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Retinol versus epigallocatechin-3-gallate (EGCG): Effects on molecular expression in photoaging

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ABSTRACT

Photoaging is a form of skin aging caused by chronic exposure to ultraviolet radiation. It is characterized by dermal matrix degradation, reduced collagen production, and accelerated collagen breakdown. In this randomized parallel-group clinical trial, 26 women aged 30-50 years with glogau II-III photoaging were randomly assigned to receive topical 5% epigallocatechin-3-gallate (EGCG) or 0.1% retinol once daily for 12 weeks. Immunohistochemical expression of TGF-β2, matrix metalloproteinase-1 (MMP-1), and type I collagen was assessed in skin punch biopsy specimens before and after treatment. Both topical EGCG and retinol induced a significant increase in TGF-β2 and type I collagen expression, indicating enhanced dermal regenerative signaling. EGCG significantly reduced MMP-1 expression, whereas retinol showed a nonsignificant decrease, suggesting a stronger anti-catabolic effect of EGCG. No significant differences were observed between treatments in increasing TGF-β2 or type I collagen expression, indicating comparable anabolic effects. Overall, EGCG and retinol demonstrated similar efficacy in improving dermal remodeling markers, with EGCG showing superior effects in suppressing collagen degradation through MMP-1 inhibition.

Keywords: photoaging, retinol, EGCG, TGF-β2, MMP-1, collagen type I

INTRODUCTION

Photoaging refers to the premature aging of skin resulting from prolonged and repeated exposure to ultraviolet (UV) radiation [1]. This process leads to significant structural changes in the dermis, primarily through decreased collagen synthesis and increased collagen degradation [2]. The central mechanism underlying these changes is an imbalance between collagen production by fibroblasts and the activity of proteolytic enzymes, particularly matrix metalloproteinase-1 (MMP-1), which plays a major role in collagen breakdown within the dermal extracellular matrix [3, 4].

Type I collagen is the predominant structural protein in the extracellular matrix of the dermis, providing skin with strength and elasticity. It is synthesized by fibroblasts through the TGF-β-Smad signaling pathway, in which TGF-β2 is one of the key isoforms involved. Reduced TGF-β2 expression impairs collagen synthesis and contributes to the clinical manifestations of skin aging [5, 6]. In addition, UV exposure generates reactive oxygen species (ROS), which further exacerbate photoaging. Elevated ROS levels activate mitogen-activated protein kinase (MAPK) pathways—particularly ERK and JNK—leading to the activation of the transcription factor AP-1, which, in turn, upregulates MMP-1 expression while simultaneously suppressing type I collagen synthesis [5]. The resulting loss of dermal collagen density produces the characteristic clinical features of photoaged skin.

Topical retinol is one of the most widely used cosmetic retinoids for the prevention and treatment of photoaging because of its favorable balance between efficacy and tolerability. After topical application, retinol is enzymatically converted into retinaldehyde and subsequently into retinoic acid, which binds to retinoic acid receptors (RARs) to regulate genes involved in epidermal differentiation, fibroblast activation, collagen synthesis, and extracellular matrix remodeling. These molecular effects promote dermal repair by enhancing collagen production while suppressing MMP-mediated collagen degradation. Despite its established efficacy, topical retinol may induce dose-dependent cutaneous irritation, including erythema, dryness, burning, and desquamation, particularly during the initial treatment period.

Consequently, there is growing interest in identifying alternative topical agents with comparable anti-photoaging efficacy but improved tolerability [6, 7].

Plant-derived extracts rich in natural polyphenols have attracted increasing interest for their antioxidant properties, ability to inhibit collagen breakdown, protection against UV-induced damage, and potential to counteract skin aging. Among these, green tea (camellia sinensis) stands out due to its high concentration of catechins, with epigallocatechin-3-gallate (EGCG) being the most abundant and biologically active component in humans. In animal models, topical application of EGCG has been shown to inhibit carcinogenesis, preserve cutaneous immune function, reduce UV-induced inflammatory responses, and prevent photoaging [8, 9]. In addition, EGCG exhibits minimal to no toxicity and exerts therapeutic effects on photoaging through modulation of key pathways, including MAPK, Nrf2, and NF-κB [7, 10-12].

To address the need for alternative topical anti-photoaging agents, we conducted a randomized parallel-group clinical trial comparing topical 5% EGCG with 0.1% retinol on the dorsal hand. The study aimed to evaluate and compare the effects of these treatments on dermal remodeling by assessing the immunohistochemical expression of TGF-β2, MMP-1, and type I collagen, which represent key biomarkers of collagen synthesis and extracellular matrix degradation.

MATERIALS AND METHODS

Study Design

This study was a randomized, controlled clinical trial with a parallel-group, before-and-after interventional design. It enrolled 26 women aged 30-50 years with glogau classification II-III photoaging who were willing to complete all study procedures and who provided written informed consent.

Inclusion criteria required that participants had no history of invasive facial or hand cosmetic procedures within the previous six months and had not used topical exfoliating therapies (retinoids, AHA/BHA, chemical peels, microdermabrasion, or laser treatments) within the prior four weeks. Additional requirements included no tattoos on the face or hands, no known allergy to products containing EGCG or retinol, no plans for pregnancy within the next three months, and the use of effective contraception throughout the study period. Exclusion criteria included a history of keloid formation, current pregnancy, active skin diseases (e.g., eczema, psoriasis, or bacterial/fungal infections) on the face or hands, a history of herpes infection in the study areas, coagulation disorders or use of antiplatelet medications, menopausal status, and systemic conditions such as diabetes mellitus or HIV/AIDS.

Topical Application of 5% EGCG and 0.1% Retinol

Participants applied a nightly topical cream containing either 5% EGCG or 0.1% retinol to the dorsal surface of the hands for the duration of the study. To ensure standardized photoprotection, all subjects received SPF 50 sunscreen and were instructed to apply it during the day, with reapplication every three hours. The test creams were applied each evening for 12 weeks. Participants were asked to avoid any additional skincare products or aesthetic procedures during the study period to prevent interference with outcome assessments. Compliance was monitored periodically, and any adverse events were recorded and documented throughout the trial. However, both treatment groups received formulations with an identical cream base, differing only in the incorporated active ingredient.

Sample Preparation and Histopathological Analysis

Skin punch biopsies (0.3 × 0.3 cm^2) were obtained from the dorsal hand under local anesthesia at baseline and after 12 weeks of treatment. Specimens were immediately fixed in 10% buffered formalin, dehydrated through a graded ethanol series (70%, 80%, 90%, 96%), cleared in xylene, and embedded in paraffin. Sections were cut to a thickness of 5-7 µm, deparaffinized, and processed for immunohistochemistry.

Immunohistochemical evaluation was performed on formalin-fixed, paraffin-embedded skin biopsy sections. Although intact skin tissue was examined, staining intensity was assessed specifically in the target cell populations according to marker localization. TGF-β2 and MMP-1 expression were evaluated in epidermal keratinocytes, whereas type I collagen expression was assessed in dermal fibroblasts. No isolated cell cultures were used in this study.

Antigen retrieval was performed using 0.025% trypsin for 15 minutes at 37 °C. Nonspecific binding was blocked with Ultra V Block solution for 5 minutes, followed by rinsing. Sections were then incubated with primary antibodies for 60 minutes at room temperature: anti-TGF-β2 (B-10) (sc-374658, 1:100 dilution, mouse monoclonal, Santa Cruz Biotechnology, Europe), anti-MMP-1 (3B6) (sc-21731, 1:200 dilution, mouse monoclonal, Santa Cruz Biotechnology, Europe), and anti-collagen type I (3G3) (sc-293182, 1:200 dilution, mouse monoclonal, Santa Cruz Biotechnology, Europe). After washing with PBS, the slides were incubated with biotinylated link reagent (yellow) for 30 minutes, rinsed, and then incubated with streptavidin reagent (yellow) for 30 minutes. Color development was achieved with DAB for 6-10 minutes, followed by counterstaining with methyl green, mounting with Entellan, and coverslipping. Histopathological analysis was performed by capturing five random fields per slide at 400× magnification using the Nikon Image System software. Immunohistochemical staining was evaluated using a modified semi-quantitative H-score approach. For each specimen, 10 representative high-power fields (400×) were examined. In each field, staining intensity was graded on a four-point scale (0 = no staining, 1 = weak, 2 = moderate, and 3 = strong), while the proportion of positively stained cells was recorded as a percentage (0-100%). A composite score for each field was calculated by multiplying the staining intensity by the percentage of positive cells, resulting in a possible score ranging from 0 to 300. The final score for each specimen was obtained by averaging the composite scores from the 10 evaluated fields. All immunohistochemical scoring was performed independently by a dermatopathologist who was blinded to treatment allocation and sampling time (baseline or post-treatment).

Statistical Analysis

Statistical analyses were performed using SPSS software. The normality of the composite immunohistochemical scores was assessed using the Shapiro-Wilk test, which is appropriate for small sample sizes. Normally distributed data are presented as the mean ± standard deviation. Within-group comparisons between baseline and post-treatment were performed using

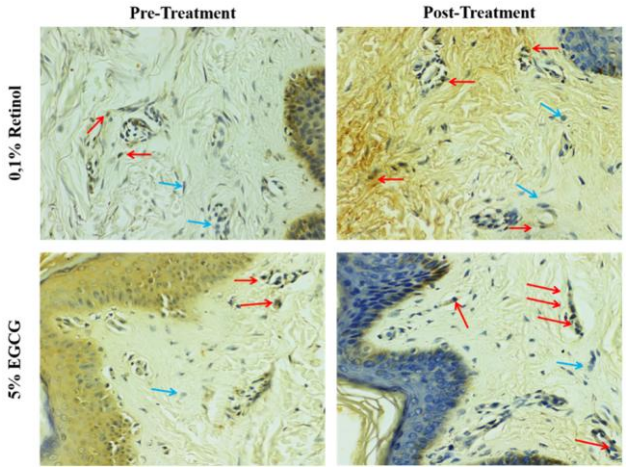

Figure 1. Immunohistochemical expression of TGF-β2 in photoaged facial skin before and after treatment with 0.1% retinol and 5% EGCG (in the retinol group [top panels], TGF-β2 expression was increased in post-treatment compared to pre-treatment group; a similar increase was observed in the EGCG group [bottom panels]; positive expression appears as brown cytoplasmic staining, while negative cells show no staining; red arrows indicate TGF-β2-positive cells, and blue arrows indicate negative cells; & images were captured under a light microscope at 400× magnification) (the authors' own images obtained from this study)

paired t-tests, whereas between-group comparisons were analyzed using independent t-tests. Path analysis was subsequently conducted to evaluate the direct and indirect relationships among treatment type, TGF-β2, MMP-1, and type I collagen expression. A two-sided p-value < 0.05 was considered statistically significant.

Path Analysis

Path analysis was performed as an exploratory analytical approach to evaluate the potential direct and indirect relationships among treatment type, TGF-β2, MMP-1, and type I collagen expression. This method was chosen because dermal remodeling in photoaging involves interconnected anabolic and catabolic pathways, in which treatment effects may not occur through isolated biomarker changes alone. In this model, treatment type was examined as an exogenous variable, while TGF-β2 and MMP-1 were assessed as potential mediating molecular markers related to type I collagen expression. For path analysis, treatment was entered as a categorical exogenous variable using numerical coding (0 = topical retinol and 1 = topical 5% EGCG). Therefore, the direction of the standardized path coefficients (β) should be interpreted according to this coding scheme, with negative coefficients indicating relatively higher values in the retinol group and positive coefficients indicating relatively higher values in the EGCG group.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Karsa Husada General Hospital, Batu (approval no. 020/1422/102.13/2024). Written informed consent was obtained from all participants before enrollment. Adverse events were documented and managed according to the approved protocol.

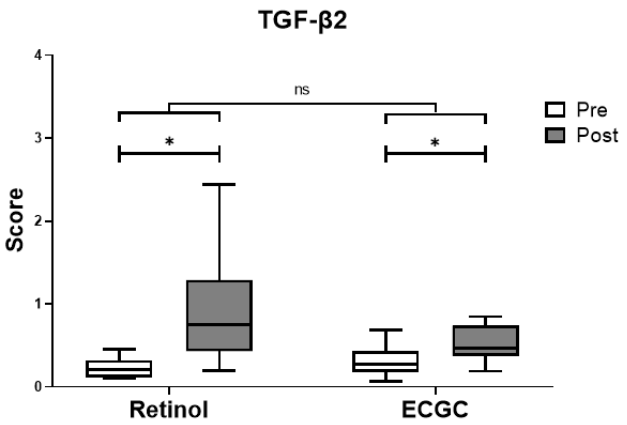

Figure 2. TGF-β2 expression scores before and after topical treatment with retinol and EGCG (both treatments significantly increased TGF-β2 expression within groups [< 0.05], with no significant difference between treatments (ns) & values are presented as mean ± standard deviation) (the authors' own images obtained from this study)

RESULTS

A total of 26 participants completed the study, with 13 participants assigned to the 5% EGCG group and 13 to the 0.1% retinol group. Overall, both treatments were well tolerated. Mild dry skin was reported by **two participants (15.4%)** in the retinol group and **one participant (7.7%)** in the EGCG group. No cases of irritation, erythema, or pruritus were observed in either treatment group throughout the 12-week study period. No participant discontinued treatment because of adverse events.

Epidermal Transforming Growth Factor β-2 (TGF-β2) Expression in Human Skin Keratinocytes Treated Topically with EGCG Compared to Retinol Treatment

Topical application of 5% EGCG significantly increased TGF-β2 expression from **0.32 ± 0.19** at baseline to **0.53 ± 0.21** after 12 weeks (paired t-test, **p = 0.046**). Similarly, the retinol group demonstrated a significant increase from **0.23 ± 0.12** to **0.88 ± 0.63** (paired t-test, **p = 0.003**). However, the magnitude of change did not differ significantly between the two treatment groups (independent t-test, **p = 0.096**) (**Figure 1** and **Figure 2**). This finding indicates that both agents are equally effective in upregulating TGF-β2 expression.

Epidermal MMP-1 Expression in Human Skin Keratinocytes Treated Topically with EGCG Compared to Retinol Treatment

Topical 5% EGCG significantly reduced MMP-1 expression from **0.51 ± 0.24** to **0.14 ± 0.09** (paired t-test, **p = 0.000**). In contrast, although the retinol group showed a reduction in MMP-1 expression (**0.24 ± 0.14** to **0.13 ± 0.09**), the change did not reach statistical significance (**p = 0.08**). The between-group comparison demonstrated a significantly greater reduction in the EGCG group (**p = 0.008**) (**Figure 3** and **Figure 4**). These findings indicate that EGCG is more effective than retinol at downregulating MMP-1 expression.

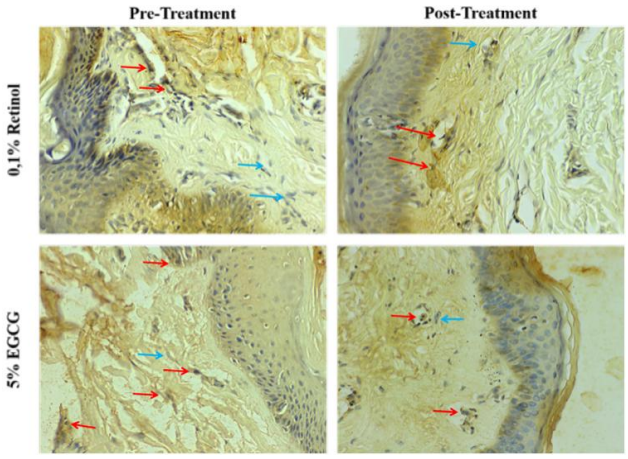

Figure 3. Immunohistochemical expression of MMP-1 in photoaged facial skin before and after treatment with 0.1% retinol and 5% EGCG (in the retinol group [top panels], MMP-1 expression was decreaded in post-treatment compared to pre-treatment group; a similar reduction was observed in the EGCG group [bottom panels]; positive expression appears as brown cytoplasmic staining, while negative cells show no staining; red arrows indicate MMP-1-positive cells, and blue arrows indicate negative cells; & images were captured under a light microscope at 400× magnification) (the authors' own images obtained from this study)

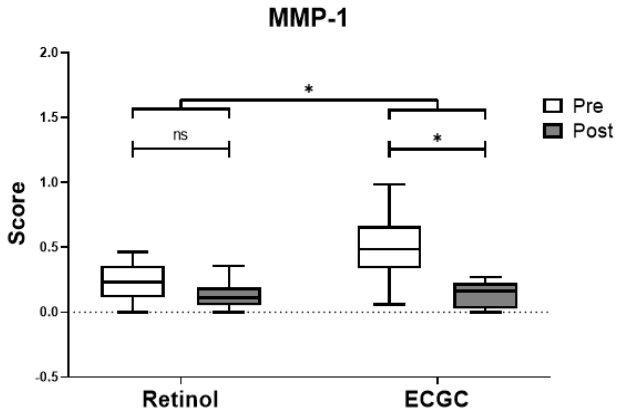

Figure 4. MMP-1 expression scores before and after topical treatment with retinol and EGCG (a significant decrease in MMP-1 expression was observed after EGCG treatment [$p < 0.05$], whereas the reduction in the retinol group was not significant (ns); comparison between treatments showed a significant difference ($p < 0.05$), indicating a greater reduction with EGCG; & values are presented as mean ± standard deviation) (the authors' own images obtained from this study)

Epidermal Collagen Type I Expression in Human Skin Fibroblasts Treated Topically with EGCG Compared to Retinol Treatment

Type I collagen expression increased significantly in both groups after treatment (EGCG: **4.15 ± 0.35** to **5.93 ± 1.37**, **p = 0.001**; retinol: **4.80 ± 0.31** to **7.88 ± 2.07**, **p = < 0.001**). No significant between-group difference was observed (**p = 0.086**) (**Figure 5** and **Figure 6**), indicating that 5% EGCG and 0.1% retinol are equally effective in enhancing collagen type I expression.

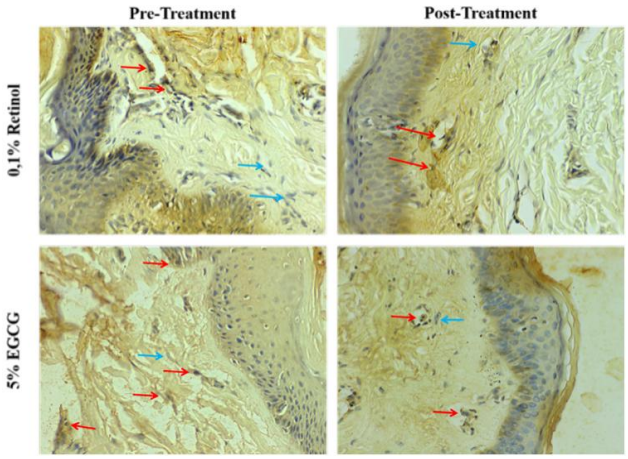

Figure 5. Immunohistochemical expression of collagen type I in photoaged facial skin before and after treatment with 0.1% retinol and 5% EGCG (in the retinol group [top panels], collagen type 1 expression was decreaded in post-treatment compared to pre-treatment group; a similar reduction was observed in the EGCG group [bottom panels]; positive expression appears as brown cytoplasmic staining, while negative cells show no staining; red arrows indicate MMP-1-positive cells, and blue arrows indicate negative cells; & images were captured under a light microscope at 400× magnification) (the authors' own images obtained from this study)

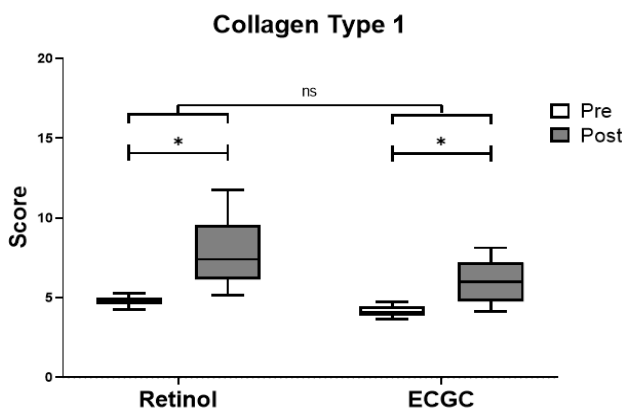

Figure 6. Collagen type I expression scores before and after topical treatment with retinol and EGCG (both treatments significantly increased collagen type I expression within groups ($p < 0.05$), with no significant difference between treatments (ns) & values are presented as mean ± standard deviation) (the authors' own images obtained from this study)

Path Analysis of Treatment Effects on Dermal Remodeling Markers

A path analysis was conducted to evaluate the relationship between treatment types and the molecular parameters involved in the dermal remodeling process (**Figure 7**). In the path analysis, the treatment variable was dummy-coded as 0 = topical retinol and 1 = topical 5% EGCG.

The model was able to explain the variance with R^2 values of 0.258 for MMP-1, 0.174 for TGF-β2, and 0.199 for collagen type I. This study found a significant direct effect of treatment type on the scores of MMP-1 (β = -0.508; p = 0.001), TGF-β2 (β = -0.417; p = 0.001), and collagen type I (β = -0.464; p = 0.049).

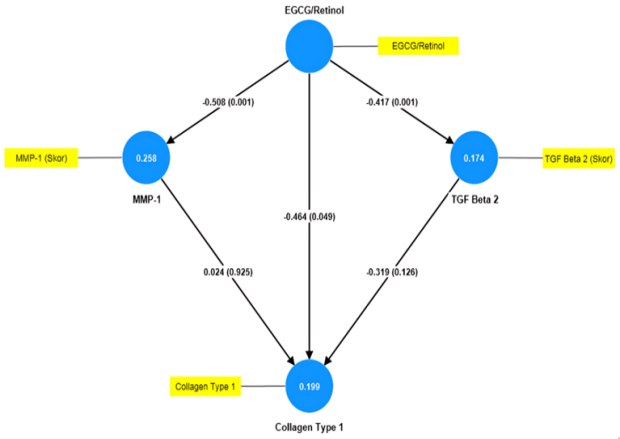

Figure 7. Path analysis comparing the effects of EGCG and retinol using SmartPLS software (the authors' own images obtained from this study)

Meanwhile, no statistical significance was observed for the paths from MMP-1 to collagen type I (β = 0.024; p = 0.925) or from TGF-β2 to collagen type I (β = -0.319; p = 0.126).

DISCUSSION

Epidermal Transforming Growth Factor β-2 (TGF-β2) Expression in Epidermal Keratinocytes of Human Skin Biopsy Specimens Following Topical EGCG or Retinol Treatment

Both topical EGCG and retinol significantly increased TGF-β2 expression after 12 weeks of treatment, with no significant difference between the two groups. These findings suggest that both agents promote dermal remodeling by activating anabolic pathways involved in collagen synthesis. TGF-β2 is a key profibrotic cytokine that stimulates fibroblast proliferation and extracellular matrix production through the canonical Smad signaling pathway, ultimately enhancing type I collagen synthesis. The observed increase in TGF-β2 expression is therefore consistent with the concurrent upregulation of type I collagen in both treatment groups.

Overall, retinol/retinoic acid improves photoaging by enhancing TGF-β2 expression and activating Smad-dependent collagen synthesis in the dermis [13]. EGCG, the major polyphenol in green tea, possesses potent antioxidant and anti-inflammatory properties. It suppresses oxidative stress, inhibits MAPK signaling, and reduces AP-1 activity. In this study, EGCG also significantly increased TGF-β2 expression. This upregulation likely results from an enhanced dermal microenvironment that allows the TGF-β2 pathway to function more effectively. Therefore, these findings support the idea that EGCG is more likely to act as a signaling intermediary that promotes balance in biological pathways rather than as a direct inducer of TGF-β2 [14, 15].

Epidermal MMP-1 Expression in Epidermal Keratinocytes of Human Skin Biopsy Specimens Following Topical EGCG or Retinol Treatment

Topical 5% EGCG significantly reduced MMP-1 expression in epidermal keratinocytes after 12 weeks of treatment, whereas the reduction observed in the retinol group did not reach statistical significance. Furthermore, the decrease in MMP-1 expression was significantly greater in the EGCG group than in the retinol group. These findings suggest that EGCG is more effective at suppressing collagen degradation, one of the principal mechanisms underlying photoaging.

EGCG is known to suppress MMP-1 expression by regulating molecular pathways associated with oxidative stress and inflammation. Additionally, this compound can reduce the production of ROS, suppress the activation of MAPK proteins (including ERK, JNK, and p38), and inhibit the AP-1 and NF-κB pathways, resulting in decreased MMP-1 gene transcription in skin fibroblasts [15, 16].

Furthermore, EGCG has been shown to increase SOD2 enzyme activity and restore the balance between MMPs and TIMPs, particularly by increasing the TIMP-1-to-MMP-1 ratio, thereby inhibiting collagen degradation [14, 17]. The results of this study demonstrate that EGCG reduces MMP-1 expression, which aligns with these established mechanisms.

These findings are also consistent with a previous study using a chronic UVB-induced hairless mouse photoaging model to evaluate the effects of topical 2.5-5% EGCG cream. That study observed a significant decrease in MMP-1 expression in the EGCG group compared with the control, confirming that EGCG reduces UV-induced collagen damage [8]. Another study using UV-exposed human dermal fibroblasts (HDF) as an in vitro photoaging model showed that EGCG administration significantly reduced MMP-1 expression and secretion while simultaneously decreasing AP-1 activation [18].

Additionally, several studies have found that EGCG reduces MMP expression across various biological models at both the cellular and organismal levels, including UV-irradiated human skin fibroblasts, HDF, human keratinocytes, artificial skin, zebrafish, and the dorsal skin of hairless mice [14]. Overall, the results from this study and prior research reinforce the evidence that EGCG reduces MMP-1 expression through antioxidant effects and modulation of dermal matrix degradation signaling pathways.

As previously described, retinol is converted into retinoic acid, which then forms a complex with RAR/RXR to regulate gene expression related to fibroblast differentiation and matrix synthesis. Retinoic acid inhibits MMP-1 expression by interfering with AP-1 activity; however, this effect is indirect and depends on the duration and concentration of UV exposure. Therefore, although a decrease in MMP-1 occurred in the retinol group, statistical significance was not reached [6, 19].

The discrepancy in efficacy between EGCG and retinol regarding MMP-1 downregulation is likely related to their respective biological mechanisms. EGCG acts directly at the onset of the oxidative stress pathway that triggers MMP-1 formation, making its inhibitory effect appear more rapid and pronounced. Retinol, however, tends to focus on enhancing anabolic pathways and improving fibroblast response to growth signals, resulting in a slower, indirect reduction of MMP-1 [5, 15]. Furthermore, in silico studies have shown that the binding affinity of EGCG for MMP-1 is stronger than that of retinol [20]. Broadly, based on in vitro, in vivo, and in silico results, EGCG is more effective at reducing MMP-1 expression by inhibiting dermal catabolic pathways—specifically the AP-1/MMP-1 axis—while retinol contributes to long-term dermal repair through the activation of anabolic pathways [13, 19, 20].

Dermal Type I Collagen Expression in Dermal Fibroblasts of Human Skin Biopsy Specimens Following Topical EGCG or Retinol Treatment

Both EGCG and retinol treatments significantly increased collagen type I expression, yet there was no significant difference between the two groups. This demonstrates that both interventions are equally effective in increasing collagen type I levels. Biologically, UV exposure triggers AP-1 activation via the MAPK pathway, which subsequently increases MMP enzyme activity and suppresses TGF-β signaling. This process leads to decreased procollagen formation and accelerated collagen degradation, resulting in reduced dermal collagen density and the clinical manifestation of photoaging. Collagen type I is a critical component of the dermal matrix produced by fibroblasts, functioning to maintain skin strength and elasticity. Consequently, increased collagen type I expression is frequently utilized as a parameter for successful dermal repair and remodeling [5, 6].

RAR/RXR receptors by retinoic acid (the converted form of retinol) can upregulate collagen type I gene expression (COL1A1 and COL1A2) and enhance fibroblast sensitivity to TGF-β signaling [19, 21]. In this study, retinol significantly increased collagen type I expression. This aligns with previous research reporting that retinol enhances dermal collagen, evidenced by increased procollagen type I expression and improved histological structure with favorable skin tolerability [22].

EGCG possesses antioxidant and anti-inflammatory properties that help maintain collagen type I by suppressing matrix degradation pathways, thereby reducing collagen damage [14]. In vivo studies using chronic UVB-induced hairless mouse photoaging models have shown that topical 5% EGCG treatment significantly improves dermal collagen repair and quantity. Additionally, a decrease in MMP-1 was observed alongside the increase in collagen, indicating that EGCG's enhancement of collagen type I occurs through the inhibition of collagen degradation rather than solely stimulating new collagen synthesis [8].

Overall, both research data and theoretical frameworks indicate that retinol and EGCG employ distinct mechanisms to increase collagen type I. Retinol plays a role in stimulating new collagen formation, whereas EGCG helps preserve existing collagen by suppressing its degradation process. This mechanistic divergence supports the potential use of retinol and EGCG in combination, as they may act synergistically to repair dermal structural damage caused by photoaging.

Path Analysis of Treatment Effects on Dermal Remodeling Markers

In this study, path analysis was utilized to evaluate the relationship between treatment types and photoaging parameters, as well as the impact of these parameters on collagen type I. The coefficients of determination indicate that the model explains a portion of the variation in biological parameters: 25.8% for MMP-1, 17.4% for TGF-β2, and 19.9% for collagen type I. These results suggest that while treatment type plays a role in shifting dermal molecular parameters, numerous factors outside the model—such as cumulative UY exposure, endogenous antioxidant status, and individual inflammatory responses—also influence the skin remodeling process [3, 4].

The results demonstrated a significant direct relationship between treatment type and MMP-1. This indicates that differences in treatment are linked to changes in matrix degradation pathway activity, including the suppression of MMP-1 expression via reduced ROS production and inhibition of MAPK pathway activation [3, 16]. Furthermore, a significant direct relationship was found between treatment type and TGF-β2, showing that both compounds influence matrix synthesis regulation pathways, albeit with differing potencies. The significant negative path coefficients observed for treatment on TGF-β2 ($\beta = -0.417$, $p = 0.001$) and type I collagen expression ($\beta = -0.464$, $p = 0.049$) indicate that retinol was associated with relatively higher expression of these anabolic markers than EGCG. These findings support the established mechanism of topical retinoids, which stimulate retinoic acid receptor signaling, enhance TGF-β-mediated fibroblast activation, and promote collagen synthesis during dermal remodeling. This finding aligns with the biological mechanism of retinoids, which are known for their direct anabolic effects on the TGF-β/SMAD pathway, whereas EGCG functions primarily by modulating oxidative stress and inhibiting extracellular matrix catabolic pathways [4, 23]. A similar trend was observed for collagen type I, where a significant direct relationship with treatment type was identified. The negative beta value indicates that retinol exerts a more potent anabolic effect on collagen synthesis than EGCG. Biologically, this is consistent with the mechanism of action of retinoids, which directly activate the TGF-β/SMAD pathway and stimulate collagen synthesis by dermal fibroblasts, while EGCG predominantly maintains matrix homeostasis through antioxidant effects and the inhibition of collagen degradation [3, 4, 23]. In contrast, EGCG demonstrated a significantly greater reduction in MMP-1 expression than retinol in the conventional comparative analysis. This finding suggests that, although retinol exerts a stronger direct anabolic effect on collagen synthesis, EGCG may preferentially preserve the extracellular matrix by suppressing collagen degradation through inhibition of oxidative stress- and AP-1-mediated MMP-1 expression. Taken together, these results indicate that the two treatments improve dermal remodeling through distinct but complementary molecular mechanisms, with retinol predominantly enhancing anabolic signaling and EGCG primarily attenuating collagen degradation [3, 17].

Study Limitations

This study has several limitations. First, a placebo or vehicle-control group was not included because the primary objective was to directly compare the biological effects of two established active interventions, 5% EGCG and 0.1% retinol. Consequently, the independent contribution of the cream vehicle or spontaneous temporal changes could not be completely excluded. Second, the sample size was relatively small, which may have limited the statistical power to detect subtle differences between treatments. Finally, this study focused on molecular markers of dermal remodeling after 12 weeks of treatment and did not evaluate long-term clinical outcomes or the durability of treatment effects. Future randomized controlled trials with larger sample sizes, a vehicle-control group, and longer follow-up are needed to further validate these findings.

CONCLUSIONS

Topical administration of 0.1% retinol and 5% EGCG both improved molecular markers of dermal remodeling in photoaged skin by significantly increasing TGF-β2 and type I collagen expression. However, a significant reduction in MMP-1 expression was observed only in the EGCG group, indicating a superior inhibitory effect on collagen degradation. Path analysis further demonstrated distinct molecular actions of the two treatments, with retinol showing a stronger association with anabolic pathways related to TGF-β2 activation and collagen synthesis, whereas EGCG predominantly suppressed extracellular matrix degradation through MMP-1 inhibition. These findings suggest that EGCG represents a promising natural alternative to retinol for photoaging management and provide mechanistic insights into the distinct biological pathways through which both agents promote dermal remodeling.

Author contributions: RNO: conceptualization, formal analysis, investigation, methodology, writing – original draft; **CRSP:** conceptualization, supervision, validation, writing – review & editing; **EH:** data curation, methodology, resources, writing – review & editing; **AE:** software, validation, formal analysis, writing – review & editing; **IKS:** formal analysis, **WEP:** formal analysis, investigation, writing – original draft. All authors have agreed with the results and conclusions.

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