Clinical Tolerability and Efficacy Establishment of a New Cosmetic Treatment Regimen Intended for Sensitive Skin

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Featured Application: This work aims to find a well-tolerated and effective therapeutic regimen option as an anti-aging treatment in subjects with sensitive skin for which skincare routines can be challenging when trying to achieve high tolerance and efficacy.

Abstract: Sensitive skin has a great impact on the quality of life of subjects. In this research, we evaluated the efficacy and tolerance of a cosmetic treatment for facial skincare, consisting of a cleanser, serum and cream. A clinical-instrumental study was carried out on 30 healthy female participants with sensitive and reactive skin and slight-to-moderate wrinkles using a new cosmetic regimen based on a new technology. Skin moisturization, skin barrier function, erythema, elasticity and firmness, and wrinkle depth (skin profilometry) were evaluated at basal time (T0), and after 14, 28 and 42 days of treatment (T14, T28 and T42). All the evaluated variables showed significant improvement at T42 when compared to T0. Moisturization, erythema, firmness, and elasticity had significant improvement at T14 and the other attributes after T28 (transepidermal water loss, wrinkle depth). A high level of tolerance and satisfaction reported by subjects were achieved. This treatment regimen combining the cleanser, the daily cream, and the nightly serum, showed a statistically significant improvement in all of the parameters evaluated, demonstrating its effectiveness as an anti-aging regimen while improving the sensitive skin condition. This regimen was well tolerated by all the participants.

Keywords: sensitive skin; TRPV1; thermal spring water; algae; TGFβ2; tolerance; anti-aging skincare

1. Introduction

Sensitive skin (SS) is one of the most prevalent issues in dermatological consultations, and selecting a good skincare routine can be a challenge for these subjects. The International Forum for the Study of Itch (IFSI) defines sensitive skin as: “Characterized by the occurrence of unpleasant sensations (stinging, burning, pain, pruritus and tingling sensations) in response to stimuli that normally do not provoke such sensations”. The skin can appear normal or be accompanied by erythema [1]. SS limits the quality of life of patients as well as the treatment options for skin aging prescribed by a dermatologist [2]. The choice of an appropriate skincare regimen for patients with SS must be made carefully, focusing on improving skin appearance while controlling the SS symptoms with a good tolerance profile. Current recommendations indicate that a complete anti-aging skin regimen should focus on protection (e.g., antioxidants and repairing actives), renewal (moisturization, exfoliation and cell turnover) and dermal activation and regeneration (e.g., dermal stimulating peptides) [2–4]. Specifically, the treatment regimen for SS patients should also include actives aimed at counteracting the psycho-chemical changes and neurosensory dysfunction present in SS; this is achieved with anti-inflammatory action, restorative barrier function and control of TRPV-upregulation and other neurosensory dysfunctions [5–11].
would also be helpful to modulate the low-intensity chronic inflammation that is known to contribute to skin aging, known as inflammaging [12]. This is characterized by increased levels of circulating proinflammatory cytokines and a shift toward cellular senescence [13]. Senescent cells secrete pro-inflammatory cytokines that considerably alter the skin microenvironment. Aged skin exhibits an augmented nonspecific proinflammatory (innate) response to environmental insults where the adaptive response is diminished [14]. Ye et al. found that the topical application of a barrier-repair emollient significantly improved the function of the epidermal permeability barrier and simultaneously, circulating levels of IL-1β and IL-6 in the treated elderly individuals returned to levels comparable to those of the young control individuals [15] (Figure 1).

Figure 1. Summary of the anti-aging molecular aspects in anti-aging skincare in sensitive skin.

The present anti-aging regimen treatment for SS combines different active ingredients that could potentially have beneficial effects on aging and on SS conditions (Figure 2). The formulation of the products in the present study is summarized as follows: Aquammunist®, which is Solia Thermal Spring Water (Solia TSW) enriched with a diatomaceous algae extract (Phaeodactylum tricornutum), combined with niacinamide 4%, vitamin E and Annona cherimola fruit extract. In addition, the serum also contained Nicotiana benthamiana hexapeptide-40 sh-polypeptide-76, which is a fusion peptide of hexapeptide-40 with a single-chain recombinant human peptide synthesized from N. benthamiana to be identical to the human gene that encodes transforming growth factor-beta-2 (Supplementary Materials INCI).

Aquammunist® combines Solia Thermal Spring Water (TSW) and Phaeodactylum tricornutum extract. These actives have anti-inflammatory and skin barrier restorative effects [16–18]. Solia TSW, a meso-thermal water from Cantabria, Spain, is an isotonic water particularly rich in sodium, calcium, magnesium, silica, and trace minerals, such as zinc, copper, manganese, boron, and selenium. TSWs have been recognized for their soothing, moisturizing, and anti-inflammatory properties [19–23]. Solia TSW is classified as chloride, bicarbonate, sulfide, carbon dioxide, and weakly mineralized water [16]. It has been declared medicinal mineral water by the Instituto Geológico y Minero de España (IGME) and the Department of Industry of Cantabria. Its hydrobiome includes Cyanophyta, Chlorophyta, and Heterokontophyta, with notable Phaeodactylum-like species [16]. Phaeodactylum tricornutum, is recognized for its adaptability, thriving in both marine and brackish water strains [24], but it has also been reported to grow in freshwater [25], showing a remarkable versatility in aquatic environments. It has been used for its anti-inflammatory and barrier repair activities, primarily due to fucoxanthin, which controls pro-inflammatory cytokines like IL-1β, IL-6, and TNF-α [26,27]. The algae extract in Aquammunist® consists of P. tricornutum extract encapsulated in liposomes, containing omega-3 fatty acids and standardized to fucoxanthin levels. This combination was clinically tested for the first time in [16]. This restorative effects have previously been observed in human keratinocytes (HaCaT cells) subjected to an irritation model, where Aquammunist® demonstrated control over key immune factors involved in skin inflammatory conditions [16].
All the products also contained niacinamide, which reinforces the skin barrier by stimulating the synthesis of ceramides and lipids in the stratum corneum and increasing the expression of involucrin, filaggrin and keratin [27]. In addition, niacinamide can protect the skin from oxidative damage from pollution, high-energy visible light and UV and reduce coloration, by inhibiting the transfer of melanosomes [28,29]. The products also had vitamin E, with very well-known antioxidative properties [30]. As for counteracting the hyperactivation of TRPV1 receptors, the cream and the serum included *Annona cherimola* fruit extract, which has previously been shown to have this effect [16,31]. *Annona cherimola* fruit extract is derived from Cherimoya fruits, which are processed and dried before extraction. Then, they are gently extracted using an aqueous buffer. The final product is obtained by subsequent filtration. *Annona cherimola* is one of the most esteemed fruits of the many edible species from the family Annonaceae.

To induce dermal stimulation, an active biotechnological TGFβ2 peptide from *N. benthamiana* seed was also included in the serum. This peptide has proven to be active regarding collagen synthesis, resulting in a consequent increase in firmness and elasticity [32]. It has been shown to increase type I collagen synthesis through the Smad metabolic pathway. Smad proteins are part of the signaling pathway orchestrated by the TGF-β family of hormones, and active ingredients with proven anti-aging efficacy, such as retinoids, also act on this pathway [32–34]. Smads form a family of transcription factors that activate and inhibit gene transcription (e.g., collagen, fibronectin), influencing key aspects such as tissue regeneration [35,36]. Subsequently, the increase in type I collagen will improve skin elasticity and firmness [32].

This study aimed to assess the efficacy and tolerance of the present regimen of combining a cleanser, a daily cream and night application serum in order to improve symptoms of SS as well as some signs of aging skin. The ingredients used in this study have previously reported beneficial properties for irritated skin [17,20,24–26,37,38].

![Figure 2](image.png)

**Figure 2.** This figure reflects the main active ingredients present in the cosmetic regimen for SS anti-aging treatment and some of their mechanisms of action for improving SS conditions and signs of aging [39].

2. Materials and Methods

2.1. Study Design

This was a prospective open-label study. The study met all ethical requirements. All the subjects were informed about the test procedures and signed a consent form.
2.2. Study Participants

Thirty healthy female subjects aged between 35 and 55 years old (±2) were recruited for the study. They had sensitive and reactive skin with slight to moderate erythema and wrinkles. Inclusion criteria are summarized as follows: healthy female subjects aged between 30 and 55 years old (±2), with sensitive and reactive skin, with slight-to-moderate erythema and wrinkles; the pharmacological therapy should be stable for at least one month without any changes expected during the study; participants willing to make the commitment to not change their daily routine or lifestyle; all subjects must understand and sign a written consent form. The exclusion criteria included: subjects who did not meet the inclusion criteria or have acute or chronic diseases that could interfere with the outcome of the study; who participated in a similar study without respecting an adequate washout period; subjects under pharmacological treatments considered incompatible with the study requirement by the investigator; subjects with known allergies to the tested products; subjects breastfeeding, pregnant or not willing to take necessary precautions to avoid pregnancy during the study.

All the study procedures complied with the ethical principles for medical research (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and its amendment).

2.3. Composition of the Tested Products

All the tested products were formulated with Aquammunist® (Solia TSW + diatom algae extract). In addition, the cream and the serum included Annona cherimola fruit extract and niacinamide 4%. The serum also had a biotechnological TGFβ2 of plant origin (seed of N. benthamiana).

2.4. Study Protocol

All subjects were instructed to follow a regimen that included applying the cleanser twice daily, the cream during the day, and the serum at night (see Table 1). Evaluations were performed at baseline (T0) and after 14 (T14), 28 (T28) and 42 days (T42) of using the regime.

Table 1. Evaluation protocol in each visit.

<table>
<thead>
<tr>
<th>Evaluation Time</th>
<th>Qualitative and Quantitative Evaluations Performed at Each Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>- Instrumental evaluations of the parameters under study (skin moisturization, TEWL, erythema index, skin elasticity and firmness and skin profilometry) before product use</td>
</tr>
<tr>
<td></td>
<td>- Dermatological evaluation of basal skin condition</td>
</tr>
<tr>
<td></td>
<td>- Clinical evaluation of skin wrinkles</td>
</tr>
<tr>
<td></td>
<td>- Acquisition of digital pictures of the treated area (face) with VisiaCR</td>
</tr>
</tbody>
</table>
Table 1. Cont.

<table>
<thead>
<tr>
<th>Evaluation Time</th>
<th>Qualitative and Quantitative Evaluations Performed at Each Visit</th>
</tr>
</thead>
</table>
| T42             | - Instrumental evaluations of the parameters under study (skin moisturization, TEWL, erythema index, skin elasticity and firmness and skin profilometry)  
                  - Dermatological evaluation of skin condition  
                  - Tolerability and adverse events  
                  - Clinical evaluation of skin wrinkles and improvement of skin appearance  
                  - Acquisition of digital pictures of the treated area (face) with VisiaCR  
                  - Volunteers are asked to express their opinion on tested products by answering a questionnaire at T42. |

2.5. Evaluation Methods

All the study procedures were carried out under temperature- and humidity-controlled conditions (temperature 18–26 °C and humidity 50 ± 10%). Before the visit, the subject undergoes a 15–20 min acclimatization period in these conditions.

Quantitative variables were evaluated with bioengineering techniques able to quantify different parameters:
- Skin moisturization Corneometer® CM 825 Courage + Khazaka, electronic at T0, T14, T28, T42.
- Transepidermal water loss (TEWL) to assess skin barrier function with Tewameter® TM 300—Courage + Khazaka Electronic at T0-T14-T28-T42.
- Skin erythema with Mexameter 18® Mexameter® MX 18—Courage + Khazaka Electronic at T0-T14-T28-T42.
- Skin firmness (R0) and elasticity (R2) with Cutometer® MPA 580, Courage + Khazaka, electronic at T0-T14-T28-T42.
- Skin profilometry (wrinkle depth) with Primos 3D (GFMesstechnik GmbH, Brandenburg, Germany) at T0-T28-T42.

In addition, some qualitative evaluations were performed:
- Skin wrinkle according to RAO Goldman scale (1–5 score) at all visits and improvement of skin appearance (1–4 score) at T14, T28 and T42.
- Dermatological evaluation and product tolerability: with collaboration of the enrolled subject, the dermatologist assessed both physical signs (skin erythema, skin edema, skin dryness, skin desquamation) and functional signs (stinging/itching sensation, burning sensation, tight feeling), scoring from 0 (no one) to 4 (severe).

The products would be classified as tested under dermatological control and safe for their use if none or at most 15% of subjects showed a clinical sign related to the application of the product that caused them to withdraw from the clinical study. And they would be classified as not tolerated during its use if more than 15% of the subjects showed a clinical sign related to the application of the product that caused them to withdraw from the clinical study.

- A self-assessment questionnaire was filled in by the enrolled subjects at the end of the study (T42), ranging from completely disagree, disagree, agree or completely agree (Table 2).
- Digital pictures of faces were acquired by means of Visia®.CR (Canfield Scientific, Parsippany, NJ, USA). This instrument ensures a reproducible subject positioning between timepoints and acquires pictures using different light modalities in order to enhance the visualization of the skin features to be analyzed.
Table 2. Self-questionnaire filled in by the enrolled subjects at the end of the study.

<table>
<thead>
<tr>
<th>Regarding the products</th>
<th></th>
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<tbody>
<tr>
<td>1 Do you find the look and smell of the products pleasant?</td>
<td></td>
</tr>
<tr>
<td>2 Do you find the texture of the products pleasant?</td>
<td></td>
</tr>
<tr>
<td>3 Is the absorption of the products into the skin rapid after application?</td>
<td></td>
</tr>
<tr>
<td>4 Do you feel freshness effect after application?</td>
<td></td>
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<tr>
<td>5 Do you notice an oily sensation during application?</td>
<td></td>
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<tr>
<td>6 Do you notice the product leave residue on the skin, or feeling stickiness?</td>
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<tr>
<td>7 Do you notice your skin is softer?</td>
<td></td>
</tr>
<tr>
<td>Regarding the scheme of use</td>
<td></td>
</tr>
<tr>
<td>8 Is it easy for you to follow the protocol using the products in your daily routine?</td>
<td></td>
</tr>
<tr>
<td>Regarding subjective efficacy</td>
<td></td>
</tr>
<tr>
<td>9 You notice your skin more hydrated, immediately after application.</td>
<td></td>
</tr>
<tr>
<td>10 You notice your skin is more hydrated at the end of treatment.</td>
<td></td>
</tr>
<tr>
<td>11 You notice your skin tone is more even</td>
<td></td>
</tr>
<tr>
<td>12 The product relieves tone is more even</td>
<td></td>
</tr>
<tr>
<td>13 Does the product relieve skin tightness?</td>
<td></td>
</tr>
<tr>
<td>14 The treatment reduces symptoms associated with sensitive/reactive skin</td>
<td></td>
</tr>
<tr>
<td>15 Reduce the sensation of heat on the skin</td>
<td></td>
</tr>
<tr>
<td>16 Reduce the dryness of the skin.</td>
<td></td>
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<tr>
<td>17 Reduce the redness of the skin.</td>
<td></td>
</tr>
<tr>
<td>18 Instantly calms the feeling of discomfort</td>
<td></td>
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<tr>
<td>19 The treatment helps control sensations of irritation and tingling.</td>
<td></td>
</tr>
<tr>
<td>20 Notice more renewed and repaired skin</td>
<td></td>
</tr>
<tr>
<td>21 You notice fewer reactions and less sensitivity in your skin since using the products</td>
<td></td>
</tr>
<tr>
<td>Regarding the purchase intention</td>
<td></td>
</tr>
<tr>
<td>22 Would you recommend this protocol?</td>
<td></td>
</tr>
<tr>
<td>23 Did product protocol meet your expectations?</td>
<td></td>
</tr>
</tbody>
</table>

2.6. Statistical Analysis

The instrumental data were submitted to 2-way Student’s test \( t \) for paired data, while clinical data were submitted to Wilcoxon signed test (intra-group analysis vs. T0). The variation was considered statistically significant when the \( p \) value was <0.05. The statistical software used for statistical analysis is NCSS 10—PROFESSIONAL. In addition, for clinical evaluations, the positive effect of the product on the evaluated parameter was confirmed if more than 50% of the subjects registered an improvement. For the self-assessment questionnaires, the benefit of the product must be perceived by at least 60% of the subjects.

3. Results

Twenty-nine of the subjects finished the study. One subject withdrew from the study for personal reasons not related to product use.

3.1. Quantitative Variables

3.1.1. Skin Moisturization

Significant improvement in skin moisturization was obtained with Corneometer® from T14 onwards. The tested treatment determined a statistically significant increase in skin moisturization by +5.7% at T14, by + 9.4% at T28 and by +14.3% at T42 (Figure 3).
Figure 3. Skin moisturization was checked at every visit. A significant improvement was detected at T14 (left image) *** *p < 0.001. The increase percentage reached up to 14% at T42 * * p < 0.05 (right image).

3.1.2. TEWL

A significant decrease in TEWL was detected with Tewameter® at T28 (−3.4%) and was maintained at T42 (−5.5%), representing an improvement in skin barrier function.

3.1.3. Skin Erythema

After 14, 28 and 42 days of use, the tested treatment determined a statistically significant decrease (p < 0.05) in the erythema index with Mexameter 18® (related to a decrease in skin redness) that was progressive along the study and reached up to 13.5% at T42 (Figure 4).

Figure 4. Percentages describe parameter (skin erythema) variation versus baseline (T0) at T14, T28 and T42. Asterisks signal a significant difference versus baseline. * * p < 0.05.

3.1.4. Skin Firmness (R0)

From T14 onwards, the tested treatment determined a statistically significant decrease (p < 0.05) in the R0 parameter (penetration depth in mm/time) of −4.1% at T14 and T28 and −7.3% at T42, showing an improvement in skin firmness with Cutometer® MPA 580.

3.1.5. Skin Elasticity (R2)

A statistically significant increase (p < 0.05) in the R2 parameter (improvement in skin elasticity) was obtained with Cutometer® MPA 580 from T14 onwards with increases of +2.8% at T14, +6.2% at T28 and +6.4% at T42 (Figure 5).
and T28 and −7.3% at T42, showing an improvement in skin firmness with Cutometer® MPA 580.

3.1.5. Skin Elasticity (R2)

A statistically significant increase ($p < 0.05$) in the R2 parameter (improvement in skin elasticity) was obtained with Cutometer® MPA 580 from T14 onwards with increases of +2.8% at T14, +6.2% at T28 and +6.4% at T42 (Figure 5).

![Figure 5. Percentages describe parameter variation (Skin elasticity, R2) versus baseline. Asterisks signal a significant difference versus baseline. * $p < 0.05$ (n = 30, paired t-test) R2 (Ua/Uf), gross elasticity or overall elasticity, which represent the ability of re-deformation of the skin to its basal state.](image)

3.1.6. Skin Profilometry

Wrinkle depth with Primos 3D (GF Messtechnik GmbH) determined a statistically significant decrease ($p < 0.05$) in crow’s feet wrinkle depth from T28 onwards, with decreases of −6.8% at T28 and −10.8% at T42. Images from one volunteer are shown (Figure 6).

![Figure 6. Images of periocular wrinkles obtained by Primos 3D. The images were taken at baseline (above) and at T42 (below). The skin surface is colored red (value of approximately 0 mm according](image)
to the color scale present at the bottom of each figure). Green and blue colors represent values below zero. Orange and yellow represent values above zero. Wrinkles, according to depth, are colored in green/blue (the more the color changes from green to blue, the greater the wrinkle depth). In the right part of each panel, the corner of the eye is represented in yellow/blue and has been acquired as a reference point for each time point evaluation.

3.2. Qualitative Variables

3.2.1. Clinical Evaluation

Upon clinical evaluation, we found a significant improvement in wrinkle graduation at T28, according to the RAO Goldman scale. In addition, after 28 and 42 days of use, a decrease in skin wrinkle appearance was clinically determined in 52% and 69% of enrolled subjects, respectively. (Figure 7).

![Figure 7. Values describe the percentages of subjects who had improvements and those who did not based on the RAO Goldman scale versus the baseline. The asterisks signal a significant difference in 52% of the subjects at T28 and 69% of the subjects at T42 versus baseline. * p < 0.05.](image)

An improvement in skin appearance after 14, 28 and 42 days of use was achieved in 55% of enrolled subjects at T14, in 62% at T28, and in 76% at T42 (p = 0.08).

3.2.2. Dermatological Evaluation of Tolerance

None of the subjects showed any onset of adverse events. The tolerance was excellent since only 5/29 volunteers reported a very mild skin tightness sensation. No burning sensations, itching sensations or any other tolerance problems were detected with the test product during the study period.

3.2.3. Self-Assessment

The questionnaire fulfilled by subjects reflected that at the end of the study, up to 97% of the subjects would recommend the treatment regimen and informed that the protocol regimen met their expectations. All of them found the texture of the products pleasant and the daily protocol easy to follow. As for the questions about the efficacy of the treatment, 92.5% had positive answers.

All the results discussed above were in accordance with the improvements shown in the digital pictures (Figure 8):
within the aging process and affect the components of the ECM, actives that regulate the would worsen the symptoms of subjects with SS [1].

The results showed a significant improvement in skin aging parameters, such as firmness present in the serum is a plant-derived TGF 52% of the subjects at T28 and 69% of the subjects at T42 versus baseline. *

the improvement in erythema and skin appearance at the end of the study versus baseline. 

the digital pictures (Figure 8): 

Figure 8. Clinical images of one volunteer at different evaluation times throughout the study. Note the improvement in erythema and skin appearance at the end of the study versus baseline.

An individualized anti-aging treatment regimen for SS subjects should be prescribed in order to increase tolerance and subsequently compliance and efficacy. This represents a therapeutic challenge since some of the anti-aging active ingredients with more demonstrated scientific evidence (e.g., retinoids) can induce a certain degree of skin irritation that would worsen the symptoms of subjects with SS [1].

Results obtained after 42 days in an in vivo study following the regimen combination showed an improvement in SS conditions. We present an anti-aging treatment regimen combining actives with published evidence of anti-inflammatory and barrier protection actions (Aquamuminist® and niacinamide), neurosensory function protection (Annona cherimola Fruit Extract) plus anti-aging activity based on a TGFβ2 peptide from the N. benthamiana plant focused on extracellular matrix (ECM) regeneration [16,20,26,27,31,37]. The results showed a significant improvement in skin aging parameters, such as firmness and elasticity at T14 and wrinkle depth at T28, evaluated by quantitative analysis and in accordance with wrinkle appearance referred by investigators and subjects. We hypothesize that this anti-aging effect is attributable to the synergistic mechanisms of the action of all the actives included in the cosmetic regimen. As the levels and activity of TGFβ decrease within the aging process and affect the components of the ECM, actives that regulate the synthesis of ECM proteins are especially useful. It is noteworthy that the TGFβ2 peptide present in the serum is a plant-derived TGFβ2 with proven activity in increasing epidermal thickness and improving neutral lipid levels in in vitro studies. In clinical trials, TGFβ2 showed an increase in skin elasticity, firmness, thickness, radiance and hydration, and reduced size, volume and depth of wrinkles without phototoxicity [32].

In addition, some studies reported that TRPV1 and Ca2+ regulate the expression and activation of matrix metalloproteinases (MMP-1) in UV-induced photoaging, leading to ECM degradation, wrinkle formation, laxity and skin fragility [39]. Xiao et al. suggested that the development of TRPV1-specific non-toxic inhibitors may be an effective strategy for the prevention of skin aging [39]. Annona cherimola fruit extract acts as a down-regulator of TRPV1 [16,31], and although its exact implications on skin aging have yet to be determined, it represents a cornerstone of treatment in the pathogenesis of sensitive skin, where neurogenic hyperreactivity is part of the process.

As for the parameters related to SS and its symptoms, a significant improvement in erythema and moisturization was obtained from T14 onwards, and a significant improvement in skin barrier function (<TEWL) was assessed at T28. Therefore, this sensitive skin treatment regimen was shown to induce greater skin resistance with a decrease in sensitivity and reactivity. We hypothesized a synergistic effect of the active ingredients present in the regimen [40]. Niacinamid could contribute to the improvement of these parameters due to its potential action on skin barrier function protection and decrease in coloration by inhibiting transference of melanin and antioxidative effects [27,28]. In addition, the combination of Solia Thermal Spring Water (Solia TSW) plus a diatom algae (Phaeodactylum tricornutum) extract had previously been reported to provide anti-inflammatory effects [16,20,26]. The
improvement of these parameters would also contribute to the better skin appearance perceived by both clinician and volunteers [41]. While traditional plant-derived ingredients are still extensively utilized in cosmetic formulations, they have limitations such as slow growth rates [42–44]. Marine-derived bioactive products offer viable alternatives. The use of algae as a natural resource is justified by the biological activities and potential health benefits of their isolated metabolites [45–49]. Algae, encompassing both macroalgae and microalgae, are aquatic photosynthetic organisms valued for their extensive bioactive compound profiles [45–49]. Macroalgae have attracted significant attention in the food, cosmetic, pharmaceutical, and nutraceutical sectors. The secondary metabolites derived from algae are known for their beneficial effects on the skin, including UV protection, moisturizers, antioxidants, and anti-aging treatments [48–50]. Microalgae are abundant in proteins, lipids, and vitamins, providing antioxidant, anti-aging, and regenerative properties, and are incorporated into skincare and haircare products [42,51]. The use of algal biocompounds or extracts in cosmetic formulations is increasing, providing environmentally sourced and safe materials; therefore, we found it interesting to discuss the clinical results of the present study where the treatment regimen included the use of diatoms. Diatoms are commonly used in the pharmaceutical and cosmetic industries [24,25,43,44]. In particular, *P. tricornutum* extracts are used for their anti-inflammatory and barrier function repair activities [25,26], with fucoxanthin being the bioactive molecule bearing the most relevant anti-inflammatory properties by controlling the levels of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α [26,27]. This is a marine diatom algae with documented benefits in sensitive skin treatments [26,27,37,52].

Previous results performed in SS subjects, with quantitative evaluations, showed a smaller decrease in erythema and R0 parameters (6% at T28 and 8% at T42 and 4.8% and 7.9%, respectively) [53].

We emphasize that with continued use of this treatment regimen throughout the study, all the evaluated parameters continued showing a progressive improvement by the end of the study. Furthermore, tolerance is a key factor when selecting a skincare regimen in a group of subjects with SS. We presumed that the different anti-inflammatory effects of the actives used in this protocol could contribute to the high tolerance of the present study regimen treatment.

The limitations of the study include the limited number of subjects recruited and the lack of vehicle control. This clinical study, as with others previously published in SS subjects, lacked blank samples/controls [53,54]. This would imply that, in the present study, the effects of factors other than the one being tested were not minimized. In addition, for further investigations, we would like to conduct longer follow-up evaluations that would help assess the long-term efficacy and tolerance of the regimen. It would also be interesting to include participants with diverse skin types and conditions. In the future, further studies on sensitive skin are needed to evaluate different skincare routines, with objectives encompassing not only soothing and moisturizing effects but also anti-aging goals.

4. Conclusions

This new treatment regimen, combining the cleanser, daily cream and serum applied at night, was well tolerated and received high satisfaction ratings. The regimen exhibited anti-aging efficacy in the analyzed parameters; however, these results will need to be confirmed in long-term controlled studies. Along with the anti-aging benefits, skin resistance could be increased, therefore improving the SS condition.

**Supplementary Materials:** The following supporting information can be downloaded at: [https://wetransfer.com/downloads/21bcb7ee1a22114749536c4ac2904a4220240717103805/d8d926f3c4207db2 efa448bb06d85d20240717103816/43cf30](https://wetransfer.com/downloads/21bcb7ee1a22114749536c4ac2904a4220240717103805/d8d926f3c4207db2 efa448bb06d85d20240717103816/43cf30) (accessed on 15 July 2024).

**Author Contributions:** All authors contributed to the conceptualization and methodology, formal analysis, and writing—review and editing; M.T.T. participated in the original draft preparation; M.J.G.-S. participated in the project administration; M.V. and V.N. contributed to the conceptualiza-
tion, methodology, formal analysis and writing; All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki. Ethical review and approval were waived for this study. According to the EU cosmetic Regulation no. 1223/2009, the cosmetic product must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use and must be assessed for its safety of use before human subjects are exposed to it, and as such, further ethical approval is not required.

**Informed Consent Statement:** Written informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The raw data supporting the conclusions of this article will be made available by the authors on request.

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**Abbreviations**


**References**


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