International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	THE ROLE OF RETINOIDS IN THE TREATMENT OF SKIN AGING: A LITERATURE REVIEW
DOI	https://doi.org/10.31435/ijitss.1(49).2026.5013
RECEIVED	10 January 2026
ACCEPTED	02 March 2026
PUBLISHED	17 March 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

THE ROLE OF RETINOIDS IN THE TREATMENT OF SKIN AGING: A LITERATURE REVIEW

Ewa Bąkowska *(Corresponding Author, Email: Ewaabakowskaa@gmail.com)*
Medical University of Lublin, Lublin, Poland
ORCID ID: 0009-0007-4135-9748

Wojciech Janikowski
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-4078-9698

Agnieszka Jóźwicka
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-1130-1518

Aleksandra Stępka
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0007-5034-0037

Lena Jaworowicz
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-4210-7216

Weronika Plichtowicz-Kordowska
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0009-7713-8597

Karina Lewandowska
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0004-5298-1426

Maria Wieczorek
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0000-9951-7509

ABSTRACT

Skin aging is a progressive biological process involving structural and functional changes such as the thinning of the epidermis, loss of structural integrity, and the development of wrinkles and uneven pigmentation. Retinoids, biologically active compounds derived from vitamin A, represent the most extensively studied pharmacological agents for addressing these age-related alterations. This review synthesized evidence from a comprehensive literature search of PubMed and Google Scholar databases, utilizing Boolean operators and keywords such as "retinoids," "photoaging," and "collagen remodeling" to identify relevant clinical trials, systematic reviews, and histological studies. These agents exert their effects by modulating gene expression via interaction with nuclear receptors, which leads to increased synthesis of type I and III procollagen and the inhibition of matrix metalloproteinases. Tretinoin continues to be the gold standard in therapy, offering the strongest clinical and histological evidence for improving photodamaged skin, although its use is often limited by dose-dependent irritation. Derivatives such as retinol and retinaldehyde provide significant clinical benefits with improved tolerability, making them suitable for long-term maintenance and individuals with sensitive skin. Furthermore, tazarotene shows robust efficacy for photodamage comparable to tretinoin, while isotretinoin remains a potent off-label option restricted by its systemic safety profile. Clinical selection of retinoids should be individualized, balancing efficacy with patient adherence, while future research should focus on advanced delivery systems and the separate evaluation of intrinsic and extrinsic aging pathways.

KEYWORDS
Retinoids, Skin Aging, Photoaging, Tretinoin, Retinol, Retinaldehyde, Tazarotene, Collagen Remodeling

CITATION
Ewa Bąkowska, Wojciech Janikowski, Agnieszka Jóźwicka, Aleksandra Stępka, Lena Jaworowicz, Weronika Plichtowicz-Kordowska, Karina Lewandowska, Maria Wieczorek. (2026) The Role of Retinoids in the Treatment of Skin Aging: A Literature Review. *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.5013

1 Introduction

The skin is the largest organ of the human body and undergoes progressive structural and functional changes with aging. These changes include thinning of the epidermis and dermis and loss of structural integrity, leading to impaired function and increased susceptibility to skin diseases, including skin cancer[1]. Clinically, skin aging is characterized by the development of wrinkles, loss of elasticity, uneven pigmentation, and increased dryness, resulting in a decline in overall skin quality[2]. Skin aging occurs through intrinsic (chronological) processes and extrinsic factors, primarily ultraviolet (UV) radiation exposure. While intrinsic aging reflects natural biological processes, extrinsic aging, referred to as photoaging, accelerates age-related changes. Both processes share common features, such as reduced collagen synthesis and increased collagen degradation, and involve overlapping molecular pathways[3, 4]. UV-induced degradation of the extracellular matrix plays a central role in photoaging[4]. Retinol belongs to the retinoid class and is widely used in anti-aging cosmetics and aesthetic dermatology[5]. Retinoids are biologically active compounds derived from vitamin A, including its active metabolite all-trans-retinoic acid (ATRA). They regulate essential physiological processes such as cell growth, differentiation, and immune function. Retinoids have well-established clinical applications in dermatology and oncology, including the treatment of acne, psoriasis, disorders of keratinization, and skin cancer, as well as in differentiation therapy for acute promyelocytic leukemia[6]. All-trans retinol, a precursor of retinoic acid, is commonly used in topical

skincare products due to its favorable safety profile and anti-aging effects. Topical retinoic acid is considered more potent; however, direct comparative studies evaluating the effects of retinol and retinoic acid on human skin remain limited[4]. Topical retinol has been shown to reduce fine wrinkles associated with intrinsic skin aging and to improve overall skin appearance. These effects are linked to increased extracellular matrix production and improved skin hydration, which may enhance skin resilience in aged individuals[5, 7]. Despite their documented benefits, retinoids are associated with limitations and ongoing controversies. Topical application may result in adverse effects such as irritation, dryness, erythema, and increased skin sensitivity, particularly during the initial phase of treatment. In addition, individual retinoids differ in potency, tolerability, and clinical efficacy, which may influence patient adherence. To address these challenges, novel formulations and application strategies, including lower concentrations and encapsulated retinoids, have been developed to improve tolerability while preserving effectiveness. Systemic retinoids, particularly isotretinoin (13-cis retinoic acid), are highly effective in the treatment of severe dermatological conditions but are limited by adverse effects such as mucocutaneous symptoms, metabolic disturbances, and teratogenicity, necessitating strict monitoring and safety measures[8]. Nevertheless, retinoids provide long-lasting improvements in skin morphology. The visible signs of skin aging may negatively affect self-esteem and quality of life, contributing to an increasing demand for effective and well-tolerated anti-aging therapies[9].

Although numerous studies have investigated the role of retinoids in skin aging, the available evidence remains heterogeneous with respect to study design, populations, treatment regimens, and retinoid formulations. Therefore, a concise and up-to-date synthesis of current and clinically relevant data is warranted. This review aims to summarize and critically evaluate current evidence on the use of retinol and other retinoids in skin aging, with particular emphasis on efficacy, safety, tolerability, and emerging strategies to optimize clinical outcomes.

2 Methodology

A comprehensive literature search was performed across the PubMed and Google Scholar databases to identify relevant studies on retinoids in anti-aging therapy. The search strategy utilized combinations of the following keywords and Medical Subject Headings (MeSH): “retinoids,” “skin aging,” “photoaging,” “tretinoin,” “retinol,” “retinaldehyde,” and “collagen remodeling.” Search terms were combined using Boolean operators (AND, OR) to ensure an exhaustive retrieval of evidence.

3 Results

3.1 Molecular Mechanisms of Retinoid Action in Skin Aging

Retinoids exert their potent anti-aging effects by modulating gene expression through interaction with specific nuclear receptors, namely retinoic acid receptors (RARs) and retinoid X receptors (RXRs)[1,10]. Upon topical application and metabolic conversion to all-trans retinoic acid, these ligands bind to RAR/RXR heterodimers, which subsequently interact with retinoic acid response elements (RAREs) in the promoter regions of target genes[11]. In the context of cutaneous aging, this molecular cascade leads to the significant upregulation of type I and type III procollagen synthesis by activating dermal fibroblasts[3, 10]. Concurrently, retinoids effectively mitigate the degradation of the extracellular matrix by inhibiting the expression of matrix metalloproteinases (MMPs), such as MMP-1 (collagenase) and MMP-3 (stromelysin), often through the antagonism of the transcription factor activator protein-1 (AP-1)[1, 12]. Furthermore, retinoids enhance epidermal thickness by promoting keratinocyte proliferation and strengthening the skin barrier function, while also stimulating angiogenesis in the papillary dermis to improve overall skin vitality and texture[11, 13].

3.2 Clinical Evidence for Individual Retinoids

3.2.1 Tretinoin

Tretinoin (all-trans retinoic acid) was identified in the reviewed literature as the most extensively studied topical retinoid in the treatment of photoaged skin. Across the analyzed studies, tretinoin was frequently evaluated in clinical trials and systematic reviews as a topical intervention for skin aging. The majority of these studies investigated formulations containing tretinoin at concentrations ranging from 0.025% to 0.1%, applied once daily or every other day over prolonged treatment periods[14]. In multiple randomized controlled trials and systematic analyses, topical tretinoin was reported to improve several clinical signs of photoaging, including fine and coarse wrinkles, mottled hyperpigmentation, sallowness, and lentigines. In these studies, clinical benefits were observed within the first months of treatment and were maintained during longer treatment durations [1, 15]. Overall, the reviewed evidence demonstrated consistent clinical effects of topical tretinoin in reducing visible features of skin aging in photoaged populations[15, 16].

The reviewed clinical studies consistently reported that topical tretinoin treatment resulted in improvements across multiple visible signs of skin aging, particularly in photoaged skin. Documented clinical outcomes included a reduction in fine and coarse wrinkles, improvement in skin roughness, and enhancement of overall skin texture [17]. Several randomized controlled trials also reported a visible decrease in mottled hyperpigmentation, solar lentigines, and sallowness following regular application of tretinoin. Improvements in skin tone uniformity and brightness were commonly observed across studies[18]. The degree of clinical improvement was generally associated with treatment duration, with more pronounced effects reported after several months of continuous use. Across the reviewed studies, treatment was associated with measurable improvements in the overall clinical appearance of aged skin, as assessed using investigator-rated evaluations and patient-reported outcome measures.

Histological analyses described in the reviewed literature indicated that topical tretinoin induced structural changes consistent with skin remodeling. These changes included increased epidermal thickness, normalization of keratinocyte differentiation, and compaction of the stratum corneum. In the dermis, multiple studies documented increased collagen content, particularly collagen types I and III, along with improved organization of collagen fibers[19, 20]. Molecular assessments further reported up-regulation of genes involved in extracellular matrix synthesis and downregulation of matrix-degrading enzymes, including matrix metalloproteinases. In addition, tretinoin treatment was associated with increased glycosaminoglycan content and improvements in dermal matrix integrity. These histological and molecular changes were reported alongside the clinical improvements observed in the analyzed studies.

Across the reviewed studies, both clinical and histological effects of topical tretinoin were reported to be dependent on treatment duration. Initial changes, such as mild improvements in skin texture and brightness, were commonly observed after several weeks of regular application. More pronounced clinical effects,

including reduction of fine wrinkles and improvement in pigmentation irregularities, were generally reported after three to six months of continuous treatment[18]. Long-term studies indicated that continued use of tretinoin was associated with maintenance of the observed clinical and structural improvements. Several investigations reported that discontinuation of retinoin therapy was followed by gradual attenuation of treatment effects.

The reviewed literature consistently reported local cutaneous adverse effects associated with topical tretinoin treatment. The most frequently documented reactions included erythema, skin dryness, scaling, burning sensations, and increased skin sensitivity. These effects were most commonly observed during the initial phase of treatment and were reported to be dose-dependent, with higher concentrations and more frequent application associated with increased irritation. In the majority of studies, adverse effects were described as mild to moderate and transient, with symptom severity decreasing over time or following adjustments in application frequency. Serious adverse events were rarely reported, and treatment discontinuation due to intolerance occurred in a minority of participants across the analyzed clinical trials.

3.2.2 Isotretinoin

Available evidence indicates that isotretinoin affects several clinical and histological parameters associated with skin aging, particularly photoaging[21, 22]. Both topical and systemic formulations have been evaluated, although the overall body of evidence remains limited compared with other retinoids [22].

Randomized, double-blind clinical trials demonstrated that topical isotretinoin (0.05-0.1%) significantly improves fine wrinkles, skin texture, and overall severity of photodamage compared with vehicle control [21]. These findings were supported by standardized photographic assessments performed by independent dermatologists [23]. Histological analyses revealed increased epidermal thickness and improved dermal collagen organization, suggesting enhanced dermal remodeling and partial reversal of solar elastosis [21, 23].

Low-dose oral isotretinoin has also been investigated in photoaged skin. Randomized and prospective studies reported improvements in skin texture, pigmentation irregularities, and wrinkle depth following systemic treatment [24]. Histological and biochemical evaluations demonstrated increased collagen fiber density and upregulation of collagen types I and III, with some effects persisting after treatment discontinuation [25]. Serum biomarker studies further supported modulation of collagen metabolism during systemic isotretinoin therapy [26]. Despite these findings, oral isotretinoin is associated with a higher risk of adverse effects and remains an off-label option for skin aging [22].

3.2.3 Retinaldehyde

Retinaldehyde (RAL) has been evaluated as a topical retinoid for photoaged skin, with clinical evidence showing improvement in several aging-related parameters and generally favorable tolerability. In a randomized double-blind controlled trial, both RAL 0.05% and 0.1% improved skin hydration and texture; however, only the 0.1% formulation produced a significant improvement in melanin index, suggesting a stronger effect on pigmentation-related features of photoaging at higher concentration[27].

Earlier controlled clinical work using objective profilometric assessment demonstrated that topical RAL (0.05%) reduced markers of photodamage (wrinkle/roughness parameters) compared with vehicle, while being better tolerated than topical retinoic acid in terms of irritation, which may support adherence in long-term anti-aging regimens[28]. Evidence from split-face randomized studies indicates that multi-lamellar vehicle retinaldehyde creams can improve wrinkle appearance, facial contour and biophysical parameters associated with aging, supporting measurable clinical and instrumental benefits under controlled conditions[29].

In addition, an open multicenter study of a combination product containing RAL with intermediate-size hyaluronic acid fragments reported significant improvement in overall photoaging severity over a 90-day period in a large cohort, suggesting potential additive benefits of combination strategies, although the open-label design limits causal inference[30].

Overall, the available studies consistently suggest that retinaldehyde can improve clinical and instrumental markers of photoaging with a tolerability profile that may be advantageous versus retinoic acid, but heterogeneity in formulations, endpoints and trial designs limits direct comparisons across studies [27–30]. Reviews of topical antiaging retinoids position retinaldehyde as an effective OTC/dermocosmetic retinoid option supported by clinical evidence, while emphasizing differences in study quality and outcome measures[31].

3.2.4 Tazarotene

Topical tazarotene, a receptor-selective retinoid, has been evaluated in several clinical studies for its effects on photodamaged skin, with evidence supporting improvements in both clinical and histological features associated with photoaging. Early randomized controlled trials demonstrated that tazarotene 0.1% cream applied once daily was significantly more effective than vehicle in reducing fine wrinkles, mottled hyperpigmentation, and other signs of facial photodamage, with improvements reported as early as 4–8 weeks of treatment[32]. Similar findings were observed in a multicenter randomized trial comparing multiple concentrations of tazarotene, in which the 0.1% formulation showed the greatest clinical efficacy among the tested doses[33]. Histological assessments corroborated these clinical observations, showing that treatment with tazarotene was associated with increased epidermal thickness, improved epidermal polarity, and reductions in keratinocytic and melanocytic atypia compared with vehicle, indicating beneficial effects on skin structure at the microscopic level[34]. Moreover, evidence from multiple randomized controlled trials summarized in narrative reviews has confirmed that topical tazarotene is both safe and effective in the treatment of photodamaged skin, with adverse effects largely limited to mild to moderate, transient cutaneous irritation typical of topical retinoid therapy[35]. Comparative studies have also evaluated tazarotene relative to other topical retinoids. In one randomized trial, tazarotene 0.1% cream demonstrated equal or superior efficacy compared with tretinoin 0.05% emollient cream in improving clinical signs of photodamage, although tazarotene was associated with a higher frequency of early application-site discomfort, which generally diminished with continued use[36]. Additional clinical investigations suggest that combination approaches, such as co-administration of tazarotene with topical antioxidants, may further enhance improvements in fine wrinkles, skin hydration, and elasticity compared with tazarotene monotherapy; however, these findings require confirmation in larger, well-controlled studies[35].

Overall, the available evidence supports the efficacy of topical tazarotene in improving visible and histological features of photoaged skin in controlled clinical settings. Its safety profile is comparable to that of other topical retinoids and is primarily characterized by localized, reversible irritation, supporting its role as an effective option for targeted treatment of photodamage in dermatological practice.

4 Discussion

The present review confirms that retinoids represent the most extensively studied and mechanistically substantiated class of topical agents for the prevention and treatment of skin aging, particularly photoaging. Across the analyzed clinical and experimental studies, consistent improvements were observed in key clinical features of aged and photodamaged skin, including fine and coarse wrinkles, pigmentation irregularities, roughness, and overall skin texture. These effects are supported by well-characterized molecular mechanisms involving retinoid-mediated regulation of gene transcription through RAR/RXR signaling pathways, leading to stimulation of collagen synthesis, inhibition of matrix metalloproteinases, normalization of epidermal differentiation, and enhancement of dermal extracellular matrix integrity.

Among topical retinoids, tretinoin remains the gold standard with the strongest level of clinical and histological evidence. Randomized controlled trials and long-term studies demonstrate that tretinoin induces epidermal thickening, increases dermal collagen types I and III, and improves dermal organization, which translates into visible and sustained clinical rejuvenation. However, its clinical use is frequently limited by dose-dependent irritant reactions, particularly during the initial phase of therapy, which may compromise patient adherence. These findings highlight the importance of gradual dose escalation, optimized formulations, and patient education in maximizing therapeutic outcomes.

Retinol and retinaldehyde exhibit a more favorable tolerability profile and have demonstrated significant efficacy in improving intrinsic and extrinsic aging parameters, albeit with generally lower biological potency compared with retinoic acid. Their ability to induce retinoic-acid–like molecular responses in the skin, while causing less irritation, supports their widespread use in cosmeceutical and preventive anti-aging strategies. Retinaldehyde, in particular, appears to provide an optimal balance between efficacy and tolerability and may represent an attractive option for long-term maintenance therapy and for individuals with sensitive skin.

Isotretinoin has shown histological and clinical effects suggestive of dermal remodeling in photoaged skin; however, its systemic adverse-effect profile and teratogenicity restrict its use to selected off-label indications and preclude routine application in aesthetic dermatology. Similarly, tazarotene demonstrates robust clinical and histological efficacy comparable or superior to tretinoin in some studies, but its higher irritation potential requires careful patient selection and treatment monitoring.

From a clinical perspective, these findings support the individualized selection of retinoids based on the balance between efficacy, tolerability, and patient adherence, taking into account skin type, severity of photoaging, and the patient's ability to tolerate initial irritation. The efficacy of retinoid therapy should also be considered in conjunction with strict photoprotection, which remains a cornerstone of anti-aging management and is essential for preventing further UV-induced degradation of the extracellular matrix. Despite the substantial body of evidence supporting retinoids in skin aging, the reviewed literature is characterized by heterogeneity in study design, outcome measures, treatment regimens, and duration of follow-up. Direct head-to-head comparisons between different retinoids remain limited, and standardized biomarkers correlating molecular changes with long-term clinical outcomes are still lacking. Furthermore, most available data focus on photoaging, whereas intrinsic aging processes are less extensively investigated in controlled clinical settings.

5 Conclusions

Retinoids are the most evidence-based pharmacological agents for the treatment and prevention of skin aging, exerting their effects through well-defined molecular mechanisms that promote collagen synthesis, inhibit extracellular matrix degradation, and normalize epidermal differentiation. Tretinoin provides the strongest and most consistent clinical and histological anti-aging effects, while retinol and retinaldehyde offer improved tolerability and suitability for long-term and preventive use. Tazarotene represents an effective alternative for intensive treatment of photoaging, whereas systemic isotretinoin remains limited to selected off-label contexts due to safety concerns.

It should be noted that the majority of available clinical and histological evidence primarily addresses photoaging, whereas data specifically targeting intrinsic (chronological) skin aging remain comparatively limited, which represents an important limitation of the current literature and of the present review.

Future research should focus on well-designed head-to-head randomized trials comparing different retinoids using standardized clinical, instrumental, and molecular endpoints, on long-term studies assessing maintenance regimens and durability of anti-aging effects, on the development and validation of objective biomarkers linking molecular remodeling to visible clinical improvement, on the investigation of advanced delivery systems such as encapsulated and nanoformulated retinoids to enhance efficacy and tolerability, and on the separate evaluation of intrinsic versus extrinsic aging pathways to enable more personalized retinoid-based therapeutic strategies.

Such approaches will further refine the clinical use of retinoids and support evidence-based optimization of anti-aging interventions in dermatological practice.

Author's contribution

Here we present a detailed description of author's contribution to the creation of this manuscript. Conceptualization Ewa Bąkowska, Wojciech Janikowski, and Agnieszka Jóźwicka; methodology, Aleksandra Stępka; software, Weronika Plichtowicz- Kordowska; check, Lena Jaworowicz, Maria Wieczorek, Aleksandra Stępka and Wojciech Janikowski; formal analysis, Karina Lewandowska; investigation, Ewa Bąkowska; resources, Maria Wieczorek; data curation, Karina Lewandowska; writing - rough preparation, Agnieszka Jóźwicka; writing - review and editing Weronika Plichtowicz- Kordowska, Wojciech Janikowski; visualization, Agnieszka Jóźwicka; supervision, Lena Jaworowicz; project administration, Ewa Bąkowska. All authors have read and agreed with the published version of the manuscript.

REFERENCES

1. Bernstein, E. F., Chen, Y. Q., Kopp, J. B., Fisher, L., Brown, D. B., Hahn, P. J., Robey, F. A., Lakkakorpi, J., & Uitto, J. (1996). Long-term sun exposure alters the collagen of the papillary dermis: Comparison of sun-protected and photoaged skin by northern analysis, immunohistochemical staining, and confocal laser scanning microscopy. *Journal of the American Academy of Dermatology, 34*(2, Pt. 1), 209–218. https://doi.org/10.1016/S0190-9622(96)80114-9
2. Pandel, R., Poljšak, B., Godic, A., & Dahmane, R. (2013). Skin photoaging and the role of antioxidants in its prevention. *International Scholarly Research Notices, 2013*, Article 930164. https://doi.org/10.1155/2013/930164
3. Quan, T. (2023). Human skin aging and the anti-aging properties of retinol. *Biomolecules, 13*(11), Article 1614. https://doi.org/10.3390/biom13111614
4. Kong, R., Cui, Y., Fisher, G. J., Wang, X., Chen, Y., Schneider, L. M., & Majmudar, G. (2016). A comparative study of the effects of retinol and retinoic acid on histological, molecular, and clinical properties of human skin. *Journal of Cosmetic Dermatology, 15*(1), 49–57. https://doi.org/10.1111/jocd.12193
5. Kafi, R., Kwak, H. S. R., Schumacher, W. E., Cho, S., Hanft, V. N., Hamilton, T. A., King, A. L., Neal, J. D., Varani, J., Fisher, G. J., Voorhees, J. J., & Kang, S. (2007). Improvement of naturally aged skin with vitamin A (retinol). *Archives of Dermatology, 143*(5), 606–612. https://doi.org/10.1001/archderm.143.5.606
6. Szymański, Ł., Skopek, R., Palusińska, M., Schenk, T., Stengel, S., Lewicki, S., Kraj, L., Kamiński, P., & Zelent, A. (2020). Retinoic acid and its derivatives in skin. *Cells, 9*(12), Article 2660. https://doi.org/10.3390/cells9122660
7. Mukherjee, S., Date, A., Patravale, V., Korting, H. C., Roeder, A., & Weindl, G. (2006). Retinoids in the treatment of skin aging: An overview of clinical efficacy and safety. *Clinical Interventions in Aging, 1*(4), 327–348. https://doi.org/10.2147/ciia.2006.1.4.327
8. Ellis, C. N., & Krach, K. J. (2001). Uses and complications of isotretinoin therapy. *Journal of the American Academy of Dermatology, 45*(5 Suppl.), S150–S157. https://doi.org/10.1067/mjd.2001.113717
9. Bagatin, E., & Costa, C. S. (2020). The use of isotretinoin for acne – an update on optimal dosing, surveillance, and adverse effects. *Expert Review of Clinical Pharmacology, 13*(8), 885–897. https://doi.org/10.1080/17512433.2020.1796637
10. Milosheska, D., & Roškar, R. (2022). Use of retinoids in topical antiaging treatments: A focused review of clinical evidence for conventional and nanoformulations. *Pharmaceutics, 14*(11), Article 2395. https://doi.org/10.3390/pharmaceutics14112395
11. Ghyselinck, N. B., & Duester, G. (2019). Retinoic acid signaling pathways. *Development, 146*(13), Article dev167502. https://doi.org/10.1242/dev.167502
12. Li, Z., Ding, J., Ma, Z., Sun, X., Wang, Y., Chen, J., & Wang, J. (2017). Retinoic acid ameliorates photoaged skin through RAR-mediated pathway in mice. *Molecular Medicine Reports, 16*(5), 6240–6247. https://doi.org/10.3892/mmr.2017.7344
13. Rusu, A., Tanase, C., Pascu, G.-A., & Todoran, N. (2020). Recent advances regarding the therapeutic potential of adapalene. *Pharmaceuticals, 13*(9), Article 217. https://doi.org/10.3390/ph13090217
14. Griffiths, C. E., Kang, S., Ellis, C. N., Kim, K. J., Finkel, L. J., Ortiz-Ferrer, L. C., White, G. M., Datloe, J. S., Hanifin, J. M., & Gadgeel, V. G. (1995). Two concentrations of topical tretinoin (retinoic acid) cause similar improvement of photoaging but different degrees of irritation: A double-blind, vehicle-controlled comparison of 0.1% and 0.025% tretinoin creams. *Archives of Dermatology, 131*(9), 1037–1044. https://doi.org/10.1001/archderm.1995.01690210057010
15. Sitohang, I. B. S., Makes, W. I., Sandora, N., & Suryanegara, J. (2022). Topical tretinoin for treating photoaging: A systematic review of randomized controlled trials. *Journal of Dermatological Treatment, 8*(1). https://doi.org/10.1097/JW9.0000000000000003
16. Huang, H.-Y., & Lee, L. T.-J. (2025). Tretinoin for photodamaged facial skin: Systematic review and meta-analysis of randomized controlled trials. *Dermatology Practical & Conceptual, 15*(4). https://doi.org/10.5826/dpc.1504a5172
17. Chien, A. L., Kim, D. J., Cheng, N., Shin, J., Leung, S. G., Nelson, A. M., Zang, J., Suh, H., Rainer, B., Wallis, L., Okoye, G. A., Loss, M., & Kang, S. (2022). Biomarkers of tretinoin precursors and tretinoin efficacy in patients with moderate to severe facial photodamage: A randomized clinical trial. *JAMA Dermatology, 158*(8), 879–886. https://doi.org/10.1001/jamadermatol.2022.1891
18. Weiss, J. S., Ellis, C. N., Headington, J. T., Tincoff, T., Hamilton, T. A., & Voorhees, J. J. (1988). Topical tretinoin improves photoaged skin: A double-blind vehicle-controlled study. *JAMA, 259*(4), 527–532. https://doi.org/10.1001/jama.1988.03400040081027
19. Griffiths, C., Russman, A. N., Majmudar, G., Singer, R. S., Hamilton, T. A., & Voorhees, J. J. (1993). Restoration of collagen formation in photodamaged human skin by tretinoin (retinoic acid). *New England Journal of Medicine, 329*(8), 530–535. https://doi.org/10.1056/NEJM199308193290803

20. Federspiel, S. J., DiMari, S. J., Guerry-Force, M. L., & Haralson, M. A. (1991). Extracellular matrix biosynthesis by cultured fetal rat lung epithelial cells. IV. Effects of chronic exposure to retinoic acid on growth, differentiation, and collagen biosynthesis. *[Journal title not provided], 65*(4), 441–450.
21. Maddin, S., Lauharanta, J., Agache, P., Burrows, L., Zultak, M., & Bulger, L. (2000). Isotretinoin improves the appearance of photodamaged skin: Results of a 36-week, multicenter, double-blind, placebo-controlled trial. *Journal of the American Academy of Dermatology, 42*(1 Pt. 1), 56–63. https://doi.org/10.1016/S0190-9622(00)90009-4
22. Paichitrojjana, A., & Paichitrojjana, A. (2023). Oral isotretinoin and its uses in dermatology: A review. *Drug Design, Development and Therapy, 17*, 2573–2591. https://doi.org/10.2147/DDDT.S427530
23. Rigel, D. S., Weiss, R. A., Lim, H. W., & Dover, J. S. (Eds.). (2004). *Photoaging* (Vol. 28). CRC Press.
24. Bagatin, E., Guadalupe, F., Enokihara, M. Y. S. S., Aguiar, M. S., Aguiar, L. M., Pereira, B. M., & Sanudo, A. (2010). A randomized and controlled trial about the use of oral isotretinoin for photoaging. *International Journal of Dermatology, 49*(2), 207–214. https://doi.org/10.1111/j.1365-4632.2009.04310.x
25. Azulay, D. R., Bagatin, E., Roche, L., Kalil, C. L., Rezende, R., & Pérez-Maldonado, A. (2023). Durability of the improvement of collagen I and collagen III with the use of oral isotretinoin in the treatment of photoaging. *International Journal of Dermatology, 62*(12), 1538–1542. https://doi.org/10.1111/ijd.16868
26. Autio, P., Risteli, J., Risteli, L., & Oikarinen, A. (1993). Effects of systemic isotretinoin on serum markers of collagen synthesis and degradation. *Acta Dermato-Venereologica, 73*(2), 108–112. https://doi.org/10.2340/0001555573108112
27. Kwon, H. S., Lee, J. H., Kim, M. N., Seong, G.-H., Kim, B.-R., Pyun, J.-H., Kim, G.-H., Choi, G.-S., & Youn, S.-W. (2018). Efficacy and safety of retinaldehyde 0.1% and 0.05% creams used to treat photoaged skin: A randomized double-blind controlled trial. *Journal of Cosmetic Dermatology, 17*(3), 471–476. https://doi.org/10.1111/jocd.12551
28. Monteil, C., Barreto-Campos, V., Lain, E., Guillou, E., Doat, G., & Nocera, T. (2025). Enhancing facial rejuvenation outcomes with a novel retinaldehyde-based cream: A comparative randomized intra-individual study. *Journal of Cosmetic Dermatology, 24*(12). https://doi.org/10.1111/jocd.70555
29. Brown, A., Furmanczyk, M., Ramos, D., Ribes, A., Pons, L., Bustos, J., Fernández de Henestrosa, A. R., Granger, C., & Jourdan, E. (2023). Natural retinol analogs potentiate the effects of retinal on aged and photodamaged skin: Results from in vitro to clinical studies. *Dermatology and Therapy, 13*(10), 2299–2317. https://doi.org/10.1007/s13555-023-01004-z
30. Creidi, P., Vienne, M.-P., Ochonisky, S., Lauze, C., Turlier, V., Lagarde, J.-M., & Dupuy, P. (1998). Profilometric evaluation of photodamage after topical retinaldehyde and retinoic acid treatment. *Journal of the American Academy of Dermatology, 39*(6), 960–965. https://doi.org/10.1016/S0190-9622(98)70270-1
31. Konisky, H., Cook-Bolden, F. E., Guenin, E., Jarratt, M., Rossi, A., & Zeichner, J. (2024). The clinical efficacy and tolerability of a novel retinaldehyde serum with firming peptides to improve skin texture and signs of photoaging. *Journal of Drugs in Dermatology, 23*(11), 992–997. https://doi.org/10.36849/JDD.8058
32. Kang, S., Leyden, J. J., Lowe, N. J., Ortiz-Ferrer, L. C., Zweig, J. S., Jarratt, M. T., Savin, R. C., Shavin, J. S., Stough, D. B., Weiss, J. S., et al. (2001). Tazarotene cream for the treatment of photodamaged facial skin: A multicenter, randomized, double-blind, vehicle-controlled study. *Archives of Dermatology, 137*(12), 1597–1604. https://doi.org/10.1001/archderm.137.12.1597
33. Phillips, T. J., Gottlieb, A. B., Leyden, J. J., Lowe, N. J., Lew-Kaya, G. W., Dixon, D. B., Gibson, J. R., & Walker, P. S. (2002). Efficacy of tazarotene cream for the treatment of facial photodamage: A 24-week, multicenter, randomized, double-blind, vehicle-controlled study. *Archives of Dermatology, 138*(11), 1444–1450. https://doi.org/10.1001/archderm.138.11.1444
34. Machtinger, L., Kang, S., Leyden, J. J., et al. (2004). Histologic effects of tazarotene 0.1% cream in the treatment of photodamaged facial skin. *Journal of Investigative Dermatology, 122*(5), 1223–1229. https://doi.org/10.1111/j.0022-202X.2004.22433.x
35. Ogden, S., Samuel, M., & Griffiths, C. E. M. (2008). Tazarotene in the treatment of photodamaged skin. *Clinical Interventions in Aging, 3*(1), 71–76. https://doi.org/10.2147/CIA.S125
36. Lowe, N. J., Gibson, J. R., Leyden, J. J., & Kang, S. (2004). Tazarotene 0.1% cream versus tretinoin 0.05% emollient cream in the treatment of photodamaged facial skin: A comparative study. *Journal of the American Academy of Dermatology, 50*(3), 397–406. https://doi.org/10.1016/j.jaad.2003.10.664