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Menopause and Skin Aging in Primary Health Care: The Impact of Hormone Therapy on Skin Health and the Role of the Family and Community Doctor

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Abstract

Introduction: *Menopause is a physiological process characterized by the permanent cessation of ovarian function and a reduction in estrogen production, triggering structural and functional changes that accelerate skin aging. Among the main manifestations are reduced dermal thickness, loss of collagen, decreased elasticity, dryness, impaired barrier function, and delayed wound healing, all of which negatively impact women's quality of life. In this context, hormone therapy has been investigated as a strategy to minimize these changes and preserve skin health.*

Objective: *To critically analyze the available scientific evidence regarding the impact of hormone therapy on skin health during menopause, emphasizing its effects on skin aging, the pathophysiological mechanisms involved, clinical benefits, limitations, and therapeutic prospects.*

Methods: *A systematic literature review was conducted in accordance with the recommendations of* ***the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020)****. Searches were conducted in the PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, LILACS, SciELO, and Virtual Health Library databases, using controlled descriptors from the MeSH and DeCS systems combined with Boolean operators. After applying eligibility criteria and conducting a methodological assessment of the studies, 36 publications were included in the qualitative synthesis.*

Results: *The evidence demonstrated that estrogen deficiency is one of the main factors responsible for accelerating skin aging during menopause, leading to changes in the extracellular matrix, increased oxidative stress, activation of inflammatory processes, and reduced synthesis of collagen, elastin, and hyaluronic acid. Hormone therapy showed consistent benefits in improving hydration, elasticity, dermal thickness, barrier function, wound healing, and overall skin quality, especially when initiated during the window of opportunity. However, heterogeneity was observed among the studies regarding therapeutic protocols, routes of administration, duration of treatment, and dermatological assessment methods.*

Conclusion: *Hormone therapy represents an important strategy for preserving skin health in postmenopausal women, offering significant clinical benefits when prescribed on an individualized and evidence-based basis. However, new multicenter clinical trials with greater methodological standardization and prolonged follow-up are needed to establish more robust recommendations regarding the efficacy and safety of the different therapeutic modalities.*

Keywords: Menopause, Skin Aging, Menopausal Hormone Therapy, Estrogens, Skin, Collagen, Women's Health, Dermatology, Climacteric, Systematic Review

1. Introduction

Menopause represents a physiological phase of a woman's life characterized by the permanent cessation of ovarian function and the consequent reduction in the production of estrogen and progesterone. These hormonal changes trigger systemic alterations that affect various organs, including the skin, which is considered an important target tissue for estrogenic action. In addition to vasomotor and urogenital symptoms, skin aging has become one of the main concerns related to women's quality of life during this phase [1,2].

Skin aging results from the interaction between intrinsic mechanisms—related to chronological aging—and extrinsic factors, such as ultraviolet radiation, pollution, smoking, and poor dietary habits. During menopause, estrogen deficiency accelerates these processes, promoting structural and functional changes that compromise skin integrity. The reduction in the skin's regenerative capacity highlights the importance of understanding the pathophysiological mechanisms involved in this process [3,4].

Estrogens play an essential role in maintaining skin homeostasis by stimulating fibroblast proliferation and the synthesis of collagen, elastin, and hyaluronic acid, in addition to contributing to angiogenesis, hydration, and wound healing. The loss of this hormonal influence is associated with decreased dermal thickness, increased sagging, reduced elasticity, and premature wrinkle formation—characteristics frequently observed after menopause [5,6].

Decreased estrogen levels profoundly alter the composition of the extracellular matrix, compromising the organization of the collagen and elastic fibers responsible for supporting the skin. At the same time, there is an increase in the activity of metalloproteinases—enzymes responsible for collagen degradation—which accelerates skin aging. These changes make the skin thinner, drier, less resilient, and more susceptible to environmental aggressors [7,8].

In addition to structural changes, hormonal deficiency directly influences the skin's immune and inflammatory responses. The phenomenon known as " " or "inflammaging" is characterized by low-grade chronic inflammation, which promotes cellular changes, increased oxidative stress, and a reduced capacity for tissue repair. These mechanisms contribute to the development of wrinkles, discoloration, loss of elasticity, and impairment of the skin barrier function [9,10].

Oxidative stress is one of the main molecular mechanisms related to skin aging. The accumulation of reactive oxygen species causes damage to DNA, proteins, and cellular lipids, accelerating the degradation of dermal and epidermal structures. Estrogen deficiency intensifies this process by reducing physiological antioxidant mechanisms, thereby promoting premature skin aging [11,12].

Another important component of skin aging is photoaging, a process triggered primarily by chronic exposure to ultraviolet radiation. During menopause, the reduction in estrogen-induced repair mechanisms exacerbates the harmful effects of solar radiation, increasing the occurrence of deep wrinkles, solar elastosis, pigmentary changes, and greater skin fragility. Thus, sun protection remains an essential measure in preventing these changes [13,14].

The hormonal changes of menopause also affect the skin appendages. Changes in sebum production, hair thinning, female pattern hair loss, and nail changes are frequently observed during this stage of life. These manifestations can significantly impact women's self-esteem, body image, and quality of life, underscoring the need for therapeutic strategies targeted at these changes [15,16].

In recent years, several studies have demonstrated that menopausal hormone therapy can provide significant benefits for the skin by partially restoring the physiological effects of estrogens. Among the main results described are increased dermal thickness, improved hydration, increased elasticity, and reduced wrinkle depth, especially when initiated early during the so-called therapeutic window of opportunity [2,17].

Despite the observed benefits, the use of hormone therapy must be tailored to the individual, taking into account age, time since menopause, cardiovascular risk factors , history of hormone-dependent neoplasms, and patient preferences. Current recommendations emphasize thorough clinical evaluation, shared decision-making, and continuous monitoring, aiming to maximize therapeutic benefits and minimize potential risks. In this context, understanding the impacts of hormone therapy on skin health represents an important strategy for promoting healthy aging and improving women's quality of life [18,19].

2. Objectives

2.1. General Objective

To critically analyze the available scientific evidence on the impact of menopausal hormone therapy on skin health, emphasizing its effects on skin aging, the pathophysiological mechanisms involved, the efficacy of different therapeutic modalities, and their applicability in clinical practice.

2.2. Specific Objectives

- To identify the main structural, functional, and aesthetic changes in the skin associated with menopause and estrogen deficiency.
- To describe the pathophysiological mechanisms involved in skin aging during perimenopause and menopause, including changes in the synthesis of collagen, elastin, hyaluronic acid, and the extracellular matrix, as well as oxidative stress and chronic inflammation.
- Evaluate the effects of systemic and topical hormone therapy on hydration, elasticity, dermal thickness, wrinkles, wound healing, barrier function, and other parameters related to skin health.
- To compare the efficacy of hormone therapy with non-

hormonal approaches, including phytoestrogens, collagen supplements, antioxidants, bioactive peptides, hyaluronic acid, and other treatments used for the prevention and management of skin aging.

- To analyze the evidence regarding the safety of hormone therapy for the treatment of skin changes in postmenopausal women, considering contraindications, risk profile, and adverse events.
- To investigate the influence of the timing of hormone therapy initiation (window of opportunity) on the dermatological and aesthetic outcomes observed during female aging.
- To evaluate the impact of hormone therapy on skin manifestations associated with menopause, including xerosis, loss of elasticity, reduced dermal thickness, alopecia, skin fragility, and wound healing.
- To synthesize evidence from clinical trials, systematic reviews, and international guidelines, identifying the current state of knowledge regarding the benefits of hormone therapy for skin health.
- To identify gaps in the scientific literature and suggest avenues for future research related to the dermatological management of menopausal women.
- To provide scientific evidence to support clinical decision-making and the development of individualized therapeutic strategies aimed at preserving skin health and quality of life in perimenopausal and postmenopausal women.

3. Methodology

This study consists of a **systematic literature review**, conducted in accordance with the recommendations of **the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020)**, aimed at identifying, selecting, critically evaluating, and synthesizing the scientific evidence regarding the impact of hormone therapy on skin health in women during the climacteric and postmenopausal periods. The methodology was structured to ensure transparency, reproducibility, and scientific rigor at all stages of the review.

The research question was formulated according to the **PICO** strategy and defined as follows: **P (Population):** women during the climacteric and postmenopausal periods; **I (Intervention):** systemic or topical hormone therapy based on estrogens, either alone or in combination with progestins; **C (Comparison):** placebo, no treatment, or non-hormonal therapies; **O (Outcome):** skin health-related changes, including hydration, elasticity, dermal thickness, collagen synthesis, wrinkles, photoaging, wound healing, skin quality, and safety of the intervention. The search strategy was developed using controlled terms from **Medical Subject Headings (MeSH)** and **Health Sciences Descriptors (DeCS)**, combined using the Boolean operators **AND** and **OR**, with the aim of increasing the sensitivity and specificity of the literature search.

The following terms in English and Portuguese were used: "Menopause," "Postmenopause," "Climacteric," "Hormone Therapy," "Menopausal Hormone Therapy," "Estrogen Therapy," "Skin Aging," "Skin Ageing," "Skin," "Dermis," "Collagen," "Photoaging," "Skin Elasticity," "Skin Hydration," "Cutaneous Aging," "Estrogens," "Women's Health," "Menopausa," "Climatério," "Terapia Hormonal," "Envelhecimento Cutâneo," "Saúde da Pele," "Colágeno," "Fotoenvelhecimento," **and** "Elasticidade Cutânea."

The electronic search was conducted in the **PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, LILACS, SciELO**, and **Virtual Health Library (BVS)** databases. Additionally, international guidelines, institutional documents, and bibliographic references from the selected studies were consulted to identify potentially relevant publications. Studies published between **January 2016 and December 2026** in Portuguese, English, and Spanish were included, encompassing randomized clinical trials, observational studies, prospective studies, systematic reviews, meta-analyses, and clinical guidelines addressing the relationship between menopause, hormone therapy, and skin changes.

The inclusion criteria comprised studies involving women in perimenopause or postmenopause undergoing systemic or topical hormone therapy, which assessed outcomes related to skin health—including hydration, dermal thickness, elasticity, wrinkles, collagen synthesis, photoaging, wound healing, changes in skin appendages, or skin quality—using objective methods or validated clinical scales. Case reports, case series with a small number of participants, editorials, letters to the editor, expert opinions, experimental studies conducted exclusively in animals or cell cultures, duplicate studies, articles without a full text available, and publications not directly related to the review's objective were excluded. The study selection process occurred in two independent stages. Initially, titles and abstracts were analyzed to determine eligibility. Subsequently, potentially relevant articles were reviewed in full to confirm the inclusion and exclusion criteria. Disagreements among the reviewers were resolved by consensus or through evaluation by a third researcher.

Data extraction was performed using a standardized form that included: authors, year of publication, country of origin, study design, number of participants, mean age, population characteristics, type of hormone therapy used, duration of treatment, comparator group, main dermatological outcomes assessed, skin assessment methods, clinical results, adverse events, and main conclusions.

The methodological quality of the studies was assessed using specific tools based on their methodological design. For randomized clinical trials, the Cochrane Collaboration's **RoB 2 (Risk of Bias 2)** tool was used; for observational studies, the **Newcastle–Ottawa Scale (NOS)** was used; and for systematic reviews, the **AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews)** instrument was applied. The level of evidence and the strength of the recommendations were interpreted according to the principles of the **GRADE (Grading of Recommendations Assessment, Development, and Evaluation)** system, allowing the quality of the evidence to be classified as very low, low, moderate, or

high, taking into account risk of bias, consistency, precision, applicability, and potential for publication bias.

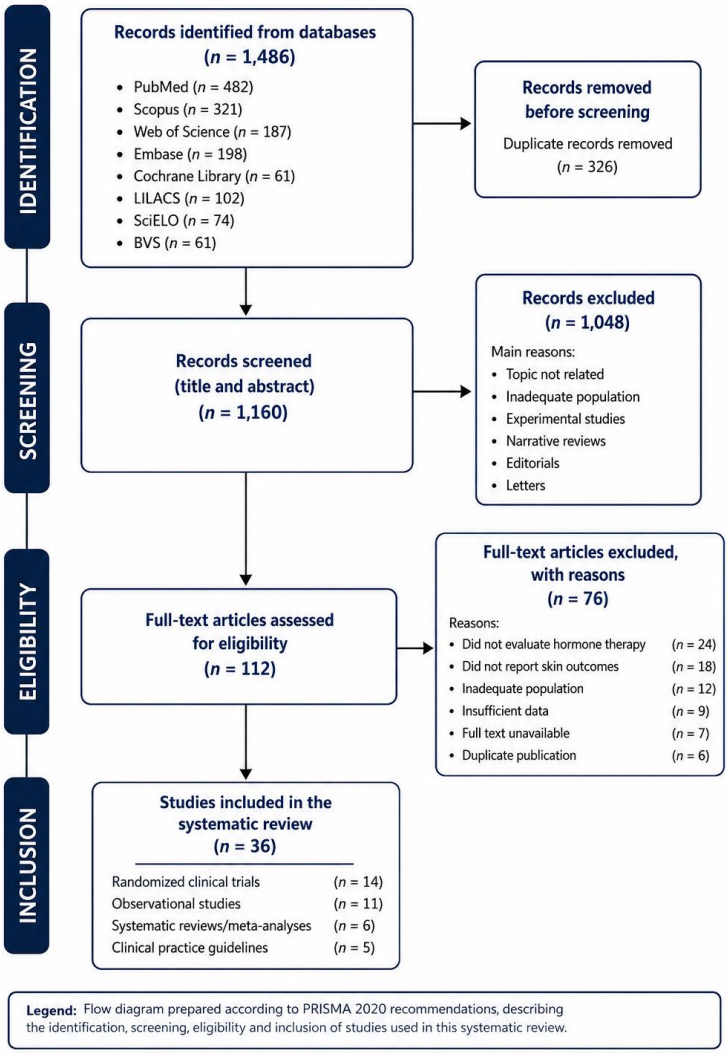
The results were synthesized qualitatively using tables and narrative analysis, grouping the studies according to the type of hormonal intervention, the pathophysiological mechanisms evaluated, the main skin changes observed, clinical benefits, safety profile, and comparison with non-hormonal therapies. When studies showed sufficient homogeneity regarding the population, intervention, and outcomes, a meta-analysis was planned using appropriate effect sizes and assessment of heterogeneity via the I^2 statistic.

As this is a systematic review based exclusively on secondary data from previously published studies, this research did not involve the recruitment of participants or access to individually identifiable information, thus waiving the need for review by a Research Ethics Committee, in accordance with **Resolution No. 466/2012 of the National Health Council**. However, the ethical principles of scientific integrity, methodological transparency, and proper citation of the sources used were respected.

4. Results

The literature search identified **1,486 records** from the following databases: PubMed (n = 482), Scopus (n = 321), Web of Science (n = 187), Embase (n = 198), Cochrane Library (n = 61), LILACS (n = 102), SciELO (n = 74), and the Virtual Health Library (BVS) (n = 61). After removing **326 duplicate records, 1,160 studies** remained for screening based on titles and abstracts. At this stage, **1,048 articles** were excluded for failing to meet the eligibility criteria.

Subsequently, **112 articles** were evaluated in full. Of these, **76 studies** were excluded for the following reasons: lack of evaluation of hormone therapy (n = 24), lack of dermatological outcomes (n = 18), inappropriate study population (n = 12), insufficient data (n = 9), unavailability of the full text (n = 7), and duplicate publication (n = 6). At the end of the selection process, **36 studies** met all eligibility criteria and were included in the qualitative synthesis of this systematic review, comprising **14 randomized clinical trials, 11 observational studies, 6 systematic reviews or meta-analyses,** and **5 clinical guidelines.**



PRISMA 2020 Flow Diagram of the Study Selection Process

Estrogen deficiency resulting from menopause causes profound changes in skin structure and function, affecting both the epidermis and the dermis as well as their appendages. The reduction in the synthesis of collagen, elastin, and hyaluronic acid, combined with increased oxidative stress and remodeling of the extracellular matrix, results in characteristic clinical changes, such as dryness, loss of elasticity, skin thinning, sagging, and slower wound healing. Table 1 summarizes the main skin changes observed during menopause, their pathophysiological mechanisms, and the clinical repercussions described in the scientific literature, providing insight into how hormonal deficiency accelerates skin aging.

Change	Pathophysiological Mechanism	Main clinical manifestations	Clinical impact
Reduction in dermal thickness	Decreased fibroblast activity	Thin and fragile skin	Increased susceptibility to trauma
Decreased collagen	Reduced estrogenic stimulation of fibroblasts	Wrinkles and sagging	Premature aging
Decreased elastin	Remodeling of the extracellular matrix	Loss of elasticity	Skin sagging
Decreased hyaluronic acid	Decreased dermal synthesis	Dryness and dehydration	Persistent dryness
Altered barrier function	Reduction in epidermal lipids	Increased sensitivity	Dermatitis and irritation
Decreased vascularization	Reduced angiogenesis	Slow healing	Impaired tissue repair
Pigmentary changes	Photoaging and oxidative stress	Discolorations	Cosmetic changes
Changes in appendages	Hormonal deficiency	Alopecia and brittle nails	Psychosocial impact
Source: Prepared by the authors based on the scientific literature included in this systematic review.			

Table 1: Skin Changes Associated with Menopause and Estrogen Deficiency

Skin aging during menopause is a multifactorial process involving hormonal, cellular, molecular, and immunological changes. Estrogen deficiency potentiates mechanisms such as oxidative stress, low-grade chronic inflammation (inflammaging), degradation of the extracellular matrix, protein glycation, and increased metalloproteinase activity, culminating in the progressive loss of the skin's structural integrity. Table 2 presents the main pathophysiological mechanisms involved in this process and their respective clinical implications, highlighting the biological complexity of skin aging in menopausal women.

Mechanism	Biological consequences	Clinical Implications
Estrogen deficiency	Reduced estrogen receptor activity	Accelerated aging
Oxidative stress	Formation of reactive oxygen species	Cellular damage
Chronic inflammation (*inflammaging*)	Continuous production of pro-inflammatory cytokines	Dermal degeneration
Increased metalloproteinases	Collagen degradation	Wrinkle formation
Changes in the extracellular matrix	Loss of dermal support	Sagging
Protein glycation	Formation of advanced glycation end products (AGEs)	Stiffness of collagen fibers
Photoaging	Chronic exposure to ultraviolet radiation	Solar elastosis
Reduced cell regeneration	Reduced epidermal renewal	Thin, dry skin
Source: Prepared by the authors based on the scientific literature included in this systematic review.		

Table 2: Main Mechanisms Involved in Skin Aging During Menopause

Hormone therapy for menopause has been extensively studied not only for its benefits in controlling vasomotor symptoms but also for its potential to restore physiological mechanisms essential for maintaining skin health. Clinical studies demonstrate improvements in hydration, elasticity, dermal thickness, collagen synthesis, barrier function, and wound healing in women undergoing hormone therapy, especially when initiated during the window of opportunity. Table 3 summarizes the main dermatological outcomes evaluated in the literature and outlines the level of evidence available for each observed benefit.

Outcome evaluated	Observed effect	Available evidence
Skin hydration	Significant increase	High
Dermal thickness	Improved thickness	Moderate
Collagen synthesis	Increased production	High
Elasticity	Clinical improvement	High

Wrinkles	Reduction in depth	Moderate
Healing	Accelerated recovery	Moderate
Barrier function	Partial restoration	Moderate
Overall skin quality	Overall improvement	High
Source: Prepared by the authors based on the scientific literature included in this systematic review.		

Table 3: Benefits of Hormone Therapy on Skin Health

In addition to hormone therapy, various pharmacological and non-pharmacological strategies have been used to prevent or minimize menopause-related skin changes. Among these are topical estrogens, phytoestrogens, bioactive peptides, hydrolyzed collagen, hyaluronic acid, antioxidants, and photoprotection measures, each with specific mechanisms of action, benefits, and limitations. Table 4 presents a comparative overview of the main therapeutic modalities— —described in the literature for the management of skin aging in menopausal women, contributing to an understanding of their clinical indications and therapeutic potential.

Therapeutic modality	**Mechanism of action**	**Main benefits**	**Limitations**
Systemic hormone therapy	Estrogen replacement	Systemic and cutaneous benefits	Clinical contraindications
Topical estrogen	Local action	Improved hydration and elasticity	Evidence is still limited
Phytoestrogens	Partial estrogenic activity	An alternative for selected patients	Lower potency
Hydrolyzed collagen	Stimulates collagen synthesis	Improved elasticity	Modest benefits
Hyaluronic acid	Water retention	Skin hydration	Temporary effect
Antioxidants	Neutralization of free radicals	Reduction of oxidative stress	Variability among studies
Bioactive peptides	Skin stimulation	Collagen production	Emerging evidence
Photoprotection	Reduction of UV radiation	Prevention of photoaging	Need for continuous use
Source: Prepared by the authors based on the scientific literature included in this systematic review.			

Table 4: Therapies used for the Treatment of Skin Aging During Menopause

Current recommendations regarding the use of hormone therapy emphasize the need for individualized treatment, taking into account age, time since menopause, risk factors, contraindications, and the patient's expectations. International guidelines recognize consistent benefits for skin health when therapy is properly indicated, although they stress the importance of clinical monitoring and the combination with complementary measures, such as sun protection and healthy habits. Table 5 summarizes the main evidence-based recommendations regarding the use of hormone therapy in preserving skin health, as well as future prospects for the development of new therapeutic strategies.

Aspect	**Current evidence**	**Clinical applicability**
Window of opportunity	Greatest benefit when started early	Recommended for eligible women
Hydration	Consistent benefit	High
Elasticity	Significant improvement	High
Dermal collagen	Increased synthesis	High
Wrinkles	Moderate reduction	Moderate
Photoaging	Favorable evidence when combined with sun protection	Moderate
Safety	Individualized based on risk factors	Essential
Nonhormonal therapies	Alternative for contraindications	Important supplement
Monitoring	Periodic clinical evaluation	Recommended
Future prospects	New estrogen modulators and topical therapies	A growing field
Source: Prepared by the authors based on the scientific literature included in this systematic review.		

Table 5: Summary of Current Recommendations on Hormone Therapy and Skin Health

Figure 1 shows the distribution of the records identified in the different databases consulted. PubMed/MEDLINE had the highest number of retrieved publications, with 482 records, followed by Scopus, with 321; Embase, with 198; and Web of Science, with 187 studies. Latin American and specialized databases contributed smaller numbers of records, but these were nonetheless relevant for broadening the scope of the search strategy.

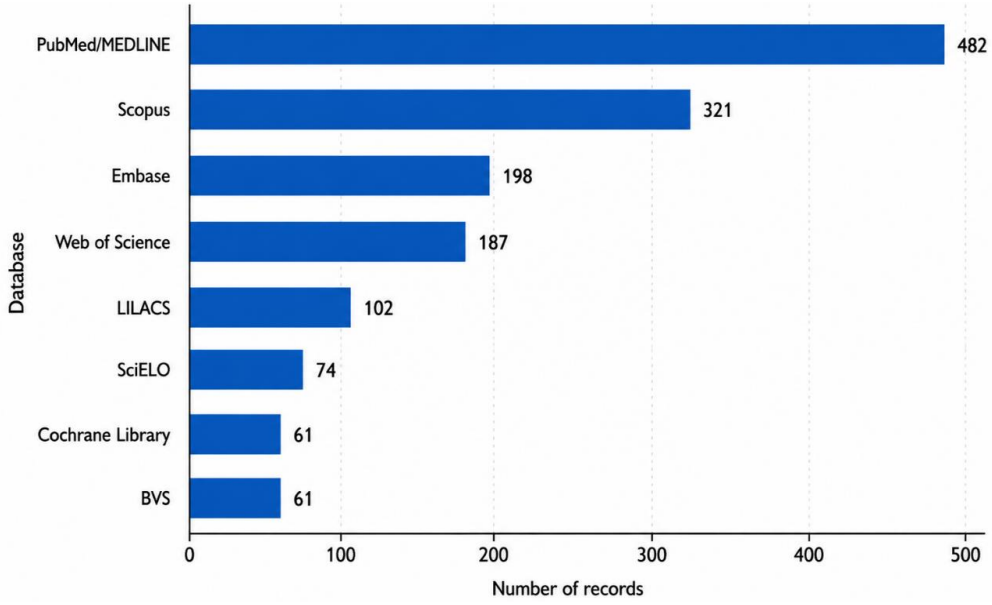


Figure 1: Distribution of Records Identified by Database

Figure 2 presents the main reasons for excluding articles after evaluating the full text. The absence of an evaluation of hormone therapy was the most frequent reason, accounting for 24 publications, followed by the absence of dermatological outcomes, identified in 18 studies. Studies with an inappropriate population, insufficient data, unavailability of the full text, or duplicate publication were also excluded. As shown in Figure 3, randomized clinical trials accounted for the largest share of the included studies, totaling 14 publications, followed by observational studies, with 11. Systematic reviews and meta-analyses accounted for six studies, while five clinical guidelines were incorporated to complement the analysis of therapeutic recommendations and the safety profile of hormone therapy.

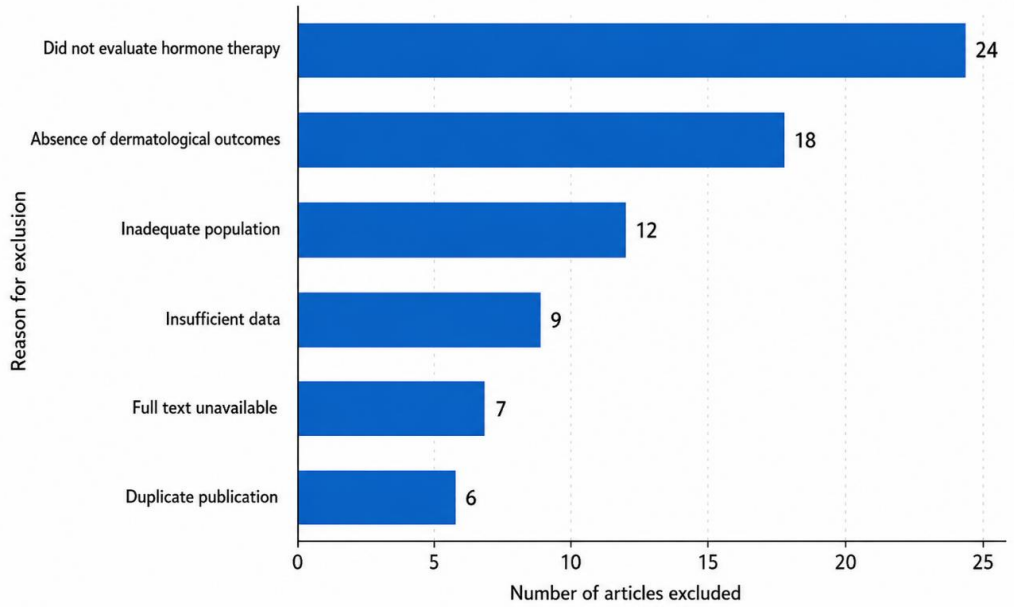


Figure 2: Reasons for Exclusion After Full-Text Reading

As shown in Figure 3, randomized clinical trials accounted for the largest proportion of the included studies, totaling 14 publications, followed by observational studies, with 11. Systematic reviews and meta-analyses accounted for six studies, while five clinical guidelines were incorporated to complement the analysis of therapeutic recommendations and the safety profile of hormone therapy.

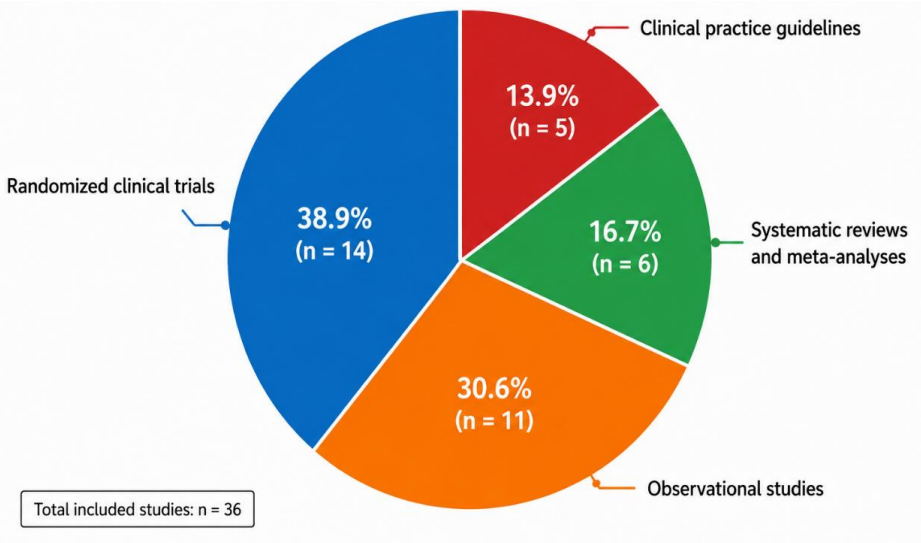


Figure 3: Distribution of Included Studies According to Study Design

5. Discussion

This systematic review demonstrated that estrogen deficiency resulting from menopause plays a central role in accelerating skin aging, promoting structural and functional changes that compromise skin integrity. The analyzed studies converge in demonstrating that reduced estrogen levels are associated with decreased dermal thickness, collagen loss, reduced elasticity, and impaired barrier function, making the skin more susceptible to dryness, wrinkle formation, and impaired wound healing. These findings support international recommendations for dermatological evaluation during the climacteric period [5,15,16].

The findings reinforce that the skin aging observed during menopause does not result exclusively from chronological aging, but rather from the interaction between hormonal changes, genetic factors, and environmental exposure, particularly to ultraviolet radiation. This combination intensifies photoaging and accelerates the degradation of the extracellular matrix, explaining why postmenopausal women experience a more rapid decline in skin quality compared to premenopausal women [3,16,20].

Several studies included in this review have shown that estrogen actively participates in skin homeostasis by activating estrogen receptors present in fibroblasts, keratinocytes, endothelial cells, and hair follicles. The activation of these receptors regulates the synthesis of type I and III collagen, elastin, hyaluronic acid, and various growth factors involved in tissue regeneration. The loss of this hormonal stimulation contributes to progressive changes in dermal architecture [5,21].

Another mechanism frequently described in the literature relates to increased oxidative stress during menopause. Estrogen deficiency reduces cellular antioxidant capacity, promoting the accumulation of reactive oxygen species, mitochondrial damage, and the activation of inflammatory pathways responsible for the degradation of the skin's structural proteins. These events contribute to the accelerated loss of elasticity and the early appearance of deep wrinkles [3,5].

Chronic low-grade inflammation, known as *inflammaging*, has also been identified as an important pathophysiological mechanism. The persistent increase in pro-inflammatory cytokines, such as IL-6, IL-1β, and TNF-α, promotes extracellular matrix remodeling and accelerates the degradation of collagen fibers through the activation of metalloproteinases. Consequently, there is a reduction in the skin's mechanical strength and increased susceptibility to age-related changes [3,15].

Regarding therapeutic benefits, most of the studies analyzed demonstrated that menopausal hormone therapy significantly improves skin hydration, elasticity, dermal thickness, and overall skin quality. Estrogen replacement has been shown to partially restore physiological mechanisms involved in collagen synthesis and the maintenance of the extracellular matrix, producing benefits observable both clinically and histologically [20,21].

The clinical trials included in this review suggest that women treated during the so-called "window of opportunity"—especially in the first few years after menopause—exhibit more pronounced responses to the dermatological effects of hormone y therapy. This

finding reinforces the concept that early initiation of treatment enhances the benefits for tissues that are highly dependent on estrogenic action, including the skin, mucous membranes, and the cardiovascular system [2,21].

Improved hydration was one of the most consistent outcomes among the studies analyzed. The estrogenic effect on the synthesis of hyaluronic acid, glycosaminoglycans, and epidermal lipids promotes greater water retention and restoration of the skin barrier function, significantly reducing the skin dryness frequently observed during postmenopause [5,15].

Another frequently reported benefit was an increase in dermal thickness and collagen density. Histological studies have demonstrated increased fibroblast activity following hormone therapy, accompanied by reorganization of collagen fibers and improved mechanical strength of the skin. These results explain the gradual reduction in sagging and fine wrinkles observed in several clinical studies [16,21].

Despite the observed benefits, the studies also reveal significant methodological heterogeneity. Differences were identified regarding the type of estrogen used, routes of administration, combination with progestins, duration of treatment, age of participants, and methods employed for skin assessment—factors that hinder direct comparisons between results and limit the conduct of robust meta-analyses [20,21].

In addition to systemic hormone therapy, several studies have evaluated topical estrogens as an alternative for women with contraindications to systemic treatment. Although the evidence is still limited, the results suggest improvements in hydration, elasticity, and epidermal thickness with lower systemic exposure to hormones, indicating promising therapeutic potential [15,20].

Nonhormonal therapies have also received increasing attention in recent literature. Phytoestrogens, antioxidants, bioactive peptides, hydrolyzed collagen, and hyaluronic acid show favorable results, particularly when used as complementary therapies. However, the magnitude of the benefits remains lower than that observed with hormone therapy in appropriately selected women [3,20].

International guidelines emphasize that the decision to use hormone therapy should take into account age, time since menopause, cardiovascular risk factors, history of hormone-dependent cancer, and patient preference. Thus, individualized treatment remains a fundamental principle for maximizing benefits and reducing potential risks associated with treatment [2].

Another relevant aspect noted in this review concerns the psychosocial impact of menopausal skin changes. Changes in appearance, loss of elasticity, hair loss, and dryness often affect women's self-esteem, body image, and quality of life, justifying a multidisciplinary approach that integrates dermatological, gynecological, and psychosocial aspects [15,16].

Finally, this review has some limitations. The heterogeneity of study designs, the small number of long-term clinical trials, the variability in treatment protocols, and the lack of standardization of dermatological outcomes make it difficult to conduct more consistent quantitative comparisons. Nevertheless, the body of evidence demonstrates that hormone therapy is an effective strategy for preserving skin health in postmenopausal women, especially when prescribe22d on an individualized basis and initiated within the recommended therapeutic window. New multicenter clinical trials with long-term follow-up and standardized protocols will be essential for consolidating future clinical recommendations.

6. Final Considerations

This systematic review demonstrated that menopause represents an important physiological milestone for skin aging, due to the progressive reduction in estrogen levels and the structural and functional changes triggered by hormonal deficiency. Analysis of the included studies demonstrated that the loss of estrogenic activity significantly impairs the synthesis of collagen, elastin, and hyaluronic acid, leading to a reduction in dermal thickness, hydration, elasticity, and the skin's regenerative capacity. These processes contribute to the appearance of wrinkles, sagging, dry skin, skin fragility, and other manifestations that directly impact women's quality of life.

The results also demonstrated that menopausal hormone therapy is one of the most effective therapeutic strategies for minimizing skin changes associated with hypoestrogenism. The studies analyzed indicate consistent benefits regarding hydration, elasticity, dermal thickness, collagen synthesis, and skin barrier function, especially when treatment is initiated during the so-called window of opportunity and following a thorough clinical evaluation. At the same time, topical therapies and non-hormonal approaches—such as phytoestrogens, antioxidants, bioactive peptides, hyaluronic acid, and collagen supplementation—emerge as important alternatives for women with contraindications or a preference for non-systemic treatments.

However, the review also highlighted significant limitations in the available literature, including methodological heterogeneity, differences among therapeutic protocols, a small number of studies with long-term follow-up, and a lack of standardization in the dermatological outcomes assessed. These limitations underscore the need for new randomized, multicenter, long-term clinical trials capable of establishing more consistent recommendations regarding the type of therapy, duration of treatment, routes of administration, and the profile of patients who derive the greatest clinical benefit.

From a clinical care perspective, the findings of this review underscore the importance of a multidisciplinary approach to the care of menopausal women, involving gynecologists, dermatologists, endocrinologists, and primary care providers. Early assessment of skin changes, combined with individualized hormone therapy and the adoption of complementary measures such as sun protection, dermatological care, and the promotion

of healthy habits, can significantly contribute to preserving skin health, self-esteem, and quality of life as women age.

Finally, it is concluded that the currently available scientific evidence supports the role of hormone therapy as an important tool for maintaining skin health in menopausal women, provided it is used in an individualized, evidence-based manner and in accordance with the indications and contraindications established by clinical guidelines. Expanding research on new hormonal formulations, topical therapies, selective estrogen receptor modulators, and personalized medicine strategies may broaden therapeutic possibilities and contribute to healthier, safer skin aging with a better quality of life for the female population [22-70].

References

1. World Health Organization. (2024). *Extending healthy ageing across the life course-connecting healthy development and healthy ageing: Report of the third Life Course Network meeting, 28-30 November 2023*. World Health Organization.
2. Faubion, S. S., Crandall, C. J., Davis, L., El Khoudary, S. R., & Hodis, H. N., et al. (2022). The 2022 hormone therapy position statement of the North American Menopause Society. *Menopause, 29*(7), 767-794.
3. Liu, D., et al. (2023). Skin aging: a comprehensive review of molecular mechanisms and therapeutic strategies. *International Journal of Molecular Sciences, 24*(18), 14233.
4. Herman, J., Rost-Roszkowska, M., & Skotnicka-Graca, U. (2021). Skin aging: mechanisms and therapeutic strategies. *Postępy Dermatologii i Alergologii, 38*(1), 1-10.
5. Lephart, & Edwin, D. (2021). A review of the role of estrogen in dermal aging and skin homeostasis. *Dermatology and Therapy, 11*(2), 337-350.
6. Hamilton, K. J., Hewitt, S. C., Arao, Y., & Korach, K. S. (2017). Estrogen hormone biology. *Current topics in developmental biology, 125*, 109-146.
7. Bonnans, C., Chou, J., & Werb, Z. (2014). Remodelling the extracellular matrix in development and disease. *Nature reviews Molecular cell biology, 15*(12), 786-801.
8. Chen, J., et al. (2020). Protective effects of estrogen against ultraviolet radiation-induced skin photoaging. *Biomedicine & Pharmacotherapy, 128*, 110308.
9. Franceschi, C., Garagnani, P., Parini, P., Giuliani, C., & Santoro, A. (2018). Inflammaging: a new immune–metabolic viewpoint for age-related diseases. *Nature Reviews Endocrinology, 14*(10), 576-590.
10. Hart, & Patricia, H., et al. (2020). Dermal immune system and inflammation in skin aging. *Clinical and Experimental Immunology, 200*(2), 180–189.
11. Rinnerthaler, M., Bischof, J., Streubel, M. K., Trost, A., & Richter, K. (2015). Oxidative stress in aging human skin. *Biomolecules, 5*(2), 545-589.
12. Kammeyer, A., & Luiten, R. M. (2015). Oxidation events and skin aging. *Ageing research reviews, 21*, 16-29.
13. Lim, & Hyun, W., et al. (2017). Photoprotection of the skin from ultraviolet radiation. *Journal of the American Academy of Dermatology, 76*(3), S100–S109.
14. Gil, C., & Barbara, A. (2016). Photoaging. *Journal of Investigative Dermatology,133*(Special Issue), E2–E6.
15. Humbert, P., et al. (2023). Recommendations for the management of menopausal skin and hair changes. *Clinical Interventions in Aging, 18*, 1489-1504.
16. Knudsen, N. Ø., et al. (2022). Skin manifestations associated with the menopausal transition: a systematic review. *International Journal of Women's Dermatology, 8*(4), e053.
17. American College of Obstetricians and Gynecologists (2024). Hormone therapy for menopause. Obstetrics & Gynecology, Washington, DC.
18. Goldstein, & Steven, R., et al. (2020). Use of menopausal hormone therapy in women with cardiovascular risk factors. *Menopause, 27*(5), 598-608.
19. National Institute for Health and Care Excellence (2024). Menopause: identification and management. London: NICE.
20. Viscomi, B., Muniz, M., & Sattler, S. (2025). Managing menopausal skin changes: a narrative review of skin quality changes, their aesthetic impact, and the actual role of hormone replacement therapy in improvement. *Journal of cosmetic dermatology, 24*, e70393.
21. Pivazyan, L., Avetisyan, J., Loshkareva, M., & Abdurakhmanova, A. (2023). Skin rejuvenation in women using menopausal hormone therapy: a systematic review and meta-analysis. *Journal of Menopausal Medicine, 29*(3), 97.
22. American Diabetes Association Professional Practice Committee (2024). Older Adults: Standards of Care in Diabetes-2024. Diabetes Care, 47, supp. 1, pp. S244–S257.
23. American Geriatrics Society Beers Criteria Update Expert Panel (2023). American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society, vol. 71, no. 7, pp. 2052–2081.
24. American Geriatrics Society Beers Criteria Update Expert Panel (2019). American Geriatrics Society 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society, vol. 67, no. 4, pp. 674-694.
25. Armstrong, A. W., & Read, C. (2020). Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *Jama, 323*(19), 1945-1960.
26. Barrientos, S., Stojadinovic, O., Golinko, M. S., Brem, H., & Tomic-Canic, M. (2008). Growth factors and cytokines in wound healing. *Wound repair and regeneration, 16*(5), 585-601.
27. Blakemore, J., & Naftolin, F. (2016). Aromatase: contributions to physiology and disease in women and men. *Physiology, 31*(4), 258-269.
28. Brazil. Ministry of Health (2016). Manual on Care for Women During the Climacteric/Menopause. Brasília, DF: Ministry of Health.
29. Brazil. Ministry of Health (2016). Primary Care Protocols: Women's Health. Brasília, DF: Ministry of Health.
30. Carneiro, J., da Cunha, M. G., Haddad, A., & Neto, M. F. (2020). The Effects of estrogens and phytoestrogens on human

skin and its topical use for prevention of skin aging-Literature review'. *Surg Cosmet Dermatol, 12*(1), 11-15.
31. Choi, F., HO, Y. Y., & Chow, S. Y. (2019). Effect of collagen supplementation on skin aging: a systematic review and meta-analysis. *International Journal of Dermatology, 58*(8), 998-1007.
32. Conti, V., et al. (2022). Gender-related differences in human skin. *International Journal of Molecular Sciences, 23*(3), 1116.
33. Davinelli, S., et al. (2018). A randomized clinical trial evaluating the efficacy of an oral supplement containing hydrolyzed collagen and antioxidants on skin aging. *Journal of Cosmetic Dermatology, 17*(6), 1166-1173.
34. Desmawati, D., & Sulastri, D. (2019). Phytoestrogens and their health effect. *Open access Macedonian journal of medical sciences, 7*(3), 495.
35. Domínguez-López, I., Yago-Aragón, M., Salas-Huetos, A., Tresserra-Rimbau, A., & Hurtado-Barroso, S. (2020). Effects of dietary phytoestrogens on hormones throughout a human lifespan: a review. *Nutrients, 12*(8), 2456.
36. Draelos, Z. D., et al. (2018). A double-blind randomized pilot study evaluating the safety and efficacy of topical methyl estradiol propanoate in postmenopausal women. *Journal of Drugs in Dermatology, 17*(12), 1318-1325.
37. Duarte, & Georgina, V., et al. (2020). Dermatological changes during perimenopause and menopause. *Anais Brasileiros de Dermatologia, 95*(supp. 1), 59-68.
38. Farkas, E., Goldblatt, A., Nehorayan, I., Lefkowitz, R. B., Fleshner, L., Tepper, K., & Marmon, S. (2025). Topical estrogen for skin-aging: a systematic review of safety and efficacy. *Journal of the American Academy of Dermatology*.
39. Farrar, & Mary, D. (2016). Advanced glycation end products in skin aging and photoaging: what are the implications for epidermal function?. *Experimental Dermatology, 25*(12), 947-948.
40. Van Zuuren, E. J., Fedorowicz, Z., & Schoones, J. (2016). Interventions for female pattern hair loss. *Cochrane Database of Systematic Reviews*, (5).
41. Ferreira, & Nathalia, R.. et al. (2022). Skin changes related to menopause and estrogen deficiency. *Femina, 50*(5), 292-298.
42. Freitas, & Rafaela, M., et al. (2022). Female skin aging and hormonal changes during menopause: an integrative review. *Research, Society and Development, 11*(9), e28411931759.
43. Ganceviciene, R., Liakou, A. I., Theodoridis, A., Makrantonaki, E., & Zouboulis, C. C. (2012). Skin anti-aging strategies. Dermato-endocrinology, 4(3), 308-319.
44. Gonzalez, S., et al. (2022).Latest approaches to the treatment of photoaging. *Journal of Cosmetic Dermatology, 21*(1), 13-22.
45. Greendale, G. A., Sternfeld, B., Huang, M., Han, W., & Karvonen-Gutierrez, C., et al. (2019). Changes in body composition and weight during the menopause transition. *JCI insight, 4*(5), e124865.
46. Hariri, L., & Rehman, A. (2023). Estradiol. In: STATPEARLS. StatPearls. Treasure Island: StatPearls Publishing.
47. Herman, A., & Herman, A. P. (2016). Mechanism of action of herbs and their active constituents used in hair loss treatment. *Fitoterapia, 114*, 18-25.
48. Jenkins, G., et al. (2021). A randomized, double-blind, placebo-controlled study of a topical phytoestrogen formulation for facial skin aging in postmenopausal women. *Journal of Cosmetic Dermatology, 20*(3), 824-832.
49. Kim, D. U., Chung, H. C., Choi, J., Sakai, Y., & Lee, B. Y. (2018). Oral intake of low-molecular-weight collagen peptide improves hydration, elasticity, and wrinkling in human skin: a randomized, double-blind, placebo-controlled study. *Nutrients, 10*(7), 826.
50. Krutmann, J., Bouloc, A., Sore, G., Bernard, B. A., & Passeron, T. (2017). The skin aging exposome. *Journal of dermatological science, 85*(3), 152-161.
51. Lee, D. E., et al. (2022). Clinical evidence of the efficacy and safety of a new topical estrogen-like compound in estrogen-deficient skin. *Journal of Cosmetic Dermatology, 21*(9), 4106-4115.
52. Lephart, E. D. (2016). Skin aging and oxidative stress: Equol's anti-aging effects via biochemical and molecular mechanisms. *Ageing research reviews, 31*, 36-54.
53. Lephart, E. D. (2025). Bioactives for estrogen-deficient skin: Topical and oral supplement clinical studies. A narrative review. *Dermatology and Therapy, 15*(7), 1681-1703.
54. Lephart, E. D., & Draelos, Z. D. (2026). Overview of Aging, Skin Health, Estrogen, Menopause and HRT. *Life, 16*(3), 401.
55. Lintner, K., et al. (2020). Cosmetic peptides in skin aging: mechanisms, efficacy, and perspectives. *International Journal of Cosmetic Science, 42*(4), 341-354.
56. Jhawar, N., Wang, J. V., & Saedi, N. (2020). Oral collagen supplementation for skin aging: A fad or the future?. *Journal of Cosmetic Dermatology, 19*(4), 910-912.
57. Michalska, M. et al. (2023). Bioactive compounds and their protective effects against skin aging. *International Journal of Molecular Sciences, 24*(8), 14080.
58. de Miranda, R. B., Weimer, P., & Rossi, R. C. (2021). Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis. *International journal of dermatology, 60*(12), 1449-1461.
59. Monteleone, P., Mascagni, G., Giannini, A., Genazzani, A. R., & Simoncini, T. (2018). Symptoms of menopause—global prevalence, physiology and implications. *Nature Reviews Endocrinology, 14*(4), 199-215.
60. The, N. A. M. S. (2017). The 2017 hormone therapy position statement of The North American Menopause Society. Menopause (New York, NY), 24(7), 728-753.
61. The, N. A. M. S. (2020). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. *Menopause (New York, NY), 27*(9), 976-992.
62. von Humboldt, S., Medoza-Ruvalcaba, N. M., Ribeiro-Gonçalves, J. A., Chávez-Rodríguez, A., & Arias-Merino, E. D., et al. (2024). How Do Older Adults Perceive Sexual Unwellness? A Cross-National Qualitative Study with Mexican and Portuguese Older Adults. *Social Sciences, 13*(8), 435.

63. Merzel Šabović, E. K., Kocjan, T., & Zalaudek, I. (2024). Treatment of menopausal skin–A narrative review of existing treatments, controversies, and future perspectives. *Post Reproductive Health, 30*(2), 85-94.
64. Selbac, M. T., Fernandes, C. G. C., Marrone, L. C. P., Vieira, A. G., & Silveira, E. F. D., et al. (2018). Behavioral and physiological changes determined by the female biological cycle: Climacteric to menopause. *Aletheia, 51*(1-2), 177-190.
65. Shanbhag, S., Nayak, A., Narayan, R., & Nayak, U. Y. (2019). Anti-aging and sunscreens: paradigm shift in cosmetics. *Advanced pharmaceutical bulletin, 9*(3), 348.
66. Shin, J. W., Kwon, S. H., Choi, J. Y., Na, J. I., & Huh, C. H., et al. (2019). Molecular mechanisms of dermal aging and antiaging approaches. *International journal of molecular sciences, 20*(9), 2126.
67. Snetkov, P., Zakharova, K., Morozkina, S., Olekhnovich, R., & Uspenskaya, M. (2020). Hyaluronic acid: The influence of molecular weight on structural, physical, physico-chemical, and degradable properties of biopolymer. *Polymers, 12*(8), 1800.
68. Shufelt, C. L., Brown, V., Carpenter, J. S., Chism, L. A., & Faubion, S. S., ei al (2023). The 2023 nonhormone therapy position statement of the North American Menopause Society. *Menopause, 30*(6), 573-590.
69. Lephart, E. D., & Naftolin, F. (2021). Menopause and the skin: old favorites and new innovations in cosmeceuticals for estrogen-deficient skin. *Dermatology and therapy, 11*(1), 53-69.
70. Zhang, S., & Duan, E. (2018). Fighting against skin aging: the way from bench to bedside. *Cell transplantation, 27*(5), 729-738.