly fewer side effects than most other alopecia therapies (Paichitrojjana and Paichitrojjana 2022). In 2023, a meta-analysis was conducted based on seven articles. According to the available data, de Oliveira et al. (2023) found the following data: PRP-based methods were able to increase hair density and thickness in women with AGA. Zhang et al. (2023) also conducted a meta-analysis and found similar data on the effectiveness of PRP. Current studies, characterized by significant variability and potential bias towards publishing only successful results, suggest that PRP therapy may promote hair growth in androgenetic alopecia. However, more rigorous and high-quality randomized clinical trials are needed to reliably confirm this finding (Wu et al. 2023; Afzal et al. 2024; Kieling et al. 2024).

### Microneedling

Microneedling is a dermatological technique that involves creating multiple microscopic punctures in the skin using a special roller (Dhurat et al. 2013; Singh and Yadav 2016). These microdamages trigger a cascade of regenerative processes, including angiogenesis, platelet activation, and the release of growth factors, as well as stimulation of collagen and elastin synthesis. Furthermore, this treatment induces stem cell activation, stimulates wound healing, and increases the expression of growth-related genes, such as VEGF and components of the Wnt signaling pathway. The physical creation of microchannels also creates more favorable conditions for the action of topical AGA treatments (Jia et al. 2022a). Clinical studies have shown that microneedling in combination with minoxidil exhibits higher efficacy in the treatment of mild to moderate AGA compared to minoxidil alone (Kumar et al. 2018; English et al. 2022). Results from a subsequent meta-analysis suggest that combination therapy combining minoxidil and microneedling successfully promotes hair growth in individuals with AGA (Abdi et al. 2023). Several other studies also suggest the effectiveness of a combination of microneedling and minoxidil for the treatment of alopecia (Jia et al. 2022b; Ahmed et al. 2025).

A unique combination of mesotherapy and microneedling was demonstrated by Ding et al. (2024). They used microneedles as a promising method for transdermal administration of a hydrogel incorporating VEGF, minoxidil, and ritlecitinib in various combinations for the treatment of AGA. The use of these microneedles statistically significantly increased the efficacy of the studied drugs in mice compared to topical application.

### Low-level laser therapy

Low-level laser therapy is a physical treatment for alopecia that involves exposing the affected areas to light waves with wavelengths ranging from 650 to 900 nm (Suchonwanit et al. 2019; Darwin et al. 2018). This therapy may stimulate the transition of hair follicles to the anagen phase and prolong its duration (Gupta and Foley 2017). It can also stimulate regenerative processes and suppress inflammation in the perifollicular dermis (Dompe et al. 2020). The putative mechanism of action of laser therapy is photo-mediated release of intracellular nitric oxide, which in turn stimulates vasodilation, suppresses endothelial dysfunction in perifollicular vessels, and potentiates ATP synthesis and activation of various transcription factors (Avci et al. 2014; Shcheblykin et al. 2022). This effect stimulates regrowth mainly by increasing follicular trophism (Dompe et al. 2020). With long-term (more than a year) and regular use, laser therapy can show an efficacy of up to 80% in both male and female patients with AGA (Qiu et al. 2022). A subsequent meta-analysis confirmed the efficacy of laser therapy in patients with AGA (Perez et al. 2025). Red LED light therapy during the long-term course of COVID-19 in patients with and without AGA was conducted by Gerkowicz et al. (2024), who concluded that LED therapy is safe and well-tolerated, and promotes faster reduction of hair loss, stimulation of hair growth, and increased thickness and density.

Despite these results, there remains a need for more in-depth and systematic study of laser therapy as a treatment for AGA and other forms of alopecia. However, it is undeniable that

this method has the advantage of being non-invasive and lacking significant side effects (Zarei et al. 2016).

**Surgical treatment**

No treatment for alopecia is 100% effective. Many patients with AGA who have failed other therapies may be recommended to undergo surgical treatment, such as hair transplantation (Rose 2011; True 2021). Hair transplantation methods can be divided into follicular unit extraction and follicular unit transplantation. In the first case, follicles are extracted from the donor area individually and then transplanted into the alopecia area; in the second, the follicles are extracted as a single flap and fixed to the alopecia area with sutures. Extraction is a more popular method worldwide due to its ability to harvest follicles from a wide range of sites, the ability to select follicles by size and diameter, significantly reduced postoperative morbidity, and rapid healing. Advantages of transplantation include the simplicity and faster surgical procedure. The primary indication for any type of transplant is stable AGA without diffuse or scarring hair loss. If all requirements are met, surgery can be a highly effective treatment for alopecia. A 2020 study evaluated the results of hair transplantation using follicular unit extraction in 52 men aged 24-50. As a result, follicle density in the transplant area was consistently increased from 6 to 30 per $cm^2$ (Goldin et al. 2025).

One of the most innovative methods in hair transplantation is 3D-printed scaffolds, a technology rapidly gaining popularity. This technique uses 3D printing to create personalized scaffolds for implantation into the scalp to stimulate hair growth. These scaffolds are tailored to the individual scalp's characteristics and can be loaded with medications for gradual release, ensuring maximum therapeutic effect (Kim et al. 2025).

**Stem cell therapy**

A promising innovative method for treating alopecia is the use of stem cells. Both embryonic stem cells and adult stem cells can be used for this therapy (Llamas-Molina et al. 2022). One method of using stem cells is the formation of three-dimensional complexes of hair papilla cells and dermal progenitor cells and subsequent implantation of such complexes into the alopecic area (Castro and Logarinho 2020). Alternatively, transplantation of complexes of modified pluripotent stem cells can stimulate the formation of hair follicles in the transplantation area (Gnedeva et al. 2015; Takagi et al. 2016; Deng et al. 2021). In their article, Bran et al. (2025) showed that local injections of adipose stem cells led to complete hair restoration in mice with a model of AGA. Moreover, stem cells are capable of producing multiple growth factors, such as VEGF and IGF-1, which form the so-called "conditioned environment" that favorably influences hair follicle growth (Narita et al. 2020).

Stromal vascular fraction (SVF), a specific application of stem cells, is becoming an increasingly promising tool in regenerative medicine, particularly for hair loss. This fraction includes a complex of various cells, such as adipose stem cells, vascular cells, fibroblasts, and immune cells, which collectively stimulate regeneration. The effectiveness of SVF has been clinically confirmed: patients have observed improved hair density and thickness, as well as accelerated hair growth. SVF promotes scalp health by improving blood circulation, reducing inflammation, and accelerating regeneration (El-Khalawany et al. 2023).

One promising approach to hair follicle regeneration is the use of fibrin hydrogels containing stem cells. Chen et al. (2022) demonstrated that administration of such a gel containing skin progenitor cells allowed for the reconstruction of hair follicles, sebaceous glands, and other skin structures in mice without the formation of teratomas.

**Nanotechnology strategies**

Nanotechnology represents the practical application of knowledge to the development, production, and use of structures, devices, and systems whose unique properties are derived from the use of nanomaterials. Research has shown that topical polymer nanoparticles specifically target hair follicles (Główka et al. 2014; Chen et al. 2022). These solid particles, created from various polymers (such as chitosan, cellulose, polystyrene, polyvinyl alcohol, and polyethyleneimine), are able to penetrate deep into hair follicles despite the difficulty of penetrating the skin. Their large surface area relative to their volume facilitates enhanced interaction with target cells.

Resveratrol-loaded nanovesicles represent a promising platform for the comprehensive treatment of alopecia. Resveratrol was chosen as the base for its pronounced antioxidant and anti-inflammatory properties. Encapsulation of resveratrol in an active carrier resulted in the formation of PPD-Lip@RES, whose use in vitro and in vivo resulted in a significant increase in the expression of genetic and histological markers of proliferation (Zhang et al. 2024).

Chen et al. (2025) developed a new form of nanoparticles with excellent colloidal stability and potent antioxidant properties due to their ability to effectively scavenge reactive oxygen species. They also activate autophagy in human dermal papilla cells. This provides reliable protection against oxidative stress. In a mouse model of AGA, delivery of these particles via microneedles resulted in accelerated hair growth, stimulation of hair follicle proliferation, and enhanced angiogenesis. These effects were more pronounced than those seen with minoxidil, while side effects were minimal.

Caffeine has attracted considerable scientific interest in the context of hair loss therapy. Its therapeutic potential stems from its ability to inhibit dihydrotestosterone and potentiate the effects of other pharmacological agents. However, caffeine efficacy in this area is limited by its bioavailability at the hair follicle level. A study by Thepphankulngarm et al. (2024) presented an innovative approach to improving caffeine delivery to hair follicles using hollow mesoporous silica nanoparticles encapsulated in ultra-deformable liposomes. These liposomes demonstrated a significant reduction in reactive oxygen species levels in hair follicle cells exposed to dihydrotestosterone. These results suggest that this nanotechnological system may serve as a promising alternative to minoxidil for stimulating.

### Gene therapy

Gene therapy is also a promising approach to treating androgenetic alopecia. A study published in 2020 utilized a microvesicle gel with nanoliposomes adsorbed onto the surface, carrying the Cas9/gRNA riboprotein complex. Ultrasound activation of the microvesicles resulted in penetration of the complex into hair papilla cells. Intracellular exposure to Cas9/gRNA inhibits the synthesis of the SRD5A2 protein, which is responsible for converting testosterone to dihydrotestosterone. This treatment in mice resulted in over 90% follicle restoration and hair growth comparable to that of a control group that did not receive any testosterone (Ryu et al. 2020) by just three weeks after application. Treatment with small interfering RNAs targeting the androgen receptor improves androgenetic alopecia. The study showed that treatment with self-assembling micellar inhibitory RNA nanoparticles, based on mRNA, selectively suppressed AR gene expression in vitro. Clinical trials in which this RNA was applied to the scalp and massaged into hair follicles confirmed its efficacy in the treatment of androgenetic alopecia (Yun et al. 2022).

One form of gene therapy is to combat necroptosis – programmed cell death with an inflammatory component. This phenomenon occurs in hair sheath cells through specific proteins RIPK1, RIPK3, or MLKL, leading to their apoptosis. Reducing the expression of these proteins using necrostatin-1s has a protective effect on outer root sheath cells and promotes hair growth in mice (Zheng et al. 2020).

### Other promising methods

Recently, an innovative oligosaccharide biomaterial, OG6, was developed that possesses latent, specific activity. This material is capable of directing regulatory T cells to hair follicles, which, in turn, stimulates hair growth in mice. This process is based on physiological mechanisms of the skin's immune system that are typically used to suppress microbial inflammation. Controlled enzymatic cleavage of the polysaccharide glucomannan yields various oligosaccharide fractions with more specific properties, including the ability to induce chemokines. Intradermal administration of OG6 oligosaccharide to depilated mouse skin leads to active hair growth and promotes the accumulation of regulatory T cells in the hair follicle region. Thus, this method offers new avenues for the creation of safer and more targeted therapeutic tools based on glycan technologies (Yin et al. 2024).

Terminalia bellirica (TBR) is a popular traditional Indian medicinal plant. A study of its extract identified 15 compounds potentially active in the treatment of AGA. TBR effectively reduces reactive oxygen species, stimulates VEGF production and HUVEC migration, and inhibits type II 5α-reductase activity (with an efficacy of 82.35 ± 1.02%). Studies in C57BL6 mice showed that TBR promotes hair regrowth better than minoxidil. TBR's mechanism of action involves accelerating the transition of hair follicles from the telogen to anagen phase by reducing malondialdehyde levels and increasing VEGF expression (Xiang et al. 2025).

In their study, Bashmaluh et al. (2023) found that topical application of miliacin, a pentacyclic triterpenoid with antioxidant properties, stimulated the transition of hair follicles into the anagen phase in mice with artificially modeled androgenetic alopecia. According to the study results, 77.26% of follicles were in the anagen phase after 28 days of treatment, compared to only 7.92% in the placebo group.

Despite the wide range of treatment options, none has demonstrated a consistent and reliable therapeutic effect (Table 1). Even the most promising treatments require detailed research and rigorous trials to confirm their effectiveness and therapeutic feasibility (Correia et al. 2023).

**Table 1.** Advantages and disadvantages of the main methods of treating alopecia

| Method | Advantages | Disadvantages |
|---|---|---|
| Pharmacological therapy (drugs) | • Satisfactory clinical effect for hair growth stimulation in AGA and AA;<br>• Non-invasive method;<br>• Ease of use. | • Often provides only a temporary effect;<br>• Non-targeted (systemic) therapy;<br>• Undesirable systemic side effects;<br>• Limited long-term use. |
| Hair transplantation | • One-time surgical intervention;<br>• Natural look and appearance;<br>• A permanent solution to hair loss;<br>• Fast healing and recovery. | • Not all patients with hair loss are good candidates for transplantation;<br>• Enough donor hair is required to cover the entire balding area;<br>• Possibility of side effects (e.g., postoperative pain, scarring, infection). |
| Low-level laser therapy | • Non-surgical intervention;<br>• Satisfactory clinical effect on hair growth in patients with hair loss;<br>• Safe (minimal side effects), painless and non-invasive. | • A temporary solution: requires time and regularity;<br>• Not effective for restoring completely lost hair;<br>• Lack of protocol standardization. |
| Plasma therapy (PRP) | • Non-surgical intervention;<br>• Non-invasiveness;<br>• Autologous nature (minimal side effects and no risk of rejection);<br>• Safety and cost-effectiveness;<br>• Painlessness. | • Short-term effect: may require multiple injection sessions;<br>• Not all patients are good candidates for PRP therapy (for example, those with bleeding disorders and low platelet counts);<br>• Conflicting data on clinical efficacy in patients with AGA;<br>• Lack of standardization in PRP preparation. |
| Stem cell therapy | • Autologous nature (no risk of rejection);<br>• Safe and non-invasive;<br>• Stimulates and restores hair follicles;<br>• Natural hair look. | • Lack of standardization in preparation, quantity and intervals of treatment;<br>• The benefits of different donor stem cells are not yet clear;<br>• Clinical efficacy has not been proven: clinical trials are underway. |
| Nanotechnology strategies | • Targeted accumulation in the hair follicle;<br>• Localized therapy;<br>• Controlled release of the drug;<br>• Increased efficiency;<br>• Reduction of systemic side effects/ | • Regulatory and legal issues (lack of regulation);<br>• Commercial and approval issues;<br>• Quality and safety issues;<br>• Cost-effectiveness issues (high costs). |

***Note:*** AGA – androgenetic alopecia; PRP – platelet-rich plasma.

# Conclusion

Both androgenetic alopecia and alopecia areata significantly reduce the quality of life of patients. Currently, in terms of the optimal combination of availability, effectiveness, and safety, the treatment methods for androgenetic alopecia include topical 5% minoxidil, oral finasteride 1 mg/day, or flutamide 250 mg/day as systemic agents, laser therapy, plasma therapy, and hair transplantation. For alopecia areata, due to its predominantly autoimmune pathogenesis, such drugs include systemic corticosteroids at a dosage of 1 mg/kg/day or as pulse therapy, baricitinib at a dosage of 2-4 mg/day, or cytostatic drugs, in particular azathioprine (1 mg/kg), cyclosporine (3-5 mg/kg), and methotrexate (0.2-0.4 mg/kg). The severity of the problem is reflected in the intensity of proposals and the development of new and high-tech treatments for alopecia. These methods include the use of stem cells, gene therapy, 3D-printed skin grafts, and new delivery systems for traditional therapeutic agents in the form of self-degrading microneedles and various nanoparticles. All of these methods demonstrate diverse effectiveness in decoupling the pathogenesis of alopecia and reducing its clinical manifestations. Therefore, the topic of alopecia and its correction requires extensive intellectual and financial investment to develop and test the many therapeutic approaches described above. And with further research, even more diverse pharmacological substances and genetic and tissue engineering technologies may become important, if not key, additions to current alopecia treatment regimens, significantly improving the quality of life of those affected.

# Additional Information

**Conflict of interest**

The authors declare that they have no conflicts of interest.

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**Data availability**

All of the data that support the findings of this study are available in the main text.

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