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"Sustainable Science in Decolleté "Skinification": Merging Well-Aging, Longevity, and Advanced Technologies"

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1. Introduction

The growing demand for sustainable cosmetic solutions has reshaped the industry, driven by a consumer shift toward products that not only deliver visible efficacy but also minimize environmental impact through ethically sourced ingredients and responsible production practices [1]. This paradigm aligns with the "skinification" trend, wherein principles of advanced facial care are extended to the body—particularly the neck and décolleté regions, which are increasingly recognized as critical sites for rejuvenation [2] .

Aging in the neck and décolleté area is marked by a reduction in collagen and elastin, leading to sagging and loss of firmness. This deterioration is exacerbated by both intrinsic factors and external aggressors, such as UV exposure and pollution. The activation of cellular repair systems, including those mediated by sirtuins, is essential to counteract these aging processes [3-5].

The solution for the pressing need for effective neck and decolléte innovative, eco-conscious products could arise by merging well-aging and longevity principles with advanced technology and upcycling approaches. The focus on sustainable innovation responds to consumer preference for formulations that deliver visible efficacy and minimize environmental impact, such as those caused by the coffee and citrus sectors, which are prominent sources of waste production. Brazil, as the foremost coffee producer, not only consumed 1,260,000 tons domestically in 2022 but also exported over 2,130,000 tons, predominantly of Coffea Arabica, largely from the southeast region, especially São Paulo [6]; Furthermore, Brazil excels in citrus juice production and exportation, with a substantial waste generation of around 45% from processing, particularly in São Paulo and Minas Gerais [7.8]. These wastes offer both a challenge and an opportunity for novel waste management and valorization strategies to mitigate environmental repercussions and exploit their inherent value.

In response to these challenges, recent research has focused on integrating sustainable innovation into anti-aging strategies. The development of the *Coffea arabica* and *Citrus*

limonum Extract (CLE) embodies this integrated approach by merging empirical efficacy outcomes with eco-conscious production methodologies. This study aims to elucidate the cellular and structural improvements conferred by CLE, thereby setting a new benchmark for sustainable cosmetics that reconcile advanced skin science with environmental responsibility.

2. Materials and Methods

Green coffee seed pressing residue from Cosmetic Industry and Citrus limonum pomace residue from Beverage Industry were submitted to hydroglycolic extraction. The CLE optimized formulation was developed using a proprietary transcriptomics platform (analyzing 45 samples in an *ex vivo* model) and empirical modeling.

1.Clinical assessment

Forty-four female participants, aged between 44 and 69 years, exhibiting moderate to severe wrinkles in the cervical and décolletage regions (grades 3-5 on the Fabi/Bolton chest wrinkle scale), were selected for this study, while excluding those with a high density of photoaged spots within the Region of Interest (neck and décolletage). These subjects evaluated a formulation containing 0.5% w/w CLE or a placebo over a period of 28 days, utilizing a single-blind randomized design. The formulations were administered bi-daily to the neck and décolletage areas.

The assessment of wrinkles and surface roughness was conducted in the décolleté (frontal) region through 3D fringe-projection image analysis utilizing AEVA-HE V4 (FoV, L) equipment. High-resolution macroscopic images were captured using a Nikon D5600 camera mounted on the HeadScan Bench Light Face, which included a comprehensive professional photographic setup.

The following parameters were used to assess wrinkles: area (mm^2), perimeter (mm), and average volume of detected wrinkles. The SQ parameter was used to assess skin texture, and Stm was used to assess skin roughness.

Data collected from each participant at the designated timepoint (D28) were normalized against baseline values (D0) for the entire cohort and subjected to statistical analysis for each measured parameter. Furthermore, the participants' subjective evaluation of the product's efficacy was gauged through an individual questionnaire administered at each timepoint.

The clinical protocol received ethical approval from the Drug Research Ethics Committee (CEIm) at La Fe Hospital in Valencia, Spain. The study protocol adheres to the guidelines established by the Scientific Committee on Consumer Safety (SCCS). It complies with all international standards governing research involving human subjects, including Good Clinical Practices (ICH-GCP) and regulations set forth by the World Medical Association. The study was conducted in accordance with the Declaration of Helsinki (1864) including its amendments. All participants provided informed consent prior to their involvement in the study.

2.Immunofluorescence *ex vivo* analysis

Eyelid fragments from elective blepharoplasty surgeries were obtained from healthy patients aged 35 to 70 at the Banco de Olhos do Hospital Oftalmológico de Sorocaba (BOS-HOS). The acquisition and utilization of these human skin explants were sanctioned by the HOS Ethics Committee, referenced under report number 6.425.834. The fragments, measuring 0.5 cm^2, were cultured for 72 hours prior to treatment with CLE 0.5% w/w and a placebo. The

application rate of the products to the skin was 12 mg/cm². Following incubation with the test products and placebo, the *ex vivo* skin fragments were fixed in 4% paraformaldehyde for 24 hours and subsequently cryoprotected in 30% saccharose solution for 48 hours, with 10 µm sections collected on silanized slides using a Cryostat (Leica – CN1850).

The sections were subjected to washes with Phosphate buffer 0.1 M and incubated overnight with the primary antibody Anti-Collagen I (Sigma-Aldrich, C2456), Anti-Collagen III (Santa Cruz, sc271249), Anti-Collagen 4 (Abcam, ab6586), Anti-Fibronectin (Santa Cruz Biotech; sc69681) and Anti-Sirtuin III (Santa Cruz, sc99143). Subsequently, they were subjected to further washes with Phosphate buffer 0.1 M and incubated for 1 hour with secondary antibody Goat anti-Mouse (Invitrogen; A11001). At the end of these steps was performed further incubation (1 minute) with DAPI (4'-6-Diamidino-2-Fenilindol; DNA marker) followed by 3 washes of 5 min with Phosphate buffer 0.1 M. The slides were prepared using a specific mounting medium and analyzed by an optical fluorescence microscope (Leica – DM 6000 B) accoupled with a camera of 2.8 MP (Leica, DFC7000 T), through Software LAS (Leica Application Suite v.4.12). The evaluated parameter was the fluorescence intensity emitted by labeling with the specific antibody.

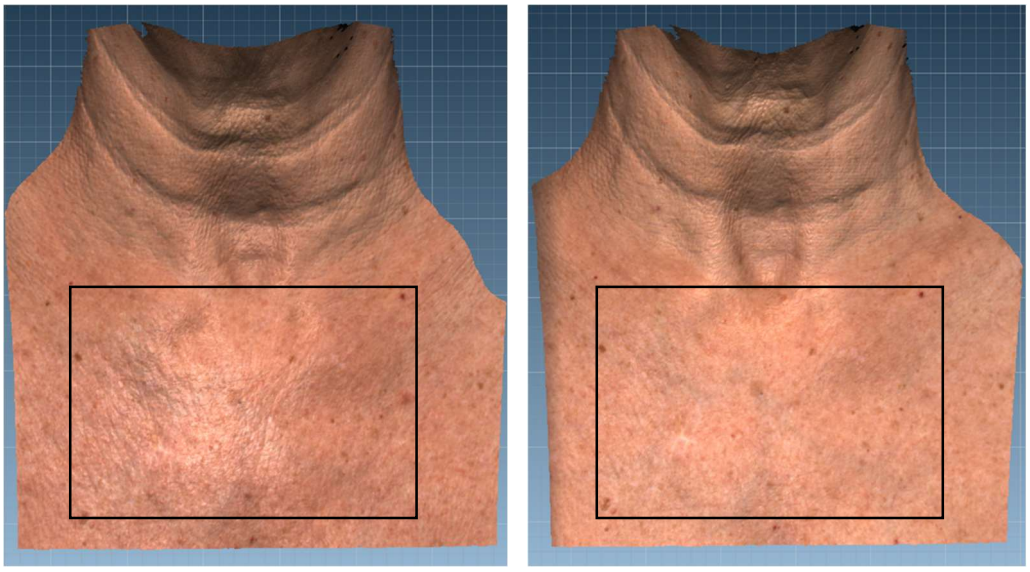
Variance analysis (ANOVA) was used for statistical analysis. The Dunnett's test is used when the analysis of variance detects significant comparative differences among groups. In all groups studied, it is considered statistically substantial those whose P values are equal to or less than 0.05.

3. Results

CLE applied at 0.5%w/w in a cosmetic formulation presented significant ($p<0.05$) enhancements in decolleté wrinkles area and skin texture (Table 1 / Figure 1), after a 28-day regimen (D28) compared to baseline (D0). The placebo group displayed nonsignificant results in both cases. In addition to instrumental findings, in the subjective evaluation, volunteers reported substantial improvements (>86%) in elasticity, skin hydration, and smoothness.

Table 1. Clinical assessment of decolleté wrinkles and skin texture. (*p<0,05 related to D0).

	Parameter	% Improvement related to D0
Decolléte Wrinkles	Area	15.0%*
	Perimeter	12.8%*
	Volume	13.5%*
Skin Texture	Surface roughness (Sq)	7.0%*
	Skin texture (Stm)	7.0%*



D0 D28

Figure 1. 3D reconstruction of the décolleté region for wrinkle reduction and texture improvement analysis at initial time (D0) and after 28-day treatment (D28) with a formulation containing CLE at 0.5%w/w.

The results (Table 2) obtained in *ex vivo* tests corroborated the improvement observed in clinical assessment. Compared to placebo, the formulation containing CLE at 0.5%w/w was able to significantly ($p<0.01$) upregulate the extracellular matrix proteins (EMC) and cellular longevity protein studied.

Table 2. *Ex vivo* evaluation by immunofluorescence. (**p<0,01 related to placebo).

	Protein	% Upregulation related to Placebo
ECM Protein	Collagen type I (COL-1)	103%**
	Collagen type II (COL-3)	106%**
	Collagen type IV (COL-4)	79%**
	Fibronectin (FN-1)	49%**
Cellular Longevity Protein	Sirtuin-III (SIRT-3)	33%**

4. Discussion

The repurposing of industrial residues generated from Brazilian coffee seed pressing and citrus juice extraction offers an environmentally responsible avenue for bioactive ingredient development. The potencial of these residues was initially tried by using a proprietary transcriptomics platform, applied to an *ex vivo* model. Empirical modeling based on efficacy outcomes allow the definition the best formulation (CLE) able to reverse or mitigate the signs of aging in the neck and décolleté regions. By leveraging these upcycled waste materials, it was possible to extract compounds that promote collagen synthesis and enhance cellular repair through the upregulation of mitochondrial function markers such as SIRT-3, ultimately contributing to structural improvement and well-aging.

A clinical study conducted on the décolleté area demonstrated significant improvements in key skin aging parameters, including a reduction in wrinkle area, perimeter, and volume, as well as marked enhancements in surface roughness (Sq) and texture (Stm). These outcomes

indicate a clear improvement in skin smoothness and a visible reduction in unevenness, contributing to a more youthful appearance.

These clinical benefits were supported by mechanistic insights from an *ex vivo* model, which revealed the upregulation of proteins essential for skin structure and repair. Notably, increased expression of collagen types I, III, and IV (COL-1, COL-3, COL-4), fibronectin (FN-1), and the mitochondrial marker SIRT-3 was observed following treatment with a synergistic extract of upcycled coffee seed cake and lemon pomace (CLE).

Collagens are critical structural proteins whose decline is a hallmark of skin aging. COL-1 is associated with intrinsic aging, COL-3 decreases progressively with age, and COL-4 is essential for dermal-epidermal cohesion [9-11]. Fibronectin plays a central role in maintaining dermal architecture, and its loss is closely linked to wrinkle formation [10-12]. SIRT-3, a mitochondrial sirtuin, supports cellular repair and protects against oxidative stress, reinforcing the biological underpinnings of skin resilience and longevity [11,13].

The coordinated upregulation of these proteins suggests a biological mechanism through which the clinical improvements were achieved by enhancing extracellular matrix remodeling and mitochondrial function, the treatment contributes to restoring skin firmness, elasticity, and texture. Thus, the ex vivo findings corroborate and help explain the clinical efficacy observed, highlighting the relevance of this upcycled extract in promoting visible and measurable signs of well-aging in the neck and décolleté regions.

5. Conclusion

CLE exemplifies a sustainable breakthrough in décolleté rejuvenation, integrating well-aging and longevity principles. By enhancing ECM protein synthesis and SIRT-3, CLE addresses aging with cellular repair and structural improvement. Derived from upcycled residues, it aligns with consumer demand for eco-conscious innovation, redefining skincare by merging efficacy with sustainability.

6. References

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