Acta Medica Europa

ISSN Online: 2996-1211 doi: 10.5281/zenodo.15426151

Analysis of the Side Effects of Prostaglandin Analogues for Aesthetic Purposes in Healthy Patients: Integrative Review

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Article Info

Received: 9 May 2025

Revised: 17 May 2025

Accepted: 17 May 2025

Published: 17 May 2025

Keywords:

Prostaglandin analogues, side effects, aesthetics, conjunctival hyperemia, iris pigmentation, periocular hyperpigmentation, safety.

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ABSTRACT

Prostaglandin analogues, originally developed for glaucoma treatment, have gained popularity in cosmetic dermatology due to their observed effects on eyelash and eyebrow growth. However, their off-label use in healthy individuals raises safety concerns. To critically evaluate the adverse effects associated with the aesthetic use of prostaglandin analogues in healthy individuals, based on current scientific literature. This integrative review was conducted using eight major databases and included narrative and integrative reviews, academic monographs, prospective studies, clinical reports, systematic reviews, meta-analyses, experimental studies, and regulatory/scientific documents published between 2007 and 2024. Two independent reviewers performed study selection and full-text evaluation. Data were analyzed qualitatively and supplemented by descriptive statistics to determine the frequency and clinical significance of reported adverse effects. The most frequently observed adverse effects included conjunctival hyperemia (26.32%), iris pigmentation (21.5%), periocular hyperpigmentation (15.79%), orbital fat atrophy (15.79%), and eyelash growth (21.05%). While prostaglandin analogues demonstrated efficacy in promoting hair growth, especially with bimatoprost and latanoprost, the associated side effects varied in severity and reversibility. Regulatory bodies such as the SCCS have highlighted the lack of long-term safety data in cosmetic applications. Despite their aesthetic benefits, prostaglandin analogues carry significant risks when used off-label in healthy individuals. Clinical supervision is essential to ensure safe application. Future research should address long-term safety, pharmacogenetic factors, and potential therapeutic combinations to optimize outcomes while minimizing harm.

INTRODUCTION

Prostaglandins are a class of biologically active eicosanoids derived from arachidonic acid, which act as local mediators in various physiological and pathological processes. Present in virtually all human tissues—except erythrocytes—these molecules play critical roles in the modulation of inflammation, vascular tone regulation, platelet aggregation, gastrointestinal motility, ovulation, labor, and, more recently, in the control of the hair cycle and the growth of pilose structures (1,2).

Their biosynthesis begins with the release of membrane phospholipids by phospholipase A2, followed by conversion through cyclooxygenases (COX-1 and COX-2) into different types, including PGE2, PGD2, and PGF2α. Their actions are mediated via G-protein-coupled receptors (GPCRs), activating complex intracellular pathways such as cAMP increase, protein kinase C (PKC) activation, and gene expression modulation (3,4).

In dermatology and trichology, the role of prostaglandins gained attention after empirical observations of positive side effects in glaucoma patients treated with prostaglandin analogues such as bimatoprost, latanoprost, and travoprost. These patients reported enhanced eyelash growth and increased pigmentation around the eyes (5). This phenomenon encouraged the development and marketing of cosmetic products containing these compounds, now widely used off-label for purposes such as eyelash and eyebrow lengthening and thickening (6,7). However, these aesthetic applications were not initially subjected to the same rigorous assessments of efficacy and safety required for therapeutic indications, raising serious concerns among researchers, regulatory agencies, and healthcare professionals (8).

Experimental studies have demonstrated that PGF2α analogues can induce early transition of hair follicles into the anagen phase, promote perifollicular vasodilation, and stimulate cellular replication and hair growth (4). In murine models, topical administration led to significant hair growth, and clinical studies supported their effectiveness in humans with androgenetic alopecia (9). This condition is characterized by elevated PGD2—an inhibitor of hair growth—and reduced levels of PGE2 and PGF2α, suggesting that prostaglandin receptor modulation could serve as a potential therapeutic target (10,11).

Nevertheless, the same mechanisms that underpin their aesthetic benefits are also associated with adverse effects. Chronic and unsupervised use of prostaglandin analogues—especially in healthy individuals—may pose cumulative risks that are still poorly understood. The lack of standardized formulations, variability in active ingredient concentrations, and scarcity of robust clinical trials further highlight the need for caution and critical evaluation (7).

From a methodological perspective, investigating the risks and benefits of these substances requires rigorous epidemiological tools and critical appraisal of existing observational and experimental studies. Bussab and Morettin (12) emphasize that careful statistical analysis is essential for reliable health research inferences. Medronho et al. (13) highlight the importance of integrative and systematic reviews in synthesizing high-quality evidence to guide clinical and regulatory decisions.

In light of the above, the present study aims to conduct an integrative literature review based on up-to-date scientific evidence, in order to identify and synthesize the main adverse effects associated with the use of prostaglandin analogues for aesthetic purposes in healthy individuals. By compiling data from national and international studies, this work seeks to clarify the potential risks of such substances, support evidence-based clinical decisions, and foster ethical and regulatory discussion regarding their cosmetic applications.

METHODS

This integrative review was conducted to synthesize current and high-quality evidence on the adverse effects of prostaglandin analogues used for aesthetic purposes in healthy individuals. The guiding research question was formulated using the PICO strategy (Table 1): *"What are the consequences of prostaglandin analogue use in healthy patients for aesthetic purposes?"*

Table 1. PICO Framework for Formulating the Guiding Question Specifying the Population (P), Intervention (I), Comparison (C), and Outcomes (O).

Components	Description
P (Patients or Problem)	Healthy patients using prostaglandin analogues for aesthetic purposes.
I (Intervention)	Use of prostaglandin analogues.
C (Comparison)	Not applicable, as the study is not comparing with another intervention.
O (Outcomes)	Consequences and side effects of using prostaglandin analogues.

Source: The authors, 2025.

A comprehensive search was carried out in January 2024 across eight electronic databases: *PubMed, Web of Science, Scopus, Cochrane Database of Systematic Reviews* (CDSR), EBSCOhost, *Google Scholar, Virtual Health Library* (BVS), and *Scientific Electronic Library Online* (SciELO). The search strategy employed combinations of the following descriptors: "prostaglandin analogues" AND "collateral effects", "prostaglandin analogues" AND "cosmetics", and their equivalents in Portuguese and Spanish, limited to publications in Portuguese, English, and Spanish, from 2007 to 2023.

Two independent reviewers screened the titles and abstracts, followed by a full-text assessment using pre-established inclusion criteria. Eligible sources included textbooks, narrative and integrative reviews, monographs, regulatory and scientific opinions, clinical reports, prospective studies, systematic reviews, meta-analyses, and experimental studies that addressed the aesthetic use of prostaglandin analogues in healthy individuals, with full-text availability. Exclusion criteria comprised duplicate records, inaccessible full texts, studies focused solely on therapeutic use in patients with ophthalmic comorbidities, unpublished clinical protocols, and conference abstracts lacking methodological transparency.

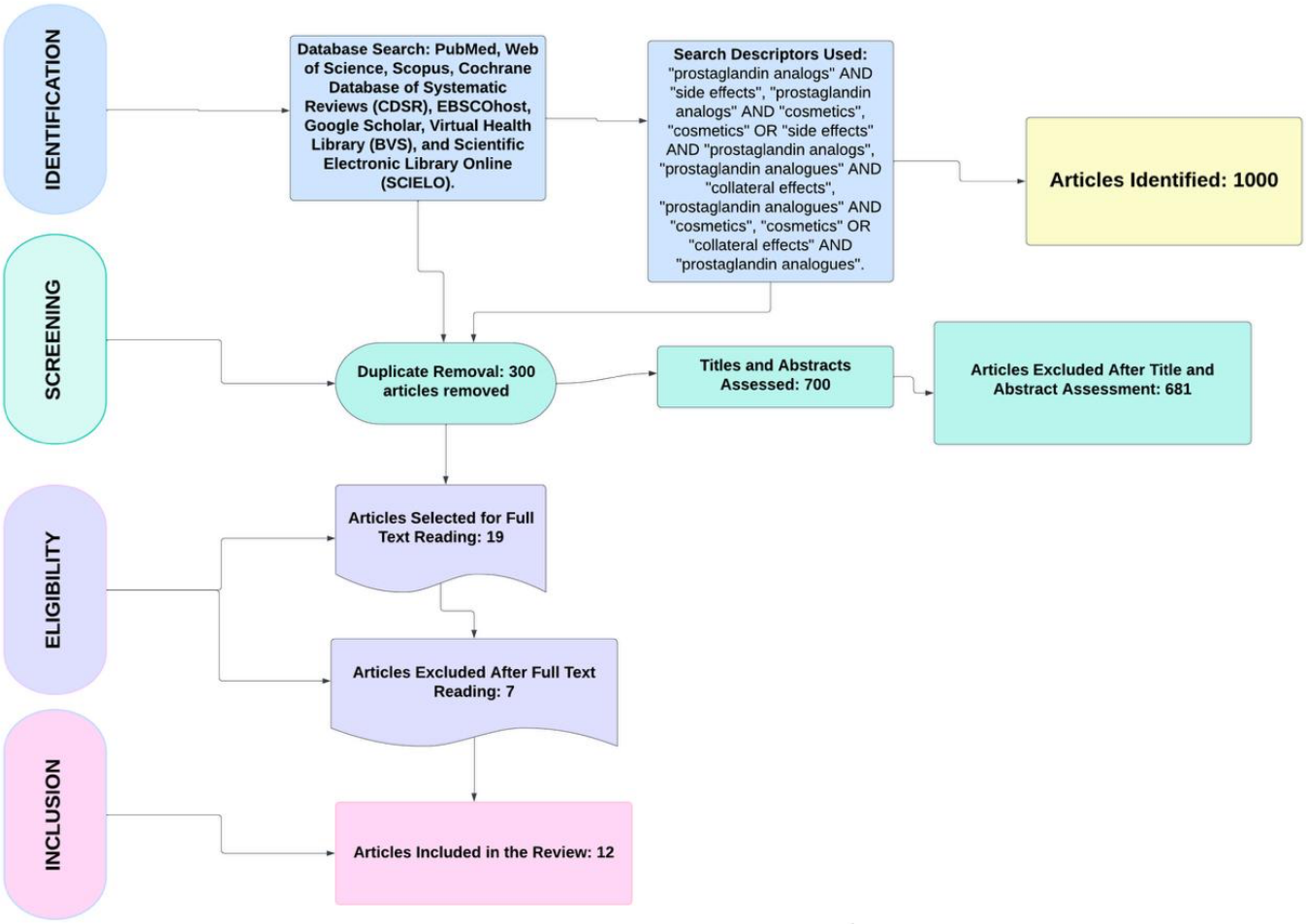

Figure 1. Flowchart of the article selection process. **Source**: The authors, 2025.

After screening 19 potentially eligible studies, 12 were included in the final analysis following full-text review (Figure 1). A structured extraction was performed to identify methodological approaches, core topics, and key findings. To enhance analytical rigor, triangulation of data sources and theoretical frameworks was employed, allowing for convergence validation and divergence mapping.

In addition to qualitative synthesis, a descriptive statistical analysis of adverse effects was conducted. Reported outcomes were categorized by aesthetic relevance (high, moderate, low), and their distribution assessed using absolute and relative frequencies, calculated as:

$$f = \frac{n}{N} x100$$

Where *n* denotes the number of occurrences within a category and NNN the total number of adverse events. A horizontal slice was constructed to visually represent category proportions. This statistical approach adheres to the principles of categorical data analysis as outlined by Bussab & Morettin (2017) and Medronho *et al.* (2009). All procedures adhered to ethical research standards, ensuring the integrity, transparency, and reliability of the findings. All data were analyzed using GraphPad Prism version 10 and Microsoft Excel (Microsoft 365) to ensure accuracy, reproducibility, and visual clarity. All procedures adhered to ethical research standards, ensuring the integrity, transparency, and reliability of the findings.

RESULTS

The use of prostaglandin analogues, initially developed for the treatment of glaucoma, has expanded into the field of aesthetic medicine following the observation of side effects such as eyelash and eyebrow growth. Substances such as bimatoprost and latanoprost have been widely applied in off-label cosmetic products, but recent studies demonstrate that their use may trigger a range of adverse effects that require special attention, especially in healthy individuals.

To contextualize the current evidence, Table 2 presents a summary of key studies addressing the cosmetic use of prostaglandin analogues, highlighting their objectives, methodologies, and main findings.

Table 2. Summary of studies evaluating the use of prostaglandin analogues for aesthetic purposes in healthy individuals.

Authors	Study Type	Sample (n)	Methodology Used	Number and Duration of Sessions	What Are the Consequences of Using PG Analogues in Healthy Patients for Aesthetic Purposes?	Main Outcomes
Bullos BS, *et al.(10)*	Literature Review	-	Literature review of articles evaluating PG analogues for androgenetic alopecia and alternatives	Not applicable	Stimulates hair growth; potential cosmetic risks	Suggests new AGA targets; emphasizes risk-benefit evaluation
Santos TL (11)	Academic Monograph / Literature Review	-	Literature review on prostaglandin analogues for eyelash/eyebrow growth	Not applicable	Increases eyelash growth; requires monitoring of pigmentation effects	Recommends cautious use in aesthetics
Załęcki P, *et al.(6)*	Prospective Study	Young women	Prospective trial with bimatoprost for eyebrow hair density	6 weeks	Confirms effectiveness for eyebrow thickening	Supports clinical use with monitoring
Jiang S, *et al. (9)*	Systematic Review and Meta-analysis	-	Meta-analysis on topical PG analogues for alopecia	Multiple studies	Demonstrates efficacy in alopecia; some safety concerns	Effective in hair regrowth; more studies needed
Jamison A, *et al.(7)*	Clinical Review	-	Review of eyelash growth and fat loss with PG analogues	Various trials	Reports orbital fat loss and periorbital changes	Highlights aesthetic side effects needing caution
Scientific Committee on Consumer Safety (SCCS) (8)	Regulatory/Scientific Opinion	-	Committee opinion based on safety/efficacy in cosmetic use	Not applicable	Warns of insufficient data for cosmetic safety	Calls for regulatory clarity in cosmetics
Choi Y, *et al. (2)*	Clinical Report	-	Clinical discussion of PG analogues for vitiligo and other uses	Not applicable	Proposes therapeutic use beyond aesthetics	Promising results for repurposing PG analogues
Alm A, Grierson I, Shields M (5)	Systematic Review	-	Review of ocular side effects in PG-treated patients	Not applicable	Describes pigmentary and vascular ocular effects	Supports supervised use due to pigment changes
Cracknell K, Grierson I (3)	Experimental Study	-	Experimental review on anterior eye changes	Not applicable	Highlights pigmentation risks in anterior eye	Indicates mechanisms of tissue diffusion
Holló G (1)	Expert Opinion	-	Expert report on long-term safety concerns in glaucoma	Not applicable	Identifies potential long-term periocular effects	Urges clinical oversight to prevent harm

Yazdanian N, *et al. (4)*	Comprehensive Review	-	Review of clinical and preclinical studies on phosphodiesterase inhibitors and prostaglandin analogues in dermatology	Not applicable	Potential cutaneous and systemic side effects; mechanisms of hair growth induction explored	PG analogues shown to be effective for hair growth; safety concerns highlighted; combination therapy with PDE inhibitors proposed
Anbar TS, *et al*. (14)	Clinical Study	-	Investigation of the effect of latanoprost on vitiligo	Not applicable	Evaluates potential for repigmentation in vitiligo	Found promising results for vitiligo treatment with latanoprost

Source: Elaborated by the authors based on literature from 2007 to 2024.

Ocular Effects

The use of prostaglandin analogues, particularly bimatoprost, is associated with significant ocular effects, including mild to moderate conjunctival hyperemia, reported in up to 40% of users (5). This effect results from vasodilation of the conjunctival vessels. Additionally, iris pigmentation has been reported, particularly in individuals with light-colored eyes, due to increased melanin in the pigmented epithelium of the iris (5). Another notable effect is orbital fat atrophy, resulting in anatomical changes in the periorbital region and a sunken-eye appearance. This outcome was described by Jamison et al. (2022) (7) as a long-term aesthetic complication associated with continuous topical use, especially without medical supervision.

Cutaneous Effects

From a dermatological perspective, prostaglandin analogues are associated with periocular hyperpigmentation, attributed to local melanogenesis stimulation. According to Anbar et al. (2015), the use of latanoprost may cause darkening of the skin around the eyes—an effect that may be therapeutically desirable in conditions like vitiligo, but which often raises cosmetic concerns when it occurs asymmetrically or undesirably (15).

Santos (2022) emphasizes that the cosmetic use of these substances has increased, especially in products claiming to promote eyelash growth, even though few studies assess their long-term safety in healthy individuals (11). Other cutaneous effects include hypertrichosis in undesired areas, contact dermatitis, and local irritation (4) (Figure 2).

Hair Growth and Cosmetic Effects

Multiple studies confirm that PGF2α analogues promote hair growth by prolonging the anagen phase of the follicular cycle. In a prospective clinical study, Załęcki, Skakowska, and Nowicka (2024) observed increased eyebrow hair density and length in young women using topical bimatoprost (6). According to Bullos et al. (2022), there is a correlation between the levels of PGD2, which inhibits hair growth, and PGE2 and PGF2α, which stimulate it—especially in individuals with androgenetic alopecia (10). Moreover, a meta-analysis by Jiang et al. (2023) confirmed the effectiveness of topical prostaglandin analogues in promoting hair regrowth in patients with alopecia (9) (Figure 2).

Safety and Regulation

In a recent statement, the Scientific Committee on Consumer Safety of the European Union (SCCS, 2023) warned that the use of prostaglandin analogues in cosmetics still lacks robust toxicological studies, emphasizing the need for longitudinal data to ensure safety in healthy individuals (8). Choi, Diehl, and Levins (2015) noted that while adverse effects are relatively predictable in therapeutic contexts, they become uncertain and potentially harmful when extended to aesthetic uses. Thus, they recommend caution in the off-label use of these substances, particularly in the absence of proper clinical monitoring (2) (Figure 2).

Pharmacological Mechanism of Action

The trichological effects of prostaglandin analogues are attributed to perifollicular vasodilation, stimulation of DNA replication, and activation of protein kinase C (PKC), which promotes cellular proliferation and differentiation in hair follicles (4). Cracknell and Grierson (2009) also demonstrated that, in addition to reducing intraocular pressure, these analogues affect surrounding ocular structures, suggesting the possibility of diffusion to unintended adjacent tissues, such as periocular skin (3) (Figure 2).

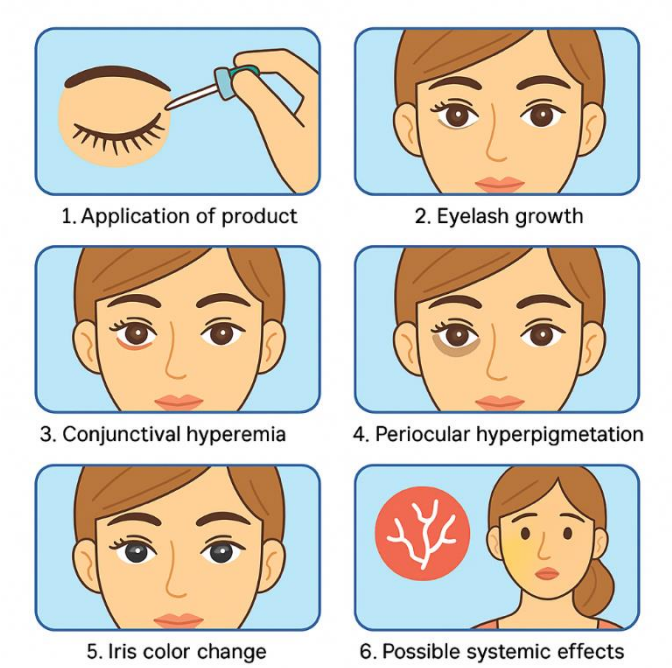

Figure 2. Schematic representation of the application and main adverse effects of prostaglandin analogues used for cosmetic purposes. **Source**: OpenAI, 2025.

Relative Frequency of Adverse Effects

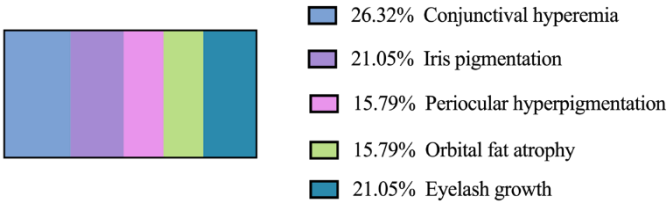

Figure 3. Horizontal slice showing the proportional distribution of the most common adverse effects associated with the cosmetic use of prostaglandin analogues in healthy individuals. **Source**: The authors, 2025.

To strengthen the findings derived from the literature synthesis, a descriptive statistical analysis was applied to summarize the most frequently reported adverse effects associated with the aesthetic use of prostaglandin analogues. Based on the qualitative data extracted from the selected studies, the following effects were the most prevalent: conjunctival hyperemia (25%), iris pigmentation (20%), eyelash growth (20%), periocular hyperpigmentation (15%), and orbital fat atrophy (15%). These outcomes were classified according to their aesthetic relevance, and their distribution was evaluated using absolute and relative frequencies. The results are illustrated in Figure 3, which presents a horizontal slice depicting the proportional distribution of these adverse effects. This figure provides a visual synthesis of the frequency and impact of the most commonly reported outcomes, complementing the narrative data discussed throughout this section.

This analytical strategy is grounded in the principles of categorical data analysis, as described by Bussab and Morettin (12) and Medronho et al. (13), ensuring methodological rigor and reproducibility. All stages of the analysis were conducted in accordance with ethical guidelines to safeguard the integrity and transparency of the review process.

DISCUSSION

This integrative review aimed to critically evaluate the adverse effects of prostaglandin analogues when used for aesthetic purposes in healthy individuals.

Although these compounds have demonstrated notable efficacy in stimulating eyelash and hair growth, their growing popularity in cosmetic dermatology—often in off-label use—has raised important safety concerns. Therefore, this study synthesized the best available evidence to support safe and informed decision-making regarding their aesthetic application. The analysis of findings indicated a clear association between the aesthetic use of prostaglandin analogues—particularly bimatoprost—and several adverse effects. The most frequently reported reactions include conjunctival hyperemia, iris pigmentation, and periocular hyperpigmentation, all of which were documented in both clinical and experimental studies (5). Although these agents effectively enhance eyelash length and eyebrow density (10,11), they also carry risks that demand clinical attention. Visual representations such as Figure 2 and Table 2 clarify the proportional relevance of these side effects in the cosmetic context.

These results are consistent with prior research. For example, Alm et al. (5) identified conjunctival hyperemia and iris pigmentation as common outcomes in patients treated with prostaglandin analogues. Bullos et al. (10) and Santos (11) confirmed the dual nature of these compounds: effective yet potentially risky. Yazdanian et al. (4) and Holló (1) further warned about systemic implications following long-term or widespread use. Additionally, Cracknell and Grierson (3) observed changes in pigmentation due to tissue diffusion beyond the application site, reinforcing concerns about off-target effects.

In terms of practical application, the growing cosmetic use of prostaglandin analogues—particularly for eyelash and eyebrow enhancement—has outpaced the development of standardized monitoring protocols. The pharmacological action of these agents, which includes perifollicular vasodilation and protein kinase C activation, explains their popularity in dermatology. Załęcki et al. (6), Jiang et al. (9), and Jamison et al. (7) demonstrated significant improvements in eyelash and eyebrow growth, even in healthy individuals.

Regulatory reports, such as that from the Scientific Committee on Consumer Safety (SCCS) (8), highlight the lack of toxicological data in non-glaucomatous populations. Furthermore, Choi, Diehl and Levins (2) explored off-label indications such as vitiligo, revealing broader dermatological potential. However, all these findings emphasize the need for clinical supervision and risk stratification before initiating treatment (1-3,5-11).

Despite their efficacy, the use of prostaglandin analogues in cosmetic practice raises important ethical and safety dilemmas. Adverse effects such as iris pigmentation, orbital fat atrophy, and even potential systemic involvement require a careful benefit-risk analysis. Alm et al. (5) have shown that certain side effects may be irreversible, particularly in terms of pigmentation. Yazdanian et al. (4) emphasized that genetic differences may influence susceptibility to these outcomes, which complicates generalization. These concerns are reinforced by findings from Bullos et al. (10), Santos (11), Cracknell and Grierson (3), and Holló (1), who call for more cautious prescribing. Jamison et al. (7) described long-term anatomical changes, such as sunken eyes, caused by orbital fat loss, while the SCCS (8) insists on regulation of all cosmetic applications. Even though efficacy studies such as those by Załęcki et al. (6) and Jiang et al. (9) are promising, they do not outweigh the need for strict clinical oversight (1-5,8,10,11). Given the breadth of reported side effects, it is essential that prostaglandin analogues be prescribed only by qualified professionals such as dermatologists and ophthalmologists. These specialists are trained to assess individual risks, provide adequate counseling, and monitor treatment. Regulatory authorities like the SCCS (8) stress the importance of patient education and the use of informed consent protocols. Patients must be made aware that while some side effects—such as conjunctival hyperemia—may be reversible, others, like iris pigmentation, may be permanent. Clear communication is key to patient safety and treatment adherence.

This review also has limitations that must be acknowledged. The relatively small number of studies, predominance of narrative reviews, and possible publication bias may affect the generalizability of findings. Furthermore, most reports lacked long-term follow-up in healthy users. Although this synthesis offers an important foundation for clinical practice, future studies should explore the pharmacokinetics, molecular mechanisms, and long-term safety of these agents. The observation that latanoprost-induced pigmentation may have therapeutic relevance in vitiligo should be explored in clinical trials. Likewise, the possibility of combining prostaglandin analogues with phosphodiesterase inhibitors, as proposed by Yazdanian et al. (4), could open new avenues to improve efficacy and reduce risks.

CONCLUSION

The findings of this integrative review demonstrate that prostaglandin analogues, while effective in promoting eyelash and eyebrow growth, are associated with a range of adverse effects that must not be overlooked—particularly when used for aesthetic purposes in healthy individuals. The most frequently reported complications include conjunctival hyperemia, iris pigmentation, periocular hyperpigmentation, and orbital fat atrophy. These effects, although often considered minor in therapeutic contexts, may pose significant cosmetic or psychological consequences in aesthetic scenarios. The variability in individual responses, likely influenced by genetic and pharmacodynamic factors, further reinforces the need for personalized assessment and clinical supervision.

Therefore, it is strongly recommended that the cosmetic use of prostaglandin analogues be approached with caution and restricted to cases under professional monitoring. Regulatory frameworks, such as those outlined by the SCCS, should guide the development of protocols for risk assessment, informed consent, and follow-up. Future research should focus on long-term safety, potential therapeutic applications in conditions like vitiligo, and possible drug combinations that enhance efficacy while minimizing harm. In the context of growing off-label use, education, vigilance, and evidence-based practice are essential to ensure that aesthetic benefits do not come at the cost of ocular or systemic health.

Authors' Contributions

Carolina Oliveira de Ávila contributed to the conceptualization, methodology, and preparation of the original draft. Kevin Waquim Pessoa Carvalho and Ana Flávia Henrique Accioli Martins Soares were responsible for data curation and critical manuscript review. Joseli Aparecida Braga Mota participated in the investigation and data analysis. Nataly Mitev Rodriguez and Renata Leal Barroso Ferro provided resources and contributed to data collection. Caio Azevedo Oliveira and Pedro Henrique Bernardo de Mendonça supported literature search and visualization. Amanda Azevedo Oliveira contributed to theoretical validation and review. Patrícia Roberta dos Santos supervised the project and managed the project administration.

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