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Research Article

Efficacy of an Anti-ageing, Hydrating and Emollient Facial Cream Containing Standardized Snail Secretion (SCA), a Lipid Fraction of Pistacia Lentiscus Tree Extract (Lakesis) and a Shiitake Mushroom-based Extract (Actifcol): The "MOIRE Trial": A Multicenter, Observational, 12-Week, Real-life, Study on 550 Subjects with Moderate-Severe Chrono-ageing

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All the authors of the MOIRE study group contributed equally to the present study

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Abstract

Introduction: A new anti-ageing cream containing a standardized snail (*Cryptomphalus aspersa*) secretion (SCA 6%), the lipid fraction of *Pistacia Lentiscus* tree extract (Lakesis) and a shiitake mushroom-based extract (Actifcol), has been recently available (SCA+A+L cream). These three components have been demonstrated to have an antioxidant effect, improve fibroblast activity, reduce skin cellular senescence markers, reduce collagen degradation, and reactivate the KLOTHO and FOXO functions, two key proteins with anti-ageing activity. This peculiar composition can restart fibroblasts and keratinocyte's cellular activity and re-densify the dermis. So far, no clinical data regarding the anti-ageing effect of this cream is available.

Materials and methods: We assessed the clinical efficacy of SCA+A+L cream in subjects with moderate-severe facial chrono-ageing. The study was a multicenter, prospective, real-life study. A total of 550 subjects with moderate-severe facial chrono-ageing (490 women and 60 men, mean age 58 ± 9 years) were enrolled after their oral informed consent. A total of 34 Italian outpatient dermo-cosmetic services participated in the trial. The main inclusion criteria were age >48 years and moderate/severe skin chrono-ageing (Glogau score >2). The SCA+L+A cream was applied to the face once daily for 12 consecutive weeks. No additional facial topical cosmetic treatments were allowed during the study duration. The main study outcome was the evaluation of a Skin Ageing Global Score (SAGS) assessing elasticity, wrinkles, skin roughness, skin pigmentation, erythema, and skin pore. For each SAGS item, a score from 0 (no alteration) to 4 (severe alteration) was used. The SAGS calculation was performed by adding the score values of a single item (Maximum SAGS score: 24). SAGS score was evaluated at baseline, and after 12 weeks. At week 12 the investigators also evaluated the global firming, plumping and nourishing effects of the treatment.

Results: All 550 subjects concluded the trial. At baseline, the mean ± SD SAGS score was 11.7 ± 4.3. SAGS significantly correlated (R = 0.5; 95% CI from 0.42 to 0.55; p = 0.0001) with age with a slope of 0.23. After 12 weeks the SAGS score was significantly reduced to 7.1 ± 3.3 (p = 0.0001) (difference between means: -4.6; 95% CI of the difference: from-5.0 to -4.1), representing a 37% reduction. At week 12, SAGS significantly correlated with age with a slope of 0.16, a -31% lower than the baseline value. The efficacy of the tested cream was similar in women and men. The greatest efficacy was observed for skin roughness and skin pores scores. The best clinical response (good or very good), assessed by the physician, was observed for the firming (62%), plumping (70%) and nourishing (95%) effects. The product was well tolerated. No relevant side effects were reported.

Discussion: In this multicentre, real-life, trial conducted on 550 subjects with moderate-severe chrono-ageing we demonstrated that the daily use of a SCA+A-L anti-ageing cream significantly improves Skin Ageing Global score with good skin tolerability.

Keywords: Skin Ageing; *Cryptomphalus Aspersa* Standardized Secretion; KLOTHO Proteins; FOXO Proteins; Real-life Trial

Introduction

Skin ageing is characterized by relevant alterations mainly at the epidermal and dermal levels [1]. A new anti-ageing cream containing a standardized snail (*Cryptomphalus aspersa*) secretion (SCA 6%) [2], a shiitake mushroom-based extract [3] (Actifcol), and the lipid fraction of *Pistacia Lentiscus* [4] tree extract (Lakesis) has been recently available (SCA+A+L cream). Lakesis increases the synthesis of two relevant proteins involved in ageing processes: KLOTHO and FOXO [5-7]. Actifcol™ an advanced botanical ingredient is a shiitake mushroom-based extract, selected to boost the synthesis, improve the quality and reduce the deterioration of collagen, favouring, therefore, skin tensile strength [8]. These three components have been demonstrated to improve fibroblast

activity [9], reduce skin cellular senescence markers [10], reduce collagen degradation [11], and reactivate the Klotho and Foxo proteins functions [12,13]. This peculiar composition can restart fibroblasts and keratinocytes cellular activity and re-densify the dermis. So far, no clinical data regarding the anti-ageing effect of this cream is available.

Study Aim

We assessed the clinical efficacy of SCA+A+L cream in subjects with moderate-severe facial chrono-ageing. The study was a multicentre, prospective, real-life study.

Material and Methods

Subjects

The study was conducted between June 2021 and April 2022. A total of 34 Italian private outpatient dermatology services participated in the trial. A total of 550 subjects with moderate-severe facial chrono-ageing (490 women and 60 men, mean age 58 ± 9 years; age range 48-87 years) were enrolled after their oral informed consent. The main inclusion criteria were age >50 years and moderate/severe skin chrono-ageing (Glogau score >2).

Study Outcomes

The main study outcome was the evaluation of a Skin Ageing Global Score (SAGS) assessing elasticity, wrinkles, skin roughness, skin pigmentation, skin redness, and pores. For each SAGS item, a score from 0 (no alteration) to 4 (severe alteration) was used. The SAGS calculation was performed by adding the score values of a single item (Maximum SAGS score: 24). SAGS score was evaluated at baseline, and after 12 weeks. At week 12 the investigators also evaluated the global firming, plumping and nourishing effects of the treatment.

Treatment

The SCA+L+A cream was applied on the face once daily for 12 consecutive weeks using 1 Fingertip Unit (0.5g of product) per application. No additional facial topical cosmetic treatments were allowed during the study duration.

Statistical Analysis

GraphPad Prism statistical software (version 9) was utilized for data analysis. Continuous variables were expressed as mean ± standard deviation (SD). The primary endpoint of the trial was the evolution of the paired t-test, the Wilcoxon test, the ANOVA test and the Chi-Square test were used for the analysis of the study outcomes. According to the nature of the trial (real-life, open not controlled) no formal sample size calculation was performed. A p-value of <.05 was considered significant.

Results

All 550 subjects concluded the trial. Table 1 shows the characteristics of the subject at baseline. At baseline, the mean ± SD SAGS score was 11.7 ± 4.3.

Total subjects	**550**
Men	60 (11%)
Women	490 (89%)
Age in years; mean ± SD age (range)	58 ± 9 (48-87)
SAGS score; mean ± SD (range)	11.7 (4.3) (2-24)
Subjects (%) with SAGS score <10	32%
Subjects (%) with a SAGS score of 10-20	64%
Subjects (%) with a SAGS score >20	4%

Table 1: Subjects' demographic and clinical characteristics at baseline.

Sixty-four percent of subjects have a SAGS score between 10 and 20; four percent have a SAGS score >20. SAGS significantly correlated (R = 0.5; 95% CI from 0.42 to 0.55; p = 0.0001) with age with a slope of 0.23. At week 12, SAGS significantly correlated with age with a slope of 0.16, a -31% lower than the baseline value (Figure 1).

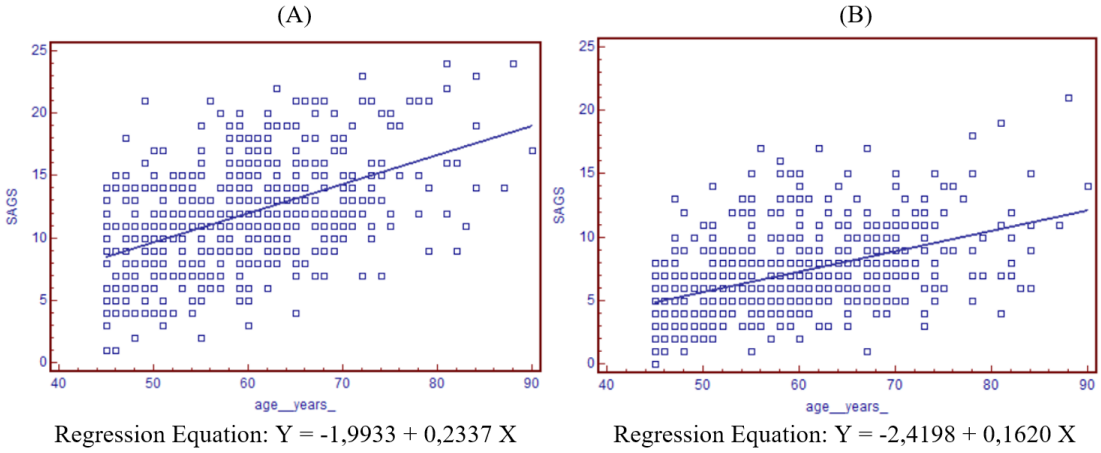

Figure 1: Scattered diagrams for regression analysis between age and SAGS score; (A: Baseline; (B: After treatment).

After 12 weeks the SAGS score was significantly reduced to 7.1 ± 3.3 (p = 0.0001) (difference between means: -4.6; 95% CI of the difference: from -5.0 to -4.1), representing a 37% reduction (Figure 2).

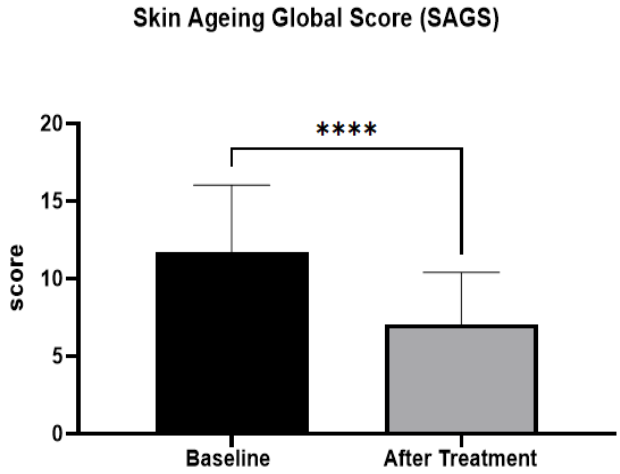

Figure 2: Evolution of SAGS Score from baseline to week; **** = P < 0.0001; Wilcoxon paired Test.

The efficacy of the tested cream was similar in women and men. Table 2 reports the evolution of each item of the SAGS score (elasticity, wrinkles, roughness, skin pigmentation, skin redness and pores) from baseline to week 12.

Parameter	Baseline	After Treatment	% Improvement	P-value
Elasticity	2.2 (1.0)	1.3 (0.8)	41%	0.001
Wrinkles	2.3 (0.9)	1.6 (0.7)	31%	0.001
Roughness	2.1 (1.0)	1.1 (0.7)	48%	0.001
Skin Pigmentation	2.0 (0.9)	1.5 (0.9)	25%	0.001
Skin redness	1.3 (1.0)	0.7 (0.8)	47%	0.001

Pores	1.7 (1.1)	0.9 (0.9)	47%	0.001

Table 2: Evolution of SAGS scores for each item (mean (SD).

The greatest efficacy in terms of % improvements was observed for skin roughness (48%) and skin pores scores (47%). The best clinical response (good or very good), assessed by the physician, was observed for the firming (62%), plumping (70%) and nourishing (95%) effects. The product was well tolerated. No relevant side effects were reported.

Discussion

Like the entire organism, also skin is subject to the intrinsic ageing process (the so-called chrono-ageing) [14]. However, skin ageing is also influenced by exogenous factors, mainly chronic sun exposure (the so-called photo-ageing) [15]. It has been estimated that 80% of facial skin ageing is attributable to UV exposure [16]. In the ageing process, the formation of reactive oxygen species and the induction of matrix metalloproteinases represent the main pathogenetic mechanisms [17]. At the dermal level senescence of fibroblasts with reduced collagen production and accumulation of fragmented collagen fibrils are the main features of skin ageing [18]. The aged skin is also characterized by xerosis and skin barrier function alteration favouring the loss of elasticity and reduced tone [19]. Increased compaction of stratum corneum, increased thickness of granular cell layer, reduced epidermal thickness and reduced epidermal mucin content are the most common histological alteration of aged skin [20]. Skin products with emollient, regenerating and UV-protecting action are widely used in anti-ageing dermo-cosmetic protocols [21]. Draelos has suggested following a "pyramid" therapeutic approach in fighting the skin ageing process: the three steps of this approach are focused on protection, renewal, activation and regeneration. The cream evaluated in this trial has three main components: a standardized snail (*Cryptomphalus aspersa*) secretion (SCA), a shiitake mushroom-based extract (Actifcol), and the lipid fraction of *Pistacia Lentiscus* tree extract (Lakesis). For all these components several published data are available showing relevant effects on ageing processes [22,23]. SCA is characterized by regenerative, antioxidant, emollient and moisturizing activities [24]. In more detail, SCA can improve fibroblast growth, increase extracellular matrix production and reduce the activity of matrix metalloproteinase [25]. All these actions could explain the anti-ageing activity of this extract. Lakesis™ increases the synthesis of two relevant proteins involved in ageing processes: Foxo and Klotho [26]. Foxo can activate the transcription of genes involved in cellular detoxification and DNA repair [27]. With advancing age, the inactive form of Foxo increases and this is caused by the activity of an anti-Foxo protein the AKT factor [28]. However, AKT could be inhibited by a specific protein, Klotho [29]. The Klotho protein is involved in many signalling pathways leading to anti-ageing effects with an improvement of cellular functions. The Klotho synthesis is reduced with age: for example, fibroblast Klotho expression at age 55 is reduced by 59% in comparison with fibroblasts of an 18-year-aged subject [30]. In vitro data demonstrate that Lakesis in 55-years fibroblast can increase Klotho expression at the same level of 35 years old fibroblast [31]. Therefore, dermo-cosmetic strategies improving the expression of Klotho synthesis could be relevant anti-ageing tools. Finally, the tested cream contains also Actifcol™ an advanced botanical ingredient. Actifcol is a shiitake mushroom-based extract, selected to boost the synthesis, improve the quality and reduce the deterioration of collagen, favouring skin tensile strength. An improvement in collagen quality is known to imply a firming effect on the skin [32]. The MOIRE trial has shown that the use of a cream containing SCA, Lakesis™ and Actifcol™ for 12 weeks is associated with a clinically relevant improvement of facial skin appearance in subjects with moderate-severe skin ageing. The present study is an open uncontrolled trial with the limitation of this kind of study. However, we adopted a "real-life" strategy approach. The "real-life" trials have the main advantage to be commonly carried out in a large sample of subjects and enrolling patients' representative of the everyday clinical routine [33]. For this reason, real-life studies are thought to have relevant external validity [34]. Our study has enrolled 550 subjects; the high statistical direct correlation between the subjects' age and the SAGS score both at baseline and after treatment support, the good quality of data collected.

Conclusion

In this multicentre, real-life, trial conducted on 550 subjects with moderate-severe chrono-ageing, we demonstrated that the daily use of a SCA+A+L anti-ageing cream significantly improves Skin Ageing Global score with good skin tolerability.

Authors Contribution

All the investigators of The MOIRE study group contributed equally to the enrolment and the visits of the participating subjects. All authors had full access to all the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work, and have given their approval for this version to be published.

Acknowledgement

The authors thank the participants of the study

Conflict of Interest

Massimo Milani declares that he is employed by Cantabria Labs Difa Cooper. All the other authors have nothing to disclose.

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