Journal of Cosmetic and Laser Therapy

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ijcl20

Management of androgenic alopecia: a systematic review of the literature

Amanda Rosenthal, Geena Conde, Joseph F. Greco & Nima M. Gharavi

To cite this article: Amanda Rosenthal, Geena Conde, Joseph F. Greco & Nima M. Gharavi (09 Jun 2024): Management of androgenic alopecia: a systematic review of the literature, Journal of Cosmetic and Laser Therapy, DOI: 10.1080/14764172.2024.2362126

To link to this article: https://doi.org/10.1080/14764172.2024.2362126

Published online: 09 Jun 2024.

JOURNAL OF COSMETIC AND LASER THERAPY
https://doi.org/10.1080/14764172.2024.2362126

Taylor & Francis
Taylor & Francis Group

Management of androgenic alopecia: a systematic review of the literature

Amanda Rosenthal[a], Geena Conde[b], Joseph F. Greco[c], and Nima M. Gharavi[d]

[a]Department of Dermatology, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA, USA; [b]Department of Dermatology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA; [c]Department of Research, Greco Hair Restoration, Sarasota, FL, USA; [d]Department of Dermatology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

ABSTRACT

We aimed to determine the efficacy of the various available oral, topical, and procedural treatment options for hair loss in individuals with androgenic alopecia. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a systematic review of the National Library of Medicine was performed. Overall, 141 unique studies met our inclusion criteria. We demonstrate that many over the counter (e.g. topical minoxidil, supplements, low-level light treatment), prescription (e.g. oral minoxidil, finasteride, dutasteride), and procedural (e.g. platelet-rich plasma, fractionated lasers, hair transplantation) treatments successfully promote hair growth, highlighting the superiority of a multifaceted and individualized approach to management.

ARTICLE HISTORY
Received 8 January 2024
Revised 1 June 2024
Accepted 28 May 2024

KEYWORDS
Hair; hair loss; hair growth; hair cycle; hair follicle; oxygen; ischemia; hyperoxygenation; androgenic alopecia; patterned hair loss; minoxidil; finasteride; dutasteride; adenosine; cetirizine; platelet rich plasma; PRP; stem cells; growth factors; low level light therapy; LLLT; LED light; fractionated lasers; microneedling; drug delivery devices; JetPeel; nutraceuticals; oral supplements; topical supplements; plant oils; botanicals; amino acids; caffeine; rosemary; antioxidants; 5-alpha reductase; dihydrotestosterone; spironolactone; androgens; estrogens; progesterones; tretinoin; valproic acid; fulvestrant; prostaglandins; latanoprost; botulinum toxin; botox; monofilament threads; thread embedding therapy; poly-l-lactic acid; ketoconazole; photodynamic therapy; hair transplant; transplantation; hair restoration surgeries; follicular unit extraction; follicular unit excision; follicular unit transplantation; FUT; graft holding solution

Introduction

Hair plays a vital role in self-identity, and hair loss can profoundly impact self-perception and life satisfaction. Patterned hair loss, or androgenic alopecia (AGA), is the most common form of hair loss, affecting more than half the adult population (1). Despite advancements in understanding the hair follicle and its natural cycle, hair loss remains a complex condition influenced by various biological, genetic, hormonal, chemical, and environmental factors (Figure 1).

Normal hair cycling

Normal hair cycling is guided by distinct populations of mesenchymal stem cells, including hair follicle stem cells (HFSCs) and dermal papilla cells (DPCs). During the anagen phase, interactions between these stem cells give rise to progenitor cells responsible for producing the hair shaft. During catagen, the hair shaft cells undergo apoptosis, while the surrounding stem cells form a new hair bulge. The stem cells then recover during the telogen phase, preparing for another hair cycle (2–4).

Any disruption to the normal hair cycle can result in hair loss. For instance, the dense inflammatory infiltrate associated with disease states, such as discoid lupus erythematosus and lichen planopilaris, destroys HFSCs, resulting in a permanent alopecia (i.e. scarring alopecia). However, in disease states such as AGA, there is reduction in progenitor cells but HFSCs remain viable (5). Consequently, many believe that the reactivation of HFSCs could regenerate hair in balding scalps. This is an area of active research and has inspired several existing hair growth treatments.

Genetic influence

Population studies have reported a polygenic inheritance pattern of hair loss, with both maternal and paternal genetic influences. Of the genes identified to date, the androgen receptor (AR) gene on chromosome X represents a major determinant of hair loss (i.e. AGA) in both men and women (6). Specifically, the CAG repeat length within the AR gene influences the sensitivity of the androgen receptor to dihydrotestosterone (DHT), a hormonal derivative of testosterone. Individuals with shorter CAG repeat sequences have an increased risk of developing AGA. In contrast, men with > 40 repeats appear to be protected and have androgen insensitivity. Other implicated genes include Ectodysplasin A2 Receptor, as well as genes located on chromosomes 20p11 and 3q26; however, how these variants affect hair loss merits further investigation (4).

Hormonal influence

The role of testosterone in the pathogenesis of both male and female balding is well known and underscores the

CONTACT Amanda Rosenthal Amanda.x.Rosenthal@kp.org Department of Dermatology, Kaiser Permanente Los Angeles Medical Center, 1515 N Vermont Avenue, Los Angeles, CA 90027, USA

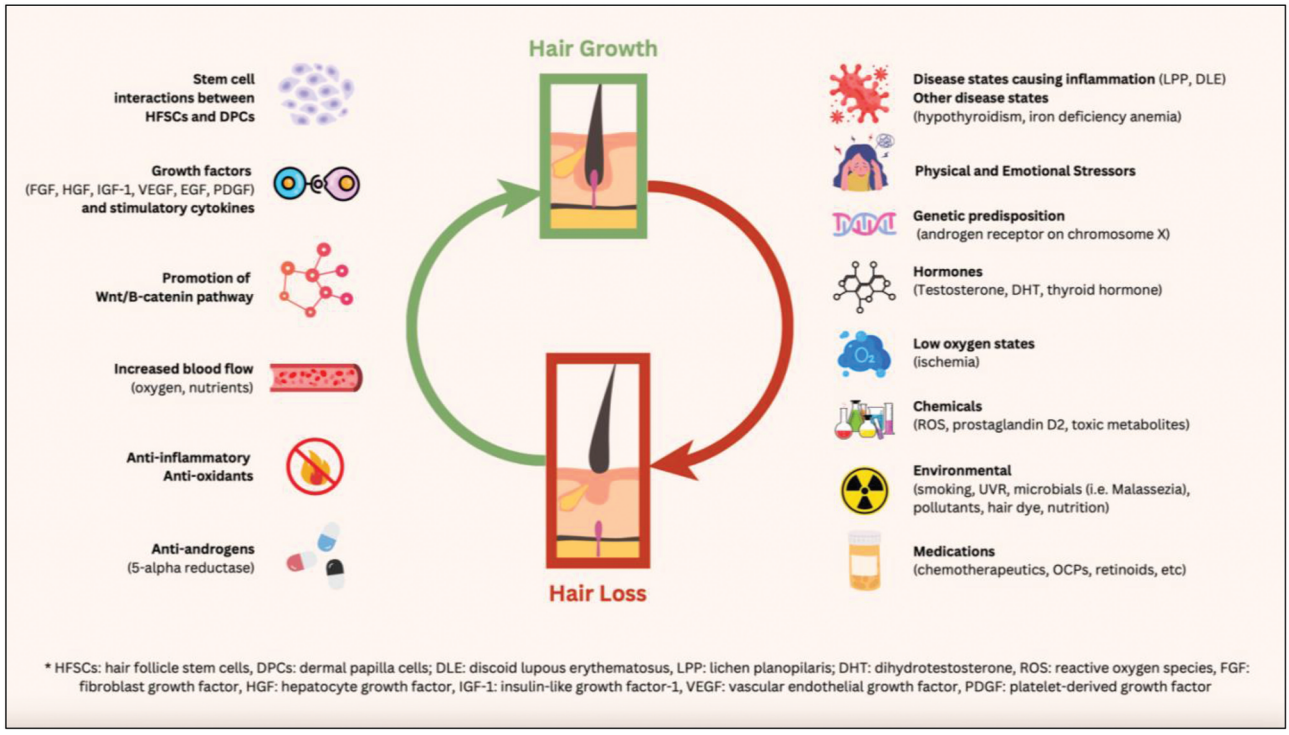

Figure 1. Factors involved in regulating the hair cycle.

prevalent use of 5-alpha reductase inhibitors. The history of this class of medications is unique and emerged from a remote village in the Dominican Republic called Las Salinas. In this village, a small group of children born with ambiguous genitalia were initially raised as female, but then developed male characteristics during puberty. Following these young men into adulthood revealed that they had no enlargement of their prostate, acne, or patterned hair loss. Endocrinologists identified a deficiency of 5-alpha reductase, an enzyme responsible for converting testosterone to DHT, within this population, ultimately resulting in the development of Proscar (i.e. finasteride) by Merck Pharmaceuticals (7).

Additional research into the role of testosterone on hair loss has shown that type I and II isoforms of 5-alpha reductase reside at the level of the hair follicle, resulting in the accumulation of DHT. DHT then binds to the androgen receptors and activates the production of proteins harmful to the follicle, leading to disruption of the normal hair growth cycle. Specifically, anagen phase is shortened, resulting in premature regression during catagen and telogen phases. With each hair cycle, the anagen phase further shortens, leading to progressive miniaturization of hair and, eventually, hair loss. Many over the counter (OTC) and prescription treatments, both oral and topical, inhibit these hormonal processes, with the intent of preventing hair loss.

Chemical factors

The relationship between specific chemical factors and hair growth regulation is an active area of research. Many have investigated the role of oxygen levels, reactive oxygen species, and ischemia on the hair cycle, hair growth, and hair loss. Studies have shown that hyper-oxygen states increase hair growth in cultured human and murine hair follicles (8). In addition, investigators examined the effects of high oxygen states following hair transplantation procedures, demonstrating lower rates of postoperative shedding, itching, and folliculitis among post-transplant patients exposed to hyperbaric oxygen therapy (9,10). Conversely, studies have demonstrated that ischemia can elicit states of alopecia. For instance, studies have found that the transcutaneous partial pressures of oxygen were much lower in bald versus hair-bearing scalps, suggesting a relative microvascular insufficiency of scalps experiencing male pattern baldness (11). Similarly, regenerated hairs in ischemic flaps experienced a slower rate of hair growth, thinner hair shafts, and decreased hair density (8).

Reactive oxygen species have also been implicated in dysregulating the hair cycle. Since lipid oxidation products are widely accepted as a biomarker of oxidative stress, their impact on the hair follicle has been studied. Murine models have demonstrated that lipid peroxides can induce apoptosis of the hair follicle, thereby inducing early catagen phase (12). Furthermore, one study revealed that the dermal papilla cells of balding scalps were less able to handle oxidative stress compared to dermal papilla cells of healthy scalps (13).

Studies have also demonstrated that several other chemical microprocesses can cause hair loss. Gene expression assays have shown that increased expression of prostaglandin D2 synthetase, an enzyme that converts prostaglandin H2 (PGH2) to D2 (PGD2), plays a pivotal role in hair cycling. Specifically, PGD2 is known to inhibit hair growth and is seen at higher concentrations in balding scalps, underlying the use of certain prostaglandin analogs and inhibitors in the management of hair loss (14). Additionally, alteration of dermal papilla microvasculature, accumulation of toxic metabolites with damage to hair follicle DNA, and imbalance of follicular

protease/antiprotease systems have all been implicated in disrupting the hair cycle, leading to hair loss (15).

Environmental factors

Various environmental factors have been shown to exacerbate or accelerate hair loss. For instance, several epidemiological studies have associated smoking with increased hair loss, which is likely related to microvasculature disruption, ischemia, and the accumulation of toxic metabolites and free radicals (15). Sun exposure has also been shown to contribute to hair loss through several mechanisms, although the relationship is not fully understood. One postulation involves the photoactivation of porphyrins produced by *Propionibacterium sp*. in the pilosebaceous duct, leading to the production of radical oxygen species and harmful cytokines (16,17). Similarly, studies have found that other environmental factors, including the presence of microbes (e.g. Malassezia spp.), pollutants, and irritants (e.g. hair dye), as well as certain disease states, such as hypothyroidism and iron deficiency, can lead to oxidative stress and hair loss (18–20).

Objective

The complexity of the hair cycle, paired with the many factors contributing to hair loss in humans, has resulted in the development of numerous therapeutic options for hair growth. Several topical, oral, and procedural treatments have emerged for managing hair loss over the past three decades. The purpose of this review is to describe the many treatment modalities for hair growth, focusing on their efficacy and the scientific studies that support their use.

Methods

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a systematic review of the National Library of Medicine was performed. A search of the following keywords, present in the title or abstract of the article, including "hair," "growth," and "treatments," yielded 7,155 results. Randomized controlled trials (RCTs), case series, case reports, cohort studies, pilot studies, and observational studies from the earliest date available through August 16, 2023, were reviewed ($n = 535$). We included only those studies performed on human subjects, written in English, and focusing on scalp hair growth. We excluded any studies focusing on treatments for hair loss due to diseases other than androgenic alopecia. Overall, 118 unique studies met our inclusion criteria. Our PRISMA search did not yield any studies focusing on the use of oral minoxidil or hair restoration surgery for hair growth. Therefore, additional searches were performed. The first included search terms "oral minoxidil" and "alopecia" and yielded 10 relevant studies. The second included the search terms "hair transplant" or "hair transplantation" or "follicular unit extraction" or "follicular unit excision" and "androgenic alopecia" or "alopecia" or "graft holding solution" or "survival" and yielded 13 relevant studies.

Results

Topical minoxidil

First introduced to the medical community as an antihypertensive medication, minoxidil became increasingly known for the common side effect of hypertrichosis. Minoxidil achieves this therapeutic effect through its vasodilatory, anti-inflammatory, and anti-androgen properties, as well as induction of the Wnt/B-catenin pathway. To date, topical minoxidil is the only Food and Drug Administration (FDA) approved treatment for hair loss in both men and women.

Over the past three decades, clinical trials have repeatedly demonstrated the efficacy of topical minoxidil in concentrations ranging from 1% to 5% (21–27). When comparing efficacy by concentration, 2% topical minoxidil was found to be equal to the 3% formulation (28–30). However, 5% topical minoxidil was found to be superior to both 1% (31), 2% (32–35), and 10% solution (36). Increasing concentration was also associated with more frequent, local side effects. For instance, a RCT of 90 males found that 10% topical minoxidil led to higher rates of local irritation and hair shedding without producing superior clinical results (36). When comparing vehicles employed for delivery of topical minoxidil, gel was found to be equivalent to solution (37), while foam resulted in significantly lower rates of local intolerance, namely pruritus and dandruff (35).

Many have also investigated compounded formulations, which combine minoxidil with other ingredients believed to regulate hair growth. Neither the addition of 0.01% tretinoin (38) nor 1% pyrithione zinc shampoo (39) demonstrated increased efficacy when compared to minoxidil monotherapy. However, improved hair growth was appreciated in trials combining 0.25% topical finasteride (40,41), sulfotransferase (the enzyme that converts the minoxidil's prodrug into its active form and physiologically resides at the level of the hair follicle (42), and a unique formulation of 0.5% diclofenac, 5% tea tree oil, 5% lauryl alcohol (43) with minoxidil solution. Decades of research support the use of topical minoxidil as a safe, effective, and easily accessible therapeutic for hair growth among men and women.

Oral minoxidil

An article published in the New York Times (NYT) in 2022 served as a catalyst for much of the recent craze surrounding oral minoxidil. In fact, a recent study out of JAMA Network Open documented soaring rates of oral minoxidil use, reporting significantly higher prescriptions 8 weeks after versus 8 weeks before the publication of the NYT article (44).

Oral minoxidil has gained popularity given its ability to promote hair growth without causing the local side effects associated with the topical formulation, potentially improving patient compliance. While oral minoxidil has its own

side effect profile (e.g. lower extremity edema and hypertrichosis), the adverse events are dose-dependent and often very well-tolerated (45). As such, many have investigated low dose oral minoxidil (LDOM) for hair loss in aging men and women, demonstrating equivalent efficacy between very low doses (as low as 0.25 mg and daily topical application (46–48). We also identified one pilot study focusing on the use of LDOM (0.25 mg) combined with 25 mg of spironolactone, demonstrating decreased hair shedding after one year of use (49).

Studies have also shown that higher doses of minoxidil may lead to improved hair growth (50–53). For example, a RCT of 26 women found that 1 mg led to an increased hair count at 26 weeks when compared to 0.25 mg of minoxidil (52). Furthermore, prospective, single arm studies found that 0.25 mg of minoxidil daily led to a non-significant increase in hair density (50), while 5 mg of minoxidil daily resulted in significant increases in hair counts after 6 months of use (51). Studies have also shown that oral minoxidil produces better hair growth among individuals with mild to moderate, rather than advanced, AGA (54). The tolerable safety profile, low medication cost, and overall efficacy make oral minoxidil a desirable option for many struggling with hair loss.

Finasteride/dutasteride

The conversion of testosterone to dihydrotestosterone (DHT) by 5 alpha-reductase within the hair follicle plays a crucial role in the development of patterned hair loss. Consequently, medications that inhibit this enzyme are widely used to treat androgenic alopecia. Both dutasteride and finasteride function as anti-androgens, blocking 5 alpha-reductase; dutasteride inhibits both the type I and II isoforms, while finasteride inhibits only the type II isoform. Only finasteride is FDA-approved for the treatment of patterned hair loss in males.

Several clinical trials over the past 30 years have exhibited the benefits of finasteride (55–61). For instance, six RCTs, including over 3,000 men with AGA, compared 1 mg of finasteride to placebo, demonstrating clinically significant increases in hair count, hair weight, and global photographic assessment data (55–60) after one or more years of use. We also identified one study focusing on the use of oral finasteride alone or with topical minoxidil. This study found that combination treatment produced greater percentage of hairs in anagen phase, but no difference in overall hair count. This clinical trial only followed patients for 3 months; therefore, it is possible that adding daily topical minoxidil is beneficial, but the follow-up period was inadequate to capture this benefit (62).

While generally well tolerated, the possibility of sexual dysfunction deters some individuals from taking finasteride. As such, a recent RCT examined topical finasteride's efficacy and safety profile compared to both the oral version and placebo. The authors demonstrated significantly increased hair densities following 24 weeks of 0.25% topical finasteride compared to placebo, as well as no significant differences in hair growth compared to 1 mg of oral finasteride. Moreover, topical finasteride had fewer treatment-related sexual adverse events when compared to the oral formulation (56).

As mentioned, dutasteride acts on both isoforms of 5-alpha reductase and has also been studied for the management of hair loss. A single-arm, prospective study of 120 males with AGA prescribed 0.5 mg of dutasteride found significantly increased hair count, density, and diameter over the 52-week study period (63). In a RCT comparing 0.5 mg of dutasteride to placebo, researchers appreciated a significantly greater change in hair count after 6 months in the intervention group (64). Clinical trials have also demonstrated a dose-dependent increase in efficacy (65,66). Increasing doses, however, were associated with greater frequency of side effects, including decreased libido (65). Given the ability to block both type I and II isoenzymes, some have speculated that dutasteride may be more effective than finasteride for the management of hair loss. Three RCTs, including 1,423 men with AGA, have demonstrated the superiority of dutasteride over finasteride (65–67). Furthermore, these studies showed a similar side effect profile between finasteride and dutasteride (65–67).

These studies suggest that both finasteride and dutasteride are efficacious in treating hair loss. While relatively infrequent, the potential for sexual adverse events may deter some individuals from treatment with 5-alpha reductase inhibitors, leading them to favor a topical formulation. Additional studies focusing on topical finasteride (and possibly topical dutasteride) are needed to validate the findings presented above.

Other hormonal therapies

Hormonal dysregulation is a well-known cause of patterned hair loss, as highlighted by our discussion of 5-alpha reductase inhibitors above. The role of other hormonal agents, however, has less supporting data. For example, we identified three studies examining the effects of other hormonal therapies, including aldosterone and androgen blockers, as well as estrogens and progesterones. In a pilot study comparing spironolactone to cyproterone acetate (an androgen receptor blocker) among 80 women with AGA, authors demonstrated improvement in hair growth among nearly half of the women but failed to show differences between the two medications (68). We also identified two studies examining the effects of topical progesterone (69) and estrogen (70), which both failed to show hair growth benefits. Additional studies comparing medications such as spironolactone to finasteride are needed to fully understand the role of these hormonal blocking agents in the management of AGA.

Ketoconazole

In addition to its anti-fungal properties, ketoconazole has shown the ability to improve hair density and diameter, as well as increase the proportion of hairs in the anagen phase. Three studies have examined the benefits of ketoconazole, in topical or shampoo formulation, for hair loss in men with AGA. First, a small-scale pilot study demonstrated "remarkable hair growth" among two of six men instructed to use ketoconazole lotion on their scalp daily (71). Similarly, a double-armed, comparative trial of 39 men with AGA found that ketoconazole shampoo significantly improved hair

diameter and proportion of hairs in the anagen phase compared to placebo. Further, this study demonstrated that ketoconazole had similar efficacy to topical 2% minoxidil (72). Finally, a RCT of 100 men with AGA showed that finasteride combined with ketoconazole was superior to finasteride alone in improving hair growth, as determined by the patient and physician global assessment scores (73). These results support the use of ketoconazole as an adjunctive therapy for individuals with patterned hair loss.

Supplements

A vast array of oral natural supplements exists to achieve hair growth through their vasodilatory, antioxidant, and hormone blocking properties. For instance, both bran supercritical CO_2 extract (74) and Serenoa repens (75), have demonstrated ability to inhibit 5-alpha reductase. However, when compared to finasteride, Serenoa repens was inferior (75). Saw palmetto is another natural supplement known to inhibit 5-alpha reductase. Nutrafol, which contains many bio-optimized phytocompounds, including saw palmetto, curcumin, ashwagandha, and tocotrienols, increases hair count after 6 months of use when compared to placebo (76,77). Chinese herb extract, or Dabaoa, is well-known for its vasodilatory effects. When studied for hair growth promotion, Dabaoa significantly increased hair counts in a RCT of 373 individuals with AGA (78). Most recently, a formulation containing hydrolyzed fish-origin collagen combined with taurine, cysteine, methionine, iron, and selenium showed promise among 76 patients enrolled in a 12-week RCT (79).

Similarly, many have studied the benefits of topical, natural formulations on hair growth, including piroctone olamine (80–82), essential plant oils (83), amino acids (84,85), caffeine (85,86), rosemary (87), and plant extracts (86,88,89). Compared to placebo, antioxidant preparations, such as piroctone olamine (80–82), polyphenols combined with hexyl nicotinate, amino acids, minerals, and caffeine (85), and essential plant oils (83) demonstrated an increase in anagen hair counts and hair thickness, and a decrease in hair shedding. Further, *Curcuma aeruginosa*, a natural 5-alpha reductase inhibitor, combined with 5% minoxidil, yielded significant increases in hair growth and decreases in hair shedding after 6 months of use over either topical agent alone (88). Given its ability to increase blood flow, topical rosemary oil has also been studied, demonstrating hair growth results comparable to topical 2% minoxidil after 6 months of use (87). Finally, we identified three studies that investigated the use of proprietary topical agents. Two prospective studies found that the combination of two extracts (Coffea arabica and Larrea divaricata) called ECOHAIR spray lotion ($n = 52$ patients with AGA) (86) and a botanical-based serum called Trimax-360 ($n = 30$ patients with AGA) (89) yielded a significant increase in hair growth after 3 months of use. Additionally, a large-scale, prospective, comparative study demonstrated improved hair density and decreased hair shedding after 8 sessions of intradermal injections of QR678 Neo® solution, a peptide-based formulation, at 3-week intervals among 2,428 patients with AGA (84). Certain natural supplements, in both oral and topical formulations, have shown the ability to promote hair growth with minimal side effects and can be considered for the management of hair growth as adjunctive therapy. Considering that supplements lack FDA regulation, patients should exercise caution when contemplating their use.

Platelet-rich plasma

Platelet rich plasma (PRP), a concentrate of platelet-rich plasma proteins derived from whole blood, has become an increasingly popular treatment for many conditions ranging from athletic injuries, wound healing, and esthetic medicine (including hair loss treatment). While a standardized method of preparation is lacking, the main principle remains consistent across all fields of medicine (Figure 2). Patients' whole blood is used to prepare concentrated platelets, which then release numerous growth factors and cytokines known to promote cell proliferation, differentiation, and angiogenesis (90).

Many have studied the use of PRP for hair loss, demonstrating overwhelming efficacy with long-term success (Figures 3–4). For example, we found five split-scalp RCTs, including a total of 221 patients, comparing PRP injections to placebo. The authors showed a significant increase in hair count and density in the PRP injected scalp, with benefits lasting 12 months following the last injection (91–95). Furthermore, in a RCT by Rodrigues et al. (2019) that did not employ a split-scalp study design, 26 males were randomized to receive either four subcutaneous injections of PRP or placebo. The authors found a significant increase in hair count, hair density, and proportion of anagen hairs 3 months following the last injection among the PRP group (96). Lastly, a pilot study found significant increases in hair density following two rounds of PRP injections 3 months apart (97). We did identify one study on PRP that failed to demonstrate success. Gessenberger et al. (2020) randomized 30 patients to receive 5 sessions of PRP or saline injections at monthly intervals. Ultimately, the authors found no differences in hair count or diameter between the intervention and control groups. It is important to note that both groups in this study experienced a paradoxical decrease in hair count and an increase in hair diameter over the 3 months study period, which likely confounded results (98).

Several other investigators have compared varying formulations of PRP, with the intention of identifying which method of preparation yields the greatest efficacy. Both non-activated PRP (99) and platelet lysate (100) demonstrated non-inferiority when compared to standard, activated PRP. Double-spin PRP, however, resulted in greater improvement in hair density when compared to single-spin PRP, suggesting higher concentrations of platelets may yield improved outcomes (97,101). Finally, compared to PRP alone, the addition of growth factors produced contrasting results (93,102).

Compared to either PRP or topical minoxidil monotherapy, three studies found that combination therapy with PRP injections and daily use of topical minoxidil led to the greatest increase in hair count and density (103–105). Finally, one small pilot study evaluated the use of PRP in a topical

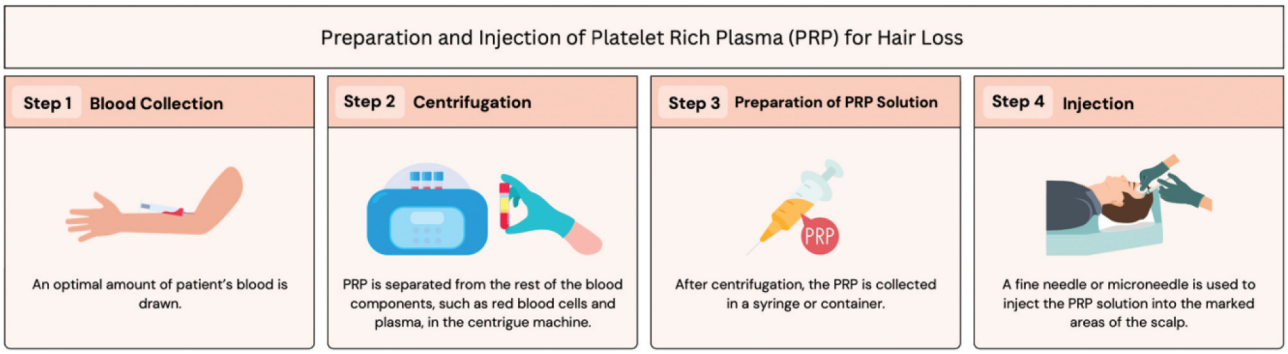

Figure 2. Schematic Diagram of Preparation and Injection of Platelet Rich Plasma (PRP) for Hair Loss.

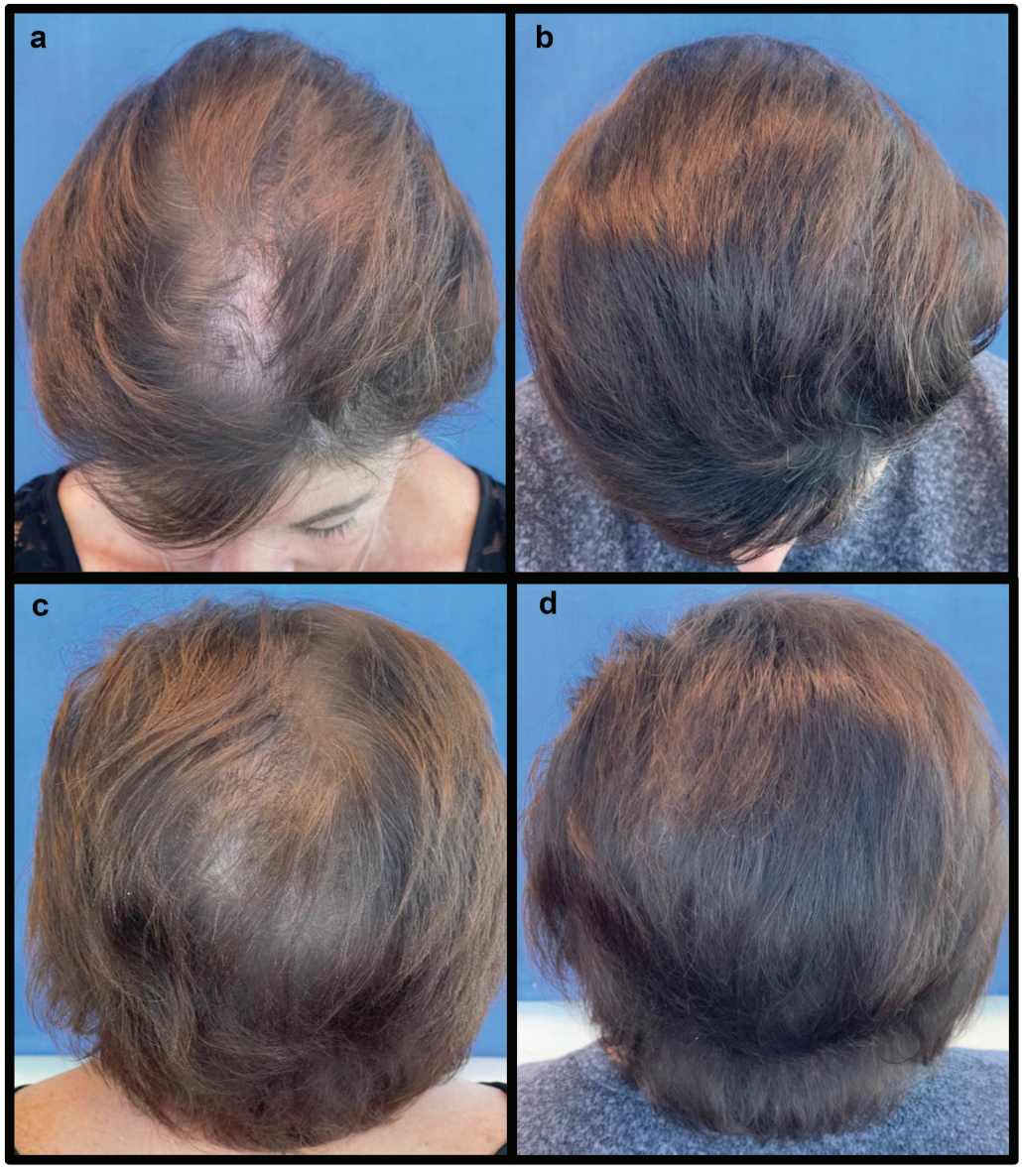

Figure 3. Female Patient with AGA: Before and 6 Months After 1 Session of PRP (from the author's clinical practice).

formulation, applied twice daily. Compared to baseline, topical PRP resulted in increased hair count and density after 3 months of treatment (106). Our pooled data suggest that it provides excellent hair regeneration results and offers a promising therapeutic with long-term benefits for patients with hair loss. The main limitation associated with this modality is the high cost of treatment, which may limit access for many patients.

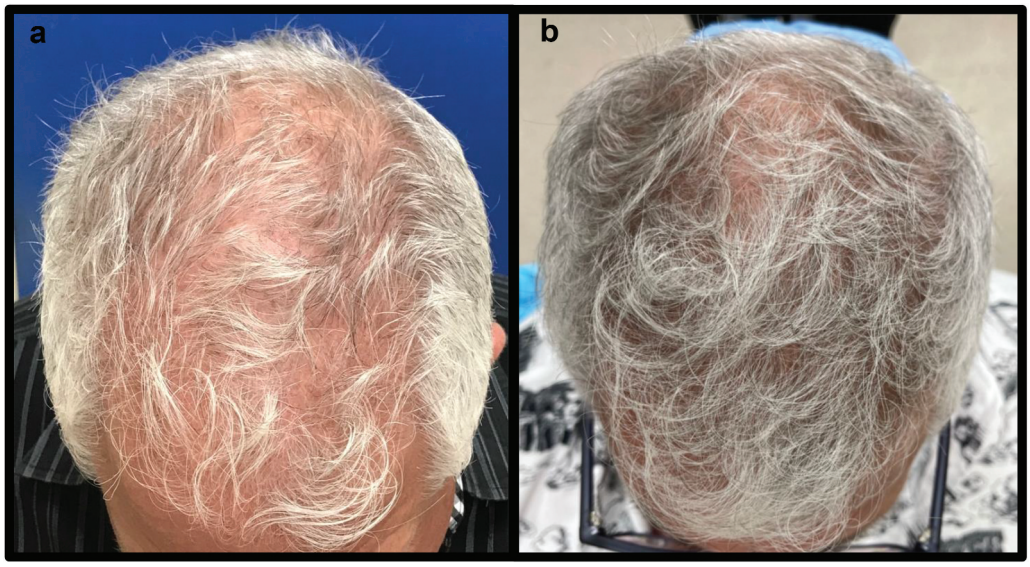

Figure 4. Male Patient with AGA: Before and 4 Months After 2 Sessions of PRP Spaced 6 Months Apart (from the author's clinical practice).

Stem cells/growth factors

Recently, much attention has focused on the hair growth-promoting effects of stem cells (Table 1). For instance, adipose-derived stem cells have been shown to release hepatocyte growth factor, insulin-like growth factor-1, vascular endothelial growth factor, and platelet-derived growth factor, which all regulate varying aspects of the hair cycle (107). Both intradermal (107) and topical (108) applications of adipose-derived stem cells have demonstrated success in increasing hair density (107,108), hair thickness (108), and anagen rate (107). Dermal sheath cup cells, which serve as progenitor cells and play a pivotal role in controlling hair growth, have also been studied in humans. In a split-scalp study by Tsuboi et al. (2020), 62 patients with AGA were randomly assigned to receive intradermal injections of autologous dermal sheath cup cells or placebo throughout their scalps over a 12-month study period. The investigators found that the scalp treated with autologous dermal sheath cup cells had significantly increased hair density compared to placebo scalp, suggesting these cells can promote dermal papillae formation (109).

Some have investigated the use of the growth factors themselves, bypassing the need for stem cells. Two studies have compared the use of topical growth factors to placebo (110) or topical minoxidil (111), demonstrating significant improvement in hair growth after 6 months of use. Similarly, in a split-scalp study design, 16 males with AGA were randomized to receive three sessions of intradermal concentrated growth factor or intradermal placebo injections, both with daily topical minoxidil, over 6 months. A greater increase in hair density was observed in the side receiving growth factor, suggesting the superiority of combination treatment approaches (112). Finally, a RCT by Zimber et al. (2011) evaluated a bioengineered, non-recombinant, human cell-derived formulation, termed Hair Stimulating Complex (HSC), containing follistatin, keratinocyte growth factor, and vascular endothelial growth factor. The authors found a significant increase in hair count after 1 year of use in scalp treated with intradermal HSC compared to placebo (113). While several studies have demonstrated the efficacy of both stem cells and growth factor therapy, we did not identify any studies comparing these modalities to PRP. Future investigations should compare these modalities, taking into consideration the associated medical costs and resources.

Thread-embedding therapy

Thread-embedding therapy is characterized by embedding dermal threads into the skin for various therapeutic effects. Poly-l-lactic acid (PLLA) threads are considered a fifth-generation polymer suture and a type of alpha hydroxy acid

Table 1. The role of stem cells and growth factors involved in hair growth (3).

Stem Cells/Growth Factors	Function in Hair Growth
Dermal Papilla Stem Cells (DPSCs)	Promote progenitor cells to proliferate and initiate hair follicle regeneration
Hair Follicle Stem Cells (HFSCs)	Proliferate, migrate and differentiate during anagen to form the hair follicle
Hepatocyte Growth factor (HGF)	Enhances the proliferation of follicular epithelial cells
Epidermal Growth Factor (EGF)	Improves the activity and growth of follicle outer root sheath cells by activation of Wnt/β-catenin flagging
Fibroblast Growth Factor (FGF)	Improves the advancement of hair follicles
Interleukein-6 (IL-6)	Involved in WIHN through STAT3 enactment
Vascular Endothelial Growth Factor (VEGF)	Promotes perifollicular angiogenesis around hair follicles
Transforming Growth Factor-Beta (TGF-β)	Stimulates the signaling pathways that manage the hair cycle
Platelet-Derived Growth Factor (PDGF)	Up-regulates the genes associated with hair follicle separation, induction, and control of anagen
Insulin-like Growth Factor (IGF-1)	Improves the migration, survival, and proliferation of hair follicle cells

known for its absorbability and biodegradability. Two RCTs investigated the use of PLLA threads among females with AGA, demonstrating increased hair density and diameter compared to both placebo (114) and topical minoxidil (115). Additional studies are needed to determine the long-term ability of this intervention to maintain and promote hair growth.

Botulinum toxin A

It has been hypothesized that Botulinum Toxin A (BTA) can increase blood flow through muscle relaxation, thereby increasing oxygen and nutrient delivery. Some have speculated that increased oxygen content inhibits the conversion of testosterone to DHT, thereby inhibiting the driving factor of patterned hair loss. Consequently, BTA has been studied for the treatment of hair growth. One split-scalp RCT found that the scalp treated with BTA had significantly higher hair density compared to the untreated scalp (116). On the other hand, a study comparing patients receiving finasteride and BTA to finasteride alone found no difference in hair counts after 4 months of treatment (117). Future investigations are needed before this modality can be recommended for the management of hair loss.

Low-level light treatment

Low-level laser light treatment (LLLT), also called laser phototherapy or photobiomodulation, has become increasingly popular over the past decade for the management of a variety of dermatologic conditions, including hair growth. While several studies have demonstrated the efficacy of LLLT in promoting hair growth, the biological mechanism is not fully understood. Various manufacturers have produced machines utilizing wavelengths in the visible spectrum (600–900 nanometers (nm)) with the intent of altering biological activity to promote hair growth. We identified six RCTs (118–123) and one pilot study (124) assessing LLLT on hair growth, with overall promising results and minimal side effects.

Two RCTs investigated the use of the HairMax LaserComb, which utilizes wavelengths between 635 and 655 nm, compared to a sham device on the change in terminal hair density after 6 months of thrice weekly use (118,120). Both studies, including a total of 339 patients with AGA, demonstrated a statistically significant increase in terminal hair density in the intervention compared to the control groups. One pilot study (124) and three RCTs (119,121,122) investigated a LLLT scalp helmet for hair growth. The pilot study showed a statistically significant increase in hair counts after 6 months of daily use of the X5 HairLaser, a precision instrument utilizing cold beam LLLT, in 48 patients with AGA (124). Two of the three RCTs including a total of 68 patients with AGA demonstrated a significant increase in hair density after 16 (119) and 24 weeks (122) of every other day use of the LLLT helmet. However, a split-scalp RCT by Ferrara et al. (2021) of 19 men with AGA found no difference in terminal or vellus hair counts between treated (cap-shaped photobiomodulation turned on) and untreated (cap-shaped photobiomodulation turned off) scalp after 6 months of daily use (121). Finally, and most recently, Choi et al. (2022) investigated the benefits of combined photobiomodulation therapy with pulsed electromagnetic therapy in a RCT of 80 patients. Compared to the control group, which was exposed to a sham machine, those individuals receiving photobiomodulation with pulsed electromagnetic therapy demonstrated a statistically significant increase in hair density after 24 weeks (123). Overall, LLLT may serve as a promising adjunctive therapy for hair loss among dedicated patients. The main limiting factor is the high cost of these devices.

Fractionated laser therapy

Fractionated laser therapy is thought to promote hair growth by two postulated mechanisms. First, microscopic injuries to the epidermis may elicit a favorable wound healing environment that promotes hair growth. Secondly, disruption of the stratum corneum may enhance delivery of hair growth-promoting topical formulations down to the level of the hair follicle. We identified four studies utilizing fractionated laser devices for the promotion of hair growth either alone (125) or in combination with topical hair growth formulations (126–128). In a prospective study, 47 men and women with AGA received 10 treatment sessions with the 1540 nm fractional erbium-glass (Er:Glass) laser at 2-week intervals. The authors demonstrated a significant increase in hair count and density five months following the last laser session, with side effects of resolving erythema and burning (125). Furthermore, when compared to topical minoxidil alone, treatment with the Er:Glass laser followed by minoxidil application significantly improved both hair density and diameter among 29 men in a split-scalp study design (128). Similarly, fractionated CO_2 laser followed by growth factor application resulted in increased hair density compared to the application of growth factor alone. In a split-scalp study design, Huang et al. (2017) randomized 27 men with AGA to 6 sessions of fractionated, ablative CO2 at 2-week intervals to one side of the scalp, followed by growth factor serum applied to the entire scalp. They demonstrated both increased hair density and greater overall improvement (as determined by the global assessment score) in the scalp treated with laser and serum (127). These results support the belief that fractionated laser technology increases the delivery of topical agents by creating microchannels in the epidermis. Finally, when compared to fractionated laser alone, addition of topical growth factors yielded improved outcomes. In a split-scalp RCT, 10 patients received 12 sessions of fractionated 1927 nm thulium laser to their entire scalp at one-week intervals, with growth factor solution applied to half the scalp. Significant increases in hair density and thickness were seen on both sides of the scalp with greatest improvements seen on scalp treated with thulium laser followed by growth factor serum (126). The use of fractionated laser therapy alone or to improve drug delivery has proven successful in promoting hair growth. These procedures, however, are both painful, requiring downtime, and costly, which may limit their use in daily clinical practice.

Drug delivery devices

Like the use of fractionated lasers to increase drug delivery of hair growth-promoting topical agents, other drug-delivery devices have been developed and studied with the intention of promoting transdermal absorption of medications, including minoxidil and growth factor serums. For instance, two prospective trials compared the use of topical minoxidil alone, microneedling alone, and the combination of microneedling with topical minoxidil over a six-month study period. Investigators demonstrated that combination treatment is clinically superior to monotherapy (129,130). Furthermore, the authors found that combination treatment resulted in an upregulation of proteins known to promote hair growth, including beta-catenin (129). Similarly, Gong et al. (2017) compared topical 5% minoxidil alone, 12 sessions of pressurized and accelerated transdermal delivery (using JetPeel technology) of 5% minoxidil weekly, and no treatment in 30 patients with AGA. The greatest increase in hair count and diameter was seen among those who received the JetPeel-assisted delivery of topical minoxidil (131). Furthermore, a RCT of 40 males with AGA found that daily minoxidil use combined with weekly microneedling procedures followed by the application of fibroblast growth factors yielded increased hair density when compared to both the use of minoxidil alone and to microneedling followed by fibroblast growth factor serum alone (132). Finally, a small pilot study demonstrated the efficacy of microneedling alone, reporting that three sessions of microneedling completely or partially halted hair loss in 50 individuals with AGA or telogen effluvium (133). These results demonstrate the efficacy of drug-delivery devices. Similar to the use of fractionated lasers, however, these procedures require access to medical resources, time, and money, which may not be available to all patients.

Hair transplantation surgery

Hair restoration surgery has significantly evolved since its initial description nearly a century ago. Originating in Japan in the 1930s, Okuda was the first physician to detail the technique of autologous hair transplantation, using large, circular punches to harvest grafts from hair bearing scalps (134,135). Hair transplantation, however, was not popularized until the 1950s when Orentreich published an article written in English describing the use of 4-mm punch grafts (136). The latter half of the 20th century marked further development in hair restoration surgery, with the use of follicular unit transplantation (FUT), also known as strip harvesting FUT, followed by the use of follicular unit extraction (FUE), which directly removes individual follicular units from donor scalp. Today, FUE has surpassed strip harvesting FUT to become the most used donor harvesting technique, yielding improved cosmetic outcomes at both the donor and recipient sites (135,137).

In 2021, nearly 150,000 hair transplants were performed in North America, primarily for AGA. This rising demand has spurred investigations seeking ways to improve graft survival. We identified three studies, including a total of 197 patients with AGA, demonstrating the superiority of hair transplantation combined with PRP to hair transplant alone (138–140). Specifically, these studies found that the use of PRP during and following hair transplantation procedures led to greater hair density (138–140), reduced catagen loss of transplanted hair (138–140), longer follicles (139), and faster healing (139,140). Finasteride has also been found to improve graft survival. For instance, in a RCT of 79 men with AGA, those randomized to receive finasteride 1 mg daily for 1 year surrounding their procedure had increased hair counts at week 48 compared to those receiving placebo (141). Finally, hyperbaric oxygen therapy has also shown promise. Decreased itching, folliculitis, and postoperative shedding was appreciated among men randomized to receive FUE with 1 week of daily hyperbaric oxygen therapy via facemask, compared to FUE alone (142). On the other hand, studies have failed to demonstrate improved graft survival when using intraoperative hydrogen peroxide compared to normal saline for wound care (143) or when de-epithelizing follicular units prior to implantation (144).

Several studies have also focused on the intraoperative storage of follicular grafts. Three studies found an increased hair density (145–147), a greater proportion of grafts in anagen phase (146), and greater improvements in skin recovery (147) among those follicular grafts stored in autologous PRP compared to saline. Two studies also demonstrated enhanced graft survival with the use of a hypothermic preservative media, called HypoThermosol, compared to saline (148,149). Furthermore, the addition adenosine triphosphate (ATP) to preservative media has also shown positive results. Decreased postsurgical shedding was appreciated when ATP was added to histidine-tryptophan-ketoglutarate solution (150) and enhanced graft survival was seen when ATP was added to HypoThermosol (148,149). In vitro studies speculate the addition of ATP leads to decreased Bcl-2 expression, thereby increasing antiapoptotic activity within follicular grafts (151).

Overall, studies have demonstrated high graft survival rates ranging from 85% to 93% (152–154), as well as very patient high satisfaction rates following hair restoration surgery (155,156). According to the International Society for Hair Restoration Surgery, bioengineering hair follicles with the use of hair cloning and stem cells are posed to be the next great leap in hair restoration (157). Until then, current hair transplantation practices produce excellent cosmetic outcomes. The high associated costs, however, may limit its widespread adaptability.

Other topical agents

A variety of other topical agents have been studied for the potential treatment of hair loss. Compared to placebo, latanoprost 0.1% (158), tretinoin 0.025% (159), and 8.3% valproic acid spray (160) proved efficacious in increasing hair counts and density, while 1% ceramide lotion (161), fulvestrant (162), and visprostol (163) did not. Furthermore, a small pilot study compared topical cyclosporine to olive oil, failing to demonstrate promising results for either agent (164).

We also identified four studies investigating the use of topical adenosine. While the exact mechanism has not yet been fully elucidated, prior reports have demonstrated the ability of adenosine to stimulate the expression of fibroblast growth factor and Wnt/B-catenin in dermal papilla

cells, thereby activating HFSCs and maintaining anagen phase (165). Three articles compared the efficacy of topical adenosine to placebo among 170 individuals with AGA, finding increases in hair density, hair thickness, and proportion of hairs in anagen phase (165–167). Topical adenosine, however, was not superior to 5% topical minoxidil (168).

Finally, we found two studies examining topical cetirizine for hair loss. Mainly known for its inhibitory effects on the histamine H1 receptor, cetirizine also promotes expression of PGE2 and inhibits PGD2, key components of the hair loss pathway. The benefits of topical cetirizine were demonstrated in a small pilot study, which found significant increases in hair density following 6 months of daily application (169). When compared to topical 5% minoxidil, however, cetirizine was inferior (170). While many topical agents have been trialed for the management of hair loss, none have proven to be superior to the FDA-approved therapeutic, topical minoxidil.

Other interventions

Several other modalities have been investigated for hair growth, including ultraviolet B (UVB) light, psoralen ultraviolet A (PUVA), and photodynamic therapy (PDT). Previous reports have demonstrated PDT's ability to promote hair follicle proliferation and induce hair growth during telogen phase in mice (171). However, a small, split-scalp RCT comparing 6 sessions of ALA-PDT to red-light therapy alone, found no difference in hair density between the two interventions (172). Furthermore, a split-scalp study of 9 males with AGA compared daily topical minoxidil alone to topical minoxidil in conjunction with twice weekly UVB or PUVA. Investigators found that the addition of UVB or PUVA did not have a synergistic effect on topical minoxidil-induced hair growth (173). Additional studies are needed to explore the role of these modalities in hair growth.

Discussion

Hair loss is a complex, multifactorial condition that holds the potential to significantly impact quality of life. While topical minoxidil (for men and women) and finasteride (for men) remain the only FDA-approved therapeutics, several other oral, topical, and procedural options exist. This literature review summarizes the key findings of 141 studies, demonstrating the greatest efficacy for those agents investigated using randomized study designs with objective hair growth parameters including hair count, density, and diameter.

Among OTC treatments, topical minoxidil is the mainstay of therapy due to its proven effectiveness, low cost, ease of accessibility, and tolerable side effect profile. Many OTC supplements have similarly proven to be beneficial as complementary treatments. These supplements are not FDA-approved; and, therefore, patients should be cautious when purchasing oral formulations as the efficacy and safety of these products may be variable. Additionally, LLLT has shown promise as a potential adjunctive treatment. These devices can be purchased online; however, they tend to be costly and regular compliance may pose a challenge for some individuals. With respect to prescription medications, oral minoxidil, finasteride, and dutasteride appear to have the highest efficacy in treating hair loss across studies. Interestingly, dutasteride may be more effective than finasteride in regrowing hair and reducing hair loss. Further, the longer half-life of dutasteride also allows for every other day or every third day dosing, thereby minimizing the side effect profile without compromising clinical efficacy. Ketoconazole shampoo is well-tolerated and inexpensive, making it an easy adjunctive therapy for patients desiring a combination treatment approach. Finally, PRP, both with and without hair restoration surgery, appears to be the most promising procedural treatment, stimulating long-lasting hair growth and enhancing overall scalp health. Use of fractionated lasers, other drug-delivery devices, and hair restoration surgery have also shown benefit. These procedural treatments, however, are not covered by insurance, can be very costly, and are oftentimes associated with pain and discomfort. In clinical practice, the ideal treatment approach should be both multifaceted and individualized, considering the degree of hair loss, patient preferences, associated costs, and comorbid conditions. Future clinical trials with sufficient sample sizes, adequate follow-up time, and standardized outcomes are necessary to better delineate the efficacy and safety of various therapeutics, alone and in combination. Finally, because AGA is a chronic condition, follow-up studies evaluating the sustainability of hair regrowth following treatment discontinuation are warranted.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

1. Salman KE, Altunay IK, Kucukunal NA, Cerman AA. Frequency, severity and related factors of androgenetic alopecia in dermatology outpatient clinic: hospital-based cross-sectional study in Turkey. An Bras Dermatol. 2017;92(1):35–40. doi:10.1590/abd1806-4841.20175241.
2. Rahmani W, Abbasi S, Hagner A, Raharjo E, Kumar R, Hotta A, Magness S, Metzger D, Biernaskie J. Hair follicle dermal stem cells regenerate the dermal sheath, repopulate the dermal papilla, and modulate hair type. Dev Cell. 2014;31(5):543–58. doi:10.1016/j.devcel.2014.10.022.
3. Gentile P, Garcovich S. Advances in regenerative stem cell therapy in androgenic alopecia and hair loss: wnt Pathway, growth-factor, and mesenchymal stem cell signaling impact analysis on cell growth and hair follicle development. Cells. 2019;8(5):466. doi:10.3390/cells8050466.
4. Wang E, de Berker D. Biology of Hair and Nails. Bologna. 2018;68:1144–61.
5. Balañá ME. Epidermal stem cells and skin tissue engineering in hair follicle regeneration. World J Stem Cells. 2015;7(4):711. doi:10.4252/wjsc.v7.i4.711.

6. Hillmer AM, Hanneken S, Ritzmann S, Becker T, Freudenberg J, Brockschmidt FF, Flaquer A, Freudenberg-Hua Y, Jamra RA, Metzen C, et al. Genetic variation in the human androgen receptor gene is the major determinant of common early-onset androgenetic alopecia. Am J Hum Genet. 2005;77(1):140–48. doi:10.1086/431425.
7. "Proscar. Merck.Com. [10 June 2020]. www.merck.com/research/proscar/.
8. Kato H, Kinoshita K, Saito N, Kanayama K, Mori M, Asahi N, Sunaga A, Yoshizato K, Itami S, Yoshimura K, et al. The effects of ischemia and hyperoxygenation on hair growth and cycle. Organogenesis. 2020;16(3):83–94. doi:10.1080/15476278.2020.1794271.
9. Fan Z, Gan Y, Qu Q, Wang J, Lunan Y, Liu B, Chen R, Hu Z-Q, Miao Y. The effect of hyperbaric oxygen therapy combined with hair transplantation surgery for the treatment of Alopecia. J Cosmet Dermatol. 2020;20(3):917–21. doi:10.1111/jocd.13665.
10. Dong X, Jin X. The effect of hyperbaric oxygen therapy combined with hair transplantation surgery for the treatment of Alopecia. J Cosmet Dermatol. 2021;21(2):857–58. doi:10.1111/jocd.14131.
11. Goldman BE, Fisher DM, Ringler SL. Transcutaneous po2 of the scalp in male pattern baldness: a new piece to the puzzle. Plast Reconstr Surg. 1996;97(6):1109–16. doi:10.1097/00006534-199605000-00003.
12. Naito A, Midorikawa T, Yoshino T, Ohdera M. Lipid peroxides induce early onset of catagen phase in murine hair cycles. Int J Mol Med. 2008;22(6):725–29. doi:10.3892/ijmm_00000078.
13. Upton JH, Hannen RF, Bahta AW, Farjo N, Farjo B, Philpott MP. Oxidative stress–associated senescence in dermal papilla cells of men with Androgenetic Alopecia. J Invest Dermatol. 2015;135(5):1244–52. doi:10.1038/jid.2015.28.
14. Garza LA, Liu Y, Yang Z, Alagesan B, Lawson JA, Norberg SM, Loy DE, Zhao T, Blatt HB, Stanton DC, et al. Prostaglandin D2 inhibits hair growth and is elevated in bald scalp of men with Androgenetic Alopecia. Sci Transl Med. 2012;4(126). doi:10.1126/scitranslmed.3003122.
15. Trüeb RM. Association between smoking and hair loss: another opportunity for health education against smoking? Dermatology. 2003;206(3):189–91. doi:10.1159/000068894. PMID: 12673073.
16. Camacho F. Telogen alopecia from UV rays. Arch Dermatol. 1996;132(11):1398–99. doi:10.1001/archderm.132.11.1398.
17. Trüeb RM. Is androgenetic alopecia a photoaggravated dermatosis? Dermatology. 2003;207(4):343–48. doi:10.1159/000074111.
18. Trüeb RM. Oxidative stress in ageing of hair. Int J Trichol. 2009 Jan;1(1):6–14. doi:10.4103/0974-7753.51923. PMID: 20805969; PMCID: PMC2929555.
19. Seo J-A, Bae I-H, Jang W-H, Kim J-H, Bak S-Y, Han S-H, Park Y-H, Lim K-M. Hydrogen peroxide and monoethanolamine are the key causative ingredients for hair dye-induced dermatitis and hair loss. J Dermatol Sci. 2012;66(1):12–19. doi:10.1016/j.jdermsci.2011.12.015.
20. Ohn J, Kim SJ, Choi S-J, Choe YS, Kwon O, Kim KH. Hydrogen peroxide (H2O2) suppresses hair growth through downregulation of β-catenin. J Dermatol Sci. 2018;8(1):91–94. doi:10.1016/j.jdermsci.2017.09.003.
21. Karam P. Topical minoxidil therapy for androgenic alopecia in the Middle East. Int J Dermatol. 1993;32(10):763–66. doi:10.1111/j.1365-4362.1993.tb02756.x.
22. Jacobs JP, Szpunar CA, Warner ML. Use of topical MINOXIDIL therapy for androgenetic alopecia in women. Int J Dermatol. 1993;32(10):758–62. doi:10.1111/j.1365-4362.1993.tb02755.x.
23. Tsuboi R, Tanaka T, Nishikawa T, Ueki R, Yamada H, Katsuoka K, Ogawa H, Takeda K. A randomized, placebo-controlled trial of 1% topical minoxidil solution in the treatment of androgenetic alopecia in Japanese women. Eur J Dermatol. 2007;17(1):37–44. doi:10.1684/ejd.2007.0187.
24. Rushton DH, Unger WP, Cotterill PC, Kingsley P, James KC. Quantitative assessment of 2% topical minoxidil in the treatment of male pattern baldness. Clin Exp Dermatol. 1989;14(1):40–46. doi:10.1111/j.1365-2230.1989.tb00881.x.
25. Whiting DA, Jacobson C. Treatment of female androgenetic alopecia with minoxidil 2%. Int J Dermatol. 1992;31(11):800–04. doi:10.1111/j.1365-4362.1992.tb04251.x.
26. Hillmann K, Garcia Bartels N, Kottner J, Stroux A, Canfield D, Blume-Peytavi U. A single-centre, randomized, double-blind, placebo-controlled clinical trial to investigate the efficacy and safety of minoxidil topical foam in frontotemporal and vertex androgenetic alopecia in men. Skin Pharmacol Physiol. 2015;28(5):236–44. doi:10.1159/000375320.
27. Blume-Peytavi U, Issiakhem Z, Gautier S, Kottner J, Wigger-Alberti W, Fischer T, Hoffmann R, Tonner F, Bouroubi A, Voisard J-J, et al. Efficacy and safety of a new 5% minoxidil formulation in male androgenetic alopecia: a randomized, placebo-controlled, double-blind, Noninferiority Study. J Cosmet Dermatol. 2019;18(1):215–20. doi:10.1111/jocd.12541.
28. Rietschel RL, Duncan SH. Safety and efficacy of topical minoxidil in the management of Androgenetic Alopecia. J Am Acad Dermatol. 1987;16(3):677–85. doi:10.1016/s0190-9622(87)70087-5.
29. Savin RC. Use of topical minoxidil in the treatment of male pattern baldness. J Am Acad Dermatol. 1987;16(3):696–704. doi:10.1016/s0190-9622(87)70090-5.
30. Koperski JA. Topical minoxidil therapy for androgenetic alopecia. a 30-month study. Arch Dermatol. 1987;123(11):1483–87. doi:10.1001/archderm.1987.01660350083018.
31. Tsuboi R, Arano O, Nishikawa T, Yamada H, Katsuoka K. Randomized clinical trial comparing 5% and 1% topical minoxidil for the treatment of androgenetic alopecia in Japanese men. J Dermatol. 2009;36(8):437–46. doi:10.1111/j.1346-8138.2009.00673.x.
32. Price VH, Menefee E, Strauss PC. Changes in hair weight and hair count in men with androgenetic alopecia, after application of 5% and 2% topical minoxidil, placebo, or no treatment. J Am Acad Dermatol. 1999;41(5):717–21. doi:10.1016/s0190-9622(99)70006-x.
33. Olsen EA, Dunlap FE, Funicella T, Koperski JA, Swinehart JM, Tschen EH, Trancik RJ. A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men. J Am Acad Dermatol. 2002;47(3):377–85. doi:10.1067/mjd.2002.124088.
34. Lucky AW, Piacquadio DJ, Ditre CM, Dunlap F, Kantor I, Pandya AG, Savin RC, Tharp MD. A randomized, placebo-controlled trial of 5% and 2% topical minoxidil solutions in the treatment of female pattern hair loss. J Am Acad Dermatol. 2004;50(4):541–53. doi:10.1016/j.jaad.2003.06.014.
35. Blume-Peytavi U, Hillmann K, Dietz E, Canfield D, Garcia Bartels N. A randomized, single-blind trial of 5% minoxidil foam once daily versus 2% minoxidil solution twice daily in the treatment of androgenetic alopecia in women. J Am Acad Dermatol. 2011;65(6):1126–34.e2. doi:10.1016/j.jaad.2010.09.724.
36. Ghonemy S, Alarawi A, Bessar H. Efficacy and safety of a new 10% topical minoxidil versus 5% topical minoxidil and placebo in the treatment of male androgenetic alopecia: a trichoscopic evaluation. J Dermatolog Treat. 2021;32(2):236–41. doi:10.1080/09546634.2019.1654070.
37. Piepkorn MW, Weidner M. Comparable efficacy of 2% minoxidil gel and solution formulations in the treatment of male pattern alopecia. J Am Acad Dermatol. 1988;18(5):1059–62. doi:10.1016/s0190-9622(88)70105-x.
38. Shin HS, Won CH, Lee SH, Kwon OS, Kim KH, Eun HC. Efficacy of 5% minoxidil versus combined 5% minoxidil and 0.01% tretinoin for male pattern hair loss. Am J Clin Dermatol. 2007;8(5):285–90. doi:10.2165/00128071-200708050-00003.
39. Berger RS, Fu JL, Smiles KA, Turner CB, Schnell BM, Werchowski KM, Lammers KM. The effects of minoxidil, 1% pyrithione zinc and a combination of both on hair density: a randomized controlled trial. Br J Dermatol. 2003;149(2):354–62. doi:10.1046/j.1365-2133.2003.05435.x.
40. Suchonwanit P, Srisuwanwattana P, Chalermroj N, Khunkhet S. A randomized, double-blind controlled study of the efficacy and

safety of topical solution of 0.25% finasteride admixed with 3% minoxidil vs. 3% minoxidil solution in the treatment of male androgenetic alopecia. J Eur Acad Dermatol Venereol. 2018;32 (12):2257–63. doi:10.1111/jdv.15171.
41. Suchonwanit P, Iamsumang W, Rojhirunsakool S. Efficacy of topical combination of 0.25% finasteride and 3% minoxidil versus 3% minoxidil solution in female pattern hair loss: a randomized, double-blind, controlled study. Am J Clin Dermatol. 2019;20 (1):147–53. doi:10.1007/s40257-018-0387-0.
42. Dhurat R, Daruwalla S, Pai S, Kovacevic M, McCoy J, Shapiro J, Sinclair R, Vano-Galvan S, Goren A. Sult1a1 (minoxidil sulfotransferase) enzyme booster significantly improves response to topical minoxidil for hair regrowth. J Cosmet Dermatol. 2022;21 (1):343–46. doi:10.1111/jocd.14299.
43. Farouk Sakr F, Gado A, Mohammed H, Ismail AA. Preparation and evaluation of a multimodal minoxidil microemulsion versus minoxidil alone in the treatment of androgenic alopecia of mixed etiology: A pilot study. Drug Des Devel Ther. Published online 2013:2013:413. doi:10.2147/dddt.s43481.
44. Goodwin Cartwright BM, Wang M, Rodriguez P, Stewart S, Worsham CM, Stucky N, Jena AB. Changes in minoxidil prescribing after media attention about oral use for hair loss. JAMA Netw Open. 2023;6(5):e2312477. doi:10.1001/jamanetworkopen.2023.12477.
45. Vañó-Galván S, Pirmez R, Hermosa-Gelbard A, Moreno-Arrones ÓM, Saceda-Corralo D, Rodrigues-Barata R, Jimenez-Cauhe J, Koh WL, Poa JE, Jerjen R, et al. Safety of low-dose oral minoxidil for hair loss: a multicenter study of 1404 patients. J Am Acad Dermatol. 2021;84(6):1644–51. doi:10.1016/j.jaad.2021.02.054.
46. Klein EJ, Karim M, Shapiro J, Sicco KL. Comparing combination low-dose oral minoxidil and topical minoxidil with oral minoxidil alone for the treatment of non-scarring alopecia: a Retrospective Chart Review. J Cosmet Dermatol. 2022;21(11):6473–75. doi:10.1111/jocd.15138.
47. Vahabi-Amlashi S, Layegh P, Kiafar B, Hoseininezhad M, Abbaspour M, Khaniki SH, Forouzanfar M, Sabeti V. A randomized clinical trial on therapeutic effects of 0.25 mg oral minoxidil tablets on treatment of female pattern hair loss. Dermatol Ther. 2021;34(6). doi:10.1111/dth.15131.
48. Ramos PM, Sinclair RD, Kasprzak M, Miot HA. Minoxidil 1 mg oral versus minoxidil 5% topical solution for the treatment of female-pattern hair loss: a randomized clinical trial. J Am Acad Dermatol. 2020;82(1):252–53. doi:10.1016/j.jaad.2019.08.060.
49. Sinclair RD. Female pattern hair loss: A pilot study investigating combination therapy with low-dose oral minoxidil and spironolactone. Int J Dermatol. 2018;57(1):104–09. doi:10.1111/ijd.13838 .
50. Pirmez R, Salas-Callo C-I. Very-low-dose oral minoxidil in male androgenetic alopecia: a study with quantitative trichoscopic documentation. J Am Acad Dermatol. 2020;82(1):e21–22. doi:10.1016/j.jaad.2019.08.084.
51. Panchaprateep R, Lueangarun S. Efficacy and safety of oral minoxidil 5 mg once daily in the treatment of male patients with Androgenetic Alopecia: an open-label and global photographic assessment. Dermatol Ther (Heidelb). 2020;10(6):1345–57. doi:10.1007/s13555-020-00448-x.
52. E Silva MN, Ramos PM, Silva MR, E Silva RN, Barbosa RN. Randomized clinical trial of low-dose oral minoxidil for the treatment of female pattern hair loss: 0.25 mg versus 1 mg. J Am Acad Dermatol. 2022;87(2):396–99. doi:10.1016/j.jaad.2022.01.017.
53. Jimenez-Cauhe J, Saceda-Corralo D, Rodrigues-Barata R, et al. Effectiveness and safety of low-dose oral minoxidil in male androgenetic alopecia. J Am Acad Dermatol. 2019;81(2):648–49. doi:10.1016/j.jaad.2019.04.054.
54. Lueangarun S, Panchaprateep R, Tempark T, Noppakun N. Efficacy and safety of Oral Minoxidil 5 mg daily during 24-week treatment in male androgenetic alopecia. J Am Acad Dermatol. 2015;72(5). doi:10.1016/j.jaad.2015.02.466.
55. Sato A, Takeda A. Evaluation of efficacy and safety of finasteride 1 mg in 3177 Japanese men with Androgenetic Alopecia. J Dermatol. 2012;39(1):27–32. doi:10.1111/j.1346-8138.2011.01378.x.
56. Piraccini BM, Blume-Peytavi U, Scarci F, Jansat JM, Falqués M, Otero R, Tamarit ML, Galván J, Tebbs V, Massana E, et al. Efficacy and safety of topical finasteride spray solution for male androgenetic alopecia: a phase III, randomized, controlled clinical trial. J Eur Acad Dermatol Venereol. 2022;36(2):286–94. doi:10.1111/jdv.17738.
57. Kaufman KD, Olsen EA, Whiting D, Savin R, DeVillez R, Bergfeld W, Price VH, Van Neste D, Roberts JL, Hordinsky M, et al. Finasteride in the treatment of men with Androgenetic Alopecia. J Am Acad Dermatol. 1998;39(4):578–89. doi:10.1016/s0190-9622(98)70007-6.
58. Gillespie JDN, Finasteride Male Pattern Hair Loss Study Group. Long-term (5-year) multinational experience with finasteride 1 mg in the treatment of men with androgenetic alopecia. Eur J Dermatol. 2002 Jan-Feb;12(3):38–49. doi:10.33589/12.3.0129.
59. Price VH, Menefee E, Sanchez M, Ruane P, Kaufman KD. Changes in hair weight and hair count in men with androgenetic alopecia after treatment with finasteride, 1 mg, daily. J Am Acad Dermatol. 2002;46(4):517–23. doi:10.1067/mjd.2002.120537.
60. Price VH, Menefee E, Sanchez M, Kaufman KD. Changes in hair weight in men with androgenetic alopecia after treatment with finasteride (1 MG Daily): three- and 4-year results. J Am Acad Dermatol. 2006;55(1):71–74. doi:10.1016/j.jaad.2005.07.001.
61. Whiting DA, Olsen EA, Savin R, Halper L, Rodgers A, Wang L, Hustad C, Palmisano J, Male Pattern Hair Loss Study Group. Efficacy and tolerability of finasteride 1 mg in men aged 41 to 60 years with male pattern hair loss. Eur J Dermatol. 2003;13 (2):150–60.
62. Van Neste D. Placebo-controlled dose-effect studies with topical minoxidil 2% or 5% in male-patterned hair loss treated with oral finasteride employing an analytical and exhaustive study protocol. Skin Res Technol. 2020;26(4):542–57. doi:10.1111/srt.12827.
63. Tsunemi Y, Irisawa R, Yoshiie H, Brotherton B, Ito H, Tsuboi R, Kawashima M, Manyak M. Long-term safety and efficacy of dutasteride in the treatment of male patients with Androgenetic Alopecia. J Dermatol. 2016;43(9):1051–58. doi:10.1111/1346-8138.13310.
64. Eun HC, Kwon OS, Yeon JH, Shin HS, Kim BY, Ro BI, Cho HK, Sim WY, Lew BL, Lee W-S, et al. Efficacy, safety, and tolerability of dutasteride 0.5 mg once daily in male patients with male pattern hair loss: a randomized, double-blind, placebo-controlled, phase III study. J Am Acad Dermatol. 2010;63(2):252–58. doi:10.1016/j.jaad.2009.09.018.
65. Olsen EA, Hordinsky M, Whiting D, Stough D, Hobbs S, Ellis ML, Wilson T, Rittmaster RS. The importance of dual 5α-reductase inhibition in the treatment of male pattern hair loss: results of a randomized placebo-controlled study of dutasteride versus Finasteride. J Am Acad Dermatol. 2006;55(6):1014–23. doi:10.1016/j.jaad.2006.05.007.
66. Gubelin Harcha W, Barboza Martínez J, Tsai T-F, Katsuoka K, Kawashima M, Tsuboi R, Barnes A, Ferron-Brady G, Chetty D. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the treatment of male subjects with Androgenetic Alopecia. J Am Acad Dermatol. 2014;70(3):489–98.e3. doi:10.1016/j.jaad.2013.10.049.
67. Shanshanwal Sujit JS, Dhurat R. Superiority of dutasteride over finasteride in hair regrowth and reversal of miniaturization in men with androgenetic alopecia: A randomized controlled open-label, evaluator-blinded study. Indian J Dermatol Venereol Leprol. 2017;83(1):47. doi:10.4103/0378-6323.188652.
68. Sinclair R, Wewerinke M, Jolley D. Treatment of female pattern hair loss with oral antiandrogens. Br J Dermatol. 2005;152 (3):466–73. doi:10.1111/j.1365-2133.2005.06218.x.
69. Van der Willigen A, Peereboom-Wynia JD, Van Joost T, Stolz E. A preliminary study of the effect of 11a-hydroxyprogesterone on the hair growth in men suffering from Androgenetic Alopecia.

Acta Derm Venereol. 1987;67(1):82–85. doi:10.2340/00015555678285.
70. Blume-Peytavi U, Kunte C, Krisp A, Bartels NG, Ellwanger U, Hoffmann R. Comparison of the efficacy and safety of topical minoxidil and topical alfatradiol in the treatment of androgenetic alopecia in women. JDDG. 2007;5(5):391–95. doi:10.1111/j.1610-0387.2007.06295.x.
71. Inui S, Itami S. Reversal of androgenetic alopecia by topical ketoconazole: relevance of antiandrogenic activity. J Dermatol Sci. 2007;45(1):66–68. doi:10.1016/j.jdermsci.2006.08.011.
72. Pierard-Franchimont C, De Doncker P, Cauwenbergh G, Pierard GE. Ketoconazole shampoo: effect of long-term use in androgenic alopecia. Dermatology. 1998;196(4):474–77. doi:10.1159/000017954.
73. Khandpur S, Suman M, Reddy BS. Comparative efficacy of various treatment regimens for androgenetic alopecia in men. J Dermatol. 2002;29(8):489–98. doi:10.1111/j.1346-8138.2002.tb00314.x.
74. Choi J-S, Park JB, Moon W-S, Moon J-N, Son SW, Kim M-R. Safety and efficacy of rice bran supercritical CO2 extract for hair growth in androgenic alopecia: a 16-week double-blind randomized controlled trial. Biol Pharm Bull. 2015;38(12):1856–63. doi:10.1248/bpb.b15-00387.
75. Rossi A, Mari E, Scarnò M, Garelli V, Maxia C, Scali E, Iorio A, Carlesimo M. Comparitive effectiveness and finasteride vs serenoa repens in male androgenetic alopecia: a two-year study. Int J Immunopathol Pharmacol. 2012;25(4):1167–73. doi:10.1177/039463201202500435.
76. Ablon G, Six-Month KSA. A six-month, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of a nutraceutical supplement for promoting hair growth in women with self-perceived thinning hair. J Drugs Dermatol. 2018;17(5):558–65.
77. Ablon G, Berkowitz S, Kogan S, Raymond I. Long-term efficacy of a nutraceutical supplement for promoting hair growth in perimenopausal, menopausal and postmenopausal women with self-perceived thinning hair. SKIN The J Cutaneous Med. 2021;5(6):s90. doi:10.25251/skin.5.supp.90.
78. Kessels AGH, Cardynaals RLLM, Borger RLL, Go MJTH, Lambers JCCA, Knottnerus JA, Knipschild PG. The effectiveness of the hair-restorer "Dabao" in males with alopecia androgenetica. A clinical experiment. J Clin Epidemiol. 1991;44(4–5):439–47. doi:10.1016/0895-4356(91)90083-l.
79. Milani M, Colombo F. Efficacy and tolerability of an oral supplement containing amino acids, iron, selenium, and marine hydrolyzed collagen in subjects with hair loss (androgenetic alopecia, AGA or Faga or telogen effluvium). A prospective, randomized, 3-month, controlled, assessor-blinded study. Skin Res Technol. 2023;29(6). doi:10.1111/srt.13381.
80. Davis MG, Piliang MP, Bergfeld WF, et al. Scalp application of antioxidants improves scalp condition and reduces hair shedding in a 24-week randomized, double-blind, placebo-controlled clinical trial. Int J Cosmet Sci. 2021;43(S1). doi:10.1111/ics.12734.
81. Davis MG, Piliang MP, Bergfeld WF. Scalp application of the antioxidant piroctone Olamine reduces hair shedding in an 8-week randomized, double-blind, placebo-controlled clinical study. Int J Cosmet Sci. 2021;43(S1). doi:10.1111/ics.12737.
82. Anzai A, Pereira AF, Malaquias KR, Guerra LO, Mercuri M. Efficacy and safety of a new formulation kit (shampoo + lotion) containing anti-inflammatory and antioxidant agents to treat hair loss. Dermatol Ther. 2020;33(3). doi:10.1111/dth.13293.
83. Bureau JP, Ginouves P, Guilbaud J, Roux ME. Essential oils and low-intensity electromagnetic pulses in the treatment of androgen-dependent alopecia. Adv Ther. 2003;20(4):220–29. doi:10.1007/bf02850093.
84. Clinic A, Asper A, Mittal A, Shome D, Parbhoo D, Thanzama J, Doshi K, Sachde N, Gaunkar R, Kapoor R, et al. Evaluation of the safety and effectiveness of intradermal administration of QR678 Neo ® hair growth factor formulation: a phase-IV, open-label, single-arm multi-ethnicity clinical trial. J Cosmet Dermatol. 2022;21(2):580–89. doi:10.1111/jocd.14715.
85. Welzel J, Wolff HH, Gehring W. Reduction of telogen rate and increase of hair density in androgenetic alopecia by a cosmetic product: results of a randomized, prospective, vehicle-controlled double-blind study in men. J Cosmet Dermatol. 2022;21(3):1057–64. doi:10.1111/jocd.14158.
86. Alonso MR, Anesini C. Clinical evidence of increase in hair growth and decrease in hair loss without adverse reactions promoted by the commercial lotion ECOHAIR®. Skin Pharmacol Physiol. 2017;30(1):46–54. doi:10.1159/000455958.
87. Panahi Y, Taghizadeh M, Marzony ET, Sahebkar A. Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial. Skinmed. 2015;13(1):15–21.
88. Pumthong G, Asawanonda P, Varothai S, Jariyasethavong V, Triwongwaranat D, Suthipinittharm P, Ingkaninan K, Leelapornpisit P, Waranuch N. curcuma aeruginosa, a novel botanically derived 5α-reductase inhibitor in the treatment of male-pattern baldness: a multicenter, randomized, double-blind, placebo-controlled study. J Dermatol Treat. 2012;23(5):385–92. doi:10.3109/09546634.2011.568470.
89. Chew S, Gajjar T, Sethi S. Safety and efficacy of Trimax-360 serum in healthy adult subjects with mild to moderate alopecia of scalp. J Cosmet Dermatol. 2022;21(10):4536–44. doi:10.1111/jocd.14998.
90. Paichitrojjana A, Paichitrojjana A. Platelet rich plasma and its use in hair regrowth: a Review. Drug Des Devel Ther. 2022;16:635–45. doi:10.2147/dddt.s356858.
91. Gentile P, Garcovich S, Bielli A, Scioli MG, Orlandi A, Cervelli V. The effect of platelet-rich plasma in hair regrowth: a randomized placebo-controlled trial. Stem Cells Transl Med. 2015;4(11):1317–23. doi:10.5966/sctm.2015-0107.
92. Qu Q, Zhou Y, Shi P, Du L, Fan Z, Wang J, Li X, Chen J, Zhu D, Ye K, et al. Platelet-rich plasma for Androgenic Alopecia: a randomized, placebo-controlled, double-blind study and combined mice model experiment. J Cosmet Dermatol. 2021;20(10):3227–35. doi:10.1111/jocd.14089.
93. Qu Q, He Y, Guo Z, Sun Y, Fan Z-X, Yi Y-H, Zhu D-C, Hu Z-Q, Miao Y. Efficacy of platelet-rich plasma plus basic fibroblast growth factor on the treatment of androgenic alopecia. Plast Reconstr Surg. 2023;151(4):630e–40e. doi:10.1097/prs.0000000000010000.
94. Siah TW, Guo H, Chu T, Santos L, Nakamura H, Leung G, Shapiro J, McElwee KJ. Growth factor concentrations in platelet-rich plasma for Androgenetic Alopecia: an intra-subject, randomized, blinded, placebo-controlled, pilot study. Exp Dermatol. 2020;29(3):334–40. doi:10.1111/exd.14074.
95. Tawfik AA, Osman MA. The effect of autologous activated platelet-rich plasma injection on female pattern hair loss: a randomized placebo-controlled study. J Cosmet Dermatol. 2018;17(1):47–53. doi:10.1111/jocd.12357.
96. Rodrigues BL, Montalvão SAL, Cancela RBB, Silva FAR, Urban A, Huber SC, Júnior JLRC, Lana JFSD, Annichinno-Bizzacchi JM. Treatment of male pattern alopecia with platelet-rich plasma: a double-blind controlled study with analysis of platelet number and growth factor levels. J Am Acad Dermatol. 2019;80(3):694–700. doi:10.1016/j.jaad.2018.09.033.
97. Schiavone G, Raskovic D, Greco J, Abeni D. Platelet-rich plasma for Androgenetic Alopecia. Dermatol Surg. 2014;40(9):1010–19. doi:10.1097/01.dss.0000452629.76339.2b.
98. Gressenberger P, Pregartner G, Gary T, Wolf P, Kopera D. Platelet-rich plasma for androgenetic alopecia treatment: a randomized placebo-controlled pilot study. Acta Dermato Venereologica. 2020;100(15):adv00247. doi:10.2340/00015555-3609.
99. Gentile P, Garcovich S. Autologous activated platelet-rich plasma (AA-PRP) and non-activated (A-PRP) in hair growth: A retrospective, blinded, randomized evaluation in Androgenetic Alopecia. Expert Opin Biol Ther. 2020;20(3):327–37. doi:10.1080/14712598.2020.1724951.

100. Guan Q, Guo Z, Dai D, Fan Z-X, Chen J, Wu S-L, Liu X-M, Miao Y, Hu Z-Q, Qu Q, et al. Platelet lysate promotes hair growth: in vitro and in vivo mechanism and randomized, controlled trial. Biomed Pharmacother. 2023;161:114517.
101. El-Husseiny RM, Saleh HM, Moustafa AA, Salem SA. Comparison between single- versus double-spin prepared platelet-rich plasma injection in treatment of female pattern hair loss: clinical effect and relation to vascular endothelial growth factor. Arch Dermatol Res. 2020;313(7):557–66. doi:10.1007/s00403-020-02134-6.
102. Takikawa M, Nakamura S, Nakamura S, Ishirara M, Kishimoto S, Sasaki K, Yanagibayashi S, Azuma R, Yamamoto N, Kiyosawa T, et al. Enhanced effect of platelet-rich plasma containing a new carrier on hair growth. Dermatol Surg. 2011;37(12):1721–29. doi:10.1111/j.1524-4725.2011.02123.x.
103. Wu S, Liu S, Chen J, Dai D, Liu W, Le D, Guan Q, Miao Y, Hu Z, Qu Q, et al. Evaluation of platelet-rich plasma plus basic fibroblast growth factor combined with minoxidil in the treatment of androgenetic alopecia: a randomized controlled trial. J Cosmet Dermatol. 2023;22(7):1995–2002. doi:10.1111/jocd.15825.
104. Singh S, Kumar V, Rai T. Comparison of efficacy of platelet-rich plasma therapy with or without topical 5% minoxidil in male-type baldness: a randomized, double-blind placebo control trial. Indian J Dermatol Venereol Leprol. 2020;86(2):150. doi:10.4103/ijdvl.ijdvl_589_18.
105. Pakhomova EE, Smirnova IO. Comparative evaluation of the clinical efficacy of PRP-therapy, minoxidil, and their combination with immunohistochemical study of the dynamics of cell proliferation in the treatment of men with Androgenetic Alopecia. Int J Mol Sci. 2020;21(18):6516. doi:10.3390/ijms21186516.
106. James R, Chetry R, Subramanian V, Ashtekar A, Srikruthi N, Ramachandran S, Koka PS, Deb K. Platelet-rich plasma growth factor concentrated spray (Keratogrow®) as a potential treatment for androgenic alopecia. J Stem Cells. 2016;11(4):183–89.
107. Narita K, Fukuoka H, Sekiyama T, Suga H, Harii K. Sequential Scalp Assessment in hair regeneration therapy using an adipose-derived stem cell–conditioned medium. Dermatol Surg. 2020;46(6):819–25. doi:10.1097/dss.0000000000002128.
108. Tak YJ, Lee SY, Cho AR, Kim YS. A randomized, double-blind, vehicle-controlled clinical study of hair regeneration using adipose-derived stem cell constituent extract in androgenetic alopecia. Stem Cells Transl Med. 2020;9(8):839–49. doi:10.1002/sctm.19-0410.
109. Tsuboi R, Niiyama S, Irisawa R, Harada K, Nakazawa Y, Kishimoto J. Autologous cell–based therapy for male and female pattern hair loss using dermal sheath cup cells: a randomized placebo-controlled double-blinded dose-finding clinical study. J Am Acad Dermatol. 2020;83(1):109–16. doi:10.1016/j.jaad.2020.02.033.
110. Lindenbaum ES, Feitelberg AL, Tendler M, Beach D, Gamliel-Lazarovich A, Har-Shai Y, Hirshowitz B. Pilot study of a novel treatment for androgenetic alopecia using enriched cell culture medium: clinical trials. Dermatol Online J. 2003;9(1). doi:10.5070/d35zp6g00d.
111. Liu C, Zhao H, Zhang Y, Wu W. Clinical observation of basic fibroblast growth factor (BFGF) combined with minoxidil in the treatment of male androgenetic alopecia. J Cosmet Dermatol. 2022;21(9):4053–59. doi:10.1111/jocd.14735.
112. Tan P-C, Zhang P-Q, Xie Y, et al. Autologous concentrated growth factors combined with topical minoxidil for the treatment of male androgenetic alopecia: a randomized controlled clinical trial. Facial Plast Surg Aesthet Med. 2021;23(4):255–62. doi:10.1089/fpsam.2020.0288.
113. Zimber MP, Ziering C, Zeigler F, Hubka M, Mansbridge JN, Baumgartner M, Hubka K, Kellar R, Perez-Meza D, Sadick N, et al. Hair regrowth following a Wnt- and follistatin containing treatment: safety and efficacy in a first-in-man phase 1 clinical trial. J Drugs Dermatol. 2011;10(11):1308–12.
114. Metwalli M, Khattab FM, Mandour S. Monofilament threads in treatment of female hair loss. J Dermatolog Treat. 2020;32(5):521–25. doi:10.1080/09546634.2019.1682499.
115. Khattab FM, Bessar H. Accelerated hair growth by combining thread monofilament and minoxidil in female androgenetic alopecia. J Cosmet Dermatol. 2019;19(7):1738–44. doi:10.1111/jocd.13228.
116. Tian K, Gao S, Jia Z, Xu W, Li K, Wu L. A study of combination unilateral subcutaneous botulinum toxin a treatment for androgenetic alopecia. J Cosmet Dermatol. 2022;21(11):5584–90. doi:10.1111/jocd.15179.
117. 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;2020:1–7. doi:10.1155/2020/1501893.
118. Leavitt M, Charles G, Heyman E, Michaels D. Hairmax Lasercomb® laser phototherapy device in the treatment of male androgenetic alopecia. Clin Drug Investig. 2009;29(5):283–92. doi:10.2165/00044011-200929050-00001.
119. Lanzafame RJ, Blanche RR, Chiacchierini RP, Kazmirek ER, Sklar JA. The growth of human scalp hair in females using visible red light laser and led sources. Lasers Surg Med. 2014;46(8):601–07. doi:10.1002/lsm.22277.
120. Jimenez JJ, Wikramanayake TC, Bergfeld W, Hordinsky M, Hickman JG, Hamblin MR, Schachner LA. Efficacy and safety of a low-level laser device in the treatment of male and female pattern hair loss: a multicenter, randomized, Sham device-controlled, double-blind study. Am J Clin Dermatol. 2014;15(2):115–27. doi:10.1007/s40257-013-0060-6.
121. Ferrara F, Kakizaki P, de Brito Ff, Contin LA, Machado CJ, Donati A, de Brito FF. Efficacy of minoxidil combined with photobiomodulation for the treatment of male androgenetic alopecia. A double-blind half-head controlled trial. Lasers Surg Med. 2021;53(9):1201–07. doi:10.1002/lsm.23411.
122. Suchonwanit P, Chalermroj N, Khunkhet S. Low-level laser therapy for the treatment of androgenetic alopecia in Thai men and women: a 24-week, randomized, double-blind, sham device-controlled trial. Lasers Med Sci. 2019;34(6):1107–14. doi:10.1007/s10103-018-02699-9.
123. Choi MS, Park BC. The efficacy and safety of the combination of photobiomodulation therapy and pulsed electromagnetic field therapy on Androgenetic Alopecia. J Cosmet Dermatol. 2022;22(3):831–36. doi:10.1111/jocd.15490.
124. Blum K, Han D, Madigan MA, Lohmann R, Braverman ER. "Cold" X5 HairlaserTM used to treat male androgenic alopecia and hair growth: An uncontrolled pilot study. BMC Res Notes. 2014;7(1). doi:10.1186/1756-0500-7-103.
125. Alhattab MK, Abdullah Mj AL, Mh A, Aljanaby WA, Alwakeel HA. The effect of 1540-nm fractional erbium-glass laser in the treatment of androgenic alopecia. J Cosmet Dermatol. 2020;19(4):878–83. doi:10.1111/jocd.13122.
126. Cho SB, Goo BL, Zheng Z, Yoo KH, Kang J-S, Kim H. Therapeutic efficacy and safety of a 1927-nm fractionated thulium laser on pattern hair loss: an evaluator-blinded, split-scalp study. Lasers Med Sci. 2018;33(4):851–59. doi:10.1007/s10103-018-2437-5.
127. Huang Y, Zhuo F, Li L. Enhancing hair growth in male androgenetic alopecia by a combination of fractional CO2 laser therapy and hair growth factors. Lasers Med Sci. 2017;32(8):1711–18. doi:10.1007/s10103-017-2232-8.
128. Suchonwanit P, Rojhirunsakool S, Khunkhet S. A randomized, investigator-blinded, controlled, split-scalp study of the efficacy and safety of a 1550-nm fractional erbium-glass laser, used in combination with topical 5% minoxidil versus 5% minoxidil alone, for the treatment of Androgenetic Alopecia. Lasers Med Sci. 2019;34(9):1857–64. doi:10.1007/s10103-019-02783-8.
129. Bao L, Gong L, Guo M, Liu T, Shi A, Zong H, Xu X, Chen H, Gao X, Li Y, et al. Randomized trial of electrodynamic microneedle combined with 5% minoxidil topical solution for the treatment of Chinese male androgenetic alopecia. J Cosmet Laser Ther. 2020;22(1):1–7. doi:10.1080/14764172.2017.1376094.
130. Bao L, Zong H, Fang S, Zheng L, Li Y. Randomized trial of electrodynamic microneedling combined with 5% minoxidil topical solution for treating androgenetic alopecia in Chinese males

and molecular mechanistic study of the involvement of the Wnt/β-catenin signaling pathway. J Dermatol Treat. 2022;33(1):483–93. doi:10.1080/09546634.2020.1770162.
131. Gong L, Bao L, Tian T, Li Y. The clinical effect of JetpPeel-assisted topical minoxidil in the treatment of androgenetic alopecia: a randomized pilot study. J Cosmet Laser Ther. 20(1):58–63. doi:10.1080/14764172.2017.1341046.
132. Yu C-Q, Zhang H, Guo M-E, Li X-K, Chen H-D, Li Y-H, Xu X-G. Combination therapy with topical minoxidil and nano-microneedle-assisted fibroblast growth factor for male androgenetic alopecia: A randomized controlled trial in Chinese patients. Chin Med J. 2020;134(7):851–53. doi:10.1097/cm9.0000000000001195.
133. Starace M, Alessandrini A, Brandi N, Piraccini BM. Preliminary results of the use of scalp microneedling in different types of alopecia. J Cosmet Dermatol. 2020;19(3):646–50. doi:10.1111/jocd.13061.
134. Okuda S. Clinical and experimental studies of transplantation of living hairs. Jpn J Dermatol Urol. 1939;46:537–87.
135. Jimenez F, Alam M, Vogel JE, Avram M. Hair transplantation: basic overview. J Am Acad Dermatol. 2021;85(4):803–14. doi:10.1016/j.jaad.2021.03.124.
136. Orentreich N. Autografts in alopecias and other selected dermatological conditions. Ann NY Acad Sci. 1959;83(3):463–79. doi:10.1111/j.1749-6632.1960.tb40920.x.
137. International Society of Hair Restoration Surgery. Practice census results. International society of hair restoration surgery. 2020. Available from: https://ishrs.org/wp-content/uploads/2020/05/Report-2020-ISHRS-Practice-Census-05-22-20.pdf.
138. Mahapatra S, Kumar D, Subramanian V, Chakrabarti SK, Deb KD. Study on the efficacy of platelet-rich fibrin matrix in hair follicular unit transplantation in androgenetic alopecia patients. J Clin Aesthet Dermatol. 2016;9(9):29–35.
139. Garg S. Outcome of intra-operative injected platelet-rich plasma therapy during follicular unit extraction hair transplant: a prospective randomised study in forty patients. J Cutan Aesthet Surg. 2016;9(3):157–64. doi:10.4103/0974-2077.191657.
140. Zhao L, Cao D. Application of hair transplantation combined with platelet-rich plasma injection for the treatment of androgenic alopecia. Eur J Dermatol. 2023; 00–00. doi:10.1684/ejd.2023.4560.
141. Leavitt M, David P-M, Rao NA, Barusco M, Kaufman KD, Ziering C. Effects of finasteride (1 mg) on hair transplant. Dermatol Surg. 2005;31(10):1268–76. doi:10.1097/00042728-200510000-00002.
142. Fan Z, Gan Y, Qu Q, Wang J, Lunan Y, Liu B, Chen R, Hu Z-Q, Miao Y. The effect of hyperbaric oxygen therapy combined with hair transplantation surgery for the treatment of Alopecia. J Cosmetic Dermatol. 2021;20(3):917–21. doi:10.1111/jocd.13665.
143. Lee S, Lee W, Na G, Kim D, Park BC. The influence of 3% hydrogen peroxide on the survival rate of hair grafts when used as an antiseptic solution for surgical wound care: experience with five patients. Dermatol Surg. 2007. doi:10.1111/j.1524-4725.2007.33316.x.
144. Fan Z-X, Liu F, Li K-T, Hu Z-Q, Miao Y. Effect of de-epithelialization on graft survival rate after follicular unit extraction. Dermatol Surg. 2021;47(8):1083–86. doi:10.1097/dss.0000000000003145.
145. Garg AK, Garg S. Use of autologous plasma as a hair follicle holding solution with clinical and histological study. Int J Innovative Research In Med Sci (IJIRMS). 2(4):674–78. doi:10.23958/ijirms/vol02-i04/08.
146. Pathania V, Sood A, Beniwal N, Baveja S, Shankar P, Patrikar S. Randomized control trial to study the efficacy and safety of platelet-rich plasma as intraoperative holding solution in hair restoration surgery: a pilot study. Med J Armed Forces India. 2023;79(1):46–53. doi:10.1016/j.mjafi.2021.04.015.
147. Abdelkader R, Abdalbary S, Naguib I, Makarem K. Effect of platelet rich plasma versus saline solution as a preservation solution for hair transplantation. Plastic And Reconstructive Surgery - Global Open. 2020;8(6):e2875. doi:10.1097/gox.0000000000002875.
148. Cooley JE. Bio-enhanced hair restoration. Int Society Of Hair Restoration Surgery. 2014;24(4):121–30. doi:10.33589/24.4.0121.
149. Beehner M. 96-hour study of fu graft "out-of-body" survival comparing saline to hypothermosol/ATP Solution. Int Soc Hair Restor Surg. 2011;21(2):33–37. doi:10.33589/21.2.0033.
150. Zhou Y, Zhang J, Fan Z, Hu Z, Miao Y. Evaluation of a novel graft-holding solution in hair transplantation: a randomized controlled clinical study. Dermatol Surg. 2023;49(7):675–81. doi:10.1097/dss.0000000000003799.
151. Rose PT, Nusbaum AG, Nusbaum BP, Morgan MB. A comparison of apoptotic activity for follicular unit extraction hair grafts stored in different holding solutions. Dermatol Surg. 2020;46(5):721–23. doi:10.1097/dss.0000000000001977.
152. Avram M, Rogers N. Contemporary hair transplantation. Dermatol Surg. 2009;35(11):1705–19. doi:10.1111/j.1524-4725.2009.01283.x.
153. Vogel JE, Jimenez F, Cole J, Keene SA, Harris JA, Barrera A, Rose PT. Hair restoration surgery: the state of the art. Aesthetic Sur J. 2013;33(1):128–51. doi:10.1177/1090820x12468314.
154. Stoneburner J, Shauly O, Carey J, Patel KM, Stevens WG, Gould DJ. Contemporary management of Alopecia: a systematic review and meta-analysis for surgeons. Aesthetic Plast Surg. 2020;44(1):97–113. doi:10.1007/s00266-019-01529-9.
155. Liu F, Miao Y, Li X, Qu Q, Liu Y, Li K, Feng C, Hu Z. The relationship between self-esteem and hair transplantation satisfaction in male androgenetic alopecia patients. J Cosmet Dermatol. 2019;18(5):1441–47. doi:10.1111/jocd.12839.
156. Liu Y, Liu F, Qu Q, Fan Z, Miao Y, Hu Z. Evaluating the satisfaction of patients undergoing hair transplantation surgery using the face-Q scales. Aesthetic Plast Surg. 2019;43(2):376–82. doi:10.1007/s00266-018-1292-x.
157. Sharma R, Ranjan A. Follicular unit extraction (FUE) hair transplant: curves ahead. J Maxillofac Oral Surg. 2019 Dec;18(4):509–17. doi:10.1007/s12663-019-01245-6.
158. 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.
159. Bazzano GS, Terezakis N, Galen W. Topical tretinoin for hair growth promotion. J Am Acad Dermatol. 1986;15(4):880–93. doi:10.1016/s0190-9622(86)80024-x.
160. Jo SJ, Shin H, Park YW, Paik SH, Park WS, Jeong YS, Shin HJ, Kwon O. Topical valproic acid increases the hair count in male patients with Androgenetic Alopecia: a randomized, comparative, clinical feasibility study using phototrichogram analysis. J Dermatol. 2014;41(4):285–91. doi:10.1111/1346-8138.12422.
161. Lee WJ, Sohng C, Kim JY, Park KD, Jang YH, Lee S. Effect of a sphingolipid-mimetic compound on the promotion of hair growth: A randomized, double-blind, placebo-controlled clinical trial. J Cosmet Dermatol. 2020;19(7):1715–22. doi:10.1111/jocd.13220.
162. Gassmueller J, Hoffmann R, Webster A. Topical fulvestrant solution has no effect on male and postmenopausal female androgenetic alopecia: results from two randomized, proof-of-concept studies. Br J Dermatol. 2007. doi:10.1111/j.1365-2133.2007.08276.x.
163. Olsen EA, DeLong E. Transdermal Viprostol in the treatment of male pattern baldness. J Am Acad Dermatol. 1990;23(3):470–72. doi:10.1016/0190-9622(90)70242-a.
164. Gilhar A, Pillar T, Etzioni A. Topical cyclosporine in male pattern alopecia. J Am Acad Dermatol. 1990;22(2):251–53. doi:10.1016/0190-9622(90)70033-e.
165. Iwabuchi T, Ideta R, Ehama R, Yamanishi H, Iino M, Nakazawa Y, Kobayashi T, Ohyama M, Kishimoto J. Topical adenosine increases the proportion of thick hair in Caucasian men with Androgenetic Alopecia. J Dermatol. 2016;43(5):567–70. doi:10.1111/1346-8138.13159.

166. Oura H, Iino M, Nakazawa Y, Tajima M, Ideta R, Nakaya Y, Arase S, Kishimoto J. Adenosine increases anagen hair growth and thick hairs in Japanese women with female pattern hair loss: a pilot, double-blind, randomized, placebo-controlled trial. J Dermatol. 2008;35(12):763–67. doi:10.1111/j.1346-8138.2008.00564.x.
167. Watanabe Y, Nagashima T, Hanzawa N, Ishino A, Nakazawa Y, Ogo M, Iwabuchi T, Tajima M. Topical adenosine increases thick hair ratio in Japanese men with Androgenetic Alopecia. Int J Cosmet Sci. 2015;37(6):579–87. doi:10.1111/ics.12235.
168. 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. 2013;21(3):155–59.
169. Rossi A, Campo D, Fortuna MC, Garelli V, Pranteda G, De Vita G, Sorriso-Valvo L, Di Nunno D, Carlesimo M. A preliminary study on topical cetirizine in the therapeutic management of Androgenetic Alopecia. J Dermatolog Treat. 2018;29(2):149–51. doi:10.1080/09546634.2017.1341610.
170. Hossein Mostafa D, Samadi A, Niknam S, Nasrollahi SA, Guishard A, Firooz 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;24:191–99. doi:10.18433/jpps31456.
171. Carrasco E, Blázquez-Castro A, Calvo MI, Á Á, Espada J. Switching on a transient endogenous ROS production in mammalian cells and tissues. Methods. 2016;109:180–89. doi:10.1016/j.ymeth.2016.08.013.
172. Cao Z, Liu X, Zhang L, Zhang Y, Zhou Z, Zhang G, Wang P, Hu W, Wang X. Treatment of androgenetic alopecia with 5-aminolevulinic acid photodynamic therapy: a randomized, placebo-controlled, split-scalp study of efficacy and safety. Photodiagnosis Photodyn Ther. 2021;36:102491. doi:10.1016/j.pdpdt.2021.102491.
173. Pestana A, Olsen EA, Delong ER, Murray JC. Effect of ultraviolet light on topical minoxidil-induced hair growth in advanced male pattern baldness. J Am Acad Dermatol. 1987;16(5):971–76. doi:10.1016/s0190-9622(87)70123-6.