IFSCC2025-503

"A New patented ingredient technology targeting molecular causes and visible signs of skin aging to promote the skin longevity"

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1. Introduction

The skin, our largest organ, is constantly exposed to environmental factors like sunlight and pollution, which accelerate aging by damaging cells and disrupting the skin's natural repair processes. Understanding the biological mechanisms behind skin aging is crucial to protecting and maintaining youthful skin [1, 2].

Skin aging is driven by both intrinsic (chronological) and extrinsic (environmental) factors. Intrinsic aging is genetically programmed and characterized by cellular senescence and increasing oxidative stress over time [3]. Extrinsic factors, such as UV radiation and pollution, exacerbate aging by causing additional cellular damage, including oxidative stress and inflammation, which accelerate molecular degradation in the skin. Intrinsic aging leads to thinning, dryness, wrinkles, and sagging, while extrinsic aging causes more pronounced wrinkles, loss of elasticity, and pigmentation disorders [4].

At the molecular level, oxidative stress, DNA damage, and inflammation play central roles in both intrinsic and extrinsic aging. Free radicals, such as reactive oxygen species (ROS), damage cellular components, including DNA, proteins, and lipids. This oxidative stress activates signaling pathways that degrade the extracellular matrix (ECM), particularly collagen, elastin, and hyaluronic acid, leading to skin thinning and loss of elasticity. Both intrinsic and extrinsic factors share common molecular pathways, but extrinsic factors, especially UV exposure, accelerate these processes. Inflammation and the resulting accumulation of reactive oxygen species (ROS) play an important role in the intrinsic and photoaging of human skin in vivo [5, 6].

Upper-regulated ROS production triggers oxidative modifications and over-stimulates stress-sensitive signaling pathways which promote aging. ROS activate the MAPK/AP-1 pathway, which increases matrix metalloproteinases (MMPs) that break down collagen, while inhibiting collagen synthesis [7]. Inflammation further accelerates aging by upregulating pro-inflammatory cytokines that break down ECM proteins. The result is an imbalance between ECM synthesis and degradation, leading to wrinkles, sagging, and reduced skin hydration [8].

UV-A radiation and pollution are key extrinsic factors in premature aging. UV-A penetrates deeply into the skin, causing oxidative stress that leads to DNA damage and collagen breakdown. It also triggers melanogenesis, leading to age spots and uneven pigmentation. Pollution, particularly particulate matter (PM10), also induces oxidative stress and inflammation, leading to pigmentation changes and further ECM degradation. Both UV-A and pollutants activate similar pathways, exacerbating oxidative damage and inflammation in the skin [9].

The skin's immune function, particularly the production of antimicrobial peptides (AMPs) like β-defensins and calprotectin, declines with age. These peptides play a key role in defending against microbial threats and regulating inflammation. Environmental stressors, including UV and pollution, can impair AMP production, leaving the skin more vulnerable to infections and inflammation. Maintaining optimal AMP levels is crucial for skin resilience [10].

To counteract premature skin aging, it is important to protect the skin from environmental factors, such as UV radiation and pollution, while supporting intrinsic repair mechanisms. This can be achieved through antioxidant treatments, sunscreens, and skincare products that strengthen the skin's defenses. Given the complexity of skin aging, comprehensive interventions that address multiple molecular pathways are necessary. The 1-LGVTY technology is an innovative solution that targets key hallmarks of aging skin like oxidative stress, inflammation, ECM degradation, microbial dysfunction, and pigmentation changes through a combination of bioactive components to preserve skin health and youthfulness.

2. Materials and Methods

1-LGVTY Technology. Aqueous composition of 5 active ingredients (called 1-LGVTY) comprising baicalin (0.25% by mass), chlorogenic acid (1% by mass), sodium carboxymethyl beta-glucan (0.25% by mass) and a mixture of inulin and alpha glucan oligosaccharide (2.55% by mass) with a mass ratio of inulin:alpha glucan oligosaccharide of 8:2.

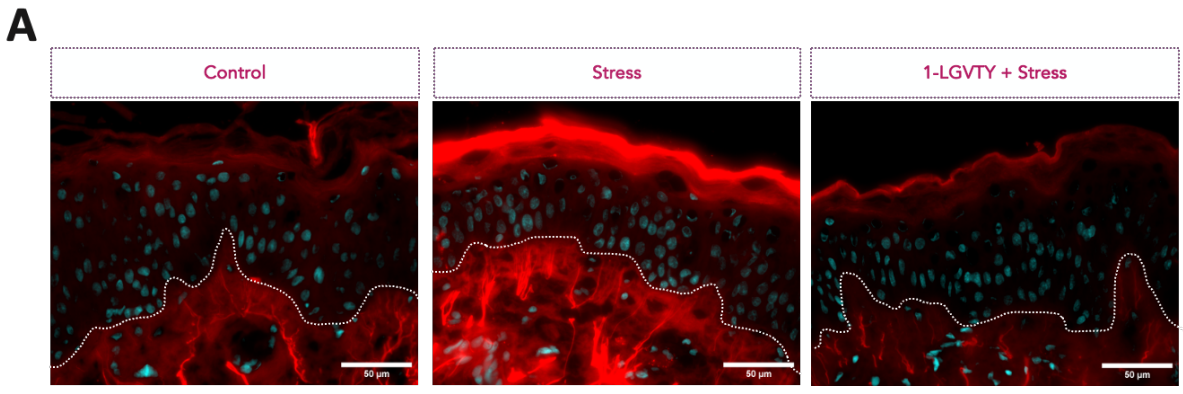
Human organotypic skin explant culture. Skin explants were obtained with the informed consent from abdominal surgery of a female Caucasian donor (25 years old, phototype II/III), distributed in 4 experimental groups (n=3) and kept alive in CO_2-humid incubator as reported previously [FRB&M]. After 48 hours of stabilization, a solution containing 1-LGVTY was topically applied once per day (30 µL/cm^2) for 3 consecutive days. Explants were then topically treated with urban dust (PM10-like; Ref. ERM-CZ100; certified European Reference Material; 0,375µg/cm^2; for 30 minutes of contact), then disposed into 2 mL of Hank's Balanced Salt Solution (HBSS) and irradiated with UV-A (LED source, emission peak at λ=365 nm; 6 J/cm^2) using the OxiProteomics® irradiation system. The control group did not receive any treatment or stress exposure. Two (2) and 24 hours after the irradiation, each explant for each lot was sampled, transferred in OCT for cryopreservation and snap-frozen in liquid nitrogen and conserved at -80°C until analysis.

Biomarkers assessment. Explant sections of 5 µm of thickness were obtained and fixed within a solution containing ethanol (95%v-v) and acetic acid (5% v-v) Oxidatively damaged (carbonylated) proteins were labelled using a fluorescent probe (Ex = 647 nm / Em = 650 nm) functionalized to specifically bind to carbonyl moieties. 4',6-diamidino-2- phenylindole (DAPI) was used for nuclear labelling in a Phosphate Buffered Saline (PBS) solution. Fontana-Masson staining (Sigma-Aldrich) was performed following provider instructions and protocols for melanin staining. For immunolabeling of other biomarkers, a saturating step of the non-

specific sites was carried out with a PBS solutioncontaining 3% (m-v) of BS. Skin sections were then incubated with previously validated antibodies for biomarker detection in the dermis: collagen 1 (ab *34710), collagen 4 (ab7046), collagen 17 (ab186415), elastin (sc-166543), CD44 (ab 254530) or epdermis and stratum corneum : tyrosinase (ab170905), IL-1a (16765-1-AP), IL-6 (M620)*, *S100A8/A9 (ab22506), Beta-DEF2 (ab63982)* The excess of primary antibodies was eliminated with washing steps with a PBS containing 0.1% Tween (PBS-T) solution, then explants were then incubated for 1 hour with the corresponding secondary antibody (*A21235 or A21244)* coupled to a fluorophorein PBS-BSA. The cellular nuclei were labeled using 4',6-diamidino-2-phénylindole (DAPI). Finally, the antibody and DAPI excess were removed with a sequence of washing steps with PBS-T. Light microscope and fluorescent images were collected with an epi-fluorescent microscope (ThermoFisher, EVOS M5000 or M7000 Imaging System). The images were collected using strictly the same acquisition time and resolution per series of acquisition (40X objective).

3. Results

Oxidative stress is a well-established mechanism behind cellular damage and dysfunction in various age-related diseases and skin conditions, and it is closely linked to inflammatory processes at both the tissue and systemic levels. A key way in which airborne particulate matter (PM) contributes to skin damage is by generating oxidative stress. Specifically, polycyclic aromatic hydrocarbons (PAHs), which are attached to the surface of PM in urban air, can activate xenobiotic metabolism, leading to the production of reactive oxygen species (ROS). This process occurs through the formation of quinone derivatives and superoxide anion radicals, both of which contribute to excessive ROS production and oxidative stress. Additionally, ultraviolet (UV) radiation harms the skin by triggering the production of ROS, primarily through UV-A exposure (320–400 nm), which penetrates deeply into the epidermis and reaches the dermis. Moreover, certain PAHs can both induce oxidative stress and enhance the effects of UV-A exposure, further amplifying the damage through photoactivation. In this context and in our explant model, a treatment with 1-LGVTY has a significant effet to counteract the production of ROS after a stress. Indeed, we can observe in the figure 1, a strong decrease of the ROS signal expression from 174 RFU units after stress to 74 RFU units after 1-LGVTY treatment and stress.



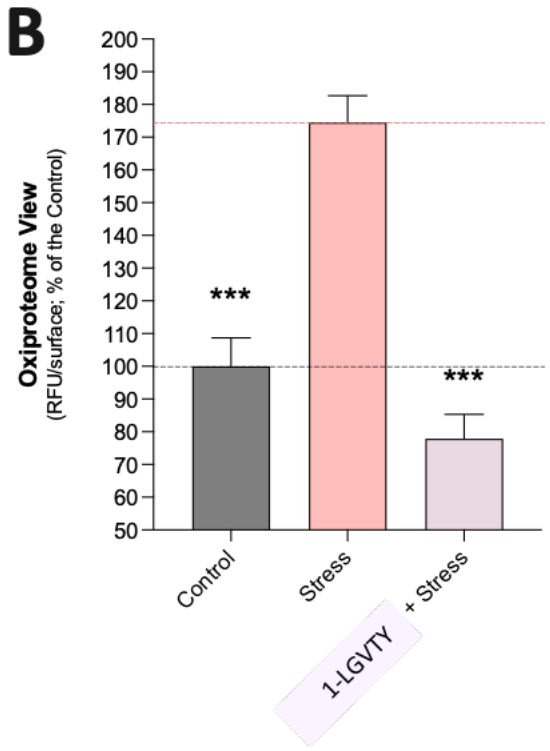


Figure 1. 1-LGVTY protects human skin from environmental-induced oxidative damage. 1-LGVTY was applied topically on the skin explant surface and left in contact for 2 days prior to apply particulate matter (PM) and UV-A exposure. Protein carbonylation was labeled on skin cryosections (5µm) by using a specific fluorophore. **A)** The carbonylation levels in the skin were visualized (in red, representative images), and, **B)** quantified by image analysis on the whole skin. Carbonylation levels (RFU/surface) were expressed as a percentage of control (vehicle) and reported as histograms of the mean ± SD (standard deviation). Comparative statistical analyses were obtained by binary t-test comparisons. ***p < 0.01.

1-LGVTY Technology Prevents Stress-Induced Inflammatory Response in Human Skin Explants

Considering the strong connection between oxidative stress and inflammation in skin aging, we investigated the ability of 1-LGVTY Technology to inhibit the upregulation of inflammatory cytokines triggered by exposure to urban pollution and UV-A radiation. These environmental stressors are known to produce high levels of reactive oxygen species (ROS), which activate inflammatory pathways and promote the release of pro-inflammatory mediators like interleukin-1α (IL-1α) and interleukin-6 (IL-6).

To evaluate the anti-inflammatory potential of the technology, human skin explants were pre-treated with 1-LGVTY Technology for three days before being exposed to a combination of PM10 and UV-A stress. As shown in Figure 2, pre-treatment with 1-LGVTY successfully prevented the increase in IL-1α (2A) and IL-6 (2B) levels, keeping them similar to those in unstressed control explants. These findings indicate that 1-LGVTY Technology not only offers antioxidant protection but also blocks the early inflammatory response typically triggered by environmental stressors.

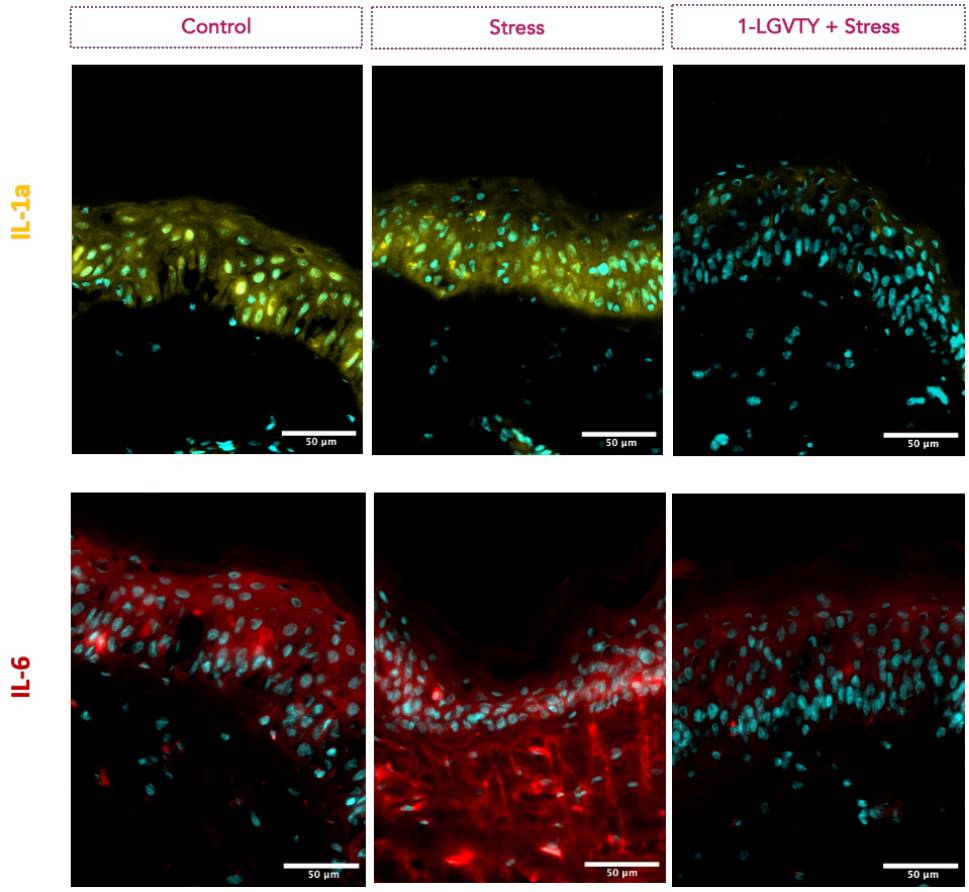


Figure 2. Preventive effect of 1-LGVTY Technology on pro-inflammatory cytokine expression in human skin explants exposed to PM10 and UV-A. Quantification of IL-1α and IL-6 expression levels in human skin explants pre-treated for 3 days with 1-LGVTY Technology, followed by exposure to urban pollution (PM10, 100 µg/mL) and UV-A irradiation (5 J/cm²). Cytokine levels were assessed by epifluorescence microscopy and normalized to untreated, unstressed explants (control). The combined PM10 + UV-A stress markedly increased IL-1α and IL-6 levels, whereas pre-treatment with 1-LGVTY effectively prevented this inflammatory response, maintaining cytokine levels close to baseline. IL-1α and IL-6 expression were labeled on skin cryosections (5µm) by using a specific fluorophore. The IL-1α levels in the skin were visualized (in yellow, representative images), and, IL-6 quantified by image analysis in red on the whole skin. Carbonylation levels (RFU/surface) were expressed as a percentage of control (vehicle).

1-LGVTY Technology Inhibits stress-induced pigmentation in the epidermis via tyrosinase downregulation

Hyperpigmentation is a well-recognized result of environmental stress, especially from the combined effects of urban pollution (PM10) and UV-A radiation, which trigger melanogenesis via oxidative and inflammatory pathways. Tyrosinase, the key enzyme in melanin production, plays a pivotal role in this process, with its overproduction leading to excessive pigmentation and uneven skin tone.

To evaluate the preventive effects of 1-LGVTY Technology on skin pigmentation, we examined the expression of melanin and tyrosinase in human skin explants pre-treated with 1.25% 1-

LGVTY for three days before exposure to PM10 and UV-A. As shown in Figure 3, stress exposure significantly increase melanin levels in the epidermis. However, pre-treatment with 1-LGVTY reduced melanin content by 80% and completely inhibited tyrosinase overexpression (100% inhibition), maintaining levels similar to unstressed controls. These findings suggest that 1-LGVTY Technology offers photoprotection and anti-pollution benefits by disrupting the melanogenesis signaling pathway, particularly through tyrosinase suppression, thereby preventing pigmentation changes caused by environmental stress and promoting skin tone uniformity.

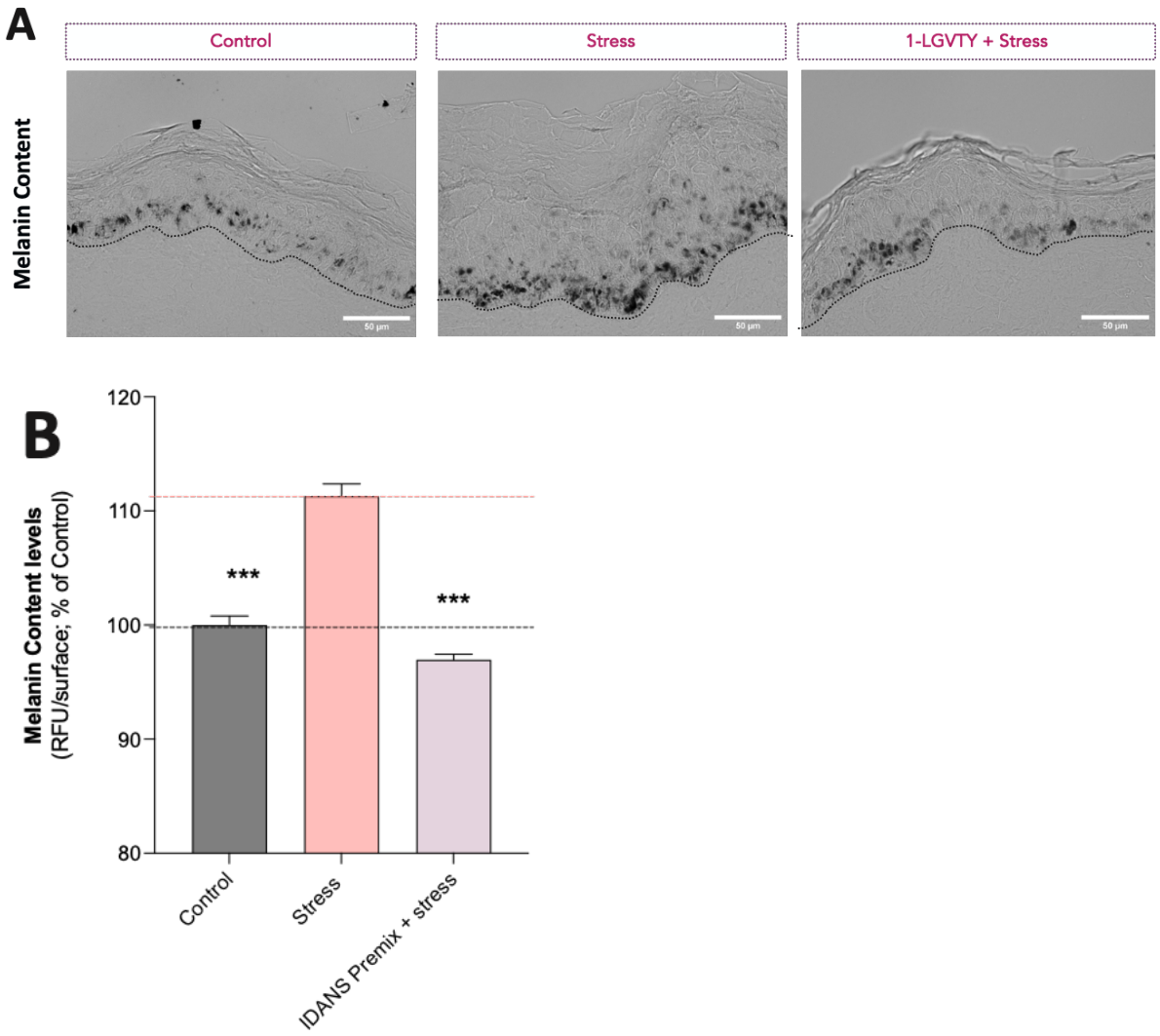


Figure 3. 1-LGVTY Technology prevents environmentally induced pigmentation in the epidermis. Epifluorescence imaging and quantitative analysis of melanin content in the epidermis of human skin explants pre-treated with 1.25% 1-LGVTY Technology for 3 days prior to exposure to PM10 (100 µg/mL) and UV-A irradiation (5 J/cm²). Untreated, unstressed explants served as negative controls; stressed, untreated explants served as positive controls. Quantitative fluorescence values are expressed as mean ± SD (n = X3). Statistical significance is indicated (***p < 0.01) vs. stressed, untreated condition).

4. Discussion

This study emphasizes the comprehensive protective effects of 1-LGVTY Technology, a novel combination of active ingredients, on human skin explants exposed to urban pollution (PM10)

and UV-A radiation, two significant environmental stressors linked to extrinsic skin aging. Our findings highlight that 1-LGVTY Technology works across multiple biological levels to support skin structure and function, offering specific benefits against oxidative stress, inflammation, extracellular matrix (ECM) integrity, pigmentation regulation, and innate immune defense.

One of the most notable outcomes was the reduction in protein carbonylation observed throughout all skin layers. Protein carbonylation is an irreversible oxidative modification of proteins, particularly long-lived structural proteins, and is a key marker of proteome damage that accelerates aging. The accumulation of carbonylated proteins disrupts cellular function and impairs tissue integrity. By mitigating stress-induced carbonylation, 1-LGVTY helps preserve the skin's proteome, a critical factor in skin resilience and longevity.

Additionally, the inhibition of pro-inflammatory cytokines IL-1α and IL-6—both closely associated with ROS production and stress signaling—demonstrates that 1-LGVTY modulates early inflammatory pathways. This anti-inflammatory effect is balanced by the stimulation of antimicrobial peptides (S100A8/A9 and β-defensin-2) under normal conditions, promoting a selective immune-boosting effect that strengthens the epidermal barrier without triggering chronic inflammation.

In the dermis, 1-LGVTY enhances the expression of Collagen I, Elastin, and CD44, proteins essential for the skin's mechanical strength and hydration, often degraded under oxidative or inflammatory conditions caused by UV-A and pollution. Furthermore, 1-LGVTY addresses pigmentation concerns. In models exposed to UV-A and pollution, it significantly reduced melanin accumulation and suppressed tyrosinase expression, preventing the hyperpigmentation typically caused by these stressors. By inhibiting tyrosinase, the enzyme responsible for melanin synthesis, 1-LGVTY helps maintain an even skin tone and prevents the development of age spots. This multifaceted approach, antioxidant, anti-inflammatory, matrix-rebuilding, antimicrobial, and pigmentation-normalizing positions 1-LGVTY as a holistic "well-aging" solution. Rather than simply concealing wrinkles or lightening spots, it works at the molecular level to strengthen the skin's defenses and repair mechanisms, addressing various aging pathways.

Together, our results suggest that 1-LGVTY promotes skin homeostasis and well-aging by targeting key molecular processes affected by environmental stress. This study underscores the importance of skincare that not only preserves the native skin proteome but also actively prevents irreversible oxidative damage.

The potential applications of 1-LGVTY are further emphasized by its antioxidant, anti-inflammatory, and pro-regenerative properties. These effects could be particularly beneficial in post-aesthetic procedures (e.g., laser resurfacing, chemical peels, or radiofrequency treatments), where its ability to reduce IL-1α, IL-6, and oxidative markers could accelerate recovery and minimize procedure-related inflammation, erythema, and post-inflammatory hyperpigmentation [11, 12]. Similarly, using 1-LGVTY topically alongside mesotherapy (without direct injection) could support dermal structure rebuilding and alleviate post-procedural irritation through its biomarker-modulating actions, such as collagen I induction and inflammatory mediator suppression [13, 14].

Incorporating 1-LGVTY into sunscreens, in combination with SPF filters, offers additional protection against both UV-A and UV-B. By counteracting UV-induced oxidative stress and inflammation, it extends skin protection beyond traditional photoprotective measures. These potential

uses highlight 1-LGVTY as a versatile, multifunctional skincare technology suitable for both restorative care following procedures and as a protective agent in daily skincare [15, 16].

5. Conclusion

In conclusion, 1-LGVTY represents a groundbreaking approach in dermatological science, focusing on treating the underlying causes of skin aging rather than just the symptoms. By modulating key aging biomarkers : from collagen I and elastin to IL-6, tyrosinase, and β-defensin-2 (not all shown in this article), this technology aims to preserve or restore youthful skin biology, even under environmental stress. With the increasing complexity of modern skin exposomes (UV, pollution, digital light, etc.), the need for multi-dimensional protective strategies has never been greater. The following sections of this publication will delve into the specific effects of 1-LGVTY on human skin explants and its potential as a comprehensive skin longevity enhancer. By addressing the interconnected mechanisms of aging like oxidative damage, inflammation, dermal integrity, immune function, and pigmentation, 1-LGVTY paves the way for a new generation of biomarker-driven cosmeceuticals for healthy skin aging.

6. References

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