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Enhancement of retinol bioactivity and extracellular matrix components through *Ex Vivo* assessments validates the important role of sunscreen and adjunctive moisturization with retinol use

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Introduction & Objectives

Retinoids are widely used to treat acne, psoriasis, and symptoms of photoaging.

Retinol is the gold-standard cosmetic antiaging treatment, clinically proven to improve numerous visible signs of photoaging with continuous benefit over time.

Despite their many beneficial effects, topical retinoids may cause both skin sensitivity under UV exposure and local irritation manifesting as redness, scaling, and dryness.

Therefore, it is often recommended for patients to use retinoid-containing treatments in combination with adjunctive sunscreens and moisturizers to enhance photoprotection and reduce potential irritation effects, respectively.

However, the biological effects of these regimens have not previously been evaluated.

Materials & Methods

In this study, human skin explants were treated for 48 hours with (1) the retinoid formula alone, (2) a 2-step regimen of retinoid + moisturizer or moisturizer + retinoid (open sandwich), or (3) a 3-step regimen of moisturizer + retinoid + moisturizer (full sandwich), where the retinoid was either retinol or tretinoin and the moisturizer was either a water gel or water cream.

Retinol bioactivity was examined via HBEGF and HAS-3 gene expression.

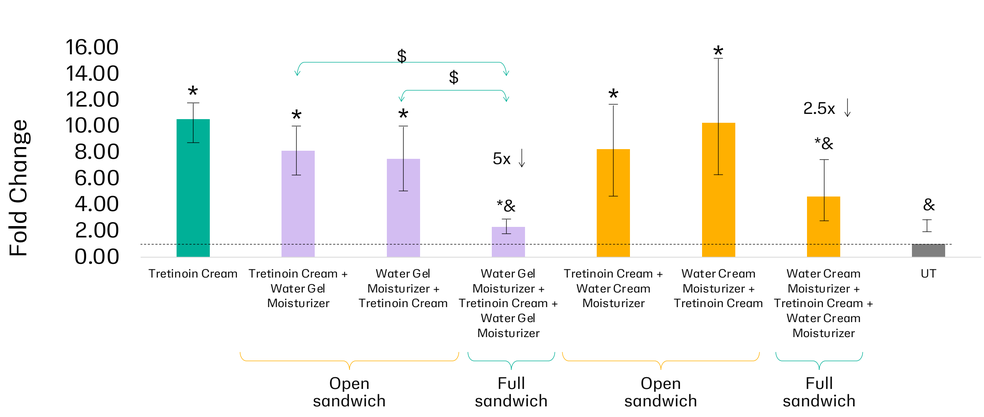
Additional skin explants were also pre-treated daily for 7 days with a stabilized retinol formulation (PM) or a PM/AM regimen with a retinol formulation (PM) followed by SPF60+ sunscreen (AM) before daily UV exposure.

Explants were assessed for 6 extracellular matrix (ECM) components – collagen types 1, 3, 4, elastin, HA, and matrixmetalloproteinase-1 (MMP-1) by immunohistochemistry (IHC).

Results

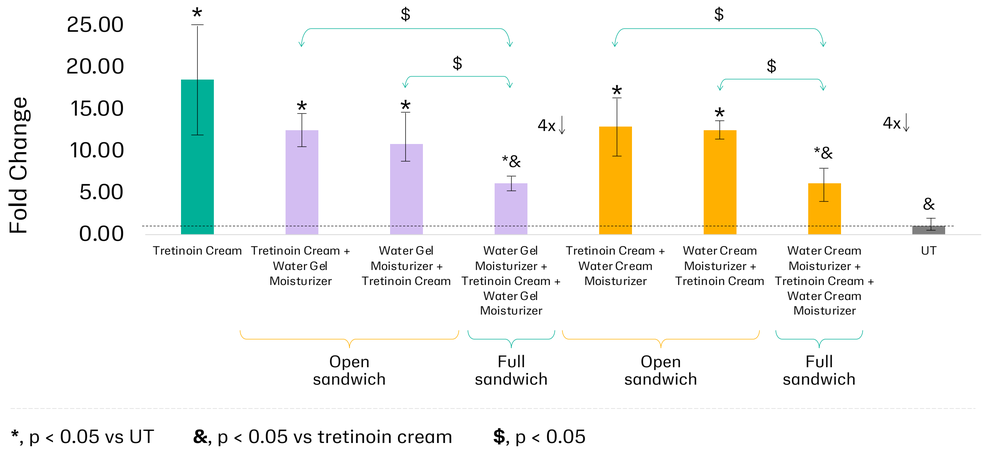
Explants treated with the “open sandwich” regimen in either order of application maintained comparable bioactivity to the retinol treatment alone (data not shown), or to the retinoid treatment alone, demonstrating compatibility of the moisturizer regimen, as shown in figures 1 and 2.

Figure 1. **Explants treated with the "full sandwich" regimen demonstrated ~ 3x reduced HbEGF expression (p<0.05), indicating lower penetration.**



*, p < 0.05 vs UT **&**, p < 0.05 vs tretinoin cream **$**, p < 0.05

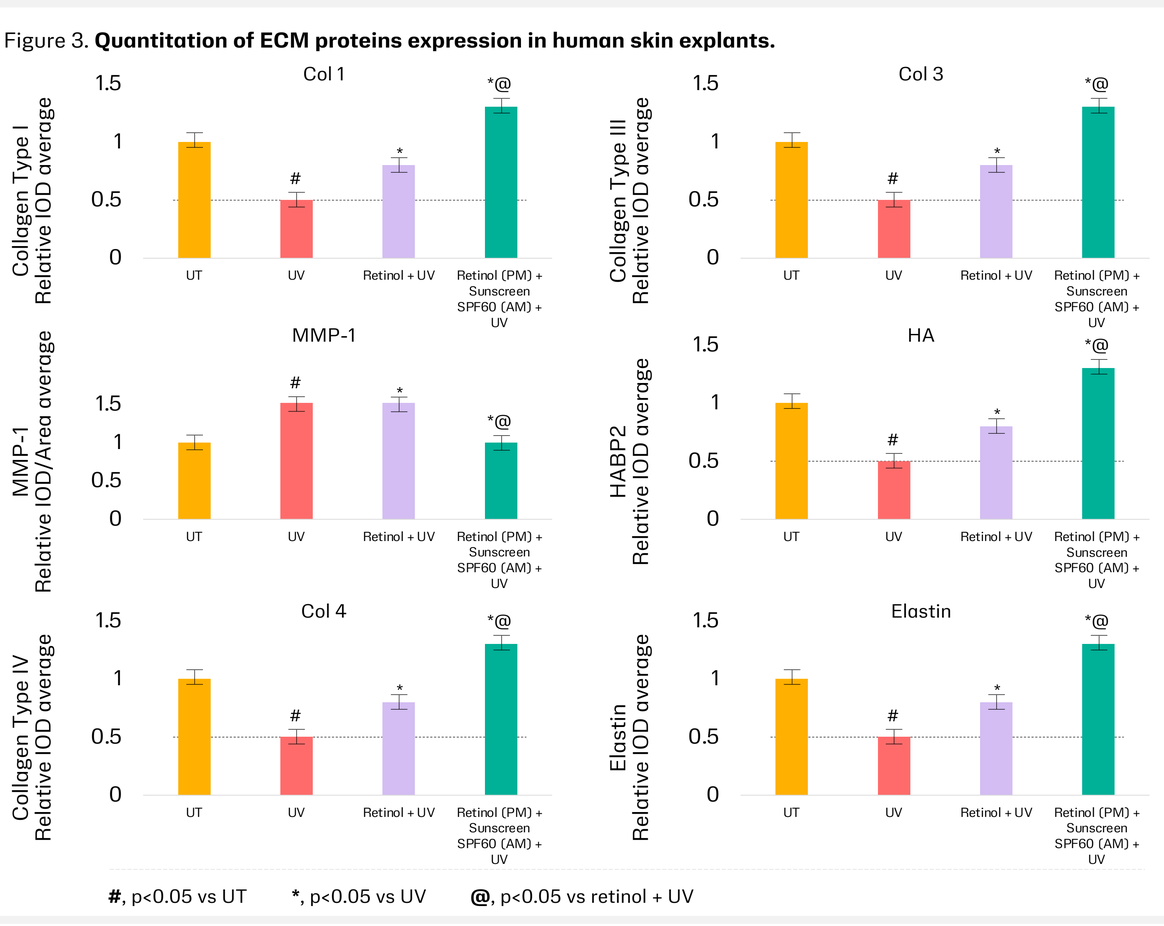
Figure 2. **Explants treated with the "full sandwich" regimen demonstrated ~ 4x reduced HAS3 expression (p<0.05), indicating lower penetration**



*, p < 0.05 vs UT **&**, p < 0.05 vs tretinoin cream **$**, p < 0.05

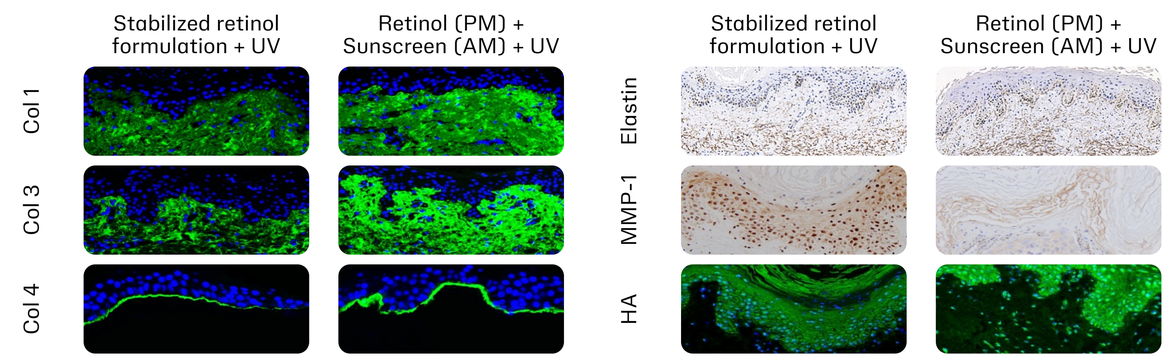
Moreover, the stabilized retinol (PM) and sunscreen SPF 60+ (AM) regimen showed enhanced photoprotection for all 6 ECM components and was significantly superior to the protection provided by retinol treatment alone, as shown in figures 3 and 4.

Figure 3. **Quantitation of ECM proteins expression in human skin explants.**



#, p<0.05 vs UT *****, p<0.05 vs UV **@**, p<0.05 vs retinol + UV

Figure 4. **Representative pictures of ECM proteins examined by IHC. Green or dark brown colors, ECM proteins. Blue color, the nuclei.**



Conclusion

These *Ex Vivo* data of retinoid + moisturizer may suggest the “full sandwich” method could be useful to reduce potency and enhance retinol tolerability during the start-up acclimation phase.

The “open sandwich” regimen can be useful for both the retinoid and the regular retinol users to provide barrier benefits and moisturization without impacting retinol bioactivity.

The data of retinol + sunscreen provides further evidence for the additive effects of a regimen including sunscreen and retinol to maintain ECM levels in skin and offset UV-induced decline.

This study provides more evidence to support the regimen recommendations to use sunscreens and adjunctive moisturizers to enhance skin anti-aging benefits while reducing irritation potential of topical retinoid use.

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