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Research Article

A Topical Scalp Serum Containing Adenosine, MgSO$_4$, Vitamin CG, and Pre- and Probiotic Fractions Reduces Discomfort and Associated Symptoms of Sensitive Scalp

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Purpose. Sensitive scalp (SScalp) is characterized by abnormal and nociceptive sensations, such as stinging and itching, that lead to scalp discomfort. This study assessed the benefit of a once-daily serum containing Adenosine, Magnesium Sulfate (MgSO$_4$), Vitamin C Glucoside (CG), and pre- and probiotic fractions in subjects with SScalp. *Methods*. An open-label, single center study in adult subjects with a Global Scalp Discomfort (GSD) score of ≥8 (0–27), defined as the sum of individual symptom scores (0–9) for itching, stinging, and warming sensations. The frequency of scratching was self-declared. Evaluations were performed immediately after the 1st application (D0Timm) and at D21, during which the cosmetic acceptability was additionally assessed. Transepidermal water loss and skin hydration were assessed at baseline, D21, and D28. Squalene (SQ) and SQOOH were analyzed at D0T0, D21T0, and D28. Tolerance was assessed throughout the study. *Results*. 42 subjects (30 women and 12 men) participated in this study. The mean age was 44.0 ± 13.0 years. At baseline, the mean GSD was 13.9 ± 3.28. The GSD and symptoms significantly ($p < 0.0001$) improved at D0Timm and lasted until the end of the study (D28), with insignificant worsening. There was a significant reduction of SQOOH at D21 and D28. Subject satisfaction was high, associated with a good tolerance. A similar and significant ($p < 0.0001$) improvement was observed for subjects with more severe symptoms and a GSD score ≥14 at baseline. *Conclusion*. The topical serum significantly reduces SScalp, global discomfort, and oxidative stress and is beneficial in the management of sensitive scalp. This TRIAL is registered with NCT05630027.

1. Introduction

Sensitive skin (or reactive/hyperreactive skin) is reported in up to 50% of the European population, with a higher incidence in women [1]. The sensitive skin syndrome is characterized by abnormal and unpleasant sensations, such as warming, stinging, and itching, and manifests as exaggerated responses to stimuli [1, 2]. Different factors, such as ultraviolet radiation, heat, cold, wind, cosmetics, soap, water, and pollution, have been reported to trigger the condition. Moreover, psychological (stress) or hormonal (menstrual cycle) factors may also play a role. Erythema is frequently, but not necessarily, associated with sensitive skin [3–5]. The syndrome is frequently reported for the face but is also present in other localizations, mainly the hands, and often the scalp and feet [6]. An incidence of 44% subjects with sensitive scalp (SScalp) has recently been observed in France [6, 7]. One-third of the population interviewed reported SScalp. Interestingly, the majority declared that the intensity of SScalp increases with age.

To date, its pathophysiology is still insufficiently understood [7]. Berardesca et al. classified sensitive skin into 3

different types, based on their physiological parameters [8]. Type I was defined as the low barrier function group, Type II as the inflammation group with normal barrier function and inflammatory changes, and Type III as the pseudo-healthy group in terms of normal barrier function and with no inflammatory changes. Compared to nonsensitive skin, a high density of nerve growth factor has been observed in the stratum corneum of all 3 types. Moreover, in types II and III, sensitivity to electrical stimuli was reported to be high, suggesting that the hypersensitive reaction of sensitive skin is closely related to the nerve fibers of the epidermis [8, 9]. Furthermore, in subjects with SScalp, an increased average temperature and increased heat sensation, dandruff, erythema of the scalp, past history of atopy, history of hair loss, and medical history of scalp disease were described [10].

Recent research has shown that sensitive skin presents with a disrupted barrier function, abnormal sebum quantity and composition, and a disturbed microbiome, which might be one of the main causes [2, 11]. In 2017, Rukwied reported that extremely high thresholds to thermal and mechanical stimuli were recorded in patients with SScalp at the vertex, compared to occipital or temporal scalp regions, or the hairy skin of other body regions, such as the trunk or distal extremities [12].

The serum tested herewith (Dercos Scalp Control Microbiome Science Complex, Laboratoires Vichy, France, hereafter topical serum) contains Adenosine, $MgSO_4$, Vitamin CG, and pre- and probiotics. Adenosine and $MgSO_4$ soothe the skin (unpublished data). Vitamin CG has an antioxidative and glycerin a moisturizing effect [13–15]. Pre- and probiotics are known for helping to rebalance the scalp microbiome [16].

The aim of this study was to assess the soothing effect of a novel topical serum in adult subjects with SScalp after 3 weeks of daily treatment followed by a one-week follow-up.

2. Materials and Methods

This open-label, observational study conformed to Good Clinical Practices and the principles of the Declaration of Helsinki, received ethics committee approval from the independant Ethics Committe of Bordeaux, France, (n° 20/ 371 01/09/2020), and was conducted at Eurofins EVIC, Bordeaux, France, between September and November 2020, according to French guidelines for the conduct of this type of study. The study received internal ethics committee approval in September 2020. All invited and participating subjects selected from the investigational site volunteer panel provided written informed consent prior to entering the study.

The study is registered in the ClinicalTrial database (NCT05630027).

Adult subjects aged between 18 and 60 years, with a skin phototype between I and V, with all scalp skin types and with a self-assessed Global Scalp Discomfort (GSD) score of at least 8 (0–27) at baseline/D0, and with no dandruff, were suitable for this study. The GSD was defined as the sum of the 3 individual scores of itching, stinging, and warming sensation, each rated on a scale from 0 = none to 9 = very much. Moreover, hair length was to be at least 2 cm.

The study included a treatment period of 21 days and a follow-up period of 7 days. At baseline/D0 and D21, participating subjects were asked to apply the serum at the investigational site under the supervision of a technician. On all other days during the treatment period, subjects were asked to apply the serum on the entire scalp in the evening. Subjects were asked to wash their hair 2 to 3 times per week using a mild shampoo between D1 and D19, as well as on the days prior to study visits (D-1, D20, and D27).

Itching, stinging sensations, warming sensations, and scratching were assessed by the subjects for the entire scalp at D0T0 (immediately before 1st application), D0Timm (immediately after application), D21T0, D21Timm, and at D28, using a 10-point, self-grading scale (0 = none, 9 = very much), as well as every evening at home between D1, D20, D22, and D27. Moreover, subjects were invited to rate the efficacy and cosmetic acceptability on a Likert scale from "totally agree" to "totally disagree" of the serum at D0Timm and at D21Timm using specific questionnaires which were developed for this study; these questionnaires are available upon request from the corresponding author.

The investigators assessed transepidermal water loss (TEWL) on an identified close-cut mini-area of about $2.25 \, cm^2$ at D0T0 (immediately before 1st application), D21Timm (immediately after first application), and at D28, using a Vapometer® SWL4001 (Delfintech, Kuopio, Finland), and the moisturizing effect on D0T0, D0Timm, D21T0, D21Timm, and D28, using a Corneometer® (Courage & Khazaka Electronic, Köln, Germany).

Biomarkers (squalene (SQ) and squalene monohydroperoxide (SQOOH)) sampled from a defined area of the scalp were taken through successive contacts between silica rods (Synelvia™, Labège, France) at D0T0, D21T0, and D28. Prior to the analysis, rods were stored at −20°C, using published analytical methods [17, 18]. In brief, after organic extraction from the rods, SQ was analyzed by gas chromatography coupled to mass spectrometry (GC-MS). SQOOH was isolated and quantified by liquid chromatography coupled to mass spectrometry (LC-MS).

Local tolerance and safety were assessed throughout the study.

SAS software and SPSS version 19 were used for statistical analysis purposes.

Quantitative variables were summarized using mean, median, minimum, and maximum, as well as measures of dispersion such as the standard deviation. Qualitative variables were described as number and percentage of the different response modalities; 95% confidence intervals were calculated, as required. All statistical analyses were performed at a 5% significance using 2-sided tests, except normality testing at 1% threshold (Shapiro–Wilk test). Evolution over time was investigated by using either Student's paired t-test or the Wilcoxon signed rank test. The count and percentage of subjects responding to questionnaires were provided for each time point.

Subgroup analyses were performed for symptoms, with scores ranging from 3 to 6 and 7 to 9 and GSD scores ranging from 8 to 13, 14 to 21, and 22 to 27.

3. Results and Discussion

3.1. Results. Overall, 42 subjects, 30 women and 12 men, participated in this study. The mean age was 44.0 ± 13 years. A majority (57%) had a normal scalp skin type; 67% had dry hair, 76% mid-short or half long, and 60% straight hair. The mean GSD score was 13.9 ± 3.28. Detailed patient demographic and baseline data are provided in Table 1.

A once-daily application for 21 days of the topical serum significantly reduced ($p < 0.0001$) global discomfort as well as itching, stinging, warming sensation, and scratching, as early as D0Timm.

The mean GSD score decreased by 12.38 points (confidence interval (CI) 95% [−13.16; −11.60]), corresponding to a reduction of 89%. The mean score for itching decreased by 4.76 (CI95% [−5.12; −4.46]), corresponding to a reduction of 89%, that of stinging by 4.08 (CI95% [−4.42; −3.73]), corresponding to a reduction of 89%, that of warming sensation by 3.51 (CI95% [−3.77; −3.25]), corresponding to a reduction of 90%, and that of scratching by 4.96 points (CI95% [−4.96; −4.63]), corresponding to a reduction of 89%. Even though a remanence was observed, the difference between D28 and baseline/D0 remained statistically significant ($p < 0.0001$) regarding global discomfort and all symptom scores.

Evolution over time of the GSD and patient-reported symptom scores is provided in Figures 1(a) and 2, respectively.

For the TEWL, no statistically significant differences to D0T0 (17.10 ± 5.74 g·m^{-2}·h^{-1}) were observed at D27T0 (17.91 ± 5.35 g·m^{-2}·h^{-1}) or D28 (17.63 ± 4.66 g·m^{-2}·h^{-1}).

Except at D0Timm (40.08 ± 15.45 a.u. (arbitrary unit), $p = 0.0001$), no statistically significant differences to D0T0 (34.20 ± 14.49 a.u.) were observed for the moisturizing effect at defined time points.

The subgroup analysis performed in subjects with symptom scores between 7 and 9 confirmed the continued and significant ($p < 0.0001$) improvement from D0T0 in 6 subjects with itching and 11 subjects with scratching, as well as that of the GSD (20 subjects with a score ranging from 14 to 21, Figure 1(b)).

At D21T0 (193.0 ± 115.8 μg/mg) and D28 (195.8 ± 118.4 μg/mg), no significant difference compared to D0T0 (192.0 ± 123.7 μg/mg) was observed for the quantity of SQ. However, the quantity of SQOOH was significantly (−10%, $p = 0.0061$) reduced at D21T0 (241.6 ± 196.3 μg/mg vs 269.7 ± 232.4 μg/mg at D0T0), only.

The SQOOH/SQ ratio significantly decreased between D0T0 (269.7 ± 232.4) and D21T0 (241.6 ± 196.3) ($p = 0.0061$).

Immediately after the first application, 95% of the subjects stated that the topical serum provided a cooling sensation, 74% that their scalp felt hydrated, 60% that their scalp breathed better, and 29% that hair and scalp were better protected from external aggressions and that the serum left the hair shiny. In total, 55% stated that itching and stinging sensations had decreased, 50% stated that "tightness" sensations had reduced, and 81% stated that warming sensations had reduced.

TABLE 1: Subject demographic and baseline data.

Total number of subjects	N	42
Age (years)	Mean	44
	SD	13
	Median	48
	Min	18
	Max	60
Sex, n (%)	Female	30 (71%)
	Male	12 (29%)
Phototype, n (%)	I	1 (2%)
	II	12 (29%)
	III	21 (50%)
	IV	7 (17%)
	V	1 (2%)
Type of skin on scalp	Dry	7 (17%)
	Normal	24 (57%)
	Oily	11 (26%)
Hair type (roots + tips)	Dry	28 (67%)
	Normal	13 (31%)
	Oily	1 (2%)
Hair length	Mid-short	16 (38%)
	Half-long	16 (38%)
	Long	10 (24%)
	Very long	0 (0%)
Hair texture	Straight	25 (60%)
	Wavy	12 (29%)
	Curly	5 (11%)
	Very curly	0 (0%)
Scalp sensitivity score	Mean	13.90
	SD	3.28
	Median	13.50
	Min	8.00
	Max	22.00

N, n: number; SD: standard deviation.

After 21 days of daily treatment, subjects highly appreciated the efficacy and product properties. Figure 3 provides a summary of results for D21.

Local tolerance was very good, with mild pruritus lasting 10 minutes immediately after application at D0 and a moderate sensation of warmth lasting 5 minutes immediately after application, both at D0 and in one subject, respectively. A third subject reported mild stinging for 2 to 3 minutes after application at home from D1 to D5. None of these adverse events led to the discontinuation of the tested product.

3.2. Discussion. Results from this open-label study provided confirmation that the tested serum efficiently and safely reduces subject-reported symptoms including itching, stinging, warming sensation, and scratching of SScalp and significantly improves global discomfort (all $p < 0.0001$), even in subjects with severe symptoms or global discomfort. Skin hydration had significantly ($p = 0.0001$) and immediately improved after the first application while only a nonsignificant reduction of the TEWL was observed. At the end of the study, the SQOOH/SQ ratio had significantly decreased ($p = 0.0061$).
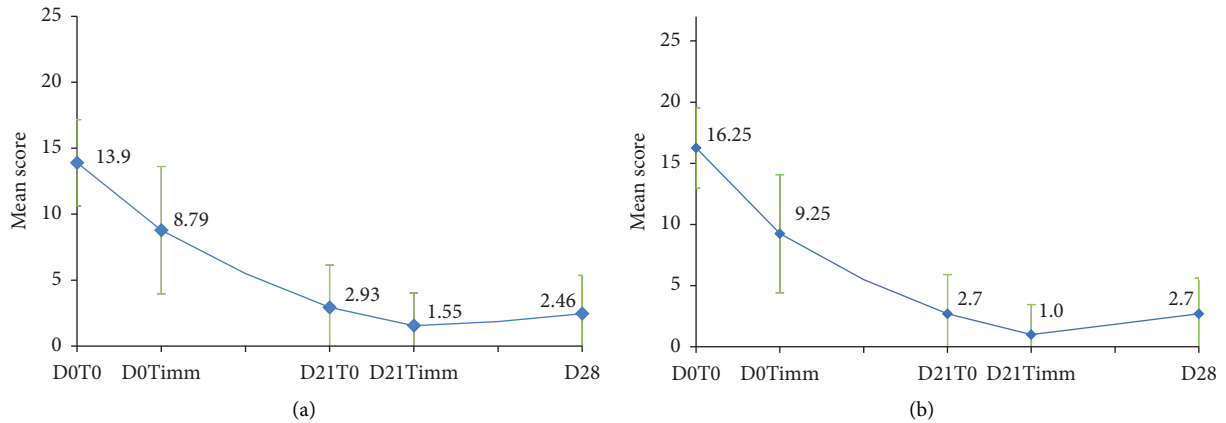
FIGURE 1: Evolution of the mean Global Scalp Discomfort score over time. (a) Study population. (b) Population with a symptom score between 14 and 21. Improvement from D0T0 was statistically significant ($p < 0.0001$) at all post-baseline visits in the overall study population and subgroup.
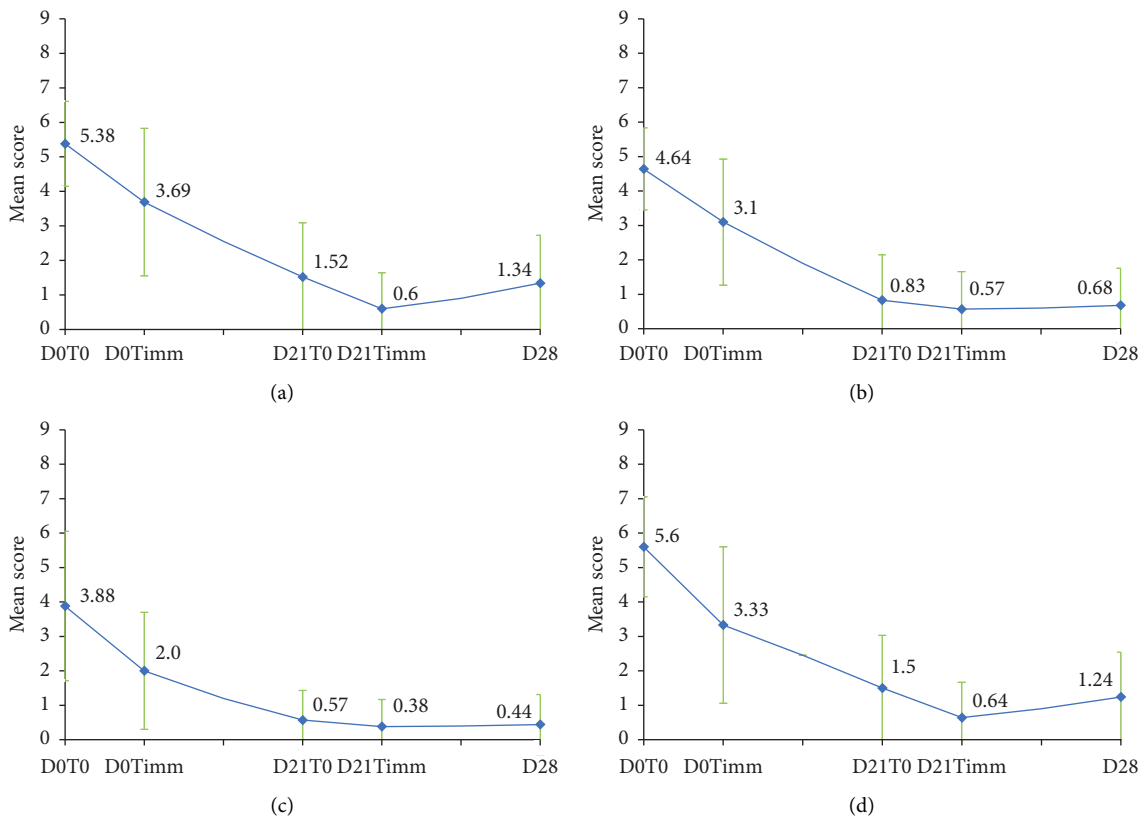

FIGURE 2: Improvement of the mean score for subject-reported symptoms over time. (a) Itching sensation. (b) Stinging sensation. (c) Warming sensation. (d) Scratching of the scalp. Improvement from D0T0 for all subject-reported symptom scores was statistically significant ($p < 0.0001$) at all post-baseline visits.

Thus, in reducing SQOOH, the tested topical serum reduces oxidative stress by rebalancing the sebum composition. According to the subjects, the serum soothes the skin and improves the scalp quality, confirming that sensitive scalp may be linked to an alteration of the surface sebum composition [2, 11, 19].

One-third of the subjects believed that their skin was better protected against exposome factors. This may be due to the restored and a better protected skin barrier.

A limitation may be the very short follow-up period of one week. Extending this period might have provided further insight of the prolonged treatment outcome of the
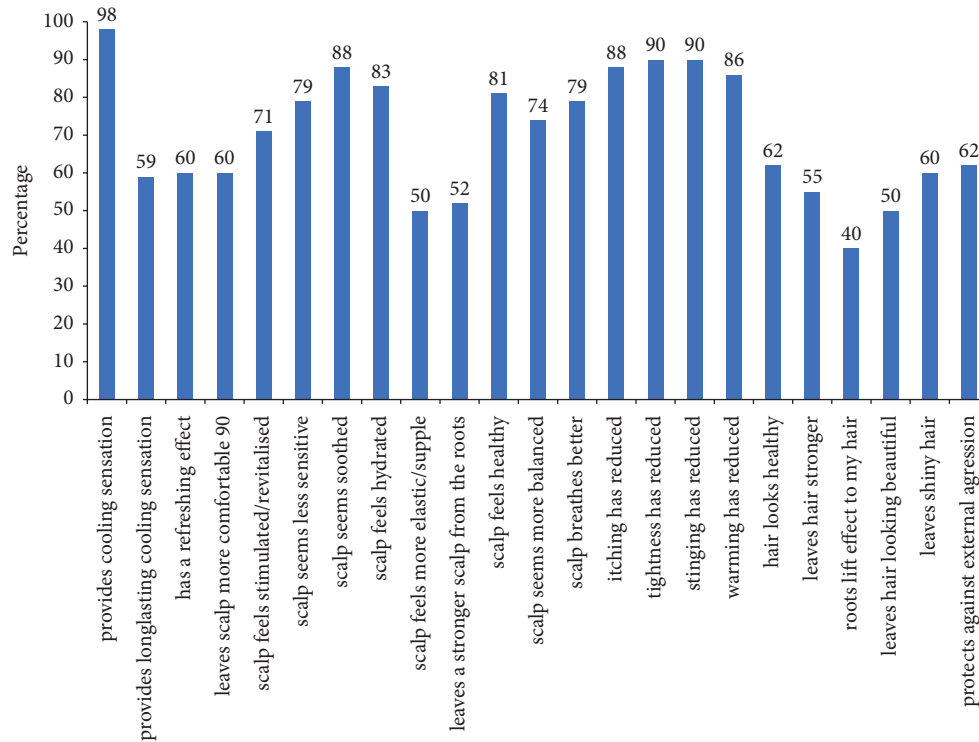
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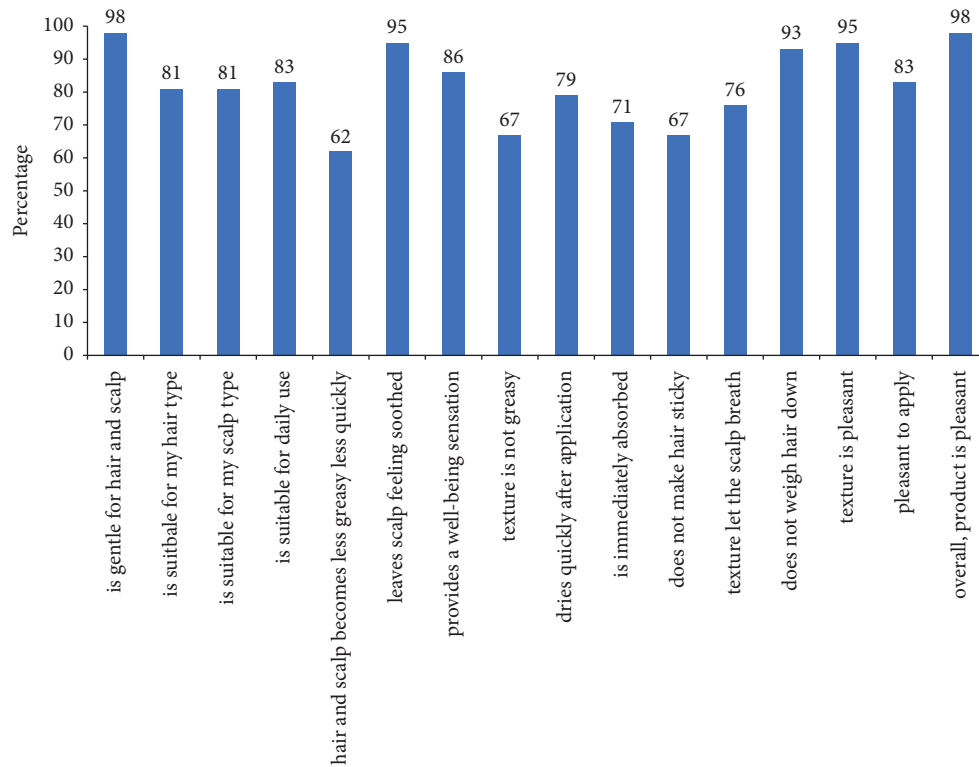
(b)

FIGURE 3: Subject appreciation of cosmetic qualities and efficacy of the topical serum after 21 days of daily use. (a) Subject appreciation of cosmetic qualities. (b) Subject appreciation of efficacy.

topical serum. Moreover, the limited results for TEWL and subjects' perception may be due to the small sample size and, potentially, to the duration of the application as well as to the fact that included subjects were not limited to those with an altered skin barrier, thus biasing the studied population. Further specific research may have to be conducted in a more important sample of subjects with SScalp to confirm that the serum also reduces TEWL and increases skin hydration, thus confirming this aspect of SScalp.

The tested serum was very well tolerated, and subjects highly appreciated its efficacy and cosmetic qualities.

Despite the limits such as a small sample size and the fact that the study was unable to show that TEWL had decreased, study objectives assessing the improvement of global discomfort and related patient-reported symptoms, as well as reducing oxidative stress, were achieved.

4. Conclusions

The tested topical serum significantly reduces SScalp global discomfort associated with subject-reported symptoms, even when severe, as well as oxidative stress, and is beneficial in the management of sensitive scalp.

Data Availability

The corresponding author will share upon reasonable request the study protocol and all data collected and statistically analyzed in relationship with this study, except identified participant data for one year after publication of this manuscript.

Ethical Approval

According to local legal requirements for the conduct of cosmetic studies, this clinical study did not require ethics committee approval.

Consent

All participants consented to participate.

Conflicts of Interest

All authors except Françoise Magne are employees of L'Oréal Group. Françoise Magne has no COI to disclose.

Acknowledgments

References

[1] L. Misery, S. Ständer, J. C. Szepietowski et al., "Definition of sensitive skin: an expert position paper from the special interest group on sensitive skin of the international forum for the study of itch," *Acta Dermato-Venereologica*, vol. 97, no. 1, pp. 4–6, 2017.

[2] L. Ma, A. Guichard, Y. Cheng et al., "Sensitive scalp is associated with excessive sebum and perturbed microbiome," *Journal of Cosmetic Dermatology*, vol. 18, no. 3, pp. 922–928, 2019.

[3] M. A. Farage and H. I. Maibach, "Sensitive skin: closing in on a physiological cause," *Contact Dermatitis*, vol. 62, no. 3, pp. 137–149, 2010.

[4] A. M. Kligman, I. Sadiq, Y. Zhen, and M. Crosby, "Experimental studies on the nature of sensitive skin," *Skin Research and Technology*, vol. 12, no. 4, pp. 217–222, 2006.

[5] L. Ma, A. Guichard, P. Humbert et al., "Evaluation of the severity and triggering factors of sensitive scalp in Chinese females," *Journal of Cosmetic Dermatology*, vol. 15, no. 3, pp. 219–225, 2016.

[6] C. Saint-Martory, A. M. Roguedas-Contios, V. Sibaud, A. Degouy, A. M. Schmitt, and L. Misery, "Sensitive skin is not limited to the face," *British Journal of Dermatology*, vol. 158, no. 1, pp. 130–133, 2008.

[7] L. Misery, V. Sibaud, M. Ambronati, G. Macy, S. Boussetta, and C. Taieb, "Sensitive scalp: does this condition exist? An epidemiological study," *Contact Dermatitis*, vol. 58, no. 4, pp. 234–238, 2008.

[8] E. Berardesca, M. Farage, and H. Maibach, "Sensitive skin: an overview," *International Journal of Cosmetic Science*, vol. 35, no. 1, pp. 2–8, 2013.

[9] T. Yokota, M. Matsumoto, and T. Sakamaki, "Classification of sensitive skin and development of a treatment system appropriate for each group," *IFSCC Magazine*, vol. 6, pp. 303–307, 2003.

[10] K. H. Park, J. Kim, B. Oh, E. Lee, J. Hwang-Bo, and J. Ha, "Evaluation of factors triggering sensitive scalp in Korean adult women," *Skin Research and Technology*, vol. 25, no. 6, pp. 862–866, 2019.

[11] H. L. Keum, H. Kim, H. J. Kim et al., "Structures of the skin microbiome and mycobiome depending on skin sensitivity," *Microorganisms*, vol. 8, no. 7, p. 1032, 2020.

[12] R. Rukwied, "[Physiology of the scalp]," *Hautarzt, Der*, vol. 68, no. 6, pp. 431–436, 2017.

[13] J. M. Pullar, A. C. Carr, and M. C. M. Vissers, "The roles of vitamin C in skin health," *Nutrients*, vol. 9, no. 8, p. 866, 2017.

[14] S. Verdier-Sévrain and F. Bonté, "Skin hydration: a review on its molecular mechanisms," *Journal of Cosmetic Dermatology*, vol. 6, no. 2, pp. 75–82, 2007.

[15] N. C. Chandrasekaran, W. Y. Sanchez, Y. H. Mohammed, J. E. Grice, M. S. Roberts, and R. T. Barnard, "Permeation of topically applied Magnesium ions through human skin is facilitated by hair follicles," *Magnesium Research*, vol. 29, no. 2, pp. 35–42, 2016.

[16] F. H. Al-Ghazzewi and R. F. Tester, "Impact of prebiotics and probiotics on skin health," *Beneficial Microbes*, vol. 5, no. 2, pp. 99–107, 2014.

[17] K. Nakagawa, D. Ibusuki, Y. Suzuki et al., "Ion-trap tandem mass spectrometric analysis of squalene monohydroperoxide isomers in sunlight-exposed human skin," *Journal of Lipid Research*, vol. 48, no. 12, pp. 2779–2787, 2007.

[18] W. M. Winnik and K. T. Kitchin, "Measurement of oxidative stress parameters using liquid chromatography-tandem mass spectroscopy (LC-MS/MS)," *Toxicology and Applied Pharmacology*, vol. 233, no. 1, pp. 100–106, 2008.

[19] A. Guichard, L. Ma, Y. Tan et al., "What if scalp flora was involved in sensitive scalp onset?" *International Journal of Cosmetic Science*, vol. 38, no. 4, pp. 429-430, 2016.