Scientific Research Publishing

Journal of Cosmetics, Dermatological Sciences and Applications, 2026, 16(3), 222-233
https://www.scirp.org/journal/jcdsa
ISSN Online: 2161-4512
ISSN Print: 2161-4105

First Assessment of *Hippophae rhamnoides* Seed Extract's Retinoid-Like Activity and Evidence for Additive/Synergistic Epidermal Reinforcement with *Harungana madagascariensis*

Sylvie Boisnic[1], Marie-Christine Branchet[1], Laxmee Caleechurn[2], Nathaniel Stroumza[1], Laura Barnaud[2], Richard Fitoussi[2]

[1]GREDECO, Paris, France
[2]Laboratoires Clarins, Pontoise, France
Email: richard.fitoussi@clarins.com

How to cite this paper: Boisnic, S., Branchet, M.-C., Caleechurn, L., Stroumza, N., Barnaud, L. and Fitoussi, R. (2026) First Assessment of *Hippophae rhamnoides* Seed Extract's Retinoid-Like Activity and Evidence for Additive/Synergistic Epidermal Reinforcement with *Harungana madagascariensis*. *Journal of Cosmetics, Dermatological Sciences and Applications*, **16**, 222-233.
https://doi.org/10.4236/jcdsa.2026.163015

Received: July 7, 2026
Accepted: September 19, 2026
Published: September 22, 2026

Abstract

Background: Skin ageing manifests as epidermal thinning, impaired barrier function, and dermal matrix degradation. Retinol and its derivatives effectively counteract these changes but can elicit irritation. Among plant-derived alternatives, a *Harungana madagascariensis* extract (HME) shows retinol-like effects. However, a comprehensive anti-ageing strategy must also reinforce the epidermis. During screenings for natural compounds, we identified a sea buckthorn (*Hippophae rhamnoides* L.) seed extract (BSE). Herein, we characterise HME and BSE effects on skin explants, benchmarking them against retinol. **Materials and Methods:** Skin explants from six female donors (26 - 47 years) were UV-irradiated and topically treated with creams containing 0.1% HME, 0.1%/0.5% BSE, HME-BSE combinations, or retinol benchmark. Treatments spanned 10 days with applications on days 2, 3, 5, 7, and 9. CRABP-II, Ki67 (day 3), COL-I, STRA6, and TJP1 (day 10) were assessed by immunofluorescence. **Results:** HME enhanced dermal COL-I/CRABP-II and epidermal CRABP-II/Ki67. BSE upregulated dermal CRABP-II (+43%), COL-I (+28% - 56%), epidermal CRABP-II (+52% - 58%), and Ki67 (+59% - 84%), mimicking retinol/HME. HME-BSE combinations showed CRABP-II antagonism yet superior epidermal responses for STRA6 (+39% - 49% *vs.* no individual effect) and TJP1 (+91% - 140% *vs.* +72% HME; +27% BSE 0.1%), suggesting additive/synergistic effects. **Conclusion:** BSE demonstrates retinol-like anti-ageing potential. HME-BSE synergy, possibly via CRABP-II-independent mecha-

nisms, should reinforce epidermal proliferation (STRA6) and the barrier function (TJP1), complementing the extracts' dermal effects. These findings position HME, BSE, and their combination as promising natural anti-ageing actives warranting clinical validation.

Keywords

Harungana madagascariensis, *Hippophae rhamnoides*, Retinol, Ageing, Skin Explant

1. Introduction

With age, the skin undergoes progressive structural and functional decline [1]-[3]. The epidermis thins due to diminished keratinocyte proliferation, yielding slower stratum corneum renewal. Diminished lipid biosynthesis impairs the permeability barrier. Senescent dermal fibroblasts display reduced proliferation as well as lower synthesis of collagens and elastin, coupled with upregulated matrix metalloproteinase activity, which all precipitates extracellular matrix catabolism. Lower levels of hyaluronic acid and proteoglycans impair hydration, while reduced vascularisation limits nutrient delivery. Flattening of the dermal-epidermal junction further impairs nutrient and cellular exchange. Collectively, these changes result in visible ageing signs, including wrinkles, sagging, loss of elasticity, dryness, and uneven skin tone.

In an ever-ageing global population, visible hallmarks of cutaneous senescence constitute a mounting aesthetic and psychosocial burden [4]. The anti-ageing cosmetics sector is accordingly witnessing exponential growth [5]. Given the pivotal role of oxidative stress in senescence, antioxidants constitute core actives in many formulations [6] [7]. Beyond this classical approach, retinol—the alcohol derivative of vitamin A—has been regarded as the reference compound for topical rejuvenation [8]. Being liposoluble, retinol penetrates the stratum corneum to reach the viable epidermis, albeit with limited efficiency. By stimulating keratinocyte proliferation, differentiation, and keratinisation, it enhances epidermal thickness, strengthens the stratum corneum, and improves barrier function [9] [10]. Within the dermis, retinol promotes extracellular matrix synthesis, particularly collagen production, thereby increasing elasticity and reducing fine wrinkles [9] [10]. Collectively, these actions account for its ability to reverse visible ageing signs [9] [11].

Although a natural compound, the widespread use of retinol has revealed that its topical application can elicit erythema, xerosis, scaling, and desquamation [12] [13]. Similar adverse reactions occur with synthetic retinoids, underscoring their limited tolerability. These drawbacks have prompted the search for better-tolerated alternatives. Bakuchiol—a meroterpene phenol derived from *Psoralea corylifolia*—has emerged as a prominent plant-based retinol analogue, mimicking retinoid-like gene expression and clinical outcomes in photodamaged skin [14] [15]. However, bakuchiol is not entirely devoid of adverse effects [16] [17]. In this con-

text, a *Harungana madagascariensis* extract (HME) has garnered interest.

In human fibroblasts, HME induces a broad transcriptional response that largely overlaps with that induced by retinol and includes upregulation of retinol receptors [18]. When formulated in a cream and topically applied to skin explants artificially aged by UV irradiation, it leads to higher levels of total collagen and type I collagen, an effect not observed with a retinol-containing cream. These findings were confirmed by the clinical evaluation of an HME-containing cream, which demonstrated improvements in multiple ageing parameters, including wrinkle depth, firmness, elasticity, and skin tone homogeneity, largely mimicking results obtained with retinol [19]. Therefore, HME appears a promising functional analogue of retinol, with potent beneficial effects on the dermis and an excellent tolerability profile, as no adverse events have been reported to date.

Reinforcing the dermis is crucial given the central role of the extracellular matrix degradation in the onset and severity of ageing signs. Indeed, it is its progressive breakdown diminishes skin strength and elasticity, ultimately resulting in the formation of static wrinkles and dynamic folds [20]. Nevertheless, a comprehensive anti-ageing approach should also strengthen the skin barrier function. During screenings for natural compounds reinforcing the epidermis, we identified a sea buckthorn (*Hippophae rhamnoides* L.) seed extract (BSE). We herein characterise the immunohistochemical effects of HME and BSE on artificially aged skin explants, alongside assessment of their synergistic action when combined.

2. Materials and Methods

2.1. Skin Explants

Skin explants were obtained from Caucasian women undergoing abdominoplasty or mammoplasty for cosmetic reasons. Procurement complied with Articles L.1245-2 and L.1211-1 of the French Code de la Santé publique, with written informed consent obtained from all donors prior to surgery.

All experiments were conducted on skin explants from six donors aged 26, 30, 42, 45, 45, and 47 years. After excision of the hypodermis, 1 cm^2 fragments were prepared from each explant. They were maintained at the air-medium interface of modified Minimum Essential Medium (Gibco, USA) supplemented with bovine pituitary extract (Gibco, USA), foetal calf serum (Biowest, France), penicillin, and streptomycin. Skin fragments were incubated at 37˚C under 5% CO_2, and 95% relative humidity.

2.2. Skin Explant Treatments

On days 0 and 1, skin fragments were irradiated with UVA (8 J/cm^2) and UVB (1 J/cm^2) to induce and homogenise their ageing. This standardized UVA/UVB irradiation protocol was used to impose a common, controlled photoageing-like state across all explants, thereby limiting donor- and age-related variability in baseline skin ageing status and improving the sensitivity of subsequent treatment

comparisons. Post-irradiation, and on days 2, 3, 5, 7, and 9, 2 mg of cream was applied topically to each fragment.

Creams were formulated in a neutral oil-in-water emulsion base deprived of ingredients known to influence the skin. Test formulations contained 0.1% (w/w) HME (CAS No. 90045-51-5), 0.1% (w/w) BSE (CAS No. 90106-68-6), or 0.5% (w/w) BSE. Combinations of HME with each BSE concentration were also evaluated. These were benchmarked against a well-established, commercially available retinol-containing cream, widely recognised as a benchmark for topical retinol efficacy. The exact retinol concentration of this cream and the possible adjuvants are not disclosed by the manufacturer, as is common for proprietary retinol formulations given retinol's known solubility, stability, and bioavailability challenges. Nevertheless, such creams typically have a retinol concentration of 0.1 to 0.01% w/w and, since June 2024, European cosmetic regulation limits retinol concentration to 0.3% (w/w) in leave-on facial products, which constrains the plausible upper bound for this comparator.

Skin fragments were harvested on days 3 and 10 for immunohistochemical studies. The day-3 timepoint was chosen to capture CRABP-II, an early retinoid-responsive marker, whereas the day-10 timepoint was chosen for COL-I, STRA6, and TJP1, which reflect slower structural and synthetic processes requiring a longer exposure to manifest measurable change. Non-irradiated and irradiated skin fragments that received no cream were used as controls.

2.3. Immunohistochemical Analysis

Day-3 fragments were formalin-fixed and paraffin-embedded for CRABP-II (cellular retinoic acid-binding protein 2) and Ki67 (marker of cellular proliferation Kiel 67) immunohistochemistry. Day-10 fragments were embedded in OCT, snap-frozen, and analysed by immunofluorescence for STRA6 (signalling receptor and transporter of retinol 6), TJP1 (tight junction protein 1), and COL-I (type I collagen).

CRABP-II was detected using a rabbit polyclonal antibody (#15998, Novus Biologicals, CO, USA) and the ImmPRESS® secondary antibody kit (#MP-7500, Vector Laboratories, CA, USA) revealed with 3-amino-9-ethylcarbazole (#ZUC042-500, Zytomed). Type I collagen was labelled with a mouse monoclonal antibody (#C2456, Sigma-Aldrich, MA, USA), subsequently detected with an Alexa Fluor™ 488-conjugated goat anti-mouse secondary antibody (#A11001 Southern Biotech, AL, USA). STRA6 employed a rabbit polyclonal antibody (#HPA040839, Sigma-Aldrich, MA, USA) revealed with goat anti-rabbit polyclonal antibody conjugated to Alexa Fluor™ 546 (#A-11010, Invitrogen, MA, USA). TJP1 was detected using a rabbit polyclonal antibody (#HPA001636, Sigma-Aldrich, MA, USA) and an Alexa Fluor™ 488-conjugated goat anti-rabbit secondary antibody (#A-11008, Invitrogen, MA, USA). Ki67 used a mouse monoclonal antibody (#M7240, DKO, France) that was revealed with the ImmPRESS® secondary antibody kit (#MP-7500, Vector Laboratories, CA, USA) and 3-amino-9-ethylcarbazole (#ZUC042-

500, Zytomed).

Imaging used a microscope Olympus (CX40RF200, Evident Scientific) that allows images to be captured with a camera Olympus DP28. CRABP-II labelled fibroblasts were counted in 10 fields. The number of epidermal CRABP-II positive cells was expressed as the percentage of basal cells (15-20 fields). COL-I associated fluorescence was analysed by calculating the percentage of immunofluorescent surface in the papillary and superficial dermis (10 fields). The intensity of the STRA6-associated fluorescence was quantified in the basal layer of the epidermis (15 fields). Ki67-positive basal cells were expressed as the percentage of basal cells (10 fields). The intensity of the TJP1-associated fluorescence was assessed in the stratum spinosum and stratum granulosum (10 fields). Image analyses were performed using cellSENS (Evident, United Kingdom) or IPSDK Explorer (Reactiv'IP, France).

All treated samples were assigned a code, withheld from investigators conducting staining and image analysis, with the exception of the UV-non-irradiated and UV-irradiated untreated controls, which served as the references for evaluating treatment-related changes.

2.4. Statistical Analysis

For each donor, one explant fragment was allocated to each experimental condition. For each marker and each explant, the multiple fields assessed were averaged to obtain a single explant-level value. To avoid pseudoreplication, statistical analyses were performed on these explant-level means (n = 6 donors per condition).

Results are expressed as means ± standard deviation. Normality was assessed via Shapiro-Wilk tests ($\alpha < 0.05$). Parametric data were compared using paired, two-sided Student's t-tests. The Wilcoxon's signed-rank test was otherwise used. Significance was set at $p < 0.05$.

3. Results

3.1. Effects on Dermal Markers

The effects of BSE, HME, and their combination on dermal markers were first evaluated, focusing on CRABP-II at day 3 and COL-I at day 10 (**Figure 1**).

UV exposure had no effect on dermal CRABP-II levels ($p = 0.180$). Compared with UV-exposed explants, topical application of creams containing BSE or HME significantly increased CRABP-II levels, from +18% ($p = 0.020$) with 0.1% HME to +43% with 0.1% BSE ($p = 0.046$). The combination of extracts increased CRABP-II only at the higher BSE concentration (+31%, $p = 0.048$). The retinol-containing cream had no significant effect ($p = 0.438$).

At day 10, UV irradiation reduced COL-I levels by 35% ($p = 0.004$). Compared with UV-exposed explants, creams containing BSE increased COL-I by +28% at 0.1% ($p = 0.030$) and +56% at 0.5% ($p < 0.001$). The HME cream increased COL-I by 53% ($p = 0.017$). Combinations of extracts yielded comparable increases of 37% regardless of BSE concentration ($p = 0.007$ for 0.1% BSE and $p = 0.013$ for 0.5% BSE). The retinol cream increased COL-I by 51% ($p = 0.002$).

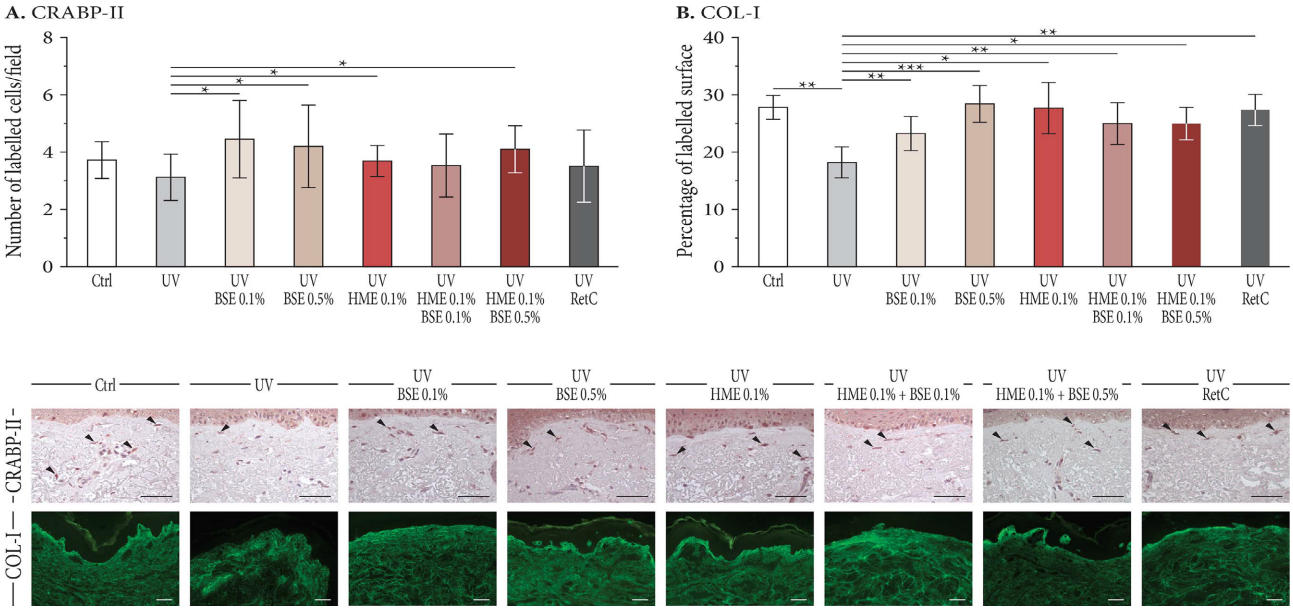

Figure 1. Immunohistochemical quantification of dermal markers. (A) CRABP-II (day 3). (B) COL-I (day 10). Statistical significance versus UV-irradiated explants: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. For the Immunohistochemical images scale bar represents 50 µm and arrowheads indicate labelling.

3.2. Effects on Retinol-Related Epidermal Markers

Retinol-related epidermal markers—CRABP-II, the cytoplasmic retinol receptor, (day 3) and STRA6, plasma membrane receptor and retinol transporter, (day 10)—were subsequently assessed (**Figure 2**).

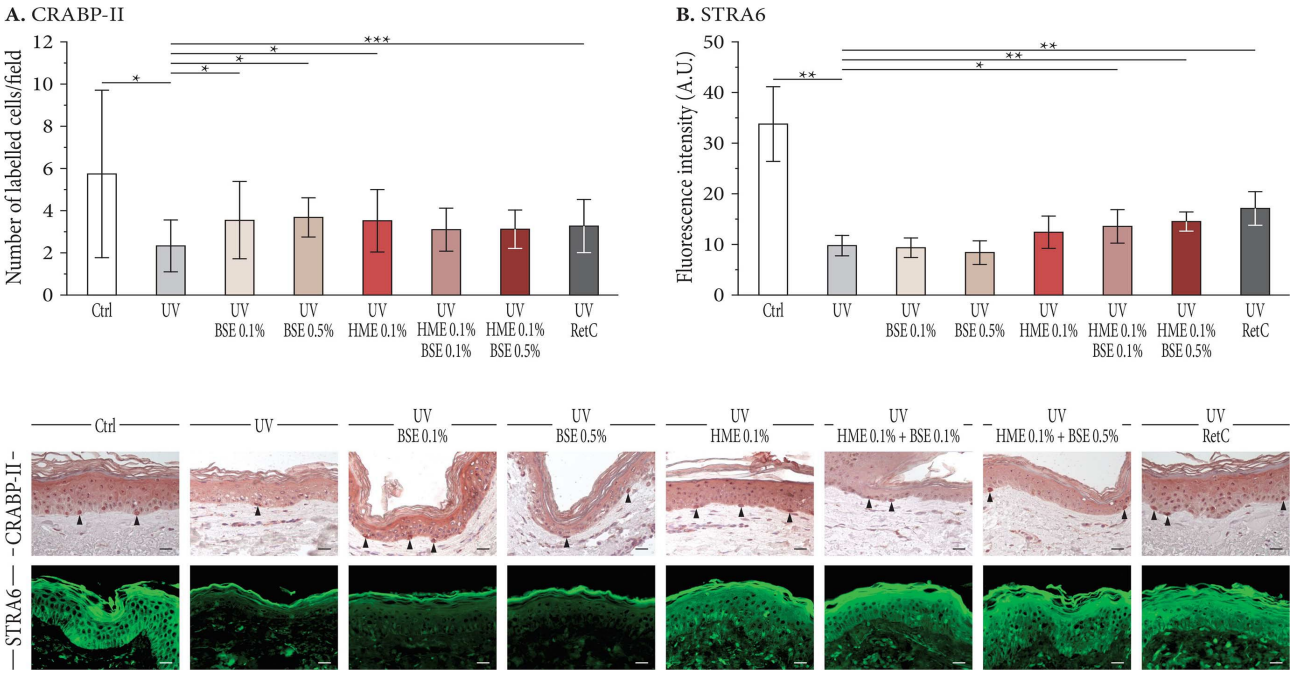

Figure 2. Immunohistochemical quantification of retinol-related epidermal markers. (A) CRABP-II (day 3). (B) STRA6 (day 10). Statistical significance versus UV-irradiated explants: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. For the Immunohistochemical images scale bar represents 20µm and arrowheads indicate labelling.

UV irradiation decreased epidermal CRABP-II by 49% ($p = 0.037$). Treatment with BSE- or HME-containing creams partially maintained CRABP-II levels (0.1% BSE: +52%, $p = 0.029$; 0.5% BSE: +58%, $p = 0.048$; 0.1% HME: +51%, $p = 0.025$), comparably to retinol (+40%, $p < 0.001$). Combinations of extracts had no significant effect ($p = 0.156$ with 0.1% BSE; $p = 0.223$ with 0.5% BSE).

UV irradiation reduced STRA6 expression by 71% ($p = 0.009$). Neither BSE nor HME alone prevented this reduction ($p = 0.509$ for 0.1% BSE; $p = 0.190$ for 0.5% BSE, and $p = 0.148$ for HME), but their combination enabled preserving higher STRA6 levels (+39%, $p = 0.042$ with 0.1% BSE; +49%, $p = 0.010$ with 0.5% BSE). Similarly, retinol preserved STRA6 at +75% ($p = 0.002$).

3.3. Effects on Epidermal Retinol Downstream Markers

Downstream markers of retinol activity were evaluated (Figure 3): epidermal proliferation (Ki67, day 3) and barrier integrity (TJP1, day 10).

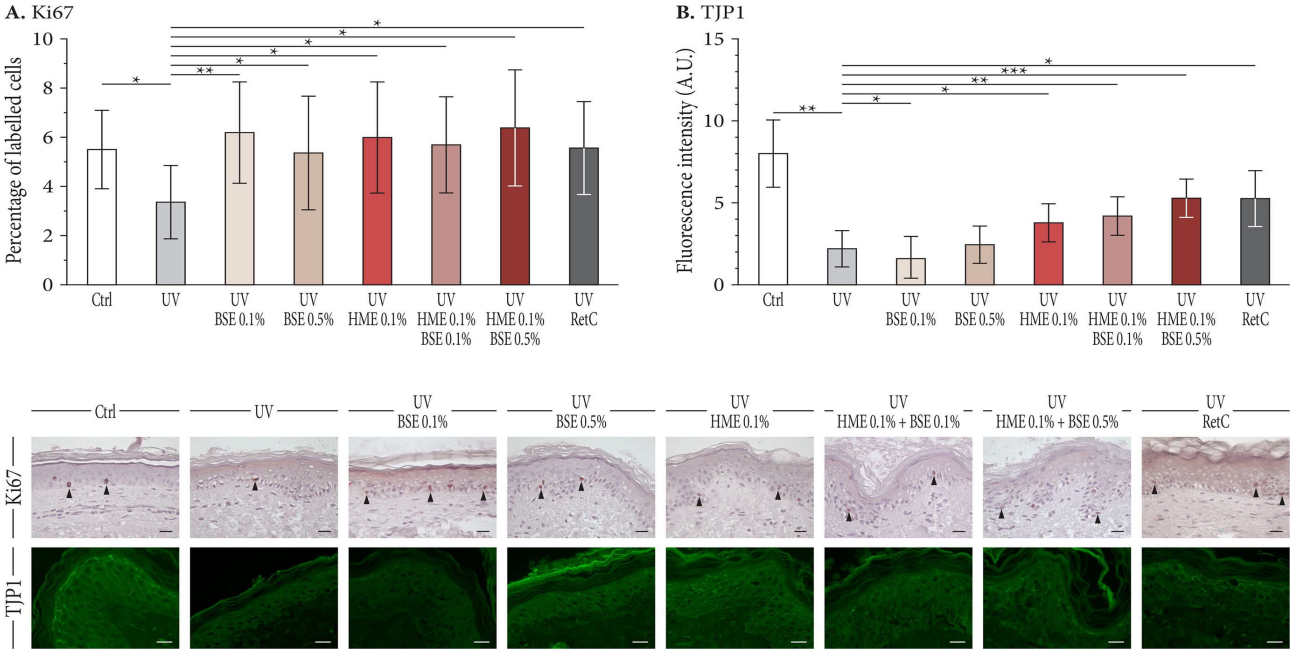

Figure 3. Immunohistochemical quantification of epidermal retinol downstream markers. (A) Ki67 (day 3). (B) TJP1 (day 10). Statistical significance versus UV-irradiated explants: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. For the Immunohistochemical images scale bar represents 20µm and arrowheads indicate labelling.

UV irradiation decreased Ki67 expression by 39% ($p = 0.012$). All creams significantly increased Ki67: 0.1% BSE (+84%, $p = 0.006$), 0.5% BSE (+59%, $p = 0.048$), 0.1% HME (+78%, $p = 0.034$), HME + 0.1% BSE (+69%, $p = 0.031$), HME + 0.5% BSE (+90%, $p = 0.015$). Retinol also increased Ki67 by 65% ($p = 0.031$).

UV irradiation reduced TJP1 expression by 73% ($p = 0.003$). Only 0.5% BSE had no effect ($p = 0.434$). Other creams increased TJP1: 0.1% BSE (+27%, $p = 0.012$), 0.1% HME (+72%, $p = 0.031$), HME + 0.1% BSE (+91%, $p = 0.002$), HME + 0.5% BSE (+140%, $p < 0.001$). Retinol achieved +139% ($p = 0.013$).

4. Discussion

Results demonstrate that HME increased dermal COL-I and CRABP-II marker levels, also enhancing epidermal CRABP-II and Ki67 levels. BSE, the effects of which are characterised here for the first time, upregulated dermal CRABP-II (+43%) and COL-I (+28% - 56%), whilst independently enhancing epidermal CRABP-II (+52% - 58%) and Ki67 proliferation (+59% - 84%). Most strikingly, the HME-BSE combinations elicited superior quantitative responses *versus* individual extracts for both STRA6 (+39% - 49% *vs.* no effect for HME/BSE) and TJP1 (+91% - 140% *vs.* +72% HME; +27% BSE 0.1%).

The effects of HME were anticipated as it was previously reported to induce a retinol-like transcriptomic profile in fibroblasts and to increase the retinol receptor CRABP-II and COL-I proteins in fibroblasts and UV-aged skin explants, also leading to higher Ki67 levels in UV-aged skin explants [18]. Our findings further support that HME recapitulates retinol's established effects: increasing dermal COL-I and CRABP-II [20] and enhancing epidermal CRABP-II and Ki67 levels [20] [21].

BSE induced effects very similar to those of HME. Both positively impact CRABP-II levels in the epidermis and the dermis, also inducing an increase in dermal COL-I, showing a strong dermal impact, while also increasing epidermal Ki67. These effects are also similar to those observed with the retinol cream, although no dermal CRABP-II increase was evidenced under our conditions. It is thus tempting to propose that BSE represents another plant extract with retinol-like properties and that both HME and BSE independently stimulate retinol effectors. Nevertheless, while BSE and HME were formulated in the same vehicle and are directly comparable, the retinol cream has a different vehicle of undisclosed composition and probably contains other active ingredients besides retinol. Comparisons should thus be made cautiously, although the results obtained align with the known impact of retinol [20] [21]. Besides, only a few proteins were evaluated, and drawing firm conclusions about BSE's retinol-like properties will require more thorough studies.

Nevertheless, the suggestion that both extracts possess retinol-like properties is further supported by their combined effects on CRABP-II. This combination did not increase epidermal CRABP-II levels, whereas each extract alone did. In the dermis, only the combination with the highest BSE concentration had an effect, whereas HME and all concentrations of BSE alone were effective. Besides suggesting potent effects of BSE on the dermis, these results suggest some interference between the extracts when combined. Whether a competitive interaction is involved remains to be elucidated, but these findings suggest that both extracts might interfere with the same CRABP-II target.

Interestingly, results also highlighted a response for STRA6 only when both extracts were combined. Besides, the expression level of TJP1 with the combination of extracts is superior to that achieved with each extract alone. These results suggest additive, and possibly synergistic, epidermal effects. Although multi-donor

consistency lends plausibility to such an additive/synergistic effect, differences across conditions were limited, restricting analyses to pairwise comparisons against UV-irradiated untreated controls and preventing multiple comparative analyses that would have strengthened this conclusion.

The additive/synergistic effect suggests that the extract combination coordinately contributes to epidermal reinforcement via a dual mechanism. On one hand, STRA6 is a membrane transporter and a cell-surface receptor that selectively binds *all-trans*-retinoic acid, constituting a central regulator of intracytoplasmic retinoid levels. When present in larger amounts, it enables higher intracellular retinoid concentrations, ultimately resulting in keratinocyte proliferation and differentiation [22] [23]. STRA6 upregulation should thus strengthen the epidermis by favouring its development. On the other hand, TJP1 is a scaffolding protein and component of the tight junction complex. This complex creates a dynamic mechanical barrier in the stratum granulosum, which—among other functions—regulates permeability to ions and solutes, also contributing to resistance against mechanical and chemical stressors [24] [25]. Increased TJP1 levels should, therefore, strengthen barrier function by stabilising tight junction complexes, reducing transepidermal water loss (TEWL), limiting solute permeability, and enhancing cellular cohesion. Both extracts also individually upregulated Ki67, a marker of basal epidermal cell proliferation [26]. Although not showing any additive/synergistic effect on this latter marker, the stimulation observed with each extract should further contribute to a strong reinforcement of the epidermis, supporting the notion that the epidermis is an important site of action of HME and BSE.

The additive/synergistic effect might appear to contradict the negative interaction we highlighted for HME-BSE combination on CRABP-II. Indeed, if such a competitive interaction exists between the extracts, one might expect reduced retinol-like properties when extracts are combined. This was not the case, as the extract combination induced changes within the range of those induced by each extract alone. Alternative explanations must therefore be sought, such as a CRABP-II-independent mode of action. This seems plausible, as *Harungana madagascariensis* and *Hippophae rhamnoides* seeds are both known to be rich in secondary metabolites, including flavonoids, proanthocyanidins, xanthones, and tocopherols [27] [28]. Such pleiotropic bioactivities might explain the preserved retinol-like efficacy despite CRABP-II antagonism, with synergy emerging via complementary modulation of STRA6/TJP1.

Taken together, this study suffers limitations that will require further work to confirm or refute our conclusions. Among these limitations are the modest effect sizes observed, highlighting the substantial inter-individual variability of skin explant responses to the various treatments, including responses to the retinol cream. This prevented detection of significant differences across treatments whilst the multi-donor design represents a methodological strength. Moreover, the analysis of only six markers limits the mechanistic breadth of the study and precludes

firm claims regarding BSE's retinol-like properties. Furthermore, the use of explants from only six Caucasian female donors aged 26 - 47 years limits the generalizability of the present findings to older individuals and to individuals with more diverse ethnic backgrounds. Although standardized UVA/UVB irradiation was used to induce a controlled photoageing-like state, this acute ex vivo UV challenge does not fully reproduce the complex intrinsic and cumulative extrinsic ageing processes occurring in older skin. Future work should encompass broader proteomic/transcriptomic profiling alongside clinical trials to validate *bona fide* retinol-like efficacy of BSE. Parallel efforts to identify BSE's active compounds would also be of interest to dissect synergy, warranting both *in vitro* mechanistic and *in vivo* translational studies.

5. Conclusion

This study provides the first evidence that *Hippophae rhamnoides* seed extract (BSE) upregulates key retinol-responsive markers (CRABP-II, COL-I, Ki67), mirroring *Harungana madagascariensis* extract (HME) effects and suggesting retinol-like anti-ageing potential. Considering the irritancy risks of retinol and its derivatives, there is a growing demand for gentler alternatives that also align with consumer preference for natural actives. Remarkably, HME-BSE synergy elevates epidermal STRA6/TJP1, complementing HME's dermal dominance with BSE's epidermal contributions to yield superior barrier/proliferative reinforcement, positioning the HME-BSE combination as a promising dual-compartment anti-ageing strategy.

Acknowledgements

The authors would like to thank Dr. Philippe Crouzet, Estium-Concept, for providing scientific writing services.

Author Contributions

SB, MCB and NS conceived and designed the study under supervision of RF. LB contributed to project administration. MCB and LC performed experiments, collected and analyzed the data, and conducted statistical analysis. SB, MCB and RF contributed to the interpretation of the results. SB, MCB and RF wrote the initial draft of the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bonté, F., Girard, D., Archambault, J.C. and Desmoulière, A. (2019) Skin Changes during Ageing. In: *Subcellular Biochemistry*, Springer, 249-280. https://doi.org/10.1007/978-981-13-3681-2_10

[2] Shin, S.H., Lee, Y.H., Rho, N.K. and Park, K.Y. (2023) Skin Aging from Mechanisms to Interventions: Focusing on Dermal Aging. *Frontiers in Physiology*, **14**, Article 1195272. https://doi.org/10.3389/fphys.2023.1195272

[3] Zhang, M., Lin, Y., Han, Z., Huang, X., Zhou, S., Wang, S., *et al.* (2024) Exploring Mechanisms of Skin Aging: Insights for Clinical Treatment. *Frontiers in Immunology*, **15**, Article 1421858. https://doi.org/10.3389/fimmu.2024.1421858

[4] Gupta, M.A. and Gilchrest, B.A. (2005) Psychosocial Aspects of Aging Skin. *Dermatologic Clinics*, **23**, 643-648. https://doi.org/10.1016/j.det.2005.05.012

[5] Grand View Research (2024) Anti-Aging Products Market (2026-2033). https://www.grandviewresearch.com/industry-analysis/anti-aging-products-market

[6] Rinnerthaler, M., Bischof, J., Streubel, M.K., Trost, A. and Richter, K. (2015) Oxidative Stress in Aging Human Skin. *Biomolecules*, **5**, 545-589. https://doi.org/10.3390/biom5020545

[7] Silva, S., Ferreira, M., Oliveira, A.S., Magalhães, C., Sousa, M.E., Pinto, M., *et al.* (2019) Evolution of the Use of Antioxidants in Anti-Ageing Cosmetics. *International Journal of Cosmetic Science*, **41**, 378-386. https://doi.org/10.1111/ics.12551

[8] Griffiths, T.W., Watson, R.E.B. and Langton, A.K. (2023) Skin Ageing and Topical Rejuvenation Strategies. *British Journal of Dermatology*, **189**, i17-i23. https://doi.org/10.1093/bjd/ljad282

[9] Zasada, M. and Budzisz, E. (2019) Retinoids: Active Molecules Influencing Skin Structure Formation in Cosmetic and Dermatological Treatments. *Advances in Dermatology and Allergology*, **36**, 392-397. https://doi.org/10.5114/ada.2019.87443

[10] Quan, T. (2023) Human Skin Aging and the Anti-Aging Properties of Retinol. *Biomolecules*, **13**, Article 1614. https://doi.org/10.3390/biom13111614

[11] Mukherjee, S., Date, A., Patravale, V., Korting, H.C., Roeder, A. and Weindl, G. (2006) Retinoids in the Treatment of Skin Aging: An Overview of Clinical Efficacy and Safety. *Clinical Interventions in Aging*, **1**, 327-348. https://doi.org/10.2147/ciia.2006.1.4.327

[12] David, M., Hodak, E. and Lowe, N.J. (1988) Adverse Effects of Retinoids. *Medical Toxicology*, **3**, 273-288. https://doi.org/10.1007/bf03259940

[13] Szymański, Ł., Skopek, R., Palusińska, M., Schenk, T., Stengel, S., Lewicki, S., *et al.* (2020) Retinoic Acid and Its Derivatives in Skin. *Cells*, **9**, Article 2660. https://doi.org/10.3390/cells9122660

[14] Chaudhuri, R.K. and Bojanowski, K. (2014) Bakuchiol: A Retinol-Like Functional Compound Revealed by Gene Expression Profiling and Clinically Proven to Have Anti-Aging Effects. *International Journal of Cosmetic Science*, **36**, 221-230. https://doi.org/10.1111/ics.12117

[15] Dhaliwal, S., Rybak, I., Ellis, S.R., Notay, M., Trivedi, M., Burney, W., *et al.* (2019) Prospective, Randomized, Double-Blind Assessment of Topical Bakuchiol and Retinol for Facial Photoageing. *British Journal of Dermatology*, **180**, 289-296. https://doi.org/10.1111/bjd.16918

[16] Malinauskiene, L., Linauskiene, K., Černiauskas, K. and Chomičiene, A. (2020) Bakuchiol—A New Allergen in Cosmetics. *Contact Dermatitis*, **80**, 398-399. https://doi.org/10.1111/cod.13211

[17] Raison-Peyron, N. and Dereure, O. (2019) A New Case of Contact Dermatitis to Bakuchiol in a Cosmetic Cream. *Contact Dermatitis*, **82**, 61-62. https://doi.org/10.1111/cod.13387

[18] Fitoussi, R., Branchet, M.C., Garnier, N., Beauchef, G., Nkengne, A., Vié, K., *et al.*

(2022) A *Harungana madagascariensis* Extract with Retinol-Like Properties: Gene Upregulations and Protein Expressions in Human Fibroblasts and Skin Explants. *International Journal of Cosmetic Science*, **44**, 201-215. https://doi.org/10.1111/ics.12768

[19] Gibielle, C., Bousseksou, L., Guéhenneux, S. and Vié, K. (2023) In a Preliminary Study on Human Subjects, a Cosmetic Cream Containing a *Harungana Madagascariensis* Plant Extract Induces Similar Anti-Aging Effects to a Retinol-Containing Cream. *Clinical, Cosmetic and Investigational Dermatology*, **16**, 1051-1058. https://doi.org/10.2147/ccid.s401290

[20] Bielli, A., Scioli, M.G., D'Amico, F., Tarquini, C., Agostinelli, S., Costanza, G., *et al.* (2019) Cellular Retinoic Acid Binding Protein-II Expression and Its Potential Role in Skin Aging. *Aging*, **11**, 1619-1632. https://doi.org/10.18632/aging.101813

[21] Saurat, J.H., Didierjean, L., Masgrau, E., Piletta, P.A., Jaconi, S., Chatellard-Gruaz, D., *et al.* (1994) Topical Retinaldehyde on Human Skin: Biologic Effects and Tolerance. *Journal of Investigative Dermatology*, **103**, 770-774. https://doi.org/10.1111/1523-1747.ep12412861

[22] Kawaguchi, R., Zhong, M., Kassai, M., Ter-Stepanian, M. and Sun, H. (2015) Vitamin A Transport Mechanism of the Multitransmembrane Cell-Surface Receptor STRA6. *Membranes*, **5**, 425-453. https://doi.org/10.3390/membranes5030425

[23] Dhokia, V. and Macip, S. (2021) A Master of All Trades—Linking Retinoids to Different Signalling Pathways through the Multi-Purpose Receptor STRA6. *Cell Death Discovery*, **7**, Article No. 358. https://doi.org/10.1038/s41420-021-00754-z

[24] Kirschner, N. and Brandner, J.M. (2012) Barriers and More: Functions of Tight Junction Proteins in the Skin. *Annals of the New York Academy of Sciences*, **1257**, 158-166. https://doi.org/10.1111/j.1749-6632.2012.06554.x

[25] Nguyen, T.P., Otani, T., Tsutsumi, M., Kinoshita, N., Fujiwara, S., Nemoto, T., *et al.* (2024) Tight Junction Membrane Proteins Regulate the Mechanical Resistance of the Apical Junctional Complex. *Journal of Cell Biology*, **223**, e202307104. https://doi.org/10.1083/jcb.202307104

[26] Ando, M., Kawashima, T., Kobayashi, H. and Ohkawara, A. (1990) Immunohistological Detection of Proliferating Cells in Normal and Psoriatic Epidermis Using KI-67 Monoclonal Antibody. *Journal of Dermatological Science*, **1**, 441-446. https://doi.org/10.1016/0923-1811(90)90014-5

[27] Happi, G.M., Tiani, G.L.M., Gbetnkom, B.Y.M., Hussain, H., Green, I.R., Ngadjui, B.T., *et al.* (2020) Phytochemistry and Pharmacology of *Harungana Madagascariensis*: Mini Review. *Phytochemistry Letters*, **35**, 103-112. https://doi.org/10.1016/j.phytol.2019.11.015

[28] Dong, W., Tang, Y., Qiao, J., Dong, Z. and Cheng, J. (2025) Sea Buckthorn Bioactive Metabolites and Their Pharmacological Potential in Digestive Diseases. *Frontiers in Pharmacology*, **16**, Article 1637676. https://doi.org/10.3389/fphar.2025.1637676