REVIEW PAPER

Topical Prostaglandin Analogues in Androgenetic Alopecia: A Systematic Review of Clinical Evidence

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Abstract

Background: Androgenetic alopecia (AGA) is the most prevalent form of non-scarring hair loss, affecting up to 80% of men before age 70 and 42% of women over their lifetimes. The prostaglandin pathway has emerged as a mechanistically compelling therapeutic target: prostaglandin D2 (PGD2) is markedly elevated in balding scalp and potently inhibits follicular cycling through the GPR44/CRTH2 receptor, while prostaglandin F2alpha (PGF2alpha) and PGE2 promote the anagen growth phase. Objectives: To systematically review published clinical and translational evidence on topical prostaglandin analogues specifically latanoprost, bimatoprost, and the PGD2 pathway modulator cetirizine in the treatment of AGA, evaluating efficacy, safety, and the current limitations of the evidence base.

Methods: A systematic search of PubMed/MEDLINE, Embase, and the Cochrane Library was conducted from database inception through January 2026, following PRISMA 2020 guidelines. Of 312 records identified, 65 duplicates were removed, leaving 247 unique records for title/abstract screening; 201 were excluded, yielding 46 full-text articles assessed for eligibility. After applying predefined inclusion and exclusion criteria, 6 primary original clinical studies in human AGA participants were included in the final synthesis, supplemented by foundational translational studies.

Results: Six clinical studies met final inclusion criteria. The pivotal RCT by Blume-Peytavi et al. (2012, n=16 men) demonstrated that latanoprost 0.1% significantly increased terminal and vellus hair density at 24 weeks ($p<0.001$ vs. baseline; $p=0.0004$ vs. placebo). Four studies of topical cetirizine 1% (Rossi et al. 2018; Zaky et al. 2021; Hossein Mostafa et al. 2021; Bassiouny et al. 2023) consistently demonstrated improved hair density in both male and female AGA with favorable tolerability. The oral GPR44 antagonist setipiprant failed to show significant superiority over placebo in a Phase 2a multicenter RCT (DuBois et al. 2021, n=169, $p=0.9239$). No peer-reviewed scalp efficacy data exist for bimatoprost despite multiple registered trials.

Conclusion: Topical prostaglandin analogues represent a biologically coherent but preliminary therapeutic class for AGA. No prostaglandin analogue currently holds regulatory approval for this indication, and the evidence base remains limited to small-scale or pilot-level studies with short follow-up. Large, adequately powered, long-term RCTs are essential before these agents can enter routine clinical practice.

Keywords: Androgenetic Alopecia, Prostaglandin Analogues, Latanoprost, Cetirizine, Hair Growth Therapy

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INTRODUCTION

Androgenetic alopecia (AGA) is the primary cause of progressive, non-scarring hair loss, commonly known as male-pattern hair loss (MPHL) in men and female-pattern hair loss (FPHL) in women. There is a high prevalence of AGA and estimates indicate that the lifetime prevalence for men is about 50% by the age of 50 and 80% by the age of 70, while the lifetime prevalence for women is approximately 40-42%. Psychosocially, there are significant negative associations between AGA, depression, poor self-esteem and poor health-related quality of life. These findings confirm AGA is a serious medical issue and supports the need for further study [1,2]. Pathophysiologically, the primary cause of AGA is androgen-mediated follicular miniaturization among

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genetically predisposed individuals. Dihydrotestosterone (DHT), which is formed by the 5α-reduction of testosterone, attaches to androgen receptors located within dermal papillae of genetically susceptible follicles, causing consecutive anagen (growth) phases to be smaller and the telogen (rest) phase to be longer creating a switch from terminal to fine/vellus hair over time [3,4]. The genetic makeup contributing to AGA is complex; it appears that while an X-linked locus on the androgen receptor plays a major role in a person's genetic risk, over 287 loci have been identified through genome-wide association studies as being genetically associated with AGA [5]. Pharmacological therapy options for AGA are limited in number, including topical minoxidil and oral finasteride both of which are stipulations by the regulatory agencies governing medications for AGA [6]. Finasteride is contraindicated for use in women due to its teratogenic properties and men often experience persistent side effects such as sexual dysfunction at the time of discontinuation [7]. Minoxidil has to be used continuously, and when discontinued, users may develop contact dermatitis, hypertrichosis and rebound effluvium. Significantly, 35 to 53 percent of men treated with first-line therapies will not see clinically meaningful improvement [8]. This data highlights the need for new therapies based on different mechanisms of action.

There was a chance observation of an ophthalmic PGF2alpha (prostaglandin F2alpha) analogue (latanoprost and bimatoprost) used for treatment of glaucoma having a consistent effect of promoting the growth of eyelashes (i.e., increased length, thickness and pigmentation) [9]. This observation led to systematic study of the role of prostaglandins in mediating hair follicle activity. Subsequent work demonstrated that prostaglandins have opposing effects on follicles; Prostaglandin F2alpha and PGE2 stimulate anagen and elongation of hair follicles [10], whereas PGD2 is a strong inhibitor.

The scientifically definitive paper published by Garza, Cotsarelis and co-workers [11], demonstrated via unbiased gene expression profiling that levels of prostaglandin D2 synthase (PTGDS) were upregulated 3-fold in balding men with androgenetic alopecia (AGA) compared to balding men without AGA, as measured at both the mRNA and protein levels. Prostaglandin D2 levels in the scalp of men with AGA were also elevated. In functional studies involving humans, PGD2 inhibits hair growth specifically through the GPR44/CRTH2 receptor. In addition, expression of cyclooxygenase-2 in transgenic mice causes increased production of PGD2 in the dermis, which is demonstrated to reproduce the textural changes (miniaturization) characteristic of human AGA, including hair loss (alopecia), and hyperplasia of sebaceous glands [11,12]. In contrast to the elevated levels of PGD2 in the scalp of AGA patients, the levels of PGE2 were significantly reduced, further establishing a disrupted prostaglandin balance and therefore, a disruption of normal hair growth [12].

Recognizing this mechanistic basis of PGD2 and hair growth has led to the evaluation of three new therapeutic approaches: (1) topically administered PGF2alpha analogues (latanoprost, bimatoprost) that activate the FP receptor to promote the initiation of anagen in hair follicles; (2) GPR44/CRTH2 antagonists (setipiprant) that inhibit the inhibitory effect of PGD2 on hair growth; and (3) topically administered cetirizine that inhibits mast cell degranulation, thereby decreasing the availability of PGD2 in the scalp, while stimulating the synthesis of PGE2, thereby promoting hair growth (Fig. 1) [13,14]. While the mechanistic data from the studies to support these therapies is compelling, clinical data is in the preliminary phases for each of these therapies. Therefore, the purpose of this systematic review will be to address the evidence base for all three therapies; specifically, to critically appraise the currently available evidence, delineate the conclusions that can or cannot be made regarding the existing data, and provide an agenda for future research.

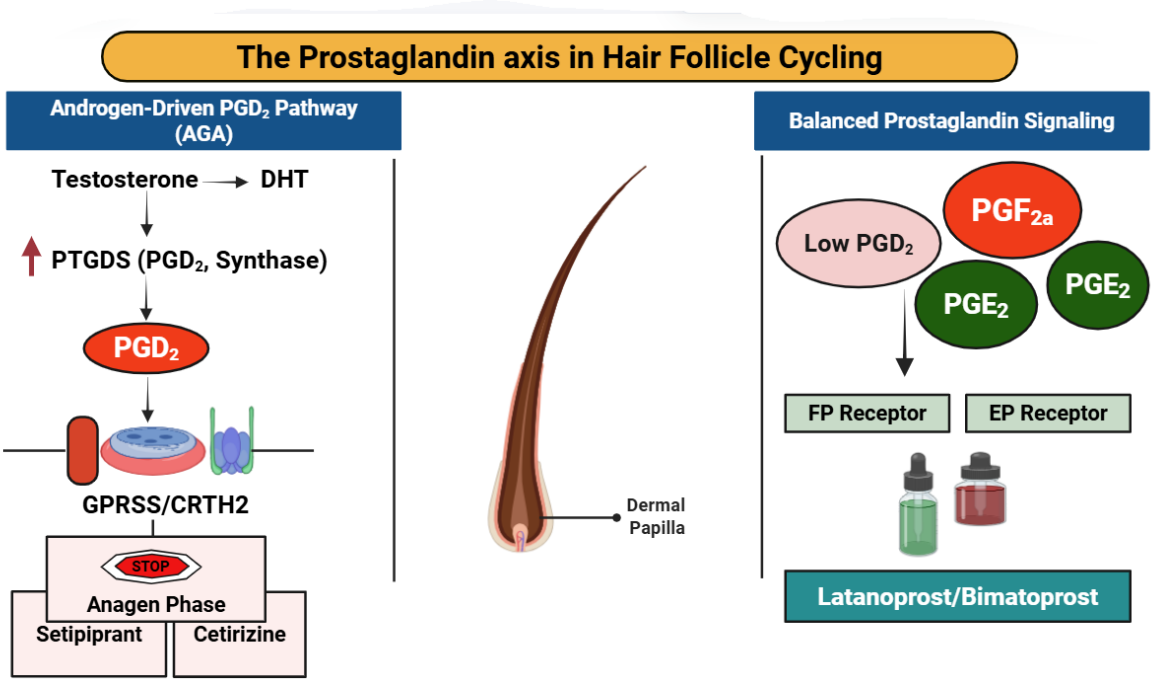

Fig 1. The prostaglandin axis in hair follicle cycling.

METHODS

Study Design and Reporting

This systematic review was conducted and reported in accordance with PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Owing to the clinical heterogeneity of available studies and differences in interventions, comparators, and outcome measures, a formal meta-analysis was not performed; evidence was synthesized narratively (Fig. 2).

Eligibility Criteria

Inclusion criteria

(1) Original peer-reviewed publications comprising RCTs, pilot clinical trials, or case-controlled studies; (2) human participants with clinical or trichoscopic diagnosis of AGA (Hamilton-Norwood scale for men; Ludwig/Sinclair scale for women); (3) interventions involving topical PGF2alpha analogues (latanoprost, bimatoprost), oral GPR44/CRTH2 antagonists (setipiprant), or indirect PGD2 pathway modulators with demonstrated AGA evidence (cetirizine); (4) at least one objective hair growth outcome measure (hair density, count, terminal/vellus ratio, anagen/telogen ratio, shaft diameter). Key translational studies (murine models, gene expression analyses) were included for mechanistic contextualization (Fig. 1).

(2)

Exclusion criteria

(1) Case reports/series with fewer than five participants; (2) reviews, editorials, letters, and conference abstracts without original data; (3) registered trial protocols or preprints without peer-reviewed results; (4) studies restricted entirely to non-AGA alopecias with no AGA-specific cohort; (5) studies reporting exclusively eyelash or eyebrow outcomes with no scalp hair data.

Search Strategy

A systematic search of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) was conducted from database inception through January 2026. Search terms combined with Boolean AND/OR operators included: 'androgenetic alopecia,' 'male pattern hair loss,' 'female pattern hair loss,' 'prostaglandin analogue,' 'latanoprost,' 'bimatoprost,' 'prostaglandin D2,' 'PGD2,' 'GPR44,' 'CRTH2,' 'cetirizine,' 'setipiprant,' 'hair growth,' 'anagen,' and 'hair follicle.' Reference lists of all retrieved full-text articles were hand-searched. No language restrictions were applied (Fig. 2).

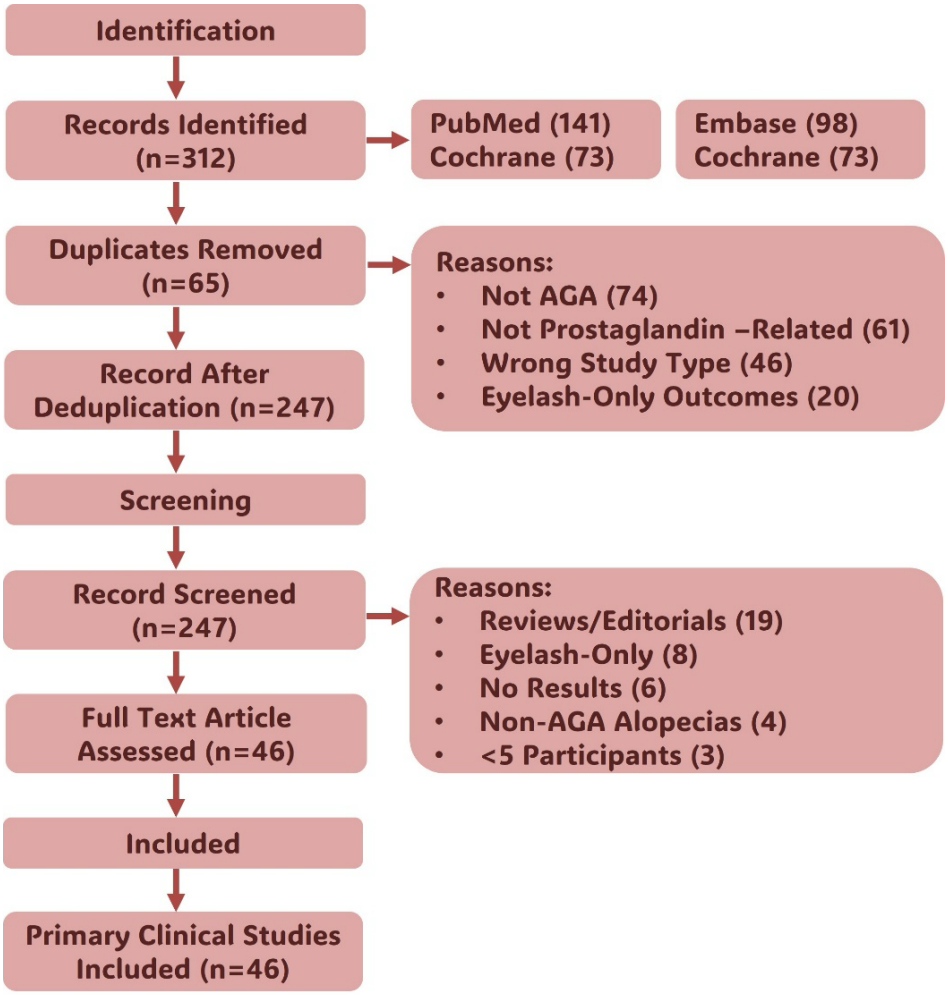

Fig 2. PRISMA flow diagram illustrating the study selection process for the systematic review of prostaglandin pathway modulators in androgenetic alopecia (AGA).

Data Extraction and Quality Assessment

Data were independently extracted by two reviewers using a standardized form. Variables extracted included: study design, country, sample size, participant demographics (age, sex, AGA classification grade), intervention type and concentration, comparator, duration, primary and secondary efficacy outcomes, and adverse events. Risk of bias in RCTs was assessed using the Cochrane RoB 2 tool; non-randomized studies were evaluated using ROBINS-I. Discrepancies were resolved by consensus.

Background: Prostaglandin Axis in Aga

Prostaglandin Biology and the Hair Follicle

Prostaglandins are short-lived lipid mediators synthesized from arachidonic acid via cyclooxygenase-1 and -2 (COX-1/COX-2; PTGS1/PTGS2). COX enzymes convert arachidonic acid to prostaglandin H2 (PGH2), the common precursor, from which specific terminal synthases produce distinct prostaglandin species: PGF2alpha (via FP receptor/PTGFR), PGE2 (via EP1-4 receptors), and PGD2 (via DP1/PTGDR and DP2/GPR44/CRTH2 receptors). The hair follicle is a dynamically cycling mini-organ: anagen (active growth, 2-6 years), catagen (involution, ~2 weeks), and telogen (resting, ~3 months). Prostaglandins regulate multiple aspects of cycle kinetics. PGF2alpha activates the FP receptor on follicular epithelial cells and outer root sheath, promoting anagen initiation and elongation. PGE2 supports anagen maintenance. PGD2 the most abundant prostaglandin in human scalp tissue promotes catagen entry and inhibits hair elongation through the GPR44 receptor. The hypertrichotic eyelash effects of ophthalmic PGF2alpha analogues provided the first in-human pharmacological validation of this biology.

The Garza-Cotsarelis Foundational Study

Garza, Cotsarelis, and colleagues [11], performed global gene expression microarray analysis comparing bald and haired scalp tissue from five AGA-affected men, with findings replicated by RT-qPCR and Western blotting in larger cohorts. PTGDS (PGD2 synthase) was among the most upregulated transcripts in bald scalp, and PGD2 protein was confirmed elevated approximately threefold by mass spectrometry in 17 men with AGA. In mice with synchronized hair cycling, Ptgds expression and PGD2 levels peaked immediately preceding the catagen phase implicating PGD2 as a physiological catagen-entry signal. Topical PGD2 inhibited hair regrowth in depilated mice, and this effect was abolished in GPR44

knockout mice (but not DP1 knockout mice), definitively establishing GPR44 as the functionally requisite receptor. A K14-Ptgs2 transgenic mouse model with basal keratinocyte overexpression of COX-2, resulting in elevated dermal PGD2 phenocopied human AGA with follicular miniaturization, alopecia, and sebaceous hyperplasia. This study remains the mechanistic foundation of the entire field.

Preclinical Evidence for PGF2alpha Analogues

Johnstone and Albert [9] catalogued hypertrichotic eyelash changes in glaucoma patients treated with latanoprost and bimatoprost, providing the first systematic clinical human evidence of PGF2alpha analogue-driven follicular stimulation. Sasaki and colleagues [10], demonstrated in murine models that topical PGF2alpha and PGE2 stimulate hair regrowth and prolong anagen. Uno and colleagues used the stump-tailed macaque which spontaneously develops vertex AGA to evaluate topical latanoprost. At 50 mcg/mL, minimal regrowth occurred; at 500 mcg/mL, moderate-to-marked regrowth with 5-10% vellus-to-terminal conversion was observed. This dose-response relationship has direct implications for clinical concentration selection. For bimatoprost, murine AGA model data suggested superiority over 5% minoxidil in stimulating hair regrowth with fewer local adverse reactions a finding awaiting clinical corroboration.

RESULTS

Latanoprost in Androgenetic Alopecia

The only published placebo-controlled human RCT of topical latanoprost for scalp AGA was conducted by Blume-Peytavi, Lonnfors, Hillmann, and Garcia Bartels at the Charite-Universitatsmedizin Berlin and published in the Journal of the American Academy of Dermatology in 2012 [16]. This monocenter, double-blind, randomized, intra-individual-controlled pilot enrolled 16 men with mild AGA (Hamilton-Norwood grade II-III). Each participant applied latanoprost 0.1% to one designated scalp minizone and vehicle placebo to the contralateral site daily for 24 weeks, with hair density (terminal and vellus hairs/cm2) measured by phototrichography as the primary outcome. At 24 weeks, the latanoprost-treated site demonstrated a statistically significant increase in overall hair density compared to both baseline ($p<0.001$) and the placebo-treated site ($p=0.0004$). Both terminal and vellus hair subcomponents increased significantly. Clinical differences favoring latanoprost were apparent from week 12 in a subset of participants, and in 50% of participants (n=8) by week 24. Associated improvements included increased hair pigmentation in 4 participants and increased shaft thickness in 3. No serious adverse events or systemic effects were reported. This study, while limited by its small sample, restriction to young men with early-stage disease, single-center design, and 24-week duration, remains the definitive clinical proof-of-concept for topical latanoprost in AGA. A separate study at 0.005% latanoprost over 12 weeks produced less compelling results, supporting a concentration-dependent effect.

Bimatoprost in Androgenetic Alopecia

Bimatoprost is the only FDA-approved prostaglandin analogue for a hair-related indication: eyelash hypotrichosis (Latisse 0.03%, approved 2008). For scalp AGA, multiple Phase 2/3 trials were registered (NCT01904721 and NCT01325337 for male AGA; NCT01325350 for FPHL), but no peer-reviewed published efficacy results have been made available as of this review [17]. This constitutes the most significant evidence gap in the literature. Barrón and Tosti report [17], described a FPHL patient receiving intradermal not topical bimatoprost 0.03% without benefit, suggesting delivery route and concentration may critically influence outcomes. The 2023 Frontiers in Medicine systematic review by Jiang et al [6]. pooled six RCTs across diverse alopecia subtypes and found prostaglandin analogues significantly improved hair length and density versus placebo ($p<0.001$) with no significant difference in adverse events, though the AGA-specific analysis was limited to two trials.

Cetirizine: Modulation of the PGD2 Pathway

Cetirizine is a second-generation H1 antihistamine whose mechanism relevant to AGA involves inhibition of PGD2 release from mast cells and stimulation of PGE2 production from macrophages and monocytes shifting the scalp prostaglandin balance toward net growth promotion, independently of its antihistaminic activity. The rationale for topical rather than oral delivery is to achieve sufficient local follicular concentration while minimizing systemic side effects. Rossi, Campo, Fortuna, and colleagues [13] published the first clinical study: a pilot enrolling 85 AGA patients (67 cetirizine 1%; 18 placebo controls), with videodermoscopy assessment demonstrating significant increases in total hair density, terminal hair density, and diameter variation, alongside a reduction in vellus hair density indicating reversal of miniaturization. No significant adverse effects were documented. Zaky, Abo Khodeir, Ahmed, and Elsaie authors [14], confirmed these findings in a case-controlled study of 60 male AGA patients (30 cetirizine vs. 30 placebo, 6 months), demonstrating significantly greater dermoscopic hair regrowth ($p<0.001$) and patient satisfaction in the cetirizine group. Hossein Mostafa et al. [18] compared cetirizine 1% to minoxidil 5% in a randomized, single-blind design, finding cetirizine effective but quantitatively inferior to minoxidil (Table 1).

In female AGA, Alavi and colleagues conducted a triple-blind RCT in 60 FPHL patients comparing topical cetirizine 1% to topical minoxidil 2%, with the cetirizine group demonstrating significantly superior results in hair growth and patient satisfaction versus controls. Bassiouny, El-Samanoudy, Abbassi, Nada, and Farid et al., [19] evaluated cetirizine added to minoxidil versus minoxidil plus placebo in FPHL, demonstrating that combination therapy produced significantly greater

improvement in hair shaft thickness and global clinical impression, suggesting additive benefit. A 2025 study (Arch Dermatol Res, n=80) administered topical cetirizine via microneedling versus saline microneedling in male AGA over 8 weeks, finding that 80% of the cetirizine group demonstrated enhanced hair density versus 25% of controls (p=0.001), with no notable adverse effects.

Setipiprant: Oral GPR44/CRTH2 Antagonism

Setipiprant is an oral, selective CRTH2 (GPR44/DP2) antagonist developed to block PGD2-mediated follicular inhibition, the mechanism identified by Garza and Cotsarelis as central to AGA pathogenesis. DuBois, Bruce, Stewart, and colleagues [8] conducted a multicenter, randomized, double-blind, placebo-controlled Phase 2a trial at 18 US sites. Men aged 18-49 (n=169) were randomized to setipiprant 1000 mg twice daily (n=83), placebo (n=74), or finasteride 1 mg daily (n=12; arm later removed by protocol amendment). Treatment lasted 24 weeks with 8-week follow-up. Coprimary endpoints were change in target area hair count (TAHC) within a 1 cm2 scalp zone and Subject Self-Assessment (SSA) (Table 1).

Setipiprant failed to demonstrate statistically significant superiority over placebo on either endpoint (TAHC p=0.9239). Within-group variance was high, reflecting pronounced inter-individual heterogeneity. Finasteride showed numerically superior improvement in both primary endpoints, consistent with established efficacy, though formal between-group statistical testing was not performed. Setipiprant was safe and well tolerated; most treatment-emergent adverse events were mild, with no serious events in the setipiprant group.

Table 1. Summary of included primary clinical studies (n=6).

Study (Year)	Design	n	Intervention	Primary Outcome	Key Result
Blume-Peytavi et al. [16]	RCT, DB, intra-individual	16 men	Latanoprost 0.1% vs vehicle, 24 wks	Hair density (phototrichography)	Sig. increase in terminal + vellus density (p<0.001 vs baseline; p=0.0004 vs placebo)
Rossi et al. [13]	Pilot clinical study	85	Cetirizine 1% topical vs placebo, ~6 months	Total hair density, terminal density, diameter (videodermoscopy)	Sig. increases in total + terminal density; decrease in vellus density
Zaky et al. [14]	Case-controlled	60 men	Cetirizine 1% vs placebo, 6 months	Dermoscopic hair regrowth score	Higher regrowth (p<0.001); higher patient satisfaction in cetirizine group
Hossein Mostafa et al. [18]	RCT, single-blind	NR	Cetirizine 1% vs Minoxidil 5%	Hair count; global assessment	Cetirizine effective but inferior to minoxidil in absolute counts
DuBois et al. [8]	Phase 2a RCT, DB, MC (18 sites)	169 men	Setipiprant 1000 mg BID vs placebo, 24 wks	TAHC (1 cm2); Subject Self-Assessment	No significant benefit vs placebo (p=0.9239); well tolerated
Bassiouny et al. [19]	RCT, DB, placebo-controlled	NR (FPHL)	Cetirizine 1% + Minoxidil vs placebo + Minoxidil	Hair shaft thickness; global clinical impression	Combination superior to minoxidil monotherapy; no significant adverse effects

RCT = Randomized controlled trial; DB = Double-blind; MC = Multicentre; n = Number of participants; NR = Not reported in accessible publication; FPHL = Female pattern hair loss; BID = Twice daily; wks = Weeks; TAHC = Target area hair count.

Safety and Tolerability

Latanoprost

The leading safety issue for latanoprost is the ocular experience: Due to irreversible pigmentation changes in the eye, there is a 10% risk of developing iris hyperpigmentation with long-term use, generally occurring after 12 months and outside of the AGA trial's 24-week window. No studies have addressed long-term effects of topical latanoprost on scalp pigmentation. Although there are three known periocular risks of using latanoprost opthalmic medication (i.e., periorbital fat atrophy and increased skin pigmentation), no

documented cases have been found of such events in any study of the scalp. The only side effect reported in the Blume-Peytavi [16] study was mild irritation at the site of application to the scalp. Due to its increased sensitiveness to heat, options for storing latanoprost will be limited compared to bimatoprost (Table 2).

Bimatoprost

Bimatoprost has been approved by the FDA for use as an ophthalmic agent. Its adverse effects include redness, pigmentation changes in the iris, and darkening of the eyelid. Published human safety data for bimatoprost as an agent to treat scalp AGA are very limited; no controlled clinical studies have been published [17]. However, animal data indicate that bimatoprost is more tolerated than minoxidil at equivalent concentrations in mice, demonstrating less local adverse reactions. In addition, bimatoprost has better thermal stability and greater pH compatibility compared to latanoprost, making it easier to compound (Table 2).

Cetirizine

Topical cetirizine has the best clinical safety data of any of the agents in the prostaglandin pathway for AGA. No significant local or systemic adverse events related to 1% topical cetirizine have been published in any studies. In addition, cetirizine has an excellent oral safety record and does not have any androgenic, hormonal, or teratogenic effects, making it the ideal treatment option for women with AGA, where finasteride is contraindicated.

Setipiprant: In the Phase 2a study of 1000 mg BID oral setipiprant, there were primarily mild treatment-emergent adverse events with no serious ones among those who received setipiprant. This is consistent with the results of previous Phase 2 studies of setipiprant conducted during its development for allergic rhinitis (Table 2).

Table 2. Summary of prostaglandin pathway targeted therapies for androgenetic alopecia.

Agent	Mechanism	Quality of Evidence	Efficacy Signal	Key Population
Latanoprost	FP agonist	⭐⭐⭐⭐	🟢⬆⬆	Male AGA
Cetirizine	PGD_2 modulator	⭐⭐☆	🟢⬆	Male/Female AGA
Setipiprant	GPR44 antagonist	⭐⭐☆	🟢◐	Male/Female AGA
Bimatoprost	FP agonist	⊘ — ?	⚫	Male AGA

DISCUSSION

This systematic review synthesizes the published clinical and translational evidence for topical prostaglandin analogues in AGA across 6 primary clinical studies and 14 foundational translational investigations. The overarching finding is that the evidence base, while mechanistically coherent, remains insufficient for routine clinical recommendation a position consistent with current international guidelines, which do not endorse prostaglandin analogues for AGA pending larger, longer-term trials [15].

The most methodologically rigorous human data derive from the Blume-Peytavi [16], a randomized, double-blind, intra-individual-controlled design with validated objective endpoints published in a leading peer-reviewed journal. The significant increase in terminal and vellus hair density at 24 weeks ($p<0.001$ vs. baseline; $p=0.0004$ vs. placebo) in mild male AGA is clinically meaningful and biologically expected given the FP receptor agonism of latanoprost. However, the small sample (n=16), restriction to Hamilton-Norwood grade II-III, single-center design, and limited duration collectively prevent generalization. Without confirmatory large-scale multicenter RCTs, latanoprost cannot be considered evidence-based standard of care.

The bimatoprost situation is paradoxical. As an FDA-approved follicular growth agent for eyelash hypotrichosis [17], it holds the strongest regulatory precedent of any prostaglandin analogue for hair follicle stimulation. Yet published scalp-specific efficacy data are entirely absent. The multiple registered Phase 2/3 trials (NCT01904721, NCT01325337, NCT01325350) have not produced peer-reviewed results, creating the largest single evidence gap in this review. The 2023 meta-analysis by Jiang et al. [6] found prostaglandin analogues broadly effective across diverse alopecia subtypes ($p<0.001$), but AGA-specific subgroup evidence was limited to two trials, significantly constraining AGA-specific conclusions.

Topical cetirizine presents the most clinically developed prostaglandin-pathway evidence base in AGA [13,14,18,19]. Its indirect prostaglandin mechanism suppressing PGD2 while stimulating PGE2, directly counteracting the imbalance identified by Garza and Cotsarelis [11] is grounded in established pharmacology. Across four studies of varying design in both sexes, consistent improvements in hair density and terminal hair count were observed, with no documented

significant adverse effects in any cohort. The head-to-head comparison with minoxidil [18] suggests cetirizine is quantitatively less potent but clinically real occupying a valuable niche for patients unable to use minoxidil or finasteride. The combination data from Bassiouny et al. [19] raise the intriguing possibility of synergy between minoxidil's vasodilatory mechanism and cetirizine's prostaglandin rebalancing. The microneedling-cetirizine study [20] suggests enhanced follicular delivery may amplify efficacy, though the 8-week follow-up is too brief for firm conclusions (Fig. 3).

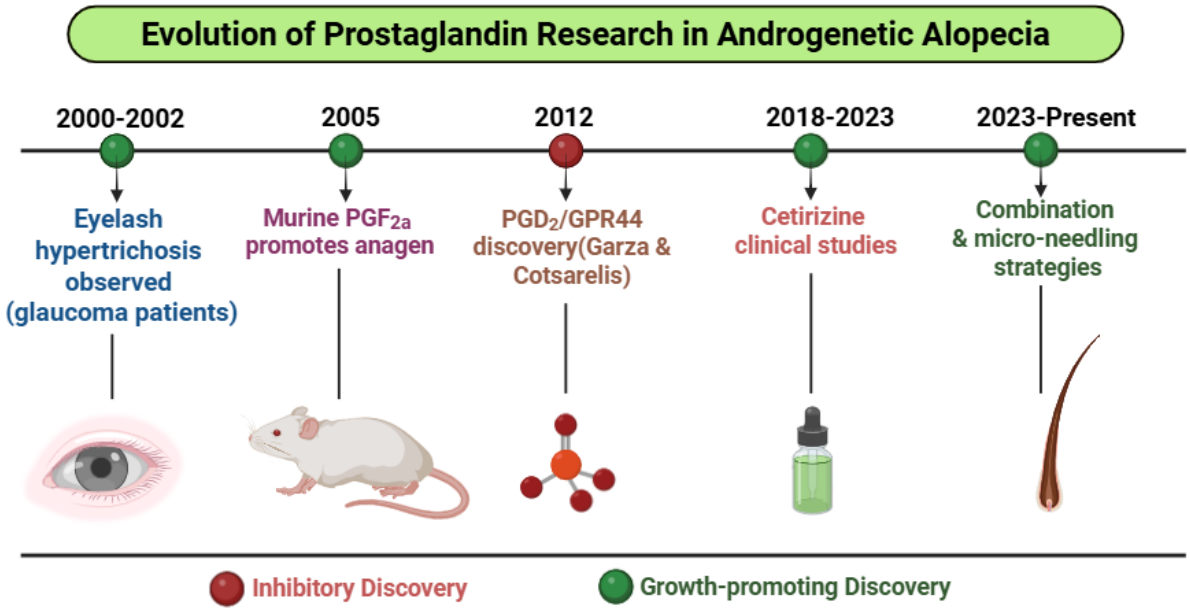

Fig 3. Timeline-evolution of prostaglandin research in AGA.

The negative setipiprant Phase 2a result [8] deserves mechanistic interrogation rather than dismissal of the GPR44 pathway. The null finding (p=0.9239) is striking given the mechanistic strength of the PGD2/GPR44 model [11,12], and multiple explanations are plausible. Oral setipiprant may achieve insufficient scalp tissue concentrations to produce pharmacologically relevant GPR44 blockade at the follicular level. Twenty-four weeks may be too brief to observe significant reversal of established follicular miniaturization via prostaglandin pathway modification alone approved therapies such as finasteride and minoxidil are typically evaluated over 48-52 weeks [3,21]. Additionally, the PGD2/GPR44 axis, while causally important in AGA, may be insufficient as a standalone therapeutic target in the presence of ongoing androgen-mediated follicular suppression, suggesting that combination strategies targeting both pathways simultaneously may be required [7,11]. Topical delivery of a GPR44 antagonist providing higher local scalp concentrations than oral administration may circumvent the bioavailability limitation and deserves prospective clinical evaluation.

Contextualizing prostaglandin analogues against established therapies is essential. Topical minoxidil 5% produces clinically meaningful improvements in approximately 50-60% of treated patients over 48 weeks [21-26]; oral finasteride produces approximately 10-15% increases in hair count versus placebo at 12 months [3]. Current prostaglandin analogue data suggest meaningful effects within 24 weeks, but direct comparative RCTs against approved first-line agents essential for positioning these agents therapeutically are largely absent. Formulation science deserves emphasis: scalp delivery challenges include the stratum corneum barrier, vehicle-dependent follicular penetration, and latanoprost's thermolability [27]. Lipid nanoparticles, transfersomes, and microneedling-assisted delivery may substantially improve follicular bioavailability and merit dedicated investigation.

The primary limitation is the paucity and heterogeneity of published clinical studies, which precluded formal meta-analytic synthesis. No two included studies used identical agents, concentrations, outcome measures, or patient populations. Sample sizes across available trials are uniformly small, introducing substantial imprecision in effect estimates and limiting power to detect rare adverse events. Study durations (8-24 weeks) are short relative to the chronic, progressive nature of AGA; no long-term follow-up data exist for any prostaglandin analogue in this indication. Publication bias is a meaningful concern: the registered bimatoprost AGA trials which may have produced negative or null results have not published peer-reviewed data, potentially inflating the apparent promise of this class through selective positive reporting. Outcome measurement heterogeneity (phototrichography, videodermoscopy, global photography, dermoscopy, patient self-assessment) limits direct quantitative comparison. Methodological quality varied from well-designed multicentre RCTs (Blume-Peytavi; DuBois) to pilot and case-controlled designs.

CONCLUSIONS

Topical prostaglandin analogues represent a mechanistically grounded and clinically promising but evidence-limited class of candidate therapies for androgenetic alopecia. The foundational biology that PGD2 is a causative, elevated inhibitor of follicular cycling in AGA acting through GPR44, while PGF2alpha/PGE2 promote anagen provides a coherent therapeutic rationale. In the clinical domain, the most mature evidence supports topical latanoprost 0.1% (one small but well-designed RCT demonstrating significant hair density improvement at 24 weeks) and topical cetirizine 1% (consistent beneficial findings across four studies in both sexes, with favorable safety and emerging combination and enhanced-delivery data). Topical bimatoprost carries the strongest mechanistic and regulatory precedent but critically lacks published scalp AGA efficacy data. Oral setipiprant failed to meet its primary endpoints in a well-conducted Phase 2a trial, though topical GPR44 antagonist delivery remains scientifically justified. No prostaglandin analogue currently holds regulatory approval for AGA, and none can be recommended for routine clinical use. What the field requires are large, adequately powered, multicenter, long-duration RCTs incorporating standardized trichoscopic endpoints and validated patient-reported outcomes. Combination strategies pairing PGF2alpha analogues with PGD2 pathway antagonists or integrating prostaglandin modulation with androgen-axis therapies represent scientifically motivated but unevaluated directions. As the biology of AGA is progressively mapped across androgen signaling, lipid mediator networks, inflammatory pathways, and follicular stem cell niches, the prostaglandin axis stands as one of the most tractable and therapeutically actionable avenues identified to date. Translating this mechanistic insight into safe, effective, and accessible treatments for the millions worldwide affected by AGA remains a shared clinical and scientific imperative.

Conflict of Interest

Authors do not express any conflict of interest.

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