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ORIGINAL CONTRIBUTION

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Polar lipids from wheat extract oil improve skin damages induced by aging: Evidence from a randomized, placebo-controlled clinical trial in women and an ex vivo study on human skin explant

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Abstract

Background: Polar lipids from wheat (*Triticum vulgare/aestivum*) extract oil (WEO) are known to improve skin hydration.

Aims: These studies aimed to assess WEO benefits on the skin appearance of middle-aged women.

Methods: A double-blind, randomized, placebo-controlled clinical study was carried out on 64 healthy women, aged from 45 to 60 years, to investigate antiaging effects and benefits for the skin. The study lasted 20 weeks including 12 weeks of oral supplementation with WEO or placebo and 8 weeks of follow-up. Wrinkles in the "crow's-feet" area were evaluated by the Lemperle score. Skin hydration was measured using a corneometer, while roughness and radiance were determined by clinical scoring. Collagen content was quantified in human skin explants exposed to ultraviolet (UV) irradiations and treated with WEO or vehicle control.

Results: Compared to the placebo group, the Lemperle score was significantly reduced in the WEO group between W0 and W8 to reach a clinically significant 1 grade at W12. Facial hydration was significantly improved in the WEO group from W0 to W12, whereas leg hydration was significantly increased after 4 weeks and lasted throughout the supplementation period. Skin roughness and radiance were also significantly improved from W0 to W8 in the WEO group compared to placebo group. A higher collagen content was measured in the UV-irradiated skin explants treated with WEO compared to the untreated ones.

Conclusion: These results confirmed the moisturizing effect of WEO and, for the first time, revealed its potential antiaging properties.

KEYWORDS

collagen, hydration, Lemperle score, polar lipids, wheat (*Triticum Vulgare aestivum*), wrinkles

Boisnic and Keophiphath equally contributed to this study.

1 | INTRODUCTION

Skin aging is genetically programmed. It accelerates through accumulation of biological events and is a result of two concomitant physiological processes.[1] Intrinsic aging comes from a slow degeneration of the tissue mainly related to reduce estrogen production, as observed in menopausal women,[2] whereas extrinsic aging is linked to environmental factors. Recently, a new concept of "skin aging exposome" has been defined as the cumulative measurement of environmental events associated with biological responses during life, including exposure to both external and internal factors such as ultraviolet (UV) exposition, nutrition, lifestyle, stress, or lack of sleep.[3] At a macroscopic level, skin aging is characterized by the progressive appearance of wrinkles, dermal atrophy due to collagen loss, degeneration in the elastic fiber network, and loss of hydration and radiance.[4] These alterations are linked to molecular, cellular, and tissue modifications of the dermis such as the reduction in the size and number of fibroblasts with substantial matrix remodeling, resulting from both a reduced production of matrix proteins and an increase in their degradation by metalloproteinases.[5,6] A causal link between nutrition and skin quality is strongly supported by the fact that cutaneous injuries such as dermatitis and depigmentation appear in some nutritional deficiencies.[7] Therefore, some diets and nutritional supplements could play an active role in skin physiology and influence its aging. Several studies have revealed the benefits of plant extracts in the prevention and improvement of skin aging symptoms.[8-10]

A lipid extract prepared from the endosperm of wheat grain (*Triticum vulgare/aestivum*) and commercially available as Lipowheat® (Robertet, France) or Ceratiq® (distributed by PLT Health Solutions)[11] is one of the first plant extracts rich in polar lipids (PoLs) used in dietary supplements for its skin moisturizing benefits. This extract has been developed in two forms, a wheat extract oil (WEO) and a wheat extract powder (WEP) to meet the galenic requirements of the industry. The composition of wheat grain lipid extracts as well as many other plant extracts is highly complex. A recent analytical study partially elucidated the lipid composition of WEO as primarily phospholipids (PLs), glycolipids (GLs), and sphingolipids (SLs).[12]

Polar lipids are complex lipids with physiological and technological properties widely studied in biology, nutrition, and cosmetics.[13,14] PoLs are also potent vectors of active molecules and show emulsifying and thickening properties.[11] Furthermore, as major components of cell membranes, they may also have beneficial effects by preventing and improving skin aging. For example, ceramides from the SL family represent 35%-40% of the lipid cement ensuring cell cohesion in the *stratum corneum*.[15-17] These ceramides are highly involved in skin hydration by limiting excessive water loss from the epidermis.[18]

Both WEO and WEP have significant clinical effects on the skin. A recent clinical study showed a significant increase in skin hydration with clinical improvements (flakiness, roughness, and redness) after 3 months of WEO supplementation.[19]

In this article, we aimed to highlight new potential antiaging effects of WEO by presenting results from two studies, a double-blind, randomized, placebo-controlled clinical trial and an ex vivo study using human skin explants. The primary outcome of the clinical trial was the efficacy of WEO on wrinkle reduction. The secondary end points were the confirmation of the hydrating properties, its positive effect on skin condition and appearance, the duration of these effects following the end of oral supplementation, and its mechanism of biological action.

2 | MATERIALS AND METHODS

2.1 | In vivo study

2.1.1 | Study design

A monocentric double-blind, randomized, placebo-controlled trial was performed on 64 healthy women for 20 weeks consisting of 12 weeks of supplementation and 8 weeks of follow-up visit every 4 weeks.

2.1.2 | Population studied

Sixty-four healthy women were recruited between January and February 2017 and randomly assigned into two groups of 32, one group received the WEO product and the other group the placebo for 20 weeks (January-June 2017) consisting of 12 weeks of supplementation and 8 weeks of follow-up. Subjects were 45-60 years old presenting with dry skin on their legs (corneometer value <40 arbitrary units [au]) and showing wrinkles of the crow's-feet area associated with a Lemperle score of between 3 and 5.

Exclusion criteria were unhealthy subjects, a BMI >30 kg/m^2, dermatological pathology, or connective tissue pathology. Additional exclusion criteria were pregnant and breastfeeding women, food allergy, and use of oral or topical treatment that could influence the cutaneous hydration, one month prior to the enrollment.

Subjects were asked to maintain their dietary and cosmetic habits throughout the study, not to depilate one week before each visit, and to avoid the use of facial makeup and body lotion before each visit.

2.1.3 | Tested products

Wheat extract oil was obtained according to a patented manufacturing process.[20] Randomly assigned subjects were instructed, in a double-blind procedure, to either take one capsule, containing either 350 mg of WEO or the placebo, daily, for 12 weeks.

One capsule of WEO contained 70 mg of GLs, mainly digalactosyldiacylglycerol (DGDG), 9.5 mg of SLs (ceramides and glycoceramides), 35 mg of PLs, and 235.5 mg of triglycerides and other lipids, while one capsule of placebo contained only triglycerides and other lipids.

2.1.4 | Wrinkle assessment by the Lemperle score

The Lemperle score was specifically developed to evaluate visible aging of the skin and to determine the efficacy of products by assessing the wrinkles in selected areas.[21] From standardized pictures

of the crow's-feet (left and right), wrinkle severity was assessed using a photonumeric scale graduated from 0 (no wrinkle) to 5 (deep wrinkles). An average of the Lemperle score on the left and the right sides was determined by a trained dermatologist.

2.1.5 | Measurement of skin hydration by corneometry

Skin hydration on the face and legs was evaluated by a Corneometer CM 825® (Courage-Khazaka) according to the established protocol.[22] An average of three successive measurements in the same area was calculated.

2.1.6 | Clinical evaluation of the skin condition by the dermatologist

A dermatologist, blinded to treatment group, evaluated skin dryness, roughness, and radiance, through visual examination and/or touch assessment using the following semi-quantitative scores:

- dryness: 0 = hydrated, 1 = slightly dry, 2 = moderately dry, and 3 = very dry;
- roughness: 0 = soft, 1 = slightly rough, 2 = moderately rough, and 3 = very rough;
- radiance: 0 = very dull complexion, 1 = dull complexion, 2 = slightly radiant, and 3 = radiant complexion.

2.1.7 | General assessment and self-assessment

The dermatologist noted the global effectiveness of the product, and each subject completed a self-assessment questionnaire about the global product efficacy on specific end points (wrinkles, skin radiance, skin complexion uniformity).

2.1.8 | Safety and tolerance

Adverse events were noted throughout the study. Product acceptance was evaluated by the dermatologist, via collection of the nature and frequency of adverse events.

2.2 | Ex vivo study

2.2.1 | Biological sample preparation

Eight human skin biopsies were obtained from healthy Caucasian women (mean age: 42.9 ± 7.5 years): four abdominal lifts, two neck-face lifts, and two breast reductions. Informed consent was obtained from each donor prior to study initiation. Skin sample preparations and cultures were performed according to the procedure previously described.[23] Briefly, skin samples were cut into 1-cm^2 full-thickness pieces and washed three times with an antibiotics solution. Subcutaneous fat and lower dermis were mechanically removed using a surgical scalpel. Skin samples were then put with the epithelium uppermost at an air/liquid interface on culture inserts (Costar, Poly-Labo Paul Block) placed in a 12-well plate. Cohesion between skin and culture inserts was obtained with a polysiloxane vinyl sea to prevent any skin retraction or lateral passage of applied product toward the dermis. A culture medium especially adapted to survival conditions (Dulbecco's minimal essential medium [Gibco BRL]) containing antibiotics and fetal calf serum was added to the wells. Skin biopsies were kept for 14 days at 37°C in a humidified incubator with 5% CO_2. The medium was renewed three times per week.

2.2.2 | Exposure to UV irradiations

To obtain premature aging of the skin with dermal alterations, skin explants were exposed to UVA (4 J/cm^2) and UVB irradiations (2 J/cm^2) on day 0 and day 1 and received a total of 8 J/cm^2 of UVA and 4 J/cm^2 of UVB irradiations with a Vilber Lourmat stimulator. This was fitted out with a UVA irradiation source (365 nm) composed of T-20.L-365 tubes (no UVB, no UVC emissions), mercury vapor tubes, low pressure, and hot cathodes. Then, the stimulator was fitted out with a UVB irradiation source (312 nm) composed of T-15.M-312 tubes (no UVA, no UVC emission). The radiometer was linked to an energy programmable microprocessor allowing the adjustment of the duration and the energy received by the skin explants. These UV irradiations were sufficient to induce reproducible alterations in the dermis, as previously described.[23]

2.2.3 | Application of WEO

Wheat extract oil was applied, at 6.7 µg/mL in the culture medium. The product was added to the medium on day 0 and day 1, just before UVA and UVB irradiations, and was renewed each time the medium was changed, until the 14 days of the culture.

2.2.4 | Measure of accumulated collagen

After 14 days of incubation, skin explants were enzymatically digested overnight at 4°C in 0.5 mol/L acetic acid solution containing 0.1 mg/mL pepsin. After grinding using a potter, the amount of collagen was determined by a spectrophotometric assay at 540 nm. Accumulated collagen corresponding to the acido-soluble collagen (µg/mg of fresh weight) was detected and quantified using the specific binding of the dye Sirius red (Sircol Collagen Assay—Interchim) and read at 540 nm.

2.3 | Statistical analysis

Statistical analyses of data from the clinical trial were performed with the software JMP® version 13.0 from SAS Institute for Windows with the intention to treat a population.

For quantitative variables, changes from baseline or from the end of the supplementation period were described and compared between groups. For the primary end point (Lemperle score changes from baseline W0-W12), the mean difference between groups was

calculated and compared using an analysis of covariance with baseline Lemperle score as covariable. A repeated measure of ANOVA followed by post hoc tests (Bonferroni correction) was carried out a posteriori to complete the analysis between W0 and W20. This was to determine when the WEO supplement reached maximum efficiency compared to the placebo and the duration of the effects seen. Results were considered as significant when the *P*-values were <0.05 (two-sided tests).

Global hydration was also calculated as the mean of face hydration and leg hydration for each study subject. Correlations between the Lemperle score and global hydration were determined using a Pearson correlation.

Statistical analyses of results from the ex vivo study were performed using the Prism software (GraphPad Software). Comparisons between the different conditions were analyzed by the Friedman test, for repeated data of independant samples, followed by the Wilcoxon test, to compare paired samples two by two. Differences were considered statistically significant when the *P*-value was <0.05.

TABLE 1 Demographic and clinical data of study groups at W0

	WEO group (n = 32)	Placebo group (n = 32)
Age (y)	54.5 ± 6.7	57.13 ± 5.7
BMI (kg/m^2)	24.04 ± 3.0	24.78 ± 3.5
Menopause	68.75%	71.88%
Lemperle score	3.46 ± 0.6	3.79 ± 0.7
Face hydration	44.44 ± 10.3	45.06 ± 6.6
Leg hydration	28.01 ± 6.3	27.81 ± 7.3
Skin dryness (legs)	2.23 ± 0.7	2.45 ± 0.5
Skin roughness	1.63 ± 0.8	1.77 ± 0.8
Skin radiance	1.59 ± 0.6	1.70 ± 0.5

Note. For the WEO group and the placebo group, age, body mass index (BMI), Lemperle score, face and leg hydration, skin dryness, roughness, and radiance are described at W0 before supplementation and expressed as means ± SD (standard deviation). The number of menopausal women is expressed as a percentage (%) in each group.

3 | RESULTS

All 64 included subjects ended the study and were analyzed.

The demographic and anthropometric data, as well as the characteristics of the skin at baseline, were comparable between the two groups, except for the Lemperle score (*P* = 0.0058—Student's *t* test; Table 1).

3.1 | Clinical assessment

3.1.1 | (Crow's-feet) Wrinkle evaluation

The Lemperle score decreased in both groups after 12 weeks of supplementation: in the WEO group, by 1.00 ± 0.7 points, and in the placebo group, by 0.34 ± 0.5 points (Figure 1A). Furthermore, the change from baseline was significant between the two groups and especially so in the WEO group from 8 weeks of supplementation (*P* < 0.0002); the effect continued for 8 weeks after the end of supplementation (Figure 1B). A visible improvement of the crow's-feet wrinkles was seen from 8 weeks and was maintained at 12 weeks (Figure 1C).

3.1.2 | Skin hydration of the face and legs

Corneometry measurements showed a significant improvement in facial skin hydration in the WEO group after 12 weeks of supplementation compared with the placebo group (+5.18 ± 2.19 au vs placebo; *P* = 0.0211; Figure 2B). Also, facial hydration increased to 8.1 ± 8.7 au compared with the baseline in the WEO group and 3.0 ± 8.8 au in the placebo group. It continued increasing during the follow-up phase in a comparable manner in the two groups (Figure 2A). The superior moisturizing effect of WEO stopped at the end of supplementation. Hydration was significantly increased on the leg skin as early as 4 weeks compared to the placebo (+5.3 ± 2.0 au vs placebo; *P* = 0.0212) and lasted throughout the supplementation period (Figure 2D). After 12 weeks, the moisturizing effect was similar to that observed on the face (+4.6 ± 1.9 au): an increase of 8.1 au in the WEO group and 3.5 au in the placebo group. The hydrating effect of the WEO on the legs continued for 8 weeks after the end of supplementation (*P* = 0.0179; Figure 2C).

3.1.3 | Correlation of skin hydration with wrinkle appearance

Considering the data from both the WEO and the placebo groups, a negative and significant correlation was observed between the Lemperle score and global skin hydration (*R* = 0.26, *P* < 0.05) after 8 (Figure 3A) and 12 weeks (Figure 3B).

3.1.4 | Skin appearance assessment by the dermatologist

Skin dryness was significantly reduced in the WEO group after 8 weeks of supplementation (−0.64 ± 0.16 points vs placebo; *P* = 0.002) (Figure 4A). Skin roughness on the legs was also significantly reduced in the WEO group after 8 weeks (−0.42 ± 0.13 points vs placebo; *P* = 0.0048; Figure 4B). Finally, skin radiance was significantly improved after 8 weeks (+0.3 ± 0.08 points vs placebo; *P* = 0.0012; Figure 4C). The beneficial effects of WEO supplementation on the skin evaluated by dermatological scores continued throughout the study.

3.1.5 | Global assessment by the dermatologist and the subjects

The dermatologist estimated the global effectiveness of the WEO supplementation as good to very good for more than 70% of the subjects and for <20% in the placebo group.

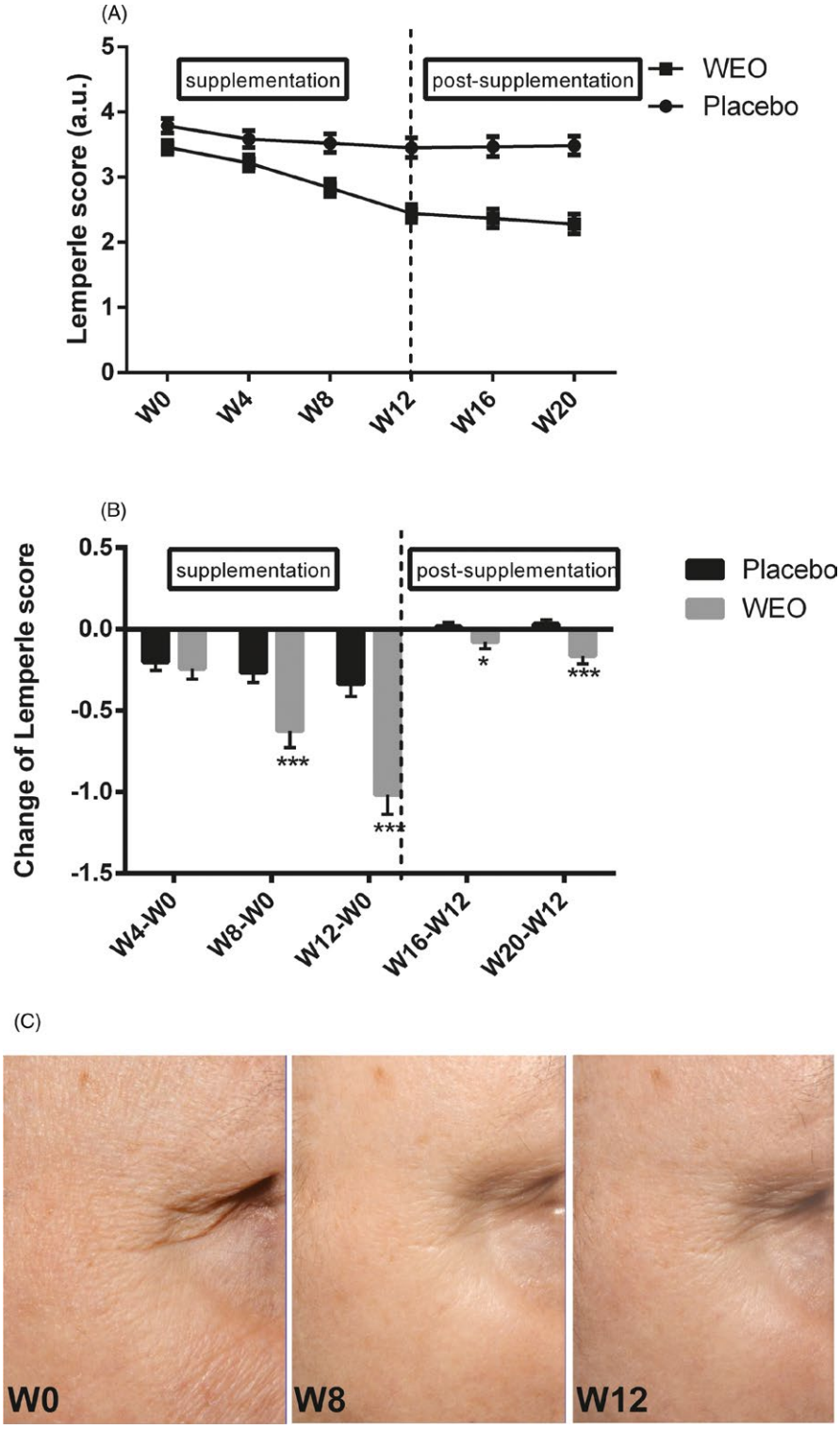

FIGURE 1 Lemperle score. A, Evolution of average Lemperle score in each group of subjects throughout the 20 wk of study (12 wk of supplements and 8 wk of follow-up): Results are expressed as means ± SEM of the Lemperle score (arbitrary unit au). B, Comparative analysis of Lemperle score variation during the supplementation period compared to W0 (W4-W0; W8-W0; W12-W0) and during the follow-up period compared to W12 (W16-W12; W20-W12): Results are expressed as means ± SEM of change in Lemperle score for each group. $^{*}P < 0.05$; $^{***}P < 0.001$ (Student's *t* test). C, Representative photographs of crow's-feet wrinkles from one woman (subject no. 44; 63 y old) in the wheat extract oil (WEO) group during the supplementation period (W0; W8; W12)

Wheat extract oil supplementation was perceived as more efficient by the subjects for the improvement of skin complexion uniformity, skin radiance, and wrinkle reduction (Table 2). Finally, more than 68% of the subjects were satisfied with the WEO supplements (vs 40% of the placebo group). Tolerance was considered as very good (95% of the subjects). No adverse event linked to the product was reported during the clinical study.

3.1.6 | Measure of accumulated collagen

In a model of human skin in survival, a significant reduction in collagen was observed in the UV-irradiated skin compared to the normal skin. A significantly higher collagen content was also reported in the UV-exposed skin explants treated with WEO compared to untreated UV-exposed skin explants. Collagen was increased by a mean of

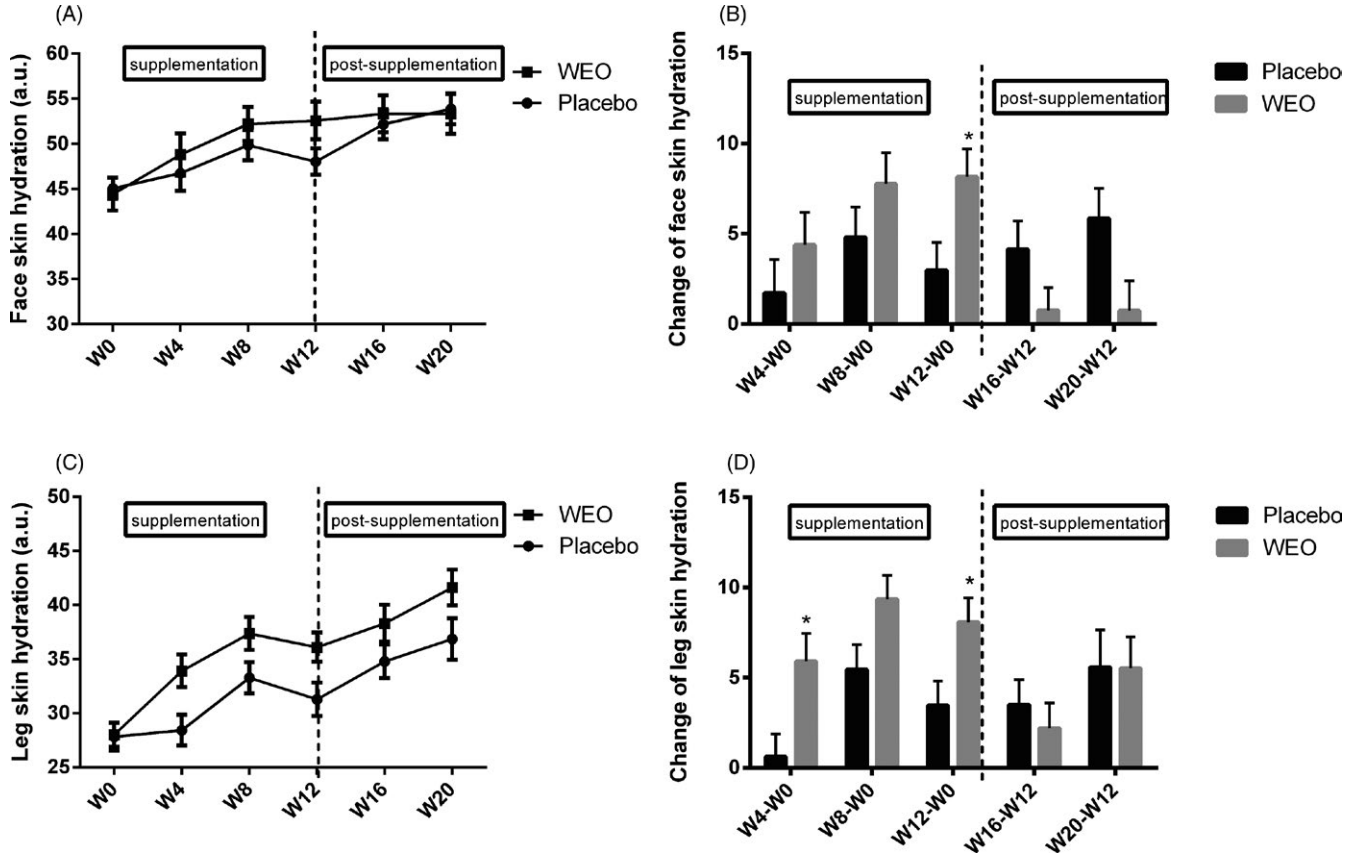

FIGURE 2 Hydration of facial and leg skins. Evolution of skin hydration of (A) the face and (C) the leg in each group, throughout the 20 wk of the study (12 wk of supplements and 8 wk of follow-up): Results are expressed as means ± SEM of skin hydration (arbitrary unit, au). Comparative analyses of the variation in hydration during the supplementation period compared to W0 (W4-W0; W8-W0; W12-W0) and during the follow-up period compared to W12 (W16-W12/W20-W12) (B) for the face and (D) for the legs: Results are expressed as means ± SEM of change in skin hydration for each group. *$P < 0.05$ (Student's t test)

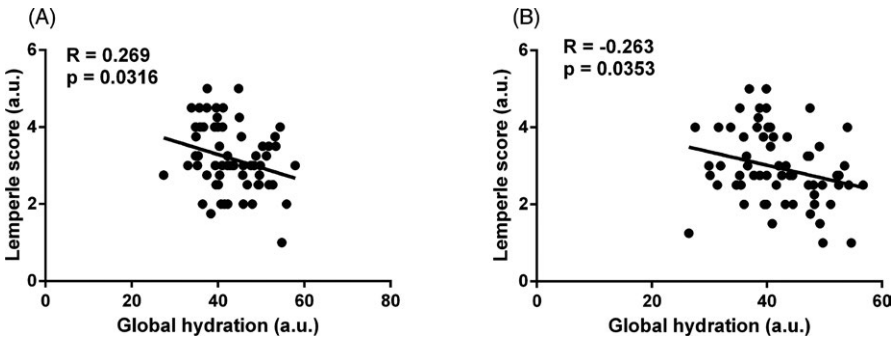

FIGURE 3 Correlation between Lemperle score (arbitrary unit a.u.) and global hydration (mean of face and legs hydration, arbitrary unit a.u.) at W8 (A) and W12 (B) (Pearson correlation R, $P < 0.05$)

48% under WEO treatment compared to untreated UV skin explants (40.09 ± 3.57 µg/mg compared to 27.06 ± 3.18 µg/mg; $P = 0.002$; Figure 5). These results suggest that WEO might stimulate the synthesis of endogenous collagen and/or prevent collagen breakdown.

4 | DISCUSSION

This new clinical study performed in women reveals first anti-wrinkle effects of WEO, and confirms its hydrating properties as seen in previous studies.[19] This present study revealed a significant reduction in crow's-feet wrinkle appearance with Lemperle scoring compared to the placebo group, after 8 weeks of supplementation. The improvement of wrinkle appearance continued to be observed during the 2 months of follow-up. Furthermore, a clinically significant difference in one grade on the Lemperle scale was observed at W12 compared to W0 in the WEO group. The effects of nutritional supplements dedicated to the skin are often difficult to assess. The Lemperle score is a validated qualitative

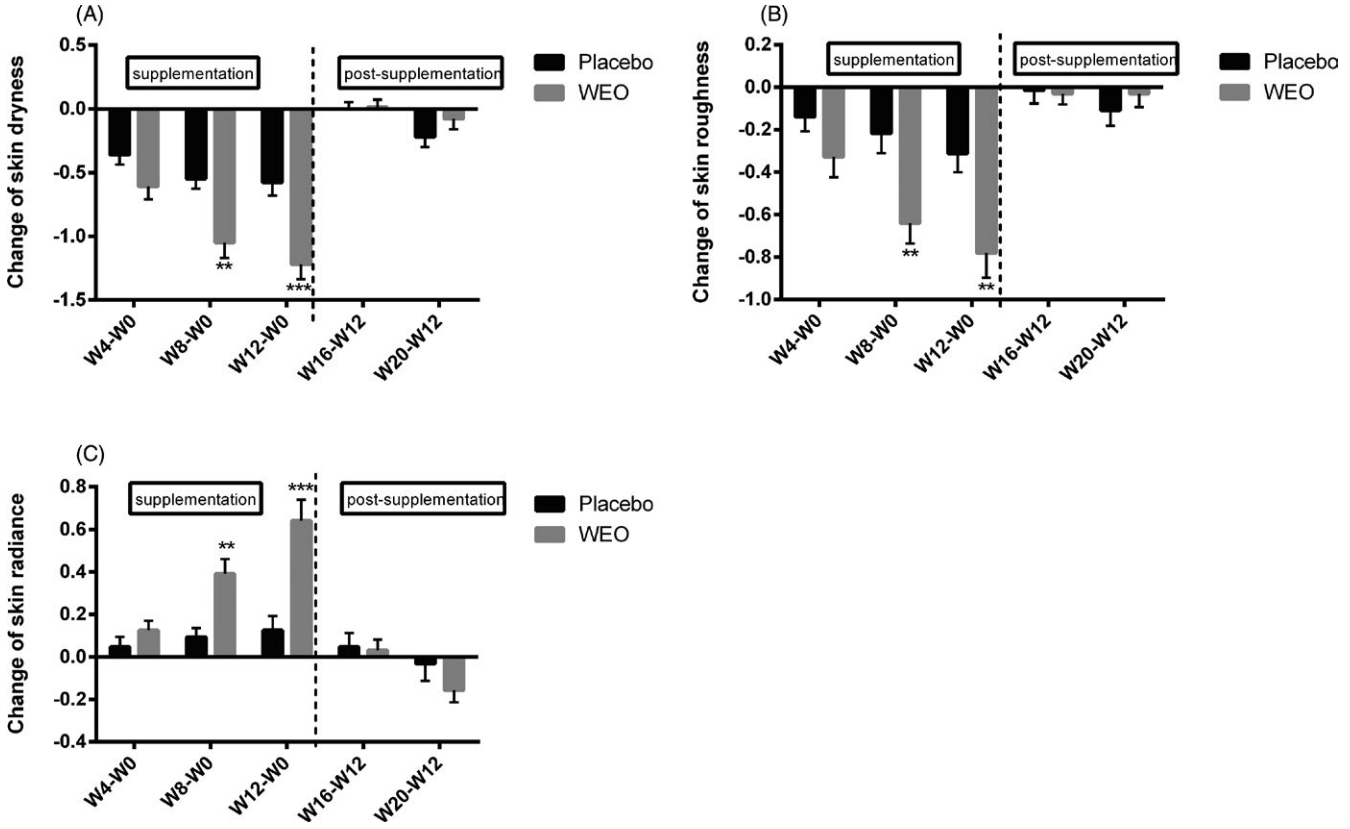

FIGURE 4 Clinical evaluation of skin quality and characteristics. Comparative analyses of variations during the supplementation period compared to W0 (W4-W0; W8-W0; W12-W0) and during the follow-up period compared to W12 (W16-W12; W20-W12) for (A) skin dryness, (B) skin roughness, and (C) skin radiance: Results are expressed as means ± SEM of change in skin condition for each group. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ (Student's *t* test). Skin dryness: score 0 = hydrated; score 1 = slightly dry; score 2 = moderately dry; and score 3 = very dry. Skin roughness: score 0 = soft; score 1 = slightly rough; score 2 = moderately rough; and score 3 = very rough. Skin radiance: score 0 = very dull complexion; 1 = dull complexion; 2 = slightly radiant; and 3 = radiant complexion

method of clinical scoring which allows a global and visible assessment of wrinkle smoothing.[21] Compared to other quantitative methods such as profilometry, Lemperle scoring is not affected by environmental or other factors (facial expression, ambient conditions such as light/luminosity).

Skin hydration was measured on two distinct areas, the face and the legs. A significant difference in the improvement of skin hydration in favor of WEO supplementation was observed as early as 4 weeks for the legs and after 12 weeks for the face. At the end of the supplementation period, the moisturizing effects of WEO were maintained on the legs but not on the face. The natural increase in skin hydration during the postsupplementation period seen in the two groups can also be explained by seasonal changes during the study. Indeed, it is already known that PoL levels in the skin are depleted in winter compared to spring and summer, and is also associated with higher dryness and a lower hydration.[24,25] Moreover, this study was performed on subjects who did not change their cosmetic habits throughout the study. In contrast, no cosmetic product was allowed on the legs. Leg skin is generally drier than facial skin. Hence, a systemic moisturizing effect can be better studied on the former area.

In the present study, the improvements in skin hydration and wrinkle reduction are concomitant with the improvement of skin qualities such as skin roughness and radiance along with global satisfaction by the subjects. Skin hydration plays an essential role in maintaining homeostasis. Skin dryness is a crucial factor leading to the formation and appearance of wrinkles. It has been demonstrated in an experimental system, reproducing the conditions of skin dryness, in reconstructed human epidermal equivalent (RHEE) models, that dry skin produces more factors such as cytokines and metalloproteases (MMP1) which participate in the degradation of the dermis matrix leading to wrinkle formation.[26] Thus, we hypothesized that, due to its moisturizing properties, WEO could lessen wrinkle appearance. Furthermore, a negative and significant correlation between global skin hydration and the Lemperle score ($R = 0.26$, $P < 0.05$) was observed after 8 and 12 weeks, in both groups, supporting the hypothesis of a link between skin hydration and wrinkle severity.

In order to get more information on the cellular processes engaged by WEO supplementation, an ex vivo study was performed on human skin explants artificially aged by UV irradiations. This ex vivo study demonstrated that WEO maintained the quantity of total collagen at the equivalent level of nonaged skin, suggesting that WEO may stimulate collagen synthesis. However, previous enzymatic tests revealed anti-collagenase properties of WEO, preventing the

TABLE 2 Global assessment of product effectiveness made by the subjects

	WEO group (n = 32)			Placebo group (n = 32)		
Week (Wx)	**W4**	**W8**	**W12**	**W4**	**W8**	**W12**
Efficacy on skin complexion uniformity						
Not efficient	62.50	18.75	9.38	62.50	46.88	40.63
Slightly efficient	18.75	25	25	18.75	28.13	25
Efficient	15.63	56.25	62.50	18.75	21.87	28.12
Very efficient	3.12	0	3.12	0	3.12	6.25
Efficacy on skin radiance						
Not efficient	65.63	15.63	9.38	68.75	46.88	43.75
Slightly efficient	18.75	31.25	28.13	18.75	28.13	25
Efficient	12.50	53.12	68.75	12.50	21.87	25
Very efficient	3.12	0	3.12	0	3.12	6.25
Efficacy on wrinkle reduction						
Not efficient	81.25	28.13	28.13	68.75	68.75	68.75
Slightly efficient	12.50	53.12	50.00	18.75	18.75	9.38
Efficient	6.25	18.75	18.75	12.50	9.38	18.75
Very efficient	0	0	3.12	0	3.12	3.12

Note. In both groups, at each study visit, subjects assessed the efficacy of the supplementation on skin complexion uniformity, on skin radiance, and on wrinkle reduction according to a four-point scale: not efficient, slightly efficient, efficient, and very efficient. Results are expressed as percentages (%) in each group.

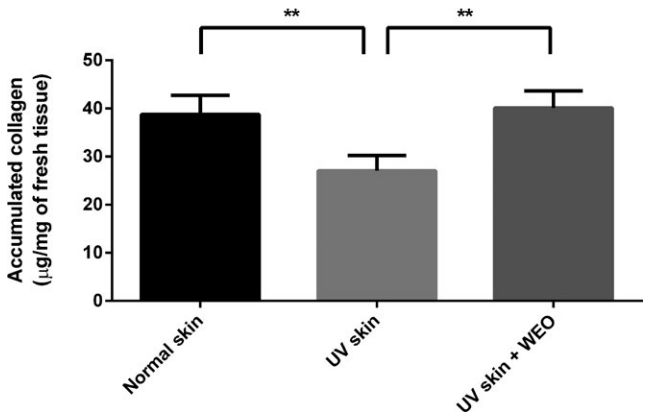

FIGURE 5 Measurement of collagen accumulation in ex vivo human skin explants. Three skin samples from each donor were prepared according to the following conditions: skin sample without UV treatment (normal skin); skin exposed to UVA and UVB (UV skin); and skin treated with Lipowheat oil at 6.7 µg/mL and exposed to UVA and UVB (UV skin + WEO). Results are expressed as means ± SEM of collagen in µg/mg of skin tissue for each condition. $^{**}P < 0.01$ (Friedman test followed by Wilcoxon test)

degradation of matrix proteins (Data S1). It would therefore be interesting to characterize the secretion profile of the proteases affected by WEO and to specify the molecular mechanisms of the WEO involved in collagen synthesis.

A study of WEO composition revealed the presence of several lipid classes, mainly PoLs, including digalactosyldiacylglycerol (DGDG), PLs, and SLs.[12] The observed effects of WEO supplementation could therefore be the consequence of a synergy of all the polar lipids. However, it would be of interest to characterize the biological effects of the different lipid fractions on the skin, particularly, the predominant form of PoLs, DGDG, whose biological roles are less known. It has already been reported that DGDGs are involved in the increased synthesis of matrix proteins such as fibronectin, thus participating in skin firmness and healing.[27,28]

A previous cellular study has shown that WEO, apart to stimulate collagen synthesis and inhibit matrix proteases, also exhibited anti-inflammatory properties. Indeed, when human adipocyte precursors, isolated after enzymatic digestion of hypodermal tissue, were cultured with the bacterial endotoxin lipopolysaccharide (LPS) in order to produce a fibro-inflammatory state of these cells,[29,30] WEO treatment led to decreased secretion of the inflammatory cytokine interleukin-6 (IL6) by these progenitors (Data S2). Several studies have shown that the hypodermis and its secreted biomolecules, mainly leptin and adiponectin, could influence dermal conditions such as collagen and hyaluronic acid production by dermal fibroblasts.[31] Also, adipocytokines produced by the hypodermis such as IL6 are known to thicken the stratum corneum.[32] Overall, new and promising prospects for WEO are in store and should be explored, like the contribution to the acceleration and improvement of the skin healing process or the reduction in dryness, itching, and red blotches in atopic dermatitis. For these reasons, it would be interesting to further assess WEO effects in models of skin inflammation or in patients with specific skin pathologies.

In conclusion, these new and promising studies performed on women and human skin explants supported the moisturizing effects of WEO and revealed the potential antiaging properties of this

extract. A more detailed characterization of the active lipid fractions contained in WEO would be the starting point for new studies on other biological functions.

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DISCLOSURE

All the studies were financed by Charabot. The clinical studies were carried out by Gredeco while SLB pharma performed all the statistics. DIVA Expertise conducted the cellular studies and wrote the article.

ETHICAL APPROVAL

This monocentric study was conducted in accordance with Good Clinical Practices and the principles of the Declaration of Helsinki. An independent ethics committee of Paris V—Hôpital Saint-Antoine (France) and the *French* National Agency of Medicine and Health Products Safety (ANSM) (registration number: 2016-A01206-45) approved the protocol. All subjects provided written informed consent prior to inclusion in the protocol.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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