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Review

Hormonal Therapies in Cosmetic Dermatology: Mechanisms, Clinical Applications, and Future Perspectives

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Abstract

Background: Hormonal fluctuations significantly influence skin physiology, affecting collagen production, sebum regulation, pigmentation, and tissue repair. Hormonal therapies are increasingly used in cosmetic dermatology to address age-related and hormone-dependent skin changes. Methods: This narrative review synthesizes the current literature on the mechanisms, clinical applications, and future directions of hormonal therapies in dermatologic aesthetics. Studies were selected through a comprehensive search on PubMed, Scopus, and Web of Science. Results: Estrogens, androgens, progesterone, and other hormones act on skin through specific receptors, modulating fibroblast, sebocyte, and melanocyte activity. Clinical applications include hormone-based strategies for anti-aging, acne, melasma, alopecia, and postmenopausal atrophy. Both systemic (e.g., HRT) and topical (e.g., clascoterone, phytoestrogens) approaches are discussed. Safety concerns, including systemic absorption and off-label use, require careful evaluation. Emerging technologies such as SERMs, nanocarriers, and regenerative combinations suggest promising future avenues. Conclusions: Hormonal therapies offer a biologically rational and increasingly evidence-based tool in cosmetic dermatology. Responsible integration into clinical practice depends on personalized approaches, ethical prescribing, and further research on long-term safety and efficacy.

Keywords: cosmetic dermatology; hormonal therapy; hormone receptors; skin aging; acne; melasma; androgenetic alopecia; hormone replacement therapy; topical hormones; regenerative dermatology

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1. Introduction

The skin is a dynamic organ equipped with specific receptors for numerous hormones that regulate fundamental processes such as cell proliferation, collagen synthesis, pigmentation, and immune response [1]. Sex hormones, in particular estrogens, progesterone, and androgens, directly influence dermal fibroblast metabolism, sebum production, and melanocyte activity [2]. Estrogens promote collagen and elastin synthesis, supporting skin hydration and firmness, while androgens modulate sebaceous gland function and keratinization [3].

Beyond sex hormones, thyroid hormones and glucocorticoids also play key roles: the former regulate epidermal turnover and cutaneous thermoregulation, while the latter modulate inflammatory responses and wound healing [4]. Hormonal actions are mediated

by nuclear and membrane receptors located in the various skin layers, whose expression levels may vary according to age, sex, and physiological status [5].

Maintaining skin trophism requires a finely tuned hormonal balance. Even minimal alterations in plasma levels or receptor sensitivity can result in visible changes in texture, pigmentation, and skin thickness. This balance is particularly critical during periods of significant endocrine change, such as puberty, pregnancy, and menopause, when the skin may exhibit fragility, hyperpigmentation, or marked dryness [1,6].

Many conditions of interest in cosmetic dermatology have a significant hormonal component. Acne, for instance, is often linked to relative androgen excess or increased sensitivity of sebaceous gland receptors [7]. Similarly, melasma is frequently associated with hormonal variations, such as those induced by pregnancy or oral contraceptive use [8].

Menopause represents a critical stage for skin aesthetics—estrogen decline leads to reduced dermal thickness and the loss of elasticity and hydration, with a consequent accentuation of wrinkles [9]. Endocrine disorders such as hypothyroidism or hypercortisolism may also impact skin appearance, causing changes in pigmentation, subcutaneous fat distribution, and the skin's regenerative capacity.

The aim of this review is to provide an updated overview of the biological mechanisms, clinical applications, and future perspectives of hormonal therapies in cosmetic dermatology. Both systemic and topical strategies will be examined, with particular attention to their efficacy, safety, and ethical considerations.

This review seeks to integrate the most recent evidence with established knowledge, offering a valuable resource for dermatologists, aesthetic physicians, and researchers interested in targeted hormonal modulation to improve skin health and appearance.

Terminology note: Throughout this review, "estrogen(s)" refers to the hormone class, whereas "estradiol (E2)" denotes the specific endogenous estrogen. When a formulation contains the native molecule, we use "17β-estradiol." American spelling ("estrogen") is adopted in the main text.

2. Methods

This review was conducted as a narrative synthesis of the current scientific literature on hormonal therapies in cosmetic dermatology. A comprehensive search on the PubMed/MEDLINE, Scopus, and Web of Science databases was performed from July 2010 to July 2025. The search included combinations of keywords such as "hormonal therapy," "cosmetic dermatology," "estrogen," "androgens," "HRT," "anti-aging," "melasma," "acne," "alopecia," "bioidentical hormones," "topical hormones," and "regenerative medicine."

Peer-reviewed clinical studies, meta-analyses, systematic reviews, and preclinical studies published in English were included. Priority was given to articles published in the last five years to ensure the inclusion of the most current evidence, while foundational studies relevant to mechanisms of action and clinical applications were also considered regardless of publication date.

Data were categorized into three main domains: (1) biological mechanisms of hormonal action in the skin; (2) clinical applications of hormone-based therapies; and (3) future directions, including personalized approaches and regenerative integrations. The selection of studies and data extraction were performed manually by the authors to ensure clinical relevance and thematic consistency.

This review does not include a formal quality assessment or meta-analysis, given its narrative nature and the heterogeneity of study designs and outcomes across the literature (Figure S1).

3. Hormonal Physiology of the Skin

To orient the reader, Figure 1 provides a schematic overview of the main hormone-activated signaling pathways in the skin (melatonin, estrogens, androgens, and IGF-1), their receptors (ERα/ERβ, GPER/mER, AR, IGF-1R), and the downstream effects on fibroblasts, sebocytes, and keratinocytes.

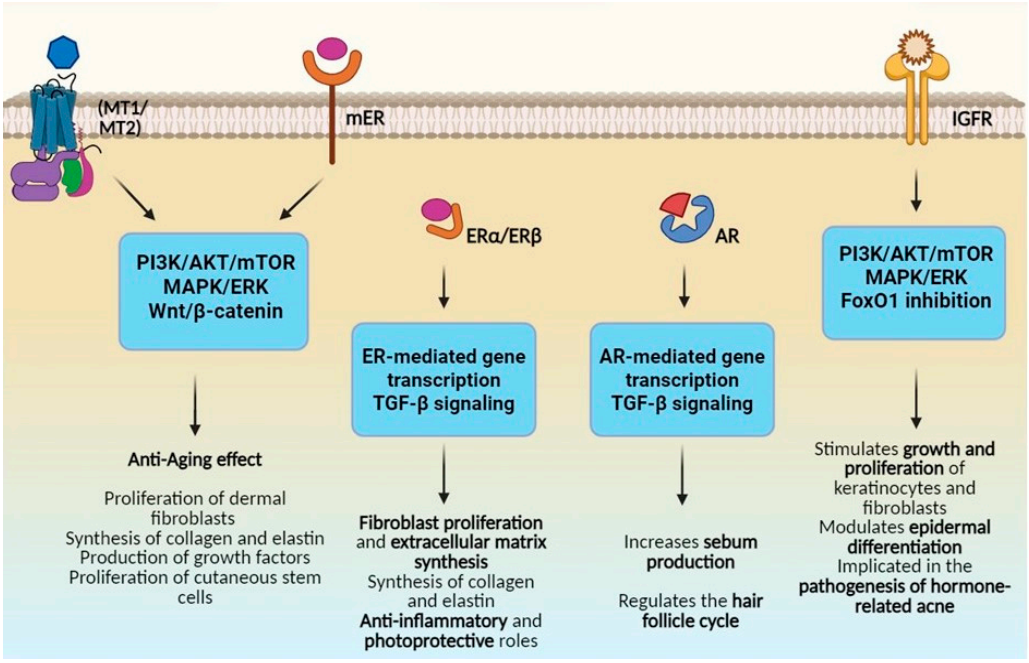


Figure 1. Intracellular pathways activated by melatonin, estrogens, androgens, and IGF-1 and their dermatologic effects. Solid arrows indicate activation/positive regulation; blunt-ended lines indicate inhibition; dashed arrows denote cross-talk or non-genomic signaling. ERα/ERβ and membrane ERs (mERs) couple to PI3K/AKT and MAPK/ERK to enhance collagen synthesis, photoprotection, and anti-inflammatory responses. Androgen receptor (AR) activation increases sebum production and modulates TGF-β and hair-cycle signaling. IGF-1 promotes proliferation and wound healing through PI3K/AKT/mTOR and MAPK/ERK. Inhibition of FoxO1 contributes to sebaceous activity and acne pathogenesis.

3.1. Structure and Function of the Skin in Relation to Hormonal Receptors

The skin is composed of three main layers—the epidermis, dermis, and hypodermis—each containing cells that express receptors for various hormones [10]. Keratinocytes in the epidermis, fibroblasts in the dermis, and sebocytes in sebaceous glands all possess nuclear and membrane receptors capable of binding steroid hormones, thyroid hormones, and peptide hormones [11].

Hormonal receptors in the skin function as molecular switches that regulate gene expression and modulate protein synthesis. For example, estrogen receptors (ER-α and ER-β) in dermal fibroblasts promote collagen synthesis and vascularization, while androgen receptors in sebocytes stimulate sebum production [12]. The distribution and density of these receptors can vary based on anatomical site, age, sex, and hormonal status [13].

Interactions between hormones and their receptors also affect immune cell behavior in the skin. Langerhans cells, mast cells, and dermal macrophages can respond to circulating hormones, influencing inflammatory responses and tissue repair [14]. This receptor-mediated signaling is central to maintaining skin homeostasis and responding to physiological changes.

3.2. Main Hormones Involved in Skin Health and Appearance

For orientation, Table 1 compiles the major hormones relevant to skin health and appearance and the canonical intracellular pathways they activate. The table also outlines the most consistent cutaneous effects reported in the literature.

Table 1. Summary of main hormones, their key pathways, and cutaneous effects.

Hormone	Key Pathways	Cutaneous Effects
Estrogens	PI3K/AKT, MAPK/ERK, Wnt/β-catenin	Increases collagen and elastin synthesis, improves hydration, reduces wrinkles
Androgens	AR-mediated transcription, TGF-β	Stimulates sebum production, regulates hair cycle, contributes to acne and alopecia
Insulin/IGF-1	PI3K/AKT/mTOR, MAPK/ERK, FoxO1	Enhances proliferation of keratinocytes and fibroblasts; implicated in acne
Melatonin	PI3K/AKT, MAPK, Wnt/β-catenin, NF-κB	Antioxidant, anti-inflammatory, stimulates skin regeneration, UV protective
DHEA	SIRT1, Nrf2/ARE, NF-κB, ERβ, AR	Anti-aging, antioxidant via SIRT1 and Nrf2, reduces inflammation via NF-κB

3.2.1. Estrogens

Estrogens have well-documented roles in enhancing dermal thickness, elasticity, and hydration through stimulation of collagen, elastin, and glycosaminoglycan synthesis [15]. They also promote angiogenesis and increase the skin's antioxidant capacity, protecting against oxidative stress [16].

3.2.2. Progesterone

Progesterone exerts regulatory effects on sebaceous gland activity and can counteract some androgen-mediated effects on the skin [17]. It also influences keratinocyte proliferation and differentiation, contributing to epidermal barrier function [18].

3.2.3. Androgens

Androgens, including testosterone and dihydrotestosterone (DHT), are potent modulators of sebaceous gland activity, stimulating sebum production and influencing acne pathogenesis [19]. They also affect hair-follicle cycling, contributing to both androgenetic alopecia and hirsutism [20]. While essential for certain anabolic skin processes, excessive androgen signaling can lead to aesthetic concerns [21].

3.2.4. Cortisol and Adrenal Hormones

Cortisol, the primary glucocorticoid, modulates skin inflammation and immune responses [22]. Short-term exposure can be beneficial for controlling inflammatory dermatoses, but chronic elevation (as seen in stress or Cushing's syndrome) leads to dermal atrophy, impaired barrier function, and delayed wound healing [23].

3.2.5. Thyroid Hormones

Thyroid hormones (T3 and T4) influence epidermal turnover, hair growth, and skin temperature regulation [24]. Hypothyroidism is associated with dry, coarse skin and hair loss, while hyperthyroidism can cause thinning skin and increased sweating. Thyroid hormone receptors in keratinocytes and fibroblasts mediate these effects at the cellular level [25].

3.3. Hormonal Changes Across Life Stages

Hormonal influence on the skin changes significantly throughout life. During puberty, androgen surges trigger increased sebaceous activity and acne development [26]. In

pregnancy, elevated estrogen and progesterone levels enhance skin hydration but may also lead to hyperpigmentation disorders such as melasma [27].

Menopause is marked by a steep decline in estrogen, leading to reduced collagen synthesis, skin thinning, dryness, and increased wrinkling [28]. In aging men, gradual decreases in testosterone can also impact skin trophism, albeit more subtly. Understanding these life-stage-related hormonal shifts is essential for tailoring cosmetic and therapeutic interventions.

4. Mechanisms of Action of Hormonal Therapies in Cosmetic Dermatology

Table 2 summarizes the main indications for hormonal therapies in cosmetic dermatology, the representative strategies, and their mechanisms/clinical effects.

Table 2. Summary of hormonal therapies and their main clinical applications in cosmetic dermatology. Numbers in square brackets refer to the references listed at the end of the manuscript.

Indication	Hormonal Strategies	Mechanisms/Clinical Effects
Skin aging and rejuvenation	Systemic HRT, topical estrogens, phytoestrogens, combination with energy-based devices	Stimulates fibroblast activity; increases collagen and ECM synthesis; improves hydration; reduces wrinkles
Hormonal acne	Systemic antiandrogens (spironolactone, cyproterone acetate), combined oral contraceptives, topical clascoterone	Reduces sebum production and inflammation via androgen receptor blockade; controls acne flares
Melasma and pigmentary disorders	Hormonal modulation (adjustment of contraceptives), topical depigmenting agents, procedural interventions (peels, lasers), tranexamic acid	Reduces melanocyte stimulation; enhances efficacy of depigmenting agents; improves hormonal stability
Androgenetic alopecia	5α-reductase inhibitors (finasteride, dutasteride), topical antiandrogens, COCs, PRP, LLLT	Reduces DHT levels; slows follicular miniaturization; promotes hair regrowth; enhances follicular response
Postmenopausal atrophy and skin dryness	Systemic HRT, topical estrogens, phytoestrogens, supportive skincare (ceramide emollients, gentle cleansers)	Restores barrier function; improves hydration; increases epidermal thickness; reduces irritation and xerosis

4.1. Modulation of Cutaneous Hormonal Receptors

Hormonal therapies exert their effects largely through modulation of skin-specific hormone receptors located in keratinocytes, fibroblasts, sebocytes, and melanocytes [29]. By binding to these nuclear or membrane receptors, hormones initiate transcriptional changes that alter cell proliferation, differentiation, and extracellular matrix production [30].

Estrogenic compounds can upregulate estrogen receptor expression in dermal fibroblasts, thereby amplifying collagen synthesis and angiogenesis [31]. Conversely, antiandrogens block androgen receptor activation in sebaceous glands, reducing sebum output and acne severity [32]. The net clinical outcome depends on receptor density, ligand affinity, and cross-talk with other signaling pathways, such as growth factors and cytokines.

4.2. Influence on Collagen and Elastin Synthesis

One of the most sought-after effects in cosmetic dermatology is the restoration of dermal elasticity and firmness through enhanced collagen and elastin production [33]. Estrogens are known to stimulate fibroblast activity, increasing type I and III collagen deposition while reducing collagen degradation by downregulating matrix metalloproteinases [34].

Hormone-based interventions—whether systemic hormone replacement therapy (HRT) or topical estrogen analogs—can improve skin thickness and smoothness by promoting extracellular matrix synthesis [35,36]. Similarly, certain growth hormone pathways influenced by sex steroids contribute indirectly to dermal structural integrity [37]. These

effects are particularly relevant in postmenopausal women and aging men, where collagen loss contributes significantly to wrinkle formation.

4.3. Regulation of Sebum Production

Sebum production is primarily controlled by androgens, particularly DHT, acting on sebaceous gland receptors [38]. Hormonal therapies that reduce androgen levels or block receptor activation can effectively lower sebum output, making them useful in treating acne-prone skin [39].

In some contexts, progesterone and estrogen derivatives are used to counteract androgen-driven sebogenesis, restoring a more balanced sebum composition [40]. The goal is to reduce excessive oiliness without inducing xerosis, thereby preserving the skin barrier and preventing secondary irritation.

4.4. Effects on Pigmentation and Melanogenesis

Hormonal regulation of melanogenesis is complex, involving direct effects on melanocyte activity and indirect modulation via keratinocytes [41]. Estrogens can enhance melanin synthesis under certain conditions, while progesterone may counterbalance this effect.

Hyperpigmentation disorders such as melasma are strongly associated with hormonal fluctuations, particularly during pregnancy or oral contraceptive use. Hormonal therapies that aim to stabilize estrogen and progesterone levels or modulate melanocyte receptor activity can help reduce pigment overproduction [42]. These interventions may be combined with photoprotection and topical depigmenting agents for optimal results.

4.5. Anti-Inflammatory and Regenerative Actions

Several hormones exert potent anti-inflammatory effects that are relevant for skin rejuvenation and repair [43]. Glucocorticoids, while immunosuppressive at high doses, can control inflammatory cascades when used judiciously in short courses [44]. Estrogens and androgens also modulate cytokine profiles, influencing wound healing speed and scar quality [45].

In regenerative dermatology, hormone-based strategies can enhance keratinocyte migration, fibroblast proliferation, and angiogenesis [46]. These mechanisms contribute not only to improved aesthetic outcomes but also to the restoration of barrier function after cosmetic procedures such as laser resurfacing or chemical peels.

5. Clinical Applications

Anti-Aging and Skin Rejuvenation

Hormonal decline, particularly estrogen deficiency, is a key driver of cutaneous aging, leading to collagen loss, reduced elasticity, and impaired barrier function [47]. Hormonal therapies (both systemic and topical) can counteract these changes by stimulating fibroblast activity, increasing extracellular matrix deposition, and improving dermal hydration [48]. Systemic hormone replacement therapy (HRT) in postmenopausal women has been shown to enhance skin thickness and reduce wrinkle depth [49]. Topical estrogen or phytoestrogen formulations provide localized benefits without significant systemic exposure, improving texture and luminosity [50]. Combination protocols incorporating hormonal therapy with energy-based devices, such as fractional lasers or radiofrequency, can amplify collagen remodeling and vascularization [51]. Because the prescribing indications, regimens, and systemic risks of hormone replacement therapy (HRT) are detailed in Section 6.1, here we have only summarized its cutaneous endpoints (increased skin thickness, elasticity, and hydration); we refer readers to Section 6.1 for clinical use and safety.

Beyond menopausal skin changes, androgen signaling is central to another highly prevalent aesthetic concern—hormonal acne.

Acne with a hormonal component is commonly observed in adolescents and adult women, particularly in the perimenstrual phase [52]. Androgen excess or increased receptor sensitivity leads to sebaceous hyperactivity and follicular hyperkeratinization [53]. Therapeutic strategies include systemic antiandrogens (e.g., spironolactone, cyproterone acetate) and combined oral contraceptives containing estrogen and progestin, which suppress ovarian androgen production and increase sex hormone-binding globulin levels [54]. Topical antiandrogen formulations, specifically clascoterone 1% cream, are now FDA-approved for the treatment of acne vulgaris in patients 12 years and older, including adolescents and adult women with hormonally mediated acne and perimenstrual flares. Clascoterone acts as a topical androgen receptor antagonist, directly inhibiting DHT binding in sebaceous glands and reducing sebum production and inflammation at the site of application, with minimal systemic absorption and no reported systemic antiandrogenic effects [55].

Phase 3 randomized controlled trials demonstrate that clascoterone 1% cream, applied twice daily, significantly reduces both inflammatory and noninflammatory lesion counts compared to vehicle, with a favorable safety profile limited to mild local skin reactions [55,56]. Long-term safety data up to 9 months support its tolerability [55–57]. Clascoterone demonstrates clinical potential as a therapeutic option for patients who are not candidates for systemic antiandrogens due to contraindications, adverse effects, or pregnancy concerns [58].

Comparatively, established systemic antiandrogens such as spironolactone (typically 50–200 mg daily), cyproterone acetate (not FDA-approved in the US), and combined oral contraceptives (COCs) are effective for hormonally mediated acne but carry risks of systemic side effects, require monitoring, and are contraindicated in certain populations [55,57]. The American Academy of Dermatology conditionally recommends spironolactone for women with acne, and COCs are established second-line therapy, but both are unsuitable for some patients due to systemic risks [54,58].

Topical spironolactone and other topical antiandrogens (e.g., canrenone, finasteride) have shown some efficacy in small studies, but the Endocrine Society currently advises against their use due to inconsistent results and the lack of robust evidence [59]. Hormonal approaches are often integrated with conventional acne therapies, such as retinoids and benzoyl peroxide, to enhance efficacy and reduce relapse rates [53,54].

Where acne exemplifies androgen-driven sebaceous activity, melasma reflects estrogen/progesterone-related melanocyte stimulation; we therefore next address hormone-informed management of pigmentary disorders.

Melasma management requires a multifaceted approach due to its chronicity, frequent association with hormonal fluctuations (e.g., pregnancy, oral contraceptives), and high relapse rates. Estrogen and progesterone increase melanocyte activity both by direct stimulation of their respective receptors on melanocytes and by inducing paracrine signaling from keratinocytes, which upregulates melanogenic factors such as stem cell factor and endothelin-1, leading to increased melanin synthesis [60–62].

First-line management is rigorous photoprotection, including daily use of broad-spectrum sunscreen covering both UV and visible light, as visible light can exacerbate melasma and reduce the efficacy of topical agents. Stabilization of hormonal status is critical; discontinuation or adjustment of estrogen/progestin-containing contraceptives should be considered if feasible, as ongoing hormonal stimulation perpetuates melanogenesis [62,63].

Topical depigmenting agents are the mainstay of therapy. Hydroquinone (2–4%) is the most effective single agent, often used in triple combination creams (hydroquinone, tretinoin, corticosteroid) for enhanced efficacy. Azelaic acid (15–20%) is an alternative,

especially in pregnancy or for those intolerant to hydroquinone [64,65]. Maintenance therapy with non-hydroquinone agents and continued photoprotection is essential to prevent relapse [63].

Hormonal modulation—such as switching to non-hormonal contraception or minimizing exogenous estrogen/progestin exposure—can be beneficial, but direct anti-estrogen or anti-progesterone receptor blockade is not established in clinical practice [62,63].

Procedural interventions (chemical peels, low-fluence Q-switched lasers, microneedling) are reserved for resistant cases and should be combined with ongoing topical therapy and photoprotection to reduce relapse risk and adverse effects. Oral tranexamic acid is an emerging adjunct for refractory melasma but requires careful patient selection [65,66].

Combining hormonal stabilization with procedural interventions addresses both the underlying drivers and the pigmentary sequelae, improving the likelihood of durable remission and reducing recurrence [66]. Periodic reassessment and individualized therapy are essential due to the relapsing nature of melasma [65].

In contrast to melanocyte dysfunction in melasma, hair-follicle miniaturization in androgenetic alopecia is primarily mediated by androgen signaling, guiding a different therapeutic strategy.

Current hormonal interventions for androgenetic alopecia (AGA) include oral 5-α-reductase inhibitors—finasteride (1 mg daily, FDA-approved for men) and dutasteride (0.5 mg daily, off-label)—which reduce DHT synthesis and slow follicular miniaturization [67–69]. Dutasteride is more potent than finasteride but is not FDA-approved for AGA and is reserved for refractory cases, especially in men and postmenopausal women due to teratogenicity and effects on fertility [67–69]. In women, particularly those with evidence of hyperandrogenism or who require contraception, COCs and antiandrogens such as spironolactone or off-label finasteride/dutasteride are used to slow progression and promote partial regrowth [70]. COCs suppress ovarian androgen production and increase sex hormone-binding globulin, reducing free DHT [71].

Topical finasteride (0.25% daily) is an emerging therapy with efficacy comparable to that of oral finasteride but with markedly lower systemic DHT suppression and reduced risk of sexual side effects. A phase III trial in men showed significant improvement in hair count with topical finasteride versus placebo and similar efficacy to oral finasteride but with >100-fold lower plasma finasteride levels [72,73]. Topical antiandrogens such as clascoterone and investigational agents (e.g., pyrilutamide) are under study, with early data suggesting benefits and minimal systemic absorption [73].

Adjunctive therapies such as platelet-rich plasma (PRP) and low-level laser therapy (LLLT) can enhance follicular response when combined with hormonal interventions. PRP delivers growth factors that may stimulate hair regrowth, and LLLT promotes follicular cycling; both have demonstrated additive effects in combination with standard therapies, though protocols are not yet standardized [74–77].

As in acne and melasma, where hormonal modulation is central to management, targeting androgen pathways in AGA is foundational, with topical formulations and procedural adjuncts offering expanded options and improved safety profiles [71,72].

Finally, because estrogen decline also compromises barrier function and hydration, we conclude this section with therapies for postmenopausal dryness and cutaneous atrophy.

Postmenopausal estrogen decline leads to decreased sebaceous gland activity, reduced natural moisturizing factor production, and thinning of the stratum corneum, resulting in clinical features such as xerosis, skin fragility, and increased susceptibility to irritation [78–82]. These changes are well-documented, with studies showing that estrogen deficiency impairs skin hydration, barrier function, and epidermal turnover, contributing to dryness and increased irritability [78–82]. Topical estrogen formulations have demon-

strated efficacy in improving skin hydration, epidermal thickness, and barrier integrity, with evidence supporting their ability to restore stratum corneum structure and function in both animal models and clinical studies. Isoflavone-based (phytoestrogen) formulations have shown some benefit in improving skin quality, though data are less robust compared to topical estrogen. Systemic HRT offers broader benefits, including increased skin collagen, thickness, and hydration, but its use should be individualized and based on a careful risk–benefit assessment, as it is not recommended solely for skin symptoms [83,84].

Adjunctive measures such as ceramide-rich emollients and gentle cleansers are recommended for maintaining skin hydration and barrier function, reducing transepidermal water loss and supporting the effects of hormonal or topical therapies [85,86]. Emollients containing humectants and occlusives remain the standard of care for xerosis in postmenopausal women [85].

In summary, estrogen decline after menopause impairs skin barrier function and hydration, and both hormonal and non-hormonal topical therapies, along with supportive skin care, are evidence-based strategies that address these changes [80,84,85].

6. Modes of Administration

6.1. Systemic Hormone Replacement Therapy (HRT)

Systemic HRT is primarily indicated for the relief of moderate to severe menopausal vasomotor symptoms, such as hot flashes and night sweats, and is also approved for the prevention of postmenopausal osteoporosis in select patients. The most common regimens involve estrogens (oral or transdermal) with or without progestins, depending on uterine status. For women with an intact uterus, a progestogen is required to reduce the risk of endometrial hyperplasia and cancer; options include micronized progesterone or synthetic progestins, and some regimens combine both hormones in a single pill or patch [86].

The dermatologic outcomes of HRT—namely improved skin thickness, elasticity, and hydration—are summarized in Section 5.

Transdermal estrogen (patches, gels) is often preferred over oral forms to avoid hepatic first-pass metabolism, resulting in more stable serum hormone levels and a lower risk of venous thromboembolism (VTE) and stroke, particularly in women with obesity or metabolic risk factors [87,88]. Oral estrogens increase hepatic production of clotting factors and inflammatory markers, which may elevate VTE risk [88]. The lowest effective dose should be used for the shortest duration necessary, with periodic reassessment of the need for continued therapy [80,89].

Systemic HRT can improve skin thickness, elasticity, and hydration, but these dermatologic benefits are not primary indications for therapy and should not outweigh consideration of risks. Potential risks include increased incidence of VTE, stroke, and hormone-sensitive cancers (notably, breast cancer with combined estrogen–progestin therapy), necessitating individualized risk assessment and patient selection [89]. The US Preventive Services Task Force and other expert groups recommend against HRT for the primary prevention of chronic conditions [90,91].

6.2. Topical Hormone-Based Therapies

Topical formulations of estrogens, androgens, and progesterone are designed to exert local effects on skin receptors, with the goal of minimizing systemic exposure. Evidence supports the use of topical estrogens to improve skin thickness, elasticity, and hydration and reduce wrinkle depth in postmenopausal women, with minimal systemic hormonal side effects when used appropriately. These benefits are attributed to increased collagen synthesis, improved barrier function, and enhanced skin moisture. Clinical studies have shown that topical estradiol and estriol creams can significantly improve skin firmness

and reduce wrinkle depth without notable systemic hormonal changes, except for mild increases in prolactin in some cases [92–94].

Percutaneous absorption of these hormones varies by formulation, concentration, and application site. In vitro and pharmacokinetic studies demonstrate that commercial estradiol gels (e.g., EstroGel) and compounded formulations achieve measurable but generally low systemic estradiol levels, with absorption profiles influenced by the vehicle and skin site. Compounded bases may provide steadier absorption compared to commercial gels, but systemic exposure remains lower than with oral or transdermal systemic therapy [95,96].

Topical progesterone has been studied less extensively. While some evidence suggests potential benefits for skin aging, the quality of data is limited, and systemic absorption is generally low, raising questions about endometrial protection when used with topical estrogens [97,98].

Combination with other topical agents (e.g., retinoids, antioxidants) is theoretically possible, but robust clinical data on synergistic effects are lacking. Overall, topical hormone therapy offers a favorable safety profile for localized skin changes associated with hormonal decline, but product selection and monitoring should consider absorption variability and the lack of long-term safety data [91,97].

6.3. Peptides and Non-Steroidal Hormonal Modulators

Non-steroidal compounds such as selective estrogen receptor modulators (SERMs), androgen receptor antagonists, and bioactive peptides are being increasingly explored as alternatives to traditional topical hormone therapies for skin rejuvenation, especially in patients contraindicated for systemic hormone replacement therapy [99,100].

SERMs (e.g., raloxifene, tamoxifen) can exert tissue-selective estrogenic effects. Preclinical and limited clinical data suggest that topical or systemic SERMs may improve skin thickness, hydration, and wound healing, with a lower risk of systemic estrogenic side effects than traditional estrogens. However, robust clinical evidence in humans for their efficacy in skin rejuvenation remains limited, and long-term safety data are lacking. The literature notes that while SERMs show promise, their use for skin aging is not yet established as standard care, and further research is needed to clarify their risk–benefit profile in this context [101–104].

Androgen receptor antagonists have not been widely studied for skin rejuvenation. Their primary dermatologic use is in conditions like acne and hirsutism, and there is insufficient evidence to support their use for age-related skin changes.

Bioactive peptides (including signal, carrier, and enzyme-inhibitor peptides) are widely used in cosmeceuticals. These peptides can stimulate collagen synthesis, enhance skin barrier function, and reduce inflammation. Clinical studies and reviews indicate that certain peptides improve skin elasticity and reduce wrinkles, but their efficacy is generally less pronounced than prescription topical retinoids or estrogens. A major limitation is poor skin penetration, though novel delivery systems (e.g., liposomes, microneedles) are under investigation to enhance effectiveness. Long-term safety appears favorable due to minimal systemic absorption, but high-quality, long-term clinical trials are sparse [105–107].

6.4. Combined Device-Based and Hormonal Approaches

Current evidence indicates that combining hormonal treatments with device-based modalities—such as fractional lasers, microneedling, or radiofrequency—can have additive or synergistic effects on skin rejuvenation, particularly in hormonally deficient or postmenopausal skin. Hormone replacement therapy (HRT), including estrogen and androgens, has been shown to restore skin thickness and stimulate neocollagenesis in

hormone-deficient individuals, likely by enhancing fibroblast activity and responsiveness [108]. Energy-based devices (EBDs), such as fractional lasers and radiofrequency, induce controlled dermal injury, activating repair pathways, upregulating TGF-β, and promoting new collagen and elastin synthesis [108,109].

Clinical studies demonstrate that combination protocols, such as the sequential or concurrent use of radiofrequency and fractional lasers, produce greater improvements in skin texture, elasticity, and wrinkle reduction than monotherapy, with evidence of synergistic effects on collagen density and fibroblast activation [110,111]. These effects are mediated by increased expression of TGF-β and other growth factors, as well as a reduction in senescent fibroblasts, which is particularly relevant in aged or hormonally deficient skin [112].

While the literature supports the safety and efficacy of these combination approaches, standardized protocols and long-term data are limited. Most studies use 3–4 treatment sessions spaced 3–4 weeks apart for device-based therapies, but optimal timing and dosing of hormonal therapy in combination protocols remain to be defined [108,110,111]. Adverse events are generally mild and transient, including erythema and edema [110,111].

7. Safety and Ethical Considerations

7.1. Risks and Contraindications

Hormonal therapies, while offering significant dermatologic benefits, can pose systemic risks depending on the type, dosage, and duration of treatment [113]. Potential adverse effects include thromboembolic events, cardiovascular complications, and stimulation of hormone-sensitive tissues, potentially increasing the risk of breast or endometrial cancer [114]. Systemic HRT should be avoided in patients with a history of thromboembolism, hormone-dependent malignancies, or uncontrolled cardiovascular disease [115]. Even topical hormonal agents may lead to systemic absorption in certain cases, necessitating careful monitoring in high-risk individuals [116].

From a cosmetic-practice perspective, adverse events can be clustered by route of administration. Topical hormone-based agents are generally associated with mild, transient local reactions and negligible systemic exposure. Transdermal systemic HRT shows a lower thromboembolic and cerebrovascular signal than oral formulations, whereas oral estrogen–progestin regimens carry uncommon but clinically relevant risks (VTE, stroke, and breast/endometrial stimulation) that increase with dose and duration. Accordingly, short-term aesthetic gains must be weighed against long-term systemic risks, prioritizing approved indications, the lowest effective dose, and individualized risk assessment (see Section 6.1).

In the Women's Health Initiative (WHI) randomized trial of conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA), there were approximately nine additional ischemic strokes and nine additional pulmonary emboli per 10,000 women-years compared to placebo. Specifically, the WHI reported an absolute excess risk of 8 more strokes and 10 more pulmonary emboli per 10,000 women-years with CEE plus MPA, with hazard ratios of 1.37 (95% CI, 1.07–1.76) for stroke and 1.98 (95% CI, 1.36–2.87) for pulmonary embolism, confirming a significant increase in these risks with combined oral hormone therapy [117].

Observational data and systematic reviews indicate that transdermal estradiol does not increase the risk of venous thromboembolism (VTE), in contrast to oral estrogen formulations. The American Heart Association/American Stroke Association guideline states that transdermal estradiol appears not to increase the risk of VTE or stroke and may be preferred in women with thrombotic risk factors, although randomized data are lacking for stroke prevention [118]. Large case–control and cohort studies further demonstrate that transdermal estrogen is not associated

with increased VTE risk, while oral estrogen—especially CEE plus MPA—confers the highest VTE risk [119–121].

7.2. Clinical Monitoring and Follow-Up

Appropriate patient selection, baseline screening, and ongoing monitoring are essential to maximize benefits while minimizing risks [122]. Baseline assessments should include a thorough personal and family history, physical examination, and relevant laboratory tests, such as hormone profiles and lipid panels [123]. Regular follow-up visits should evaluate both dermatologic outcomes and systemic parameters, with therapy adjustments made based on efficacy, tolerance, and safety markers [122,123]. Informed consent should clearly address potential risks, benefits, and alternative treatment options [115,122].

7.3. Off-Label Use and Regulatory Issues

Many hormonal agents used in cosmetic dermatology are prescribed off-label, meaning their use for skin rejuvenation or other aesthetic purposes is not officially approved by regulatory agencies [124,125]. This requires practitioners to base decisions on sound scientific evidence, expert consensus, and clinical judgment [124]. Ethical practice mandates transparency with patients regarding the experimental nature of certain treatments, as well as adherence to local and international guidelines [126]. Clinicians should remain updated on evolving regulations and safety data to ensure compliant and responsible prescribing [124].

8. Future Perspectives

8.1. Emerging Molecules and Technologies

Recent advances in molecular biology and drug delivery, such as SERMs with tissue-specific activity and nanocarrier-based delivery systems (e.g., liposomes), have the potential to improve the safety and efficacy of hormonal therapies in cosmetic dermatology by enabling more targeted, tissue-selective effects and reducing systemic exposure. SERMs and nanocarriers may minimize off-target stimulation of hormone-sensitive tissues (such as breast and endometrium), potentially lowering risks of thromboembolism and hormone-dependent cancers, although long-term safety data for these technologies in dermatologic use remain limited [127,128].

Efficacy may be enhanced through improved receptor specificity and targeted delivery, which could allow for more pronounced local skin benefits (e.g., increased collagen synthesis, improved elasticity) at lower systemic doses. However, the molecular interactions of nanocarrier systems with skin and underlying tissues are complex, and their ability to selectively modulate genomic versus non-genomic estrogen receptor pathways may alter therapeutic outcomes [127,128].

Ethical considerations are significant, especially regarding off-label use and compounded or custom formulations. The American College of Obstetricians and Gynecologists explicitly states that compounded bioidentical hormones, which are not FDA-approved, lack rigorous safety, efficacy, and quality data, and their use should be restricted to cases with clear medical necessity (e.g., documented allergy to FDA-approved products), not for routine aesthetic purposes. Clinicians must ensure transparency, obtain informed consent, and adhere to established guidelines, including comprehensive baseline assessment and ongoing monitoring [40,129,130]. Routine use of non-FDA-approved compounded bioidentical hormones for cosmetic indications is not supported by current evidence or ethical standards [130].

8.2. Personalized Therapies Based on Hormonal Profiling

The integration of precision medicine—using comprehensive hormonal panels and genetic/epigenetic testing—to tailor hormonal interventions in cosmetic dermatology has the potential to improve outcomes, reduce adverse effects, and optimize long-term skin health by enabling more individualized selection of compounds, doses, and delivery routes. This approach may be particularly valuable in populations with diverse hormonal baselines and sensitivities, as it allows for risk stratification and identification of patients most likely to benefit from specific therapies while minimizing exposure in those at higher risk of adverse events [122–124].

However, the American College of Obstetricians and Gynecologists explicitly states that current data do not support the routine use of adjunct hormone testing (including salivary, serum, or urinary panels) for individualizing hormone therapy, as these tests lack accuracy, standardization, and clinical utility for the dosing or safety monitoring of steroid hormones such as estrogen and progesterone [125]. Most hormone therapy dosing should be titrated to clinical response rather than laboratory values, except in rare circumstances. Similarly, while genetic and epigenetic profiling holds promise, robust evidence for its clinical application in guiding hormonal therapy in dermatology is not yet established [112–114].

Personalized approaches may eventually enhance safety and efficacy by identifying optimal candidates, formulations (e.g., SERMs, nanocarrier systems), and routes (e.g., transdermal vs. oral), but ethical considerations remain paramount. The use of non-FDA-approved compounded bioidentical hormones should be restricted to clear medical necessity, not routine cosmetic use, as emphasized by the American College of Obstetricians and Gynecologists [115–117]. Informed consent, transparency, and ongoing monitoring are essential, and practitioners must avoid overreliance on unvalidated testing or unapproved therapies [125–128,130].

8.3. Integrated Approaches with Regenerative Medicine

Current evidence supports the potential for combining hormonal therapies with regenerative techniques—such as stem cell therapy, PRP, and growth factor-based treatments—to enhance skin regeneration and anti-aging outcomes. Stem cell therapies, particularly those utilizing autologous adipose-derived stem cells, have demonstrated the ability to promote tissue regeneration, modulate inflammation, and secrete paracrine factors that support dermal repair and rejuvenation [113,118]. PRP, especially when combined with adipose tissue or stromal vascular fractions, can synergistically enhance the regenerative capacity of stem cells, promoting angiogenesis, fibroblast proliferation, and extracellular matrix (ECM) deposition, which are critical for skin quality improvement [120,121].

Growth factor-based treatments, including those derived from human fibroblast conditioned media and exosomes, have shown efficacy in stimulating skin regeneration, reducing signs of aging, and improving recovery after cosmetic procedures [130]. These approaches act by delivering bioactive molecules that support fibroblast activity, ECM synthesis, and tissue remodeling.

Hormonal modulation, while not directly addressed in the cited literature, is hypothesized to create a more favorable microenvironment for these regenerative interventions by influencing cellular senescence, fibroblast function, and the skin's reparative capacity [113,124]. The integration of these modalities is an area of active research, with the goal of achieving synergistic and sustained improvements in skin quality and anti-aging outcomes [124,125].

However, while preclinical and early clinical data are promising, further systematic investigation is required to establish optimal protocols, safety, and long-term efficacy for these combined strategies in advanced anti-aging regimens [130].

Extracellular vesicles—particularly exosomes (≈30–150 nm)—released by dermal fibroblasts and stem cells transport miRNAs, proteins, and lipids that modulate fibroblast proliferation, type I/III collagen synthesis, angiogenesis, and inflammation. Preclinical work and early aesthetic studies suggest improvements in texture, fine lines, and post-procedure recovery when EV preparations are applied topically or delivered via microneedling, with a favorable local safety profile. However, heterogeneity in EV sourcing, isolation, and dosing, together with the lack of regulatory approval for dermatologic indications, currently limit comparability and routine use. Rigorous, controlled trials are needed to define indications, the durability of benefits, and optimal delivery. Conceptually, EVs may synergize with hormonal modulation by supporting fibroblast function and extracellular matrix remodeling [126–128].

8.4. Practical Limitations and Evidence Gaps

Despite encouraging signals, adoption of emerging hormone-informed strategies is constrained by the following [50,79,99]: (1) heterogeneity in formulations, sourcing, and dosing—particularly for exosome-containing products; (2) small, short-duration studies that rely on surrogate end points, with few head-to-head comparisons; (3) variable cutaneous absorption and sparse pharmacokinetic data for topical and transdermal systems; (4) regulatory and ethical issues surrounding off-label and compounded preparations; and (5) uncertain durability of benefits and cost-effectiveness. Priorities include adequately powered randomized trials with standardized aesthetic and patient-reported outcomes, long-term safety registries, and comparative-effectiveness studies, including combinations with energy-based devices [130].

9. Conclusions

The skin is a complex endocrine organ, both a target and a source of hormonal signaling. As such, hormonal therapies represent a physiologically grounded and increasingly evidence-based tool in cosmetic dermatology. From adolescence to menopause, hormonal fluctuations profoundly influence key cutaneous parameters, such as collagen content, sebaceous activity, pigmentation, hydration, and immune modulation. Leveraging this biological axis, clinicians are now exploring a broadening spectrum of hormone-based strategies to address aesthetic skin concerns that were previously considered difficult to manage.

Throughout this review, we have examined the mechanisms through which hormones act on the skin, primarily by modulating receptor expression and cellular signaling pathways involved in proliferation, differentiation, inflammation, and extracellular matrix production. These pathways underpin the therapeutic effects observed with systemic hormone replacement therapy (HRT), topical estrogens and antiandrogens, and emerging agents such as clascoterone, SERMs, and bioactive peptides.

Clinically, hormonal therapies have demonstrated value across several key applications: anti-aging interventions, treatment of hormonal acne, pigmentary disorders like melasma, androgenetic alopecia, and postmenopausal xerosis. Topical routes offer promising localized effects with minimized systemic exposure, while systemic regimens require careful screening and follow-up due to potential risks, including thromboembolic events and hormone-sensitive cancers. Personalized treatment strategies, based on hormonal profiling and patient-specific factors, may further optimize outcomes, although they currently lack sufficient standardization and validation for routine implementation.

Future directions include integrating hormonal approaches with regenerative techniques—such as PRP, stem cell–based therapies, and exosome-derived growth factors—to achieve synergistic results in tissue rejuvenation. Likewise, innovations in nanocarrier delivery systems and molecular targeting may improve cutaneous bioavailability and receptor selectivity, enhancing both efficacy and safety.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/cosmetics12050207/s1, Figure S1: CONSORT flow diagram of the study method.

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