

Complementary and alternative supplements: a review of dermatologic effectiveness for androgenetic alopecia

Promise Ufomadu, BSA 

Department of Dermatology and School of Medicine, Baylor College of Medicine, Houston, TX, USA

ABSTRACT

Background: Androgenetic alopecia (AGA) is a dermatologic condition with no current cure. Treatments such as minoxidil have been proven to be effective; however, the side effects can be unpleasant. As a result, the utilization of natural remedies for treatment has increased over the years. There is limited scientific evidence that addresses the efficacy of these supplements in combating AGA.

Methods: A review was conducted of the effectiveness of popular complementary and alternative medicines (CAMs) in adult patients experiencing AGA. A literature search was performed for the period of 1993 to 2023 using PubMed, Embase, Google Scholar, Web of Science, and Cochrane.

Results: Natural ingredients like pumpkin seed oil, saw palmetto, melatonin extract, caffeine extract, and rosemary oil were effective in treating AGA either when compared to baseline or a definite AGA Western medication, such as minoxidil. These natural agents also presented minimal side effects.

Conclusion: Certain CAMs can be promising for hair loss treatment. There is a need for more scientific research to better explore the efficacy of currently identified CAMs in treating AGA.

KEYWORDS Androgenetic alopecia; baldness; caffeine; hair loss; hair; melanin; pumpkin seed oil; rosemary; saw palmetto

Female- and male-pattern baldness (FM-PB), also known as androgenetic alopecia (AGA), is a common multifactorial type of alopecia influenced by genetic, hormonal, and environmental elements.¹ Among women, this condition is a major contributor to hair loss, affecting 40% of those in their reproductive years and postmenopausal women.² In addition, this condition impacts 30% to 50% of men by age 50.³ FM-PB can be described as a nonscarring diffuse alopecia that can evolve from the progressive miniaturization of hair follicles with a significant decline in hairs, specifically in the central, frontal, and parietal scalp regions.⁴ This condition can have a negative psychological impact on affected persons, diminishing their self-esteem and confidence, especially in social situations.

Among the multifactorial contributors to FM-PB, hormonal imbalance can have a significant involvement in the progression of this condition. As with male-pattern baldness, dihydrotestosterone can also play a key role in female-pattern

baldness. When this molecule attaches to hair follicles, it leads to their shrinkage, disrupting the hair cycle and promoting hair loss.¹ Various factors, such as increased circulating androgen, menopause, stress, and underlying thyroid diseases, can promote the increase in dihydrotestosterone in women.⁵ In addition, genetics strongly impacts both male-pattern baldness and female-pattern baldness; however, the role of genetics is still ambiguous and can be speculated to be polygenic in nature with a key enzyme contributor called aromatase.⁶ Other key factors that can influence FM-PB include age, diet, medications, and environmental conditions.

The treatment and management of FM-PB are still being explored due to the rarity of randomized controlled trials with longitudinal follow-up and the lack of substantial results that explore the efficacy of available treatments and their combinations. Some current treatment regimens for FM-PB, administered either topically or systemically, include

Corresponding author: Promise Ufomadu, BSA Department of Dermatology and School of Medicine, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030 (e-mail: Promise.Ufomadu@bcm.edu)

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Table 1. Inclusion and exclusion criteria for the literature review

Inclusion criteria	Exclusion criteria
<ol style="list-style-type: none">1. Results that utilized standardized metrics and validated scales like the Ludwig scale and the Sinclair scale2. Studies published outside of the US, as long as they had significant statistical outcomes and were primarily written in English3. Blinded studies, whether single or double-blinded, as long as they met other inclusion criteria4. Studies pertaining to two alopecia variants (androgenetic and areata) due to limited scope if at least one of them was solely performed on AGA patients5. Articles published, approved for publication, or currently in press6. Studies on a specific CAM if there were at least two separate studies and at least five patients (male, female, or both) who received treatment	<ol style="list-style-type: none">1. Studies not within the category of the aforementioned type of study2. Studies not performed in vivo (i.e., ex vivo, in vitro)3. Studies with nonadult participants (<18 years)4. Studies that compared CAMs with Western medications vs. Western medications for concerns about the efficacy of the primary CAM agent5. Studies with multiplex combination regimens (>5 active ingredients) due to concerns about the efficacy of the primary agent6. Studies not published between 1993 and 20237. Studies not involving human subjects

minoxidil, finasteride, spironolactone, red light therapy, and laser-comb therapy.⁷ In addition, natural botanical remedies have also been used for FM-PB treatment. Such remedies include pumpkin seed oil, sandalwood, lavender, rosemary mint, and aloe vera.^{8,9} Complementary and alternative medicines (CAMs), like natural remedies, are widely used by affected persons in an attempt to find safe, natural, and efficacious therapies to restore hair with minimal side effects.¹⁰ In fact, studies show >30% of adults and 12% of children use treatments developed outside of mainstream Western medicine, with a total of \$30.2 billion spent out of pocket annually.¹¹ Additionally, with the recent natural hair movement embraced by African American women, there has been a shift in the utilization of CAMs and alternative hair care products in mitigating hair loss.⁹ Even though CAMs could have potential hair-growing benefits, there has been limited scientific evidence and research on the efficacy of such remedies, along with the lack of standardization of their corresponding bioactive ingredients.¹⁰

Because of the few options available for the treatment of FM-PB, there is still some ambiguity regarding how functional CAMs are and if any have a significant beneficial effect or undesirable side effects. This review was conducted to examine various CAMs utilized to treat FM-PB. It aims to provide reliable decision-making information to physicians and patients about the benefits and harms of such treatments. This study can also serve as a foundation for further research.

METHODS

A comprehensive search on various CAMs utilized in treating AGA was performed through the following databases: PubMed (January 1993 to June 2023), Cochrane Library (January 1993 to June 2023), the Web of Science (January 1993 to June 2023), Google Scholar (January 1993 to June 2023), Embase (January 1993 to June 2023), and ClinicalTrials.gov. Included keywords, while also utilizing

the MeSH function, were androgenetic alopecia, androgenic alopecia, pumpkin seed oil, rosemary oil, lavender oil, saw palmetto, dermatology, hair loss, hair loss treatment, female-pattern hair loss, and male-pattern hair loss. Search emphasis was placed on randomized control trials (RCTs), clinical trials, observational studies, case series, meta-analyses and systematic reviews of RCTs, and case reports. The bibliographies of the referenced studies were perused for further understanding and also referenced as an additional resource for this investigation. A separate search was not performed for adverse effects of the specific CAM interventions. The criteria for inclusion and exclusion are listed in *Table 1*.

RESULTS

Various AGA (and alopecia areata) studies on the efficacy of different CAMs were independently screened and reviewed. Twelve studies (*Table 2*)^{12–23} were selected and analyzed after applying the inclusion and exclusion criteria. The CAMs investigated in this review included oils and extracts like pumpkin seed, rosemary, saw palmetto, caffeine, and melatonin.^{8,9} *Table 3* addresses the level of evidence used as guidance during the review process. *Table 4* displays the side effect profile for each CAM, noting the study where the side effect was mentioned.

DISCUSSION

Pumpkin seed oil

Pumpkin seed oil, a natural remedy known for its high levels of antioxidants and essential fatty acids (β -carotenes, lutein, γ - and β -tocopherols, linolenic acid, and phytosterols), has been utilized in several countries throughout history to help treat prostate conditions, hair loss, diabetes, cardiovascular conditions, and even cancer.²⁴ Additionally, it can be an alternative approach to promoting hair growth.¹² Since it is classified as a dietary supplement, it is not approved by the Food and Drug Administration; however, studies have been conducted proving its efficacy. When compared to side

Table 2. The efficacy of complementary and alternative medicines in androgenetic alopecia in men and women

CAM	Evidence	Alopecia variant	Combination therapy?	Highest level of evidence*
PSO ^{12,13}	In a randomized, controlled trial of 60 female patients with AGA, 30 women received 1 mL of topical PSO vs. 30 women received 1 mL of minoxidil 5% foam for 3 months. For the PSO group, a significant decrease was observed in hair shaft diversity before and after treatment ($30.5 \pm 6.2\%$ vs 24.0 ± 4.02 , $P < 0.001$). For the minoxidil group, a significant decrease was observed in hair shaft diversity before and after treatment ($31.5 \pm 6.3\%$ vs 21.3 ± 2.2 , $P < 0.001$).	AGA	No	1-B
	In a randomized, double-blind controlled trial of 76 male patients with AGA, the intervention group received 2 PSO capsules twice daily before meals (400 mg daily dose) for 24 weeks vs. the placebo group. There was a 40% increase in hair count at 24 weeks in the treatment arm versus 10% in the placebo group ($P < 0.001$).	AGA	No	
RO ^{14–16}	In a single-blind, randomized clinical trial, patients with AGA were assigned to topical rosemary oil ($n = 50$) or minoxidil 2% ($n = 50$) for 6 months. Both groups had a significant increase in hair count at the 6-month endpoint ($P < 0.05$). No significant difference was found between the study groups regarding hair count (> 0.05). Scalp itching, however, was more frequent in the minoxidil group at both assessed endpoints ($P < 0.05$).	AGA	No	I-B
	In a double-blind randomized controlled study, patients ($n = 20$) with AA received aromatherapy including rosemary oil as one of the essential oils vs. placebo group ($n = 20$) for 3 months. The mean size of the affected area decreased from 6.54 ± 10.18 to 3.40 ± 7.62 in the aromatherapy group and 6.73 ± 8.88 to 5.30 ± 7.26 in the placebo group. All observed differences between these treatment groups were statistically significant ($P < 0.05$).	AA	Yes, aromatherapy (thyme oil, rosemary oil, lavender oil, evening primrose oil, atlas cedarwood oil)	
	In a double-blind, randomized controlled trial, patients ($n = 43$) in the active group massaged essential oils including rosemary with carrier oils into their scalp daily. The control group ($n = 43$) used only carrier oils for their massage, also daily for 7 months. A total of 44% of patients had improvement in the active group compared with 15% of patients in the control group ($P = 0.008$).	AA	Yes, aromatherapy (thyme oil, rosemary oil, lavender oil, cedarwood oil)	
SP ^{17–19}	In a double-blind, randomized controlled trial, patients ($n = 26$) were divided into two groups, active oral soft gel group ($n = 13$) and placebo oral soft gel group ($n = 13$), for 5.4 months; 7 dropped out of the study. For the active group, there was a 60% ($n = 6/10$) improvement at the final visit as compared to the baseline. The placebo group had an 11% ($n = 1/9$) improvement.	AGA	Yes, active soft gel capsule contained beta-sitosterol, 50 mg, and saw palmetto extract (standardized to 85%–95% liposterolic content) 200 mg	I-A
	Open-label study of 100 male patients with AGA. One group received <i>Serenoa repens</i> 320 mg vs. finasteride 1 mg group every day for 24 months. Only 38% of <i>Serenoa</i> patients had an increase in hair growth compared to 68% of finasteride patients.	AGA	No	
	Prospective cohort study of 50 men with AGA received SP products (serum and lotion) for 24 weeks. The average hair count and terminal hair count increased at weeks 12 and 24 when compared to baseline.	AGA	Yes, in serum and lotion form (saw palmetto, green tea extract, peony root extract, piroctone-olamine, oligopeptides)	
CE ^{20,21}	In an open-label, randomized trial, 210 men with AGA were divided into two groups: 0.2% caffeine vs. 5% minoxidil group for 6 months. The 5% minoxidil group showed a mean improvement of 11.68% and the 0.2% caffeine group had an improvement of 10.59% in the anagen ratio of the trichogram. The difference in mean values between both groups was 1.09%.	AGA	No, 0.2% caffeine solution	1-A
	In this prospective study, 5 AGA individuals were given a topical solution containing caffeine to apply twice daily for 6 months. On day 180, there was a global average increase of +1.05 in the patients' hair density with thicker hair and improved scalp coverage.	AGA	Yes, a topical compounded formulation (minoxidil 10%, finasteride 0.1%, biotin 0.2%, and caffeine citrate 0.05% hydroalcoholic solution)	

(Continued on next page)

Table 2. Continued

CAM	Evidence	Alopecia variant	Combination therapy?	Highest level of evidence*
Melatonin ^{22,23}	In an open-label, prospective study of 35 men with AGA, 0.0033% topical melatonin solution was applied to their scalps every night for 6 months. A digital TrichoScan showed a 42.7% increase in hair count after 6 months compared to baseline ($P < 0.001$). Hair density improved by 40.9% after 6 months compared to baseline ($P < 0.001$).	AGA	No	I-B
	A double-blind, randomized controlled trial of 12 women with AGA were given 0.1% melatonin-alcohol solution or a placebo (alcohol) solution to apply on their scalp once daily for 6 months. The group treated with the melatonin solution showed an increase of anagen hairs from 76.3% baseline to 85% at 6 months in occipital bronchograms.	AGA	No	

AA indicates alopecia areata; AGA, androgenetic alopecia; CAM, complementary and alternative medicine; CE, caffeine extract; PSO, pumpkin seed oil; RO, rosemary oil; SP, saw palmetto.

*Defined in Table 3.

effects found in minoxidil and finasteride, both Food and Drug Administration–approved medications, topical pumpkin seed oil did not have significant adverse effects.¹² The side effects usually reported from pumpkin seed oil capsule use were mild abnormal discomfort and itchy sensations; however, there were no observed changes in liver enzymes, creatinine, blood pressure, serum-free testosterone, and glucose levels.¹³

In regards to the mechanism of pumpkin seed oil in mitigating hair loss, when applied topically, β -sitosterol and linoleic acid exhibit inhibitory effects on 5α -reductase, hindering IL-6 activity.²⁵ With this mechanism of action, pumpkin seed oil has great potential to reduce hair loss and even promote hair growth while minimizing irritation to the scalp;²⁶ however, it is important to consider the route of administration to maximize efficacy while minimizing adverse effects.

Rosemary oil

Rosemary oil, known for its medicinal benefits, is a natural supplement extracted from an evergreen shrub that inhabits areas within the Mediterranean Sea and the sub-Himalayans. This remedy is used for symptoms pertaining to headaches, neuralgia, hair loss, insomnia, depression, and rheumatic diseases.²⁷ The contents of rosemary oil include rosmarinic acid, caffeic acid, camphor, and 12-methoxycarboxylic acid, which provide a summative effect contributing to the antioxidant, antimicrobial, and anti-inflammatory properties of this oil.²⁵ Rosemary oil can be administered orally, topically, or inhaled for hair loss prevention, increasing microcapillary perfusion. It is important to consider the route of administration, as it could optimize efficacy.

Saw palmetto

Saw palmetto, also called *Serenoa repens*, is a palm-like shrub that is naturally occurring in the native lands of Florida. Its extract, rich in various fatty acids and sterols, is

utilized for medicinal benefits in treating benign prostate hyperplasia, underactive bladder, prostate cancer, inflammation, and hair loss.²⁸ To achieve these therapeutic effects, saw palmetto inhibits 5α -reductase, reducing the serum levels of dihydrotestosterone and, as a result, promoting better prostate health and hair growth.²⁹ Because of the clinical benefits of saw palmetto, it is estimated that about 2.5 million US adults utilize this product regularly, both orally and topically as a lotion, regardless of its status as a supplement.³⁰ However, there has been ambiguous and limited scientific evidence that reinforces the clinical significance of saw palmetto in helping with the aforementioned conditions.^{31–33}

Caffeine extract

Caffeine, an active ingredient commonly found in coffee, has been widely used in different geographic regions over many decades. Depending on the dosage, caffeine extract provides medicinal benefits that affect different systems of human biology. Such benefits involve its role in alertness, mental health, pain relief, metabolism, cancer, and dermatologic conditions, especially hair loss.^{34–38} Though the consumption of caffeine has a plethora of health benefits, it is important to be cautious about the frequency and amount of such consumption. Ingestion of very high doses (>400 mg per day) can produce undesirable effects on physiologic functions, such as fatigue, nervousness, irritability, and possibly feelings of anger or depression.³⁹ In regards to caffeine extract's mechanism of action in mitigating hair loss, this extract, via cAMP upregulation, enhances the microvascular perfusion of cutaneous capillaries and arterioles, improving endothelium-dependent microvascular responses in the skin.^{40,41}

Melatonin

Melatonin is a widely known compound that plays a key role in sleep modulation. As a neurohormone that can be

Table 3. Level of evidence derived from the *Journal of American Academy of Dermatology* guidelines

Level	Description
I-A	Evidence from a meta-analysis of randomized controlled trials
I-B	Evidence from at least one randomized controlled trial
II-A	Evidence from at least one controlled study without randomization
II-B	Evidence from at least one other type of experimental study
III	Evidence from nonexperimental descriptive studies (comparative studies, correlation studies, and case-control studies)
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Table 4. Side effect profile of complementary and alternative medicines

CAM	Side effect?	Description
Pumpkin seed oil	Yes	Ref 13: Mild abdominal cramping and itching
Rosemary oil	Yes	Ref 14: Scalp itching Ref 15: One of the following adverse events (burning sensation, pruritus, irritation, and erythema) was minimally observed in a patient in the intervention group
Saw palmetto	Yes	Ref 17: A patient with acne in the treatment group had progressively worsened acne at the end of the study Ref 19: Mild side effects perceived: feeling of coldness (16%), mild burning (12%), an unpleasant smell (2%), an itchy scalp (2%), acne on the forehead (2%) and abrasion when using the finger that touched the products to scratch the scrotum (2%)
Caffeine extract	No	
Melatonin	Yes	Ref 20: Four patients experienced mild side effects during the course of the study, including temporary reddening, sensitivity, itching, or burning

synthesized endogenously, melatonin can help combat symptoms of jet lag, delayed or abnormal sleep-wake phase disorder, mental health, diabetes, and potentially hair loss progression.^{42,43} Pertaining to skin conditions, melatonin's antioxidative effects can provide photoprotection, preventing rapid skin aging and skin hyperpigmentation disorders, though its benefits have not been thoroughly studied.⁴⁴ As a CAM intervention with multiple uses, melatonin exhibits the potential to combat AGA.

CONCLUSION

The application of natural CAMs in hair loss prevention has rapidly expanded over the years. The reasons for this trend could be vast. Some individuals may want to avoid the harsher side effects observed from Western medications like finasteride and minoxidil, while others may prefer alternative and natural interventions to treat dermatologic conditions, minimizing the application of chemical and thermal products.⁴⁵ Hair loss affects a compelling percentage of African

Americans, and some of these individuals express dissatisfaction with hair-related physician encounters.⁴⁶ Regardless of the reason, there is a demand for an integrative approach, where natural CAMs are better utilized in clinical care. The literature review provided no sufficient scientific evidence on the use of the following CAMs: peppermint oil, castor oil, sandalwood oil, tea tree, licorice, green tea extract, cannabidiol, and aloe vera. Because of the scarcity of evidence, there is a need for randomized controlled trials and long-term clinical research that investigates the efficacy of these natural products to address the demand for an integrative approach to AGA treatment, especially in ethnic and minority populations. Among with the CAMs discussed in this review, aromatherapy and topical applications of *Serenoa repens*, caffeine extract, and rosemary oils seem to be promising and cost-effective approaches to combating hair loss like AGA. Additionally, these ingredients can be combined with well-known Western medications, such as finasteride and minoxidil, to enhance AGA treatment.

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Avocations



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