Review EMUJPharmSci ISSN 2651-3587 https://dergipark.org.tr/emujpharmsci

EMU Journal of Pharmaceutical Sciences

EMUJPharmSci

Common Treatment Formulation for Non-Scaring (Androgenetic) Alopecia: Mini Review

Jannat WH Al-Jubouri[1], Leyla B Pozharani[1], M Çelik[2,3,*]

[1]Eastern Mediterranean University, Faculty of Pharmacy, Famagusta, TRNC

[2]Pharmaceutical Technologies International, Inc., Skillman, New Jersey, USA

[3]University of New Mexico, College of Pharmacy, Albuquerque, New Mexico, USA

Abstract

In spite of being a non-life-threatening condition, hair loss (alopecia) severely impacts the quality of life of individuals who experience it. Recent studies indicate that the number of patients suffering from alopecia globally is on the rise. Androgenic alopecia (AGA) affects both genders at all ages. Genetic factors and family history are found to greatly impact the likelihood of experiencing hair loss. Statistics reveal that during the course of their lives, 80% of men experience alopecia, while 40 to 50% of women are likely to face some form of hair shedding. AGA is characterized by frontal-temporal hair shedding in men and hair thinning of the midline part of the scalp for women. A variety of herbal formulations are available on the market to combat AGA, while only two FDA-approved medications exist at the moment: oral finasteride and topical minoxidil. Topical formulations of finasteride are still under clinical trials. Minoxidil and finasteride formulations provide effective AGA treatment for both genders. Recent concerns regarding potential side effects of these two medications have drawn interest in providing new innovative alternative formulations (nutrients, minerals and vitamins) to provide a safer treatment against AGA. This article provides a brief overview of the current and alternative AGA formulations.

Keywords

Androgenetic alopecia: Finasteride: Hair loss: Minoxidil

Article History

Submitted: 29 November 2022 Accepted: 24 January 2023 Published Online: July 2023

Article Info

***Corresponding author:** Jannat W. H, Al-Jubouri **email:** jannat.aljubouri@emu.edu.tr

Research Article:

Volume: 6 Issue: 1 2023 Pages: 56-63

DOI: 10.54994/emujpharmsci.1211611

INTRODUCTION

Hair is the mirror of human health. It is an integrated system with unique physical and chemical characteristics that reflects human well-being (Araújo *et al.,* 2011). The number of patients suffering from hair loss (alopecia) and hair thinning has recently increased globally. Alopecia is a wide spread issue that affects all genders from infancy to old age. The most prevalent type of non-scaring alopecia is androgenetic alopecia (AGA) (DeVillez, 1994). The difference between male AGA (referred to as male pattern hair loss (MPHL)) and female AGA (referred to as female pattern hair loss (FPHL) is the location of hair shedding on the scalp (Al Aboud *et al.,* 2020). Figures 1 and 2 present the difference between MPHL and FPHL. Scientific data show that 80% of men get noticeable hair loss (AGA) by the age of 80, and nearly 40-50% of women suffer from alopecia during their life course. These numbers may increase by aging (Guo *et al.,* 1998; Sadick, 2018; York *et al.,* 2020).

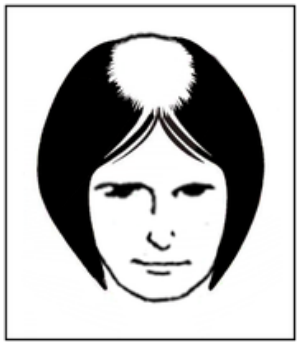

Figure 1. Androgenetic alopecia location in women (AGA).

Figure 2. Androgenetic alopecia (AGA) location in men.

Although AGA is an age-race-dependent genetic condition (Kelly *et al.,* 2016; Völker *et al.,* 2020), scientists have developed several approaches to address these issues, such as pharmacotherapy, surgery, and cosmetics. However, only two medications (oral finasteride and topical minoxidil) are approved by the Food and Drug Administration (FDA) for the treatment of reversible androgenetic alopecia (AGA). Currently two drugs are available in the market under various names

and formulations (Lee *et al.,* 2018). The main goal of AGA treatment is to arrest hair shedding progress, preventing any future miniaturization, and reversing the process if possible. Topical minoxidil is favored instead of oral finasteride due to its noticeable outcome and more minor side effects. Topically administered minoxidil is currently available as an OTC drug in solution form at a concentration of 2% or 5% and, foam and shampoo forms at 5% concentration. Finasteride is available in 1 mg oral dosage form, and clinical trials have been performed for 0.25% and 0.5% of the topical solution as a promising topical form (Ashique *et al.,* 2020; Kelly *et al.,* 2016; Lee *et al.,* 2018). The effectiveness of the FDA-approved drugs is, however, shown to be suboptimal, giving rise to greater interest for complementary therapies with reduced side effects, such as natural medications with potential medicinal constituents like vitamins, minerals, and oils (Kelly *et al.,* 2016; York *et al.,* 2020).

Common Causes of AGA

The main reason causing androgenetic alopecia (AGA) is heredity. However, improper lifestyle habits, hair styling abuse, oily scalp, the side effect of some medication, vitamin deficiency, hormonal changes (female pattern alopecia), chemotherapy, and pregnancy may cause alopecia (Nabahin *et al.,* 2017).

Treatment Strategies

Significant indicators for the etiology of various hair loss patterns and hair loss forms are presented in Table 1. The most common type of alopecia is androgenetic alopecia (AGA) which is a cumulative patterned hair loss attributed primarily to heredity and\or hormonal (androgen, estrogen, testosterone) disorders affecting almost 50% of the population in different severity levels (DeVillez, 1994; Kelly *et al.,* 2016; Yip *et al.,* 2011).

Table 1. Significant features and common types of non-scaring alopecia

Type	Considerable feature	Comments	Source
Androgenetic alopecia	Heredity (family history) and hormonal disorders are related factors leading to complete baldness starting from the frontal area of the scalp in both genders. It causes reduction of the hair thickness and length plus loss of hair pigmentation.	The most common type of hair loss, affecting 50% of the population.	(Kelly et al., 2016)
Alopecia areata	Hair loss in small patches on the scalp may prevent future hair regrowth in the affected areas. Alopecia areata happens due to immune system reaction against hair follicles.	Study shows 1.7% of the American population have the risk by the age of 50.	(Phillips et al., 2017)
Iron deficiency alopecia	Scalp hair shedding starts to be noticeable when the ferritin levels go under 40 mg/mL.	This case is a frequently seen especially in women during their life course.	(Almohanna et al., 2019)
Telogen effluvium	Stress and psychological\emotional state causes a significant amount of hair to fall while brushing the hair or in the shower.	A pervasive case that may affect each one of us can be resolved in 2-6 months to a normal state.	(Whiting, 1999)
Anagen effluvium	65% of the hair starts to fall after few days of chemotherapy exposure.	It is a common side effect of chemotherapy treatment.	(Phillips et al., 2017)

Pharmacological Treatment

Only two FDA-approved therapeutic agents demonstrated a significant effect in the treatment of AGA. The first drug launched on the market for the treatment of AGA was minoxidil**.** This drug was initially used as a hypertension medication for its potent vasodilator effect. The fact that balding patients experienced hair regrowth prompted the idea of a topical minoxidil formulation for treating androgenetic alopecia (AGA) in both male and female patients. Minoxidil is a prodrug that the hair follicle root converts to minoxidil sulfate; thus, the scientists proposed using this conversion topically to achieve more direct benefit while minimizing the drug's systemic potential side effects. The mechanism of action of minoxidil is not fully understood, but the fundamental mechanism on hair growth is due to its vasodilating and K+ channel opening properties, which provide more oxygen and higher blood flow to the region. The FDA has approved the 2% and 5% solution and 5% foam for long-term use, daily applied on a dry scalp once or twice a day, having visible results after 4-8 months. The procedure causes a substantial rise in existing hair diameter as well as an increase in hair weight. The drug's main side effects are demonstrated as scalp dryness, itching, and a burning sensation. Over 56 products have been introduced to the market under different brand names and application forms such as spray, liquid solutions, shampoos, and foam (Ashique *et al.*, 2020; Levy and Emer, 2013; Lolli *et al.*, 2017; Messenger and Rundegren, 2004; Varothai

and Bergfeld, 2014; York *et al.*, 2020; Zins, 1988).

The second FDA-approved drug is oral finasteride which is a selective type II 5-alpha reductase inhibitor with limited use to its systemic side effect, 5 mg dose is prescribed for prostate enlargement, and 1 mg is (oral dose) suggested to treat male pattern hair loss (MPHL). It is a life-long use medication, showing several side effects such as male feminization, especially in pregnant women with male gender fetuses, reduced libido, and erectile dysfunction. These side effects may be normalized when discontinued. Only the 1 mg dose oral Finasteride is FDA approved for AGA treatment; finasteride topical form is a potential future medication currently being tested in clinical trials (Kelly *et al.*, 2016; Varothai and Bergfeld, 2014; York *et al.*, 2020).

Other Common Pharmacological Alternatives for AGA Treatment

Dutasteride: A second-generation 5-alpha reductase inhibitor and is more potent than finasteride due to its dual- effect. It inhibits both type 1 and 2 of the 5-alpha reductase enzymes. It is a selective inhibitor which is considered an alternative for AGA treatment for the patients who did not show any response using finasteride for minimum of 8 months. Although dutasteride showed a significant increase in hair growth compared to finasteride, it is not an FDA approved drug (Gubelin Harcha *et al.*, 2014; York *et al.*, 2020).

Moreover, the main molecule causing androgenic alopecia is dihydrotestosterone (Olszewska *et al.*, 2005). Dutasteride is the only dual selective type I & II 5-alpha reductase enzyme (which converts testosterone to 5-alpha dihydrotestosterone) available in the market as an OTC drug (Nickel *et al.*, 2004).

Prostaglandins: The key function of prostaglandins is regulating the hair follicle cycle by normalizing PGD2 levels. There is an increase in the PGD2 levels in AGA, which has a considerable impact on hair loss. A previously made study showed that 0.03% bimatoprost (prostaglandin analog) lotion applied continuously for 12-16 weeks gives a tremendous increase in diameter & number of the hair. There is significant number of clinical trials to confirm this activity (Kelly *et al.*, 2016; Levy and Emer, 2013).

Physical Treatment Method

New therapies emerged with a positive result in the last decades to treat hair loss and AGA, having a vast population due to its direct effect on the desired area and less time consuming. Table 2 presents the available physical treatment options.

Table 2. Physical treatment options (Sadick, 2018).

Treatment Type	Description
Platelet-rich-plasma (PRP)	Taken from the patient's blood then go through a centrifuge machine; this concentrated number of platelets are injected intradermally to the affected.
Micro-Needling	Tiny little needles injected directly to the stratum corneum consist of a combination of drugs like minoxidil and some vitamins and growth factors.
Cytokines	Introduced to the AGA treatment list is very similar to the PRP in terms of the low number of side effects; it focuses on injecting growth factors like KGF into the skin.
Low-level-laser therapy (LLLT)	The near-infrared laser works on enhancing and regenerating the tissues; LLLT was proved in 2011 as a safe method for treating different types of alopecia.

Other Alternatives for the Treatment of AGA

Herbs, probiotics, minerals, and enzymes are all examples of natural ingredients sold as nutritional supplements which do not require FDA approval (Hosking *et al.*, 2019). Table 3 summarizes the natural source alternatives.

Table 3. Summary of natural source alternatives for AGA treatment.

Natural alternative	Comments	Reference
Vitamin A	Vitamin A is essential for healthy hair.	(Ashique *et al.*, 2020)
Vitamin D	Women with FPHL showed lower levels of vitamin D than usual.	(Almohanna *et al.*, 2019)
Vitamin C	Vitamin C deficiency is commonly associated with body hair abnormality.	(Almohanna *et al.*, 2019)
Vitamin E	Vitamin E has an antioxidant effect that can minimize oxidative stress throughout the scalp.	(Ashique *et al.*, 2020)
Iron	Iron deficiency is the most widespread nutritional deficiency in the world strongly associated with hair loss, especially in MPHL patients.	(Almohanna *et al.*, 2019)
Zinc	Alopecia is an eminent indication of a zinc deficiency significant regrowth occurring with zinc supplementation therapy.	(Ashique *et al.*, 2020)
Selenium	Selenium supplements improved dispersed hair growth.	(Bates *et al.*, 2000)
Onion juice	The entity of sulfur and phenolic compounds are responsible for hair regrowth.	(Sharquie and Al-Obaidi, 2002)
Rosemary oil	The procedure is quite similar to minoxidil in increasing blood circulation and the delivery of oxygen to the area.	(Ezekwe, 2020)
Green tea	Work as 5-alpha reductase.	(Ashique *et al.*, 2020)
Saw Palmetto	It is a non-selective 5-alpha reductase.	(Ashique *et al.*, 2020)

CONCLUSION

AGA is a psycho-social condition, which has a massive impact on psychological health and social acceptance. The therapy for AGA is determined by a variety of factors, including effectiveness, concerns, and costs. The goal is to limit and, if possible, reverse the alopecia process. Currently, only two synthetic drugs have been approved by the FDA for androgenetic alopecia treatment (oral finasteride, topical

minoxidil). Some side effects have been reported during the use of oral finasteride, particularly sexual dysfunction; this may cause significant worry and have a negative influence on patients' quality of life. Topical finasteride has been suggested of being a possible alternate option for minimizing systemic side effects. Although dutasteride is the only dual-effect treatment showing a significant increase in hair count and hair quality compared to finasteride, the lack of clinical trials on dutasteride efficacy is the main reason for being not FDA-approved yet. Besides hair transplantation, several new physical treatment approaches were found to be effective for the treatment of AGA. Moreover, various natural supplements that might also assist in preventing hair loss. Treatment of AGA is essential, relying on the fact that the number of patients increases by almost 5% every year. This mini-review summarizes the most widespread causes of alopecia and their chemical/physical treatment solutions and the natural source alternatives for AGA.

REFERENCES

Nabahin A, Eloun AA, Naser SSA (2017). Expert System for Hair Loss Diagnosis and Treatment, *Int. J. Eng. Inf. Syst.* **1** :160–169.

Messenger AG, Rundegren J (2004). Minoxidil: Mechanisms of action on hair growth, *Br. J. Dermatol.* **150**: 186–194

Al Aboud AM, Zito PM (2019). Alopecia, Conn's Handb. *Model. Hum. Aging*, 751–762.

Hosking AM, Juhasz M, Atanaskova MN (2019). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review, *Ski. Appendage Disord*. **5**: 72–89.

Whiting DA (1999). Dermatopathology of common hair problems, *J. Cutan. Med. Surg*. **3**: 2–13.

Lolli F, Pallotti F, Rossi A, Fortuna MC, Caro G, Lenzi A, *et al.* (2017). Androgenetic alopecia: a review, Endocrine **57**: 9–17.

Zins GR (1988). The history of the development of minoxidil, *Clin. Dermatol.* **6**: 132–147.

Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A (2019). The Role of Vitamins and Minerals in Hair Loss: A Review, *Dermatol. Ther. (Heidelb).* **9**: 51–70.

Bates JM, Spate VL, Steven MJ, Germain DL, Galton VA (2000). Effects of selenium deficiency on tissue selenium content, deiodinase activity, and thyroid hormone economy in the rat during development, *Endocrinology* **141**: 2490–2500.

Völker JM, Koch N, Becker M, Klen A (2020). Caffeine and Its Pharmacological Benefits in the Management of Androgenetic Alopecia: A Review, *Skin Pharmacol. Physiol.* **33**: 153–169.

York K, Meah N, Bhoyrul B, Sinclair R (2020). Treatment review for male pattern hair-loss, *Expert Opin. Pharmacother.* **21**: 603–612.

Sharquie KE, Al-Obaidi HK (2002). Onion juice (*Allium cepa* L.), a new topical treatment for alopecia areata, *J. Dermatol*. **29**: 343–346.

Yip L, Rufaut N, Sinclair R (2011). Role of genetics and sex steroid hormones in male androgenetic alopecia and female pattern hair loss: An update of what we now know, *Australas. J. Dermatol.* **52**: 81–88.

Levy LL, Emer JJ (2013). Female pattern alopecia: Current perspectives, *Int. J. Womens. Health* **5**: 541–556.

Olszewska M, Rudnicka L (2005). Effective treatment of female androgenic alopecia with dutasteride, *undefined*.

Ezekwe N, King M, Hollinger JC (2020). The Use of Natural Ingredients in the Treatment of Alopecias with an Emphasis on Central Centrifugal Cicatricial Alopecia: A Systematic Review, *J. Clin. Aesthet. Dermatol*. **13**: 23.

Sadick NS (2018). New-Generation Therapies for the Treatment of Hair Loss in Men, *Dermatol. Clin.* **36**: 63–67.

Nickel JC (2004). Comparison of clinical trials with finasteride and dutasteride. *Reviews in urology*, **6**(9): 31–39.

Araújo R, Fernandes M, Cavaco-Paulo A, Gomes A (2011). Biology of human hair: Know your hair to control it, *Adv. Biochem. Eng. Biotechnol*. **125**: 121–143.

DeVillez RL (1994). Androgenetic Alopecia in the Female, *Arch. Dermatol*. **130**: 303.

Ashique S, Sandhu NK, Haque SN, Koley K (2020). A Systemic Review on Topical Marketed Formulations, Natural Products, and Oral Supplements to Prevent Androgenic Alopecia: A Review, *Nat. Products Bioprospect*. **10**: 345–365.

Varothai S, Bergfeld WF (2014). Androgenetic alopecia: An evidence-based treatment update, *Am. J. Clin. Dermatol.* **15**: 217–230.

Guo S, Lilly P, Siervogel RM, Cam P, E Lea and P. D, P r e v a l e n c e o f M a l e, 0512 (1998), pp. 1330–1332.

S.W. Lee, M. Juhasz, P. Mobasher, Ekelem C, Mesinkovska NA (2018). A Systematic Review of Topical Finasteride in the Treatment of Androgenetic Alopecia in Men and Women, *J. Drugs Dermatol*. **17**: 457.

Phillips TG, Slomiany WP, Allison R (2017). Hair Loss: Common Causes and Treatment, *Am. Fam. Physician* **96**: 371–378.

Gubelin W, Harcha J, Barboza M, Tsai TF, Katsuoka K, *et al.* (2014). 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*. **70**: 489-498.e3.

Kelly Y, Blanco A, Tosti A (2016). Androgenetic Alopecia: An Update of Treatment Options, *Drugs* **76**: 1349–1364.