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ORIGINAL RESEARCH

Recovery Effects of Oral Supplementation with Polar Lipid-Rich Wheat Extracts on Acute Telogen Effluvium: A Randomized Double-Blind Placebo-Controlled Study

Vincenzo Nobile[1], Stéphanie Dudonné[2], Catherine Kern[2], Enza Cestone[3], Christine Garcia[2]

[1]R&D Department, Complife Italia S.r.l., San Martino Siccomario, Italy; [2]Research and Innovation Department, Seppic, La Garenne Colombes, France; [3]Clinical Trial Department, Complife Italia S.r.l., San Martino Siccomario, Italy

Correspondence: Stéphanie Dudonné, Research and Innovation Department, Seppic, La Garenne Colombes, France, Email stephanie.dudonne@airliquide.com

Background: Acute telogen effluvium (aTE) is a transient condition characterized by an early entry of the hair into the telogen phase.
Purpose: This clinical study aimed at demonstrating the efficacy of a standardized wheat polar lipid complex both in oil (WPLC–O) and in powder (WPLC–P) form in improving hair shedding.
Subjects and Methods: The study was carried out in 99 healthy women with aTE. Hair growth cycle related parameters (anagen/telogen hair), hair pull test, hair shaft mechanical properties (hair elongation at break) and hair growth were assessed at baseline and after 56 (D56) and/or 84 (D84) days of products use. These parameters were completed by the subject's self-assessment.
Results: Telogen hair density was decreased by up to 26.9% and 24.2% while anagen density was increased by up to 10.3% and 10.8%, for WPLC–O and WPLC–P, respectively. These effects were significant compared with the placebo as early as within 56 days. These variations corresponded to an increase in the anagen/telogen ratio by up to 62.2% and 53.3% for WPLC–O and WPLC–P, respectively. Hair growth was also significantly increased in both active groups. At the end of the study the pull test was negative for aTE, exclusively in active treatment arms.
Conclusion: Our findings demonstrated the efficacy of WPLC in both form in reducing hair shedding and in improving hair growth in women with aTE.
Keywords: hair shedding, acute telogen effluvium, sphingolipids, digalactosyl diglycerides, nutricosmetics

Introduction

Acute telogen effluvium (aTE) is a transient and reversible dermatological condition occurring 3 months after a stressful event that causes diffuse hair shedding and lasts up to 6 months.[1–4] The triggering factors behind aTE include metabolic stress, hormonal change, dietary deficiencies or medications.[5] aTE is a reactive, diffuse, not pathological, and self-limited condition with a spontaneous remission rate in around 95% of cases[5,6] and with hair starting to regrowth when the triggering cause is corrected or removed.[7,8] While transient, this condition is a major source of psychological distress for affected people.

The true incidence and prevalence of aTE is not clearly known since most cases of telogen effluvium are subclinical.[9,10] No ethnicity or gender predilection has been recognized, even if the incidence rate is higher in women. The higher incidence in women is overrepresented probably due to unawareness or underreporting in males.[11] In addition, women have a greater tendency to experience hair shedding since hormonal changes in the postpartum period are a common cause of aTE (telogen gravidarum).[11–14] The association of aTE with age is unclear even if there is evidence of a greater susceptibility of elderly women to experience aTE because of hormonal and age-related physiologic changes, such as the onset of menopause.[11] Even if aTE is a transitory condition, the massive hair shedding significantly

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impacts the subject's self-esteem and quality of life especially in women, who usually rate the hair shedding as more severe than the dermatologist.[15] Hair shedding and thinning associated with aTE can be solved by removing or correcting the underlying cause. However, the multifactorial cause, its psychological component, and the absence of targeted treatments for aTE makes the clinical management of aTE challenging for physicians.[16,17] On the other hand, very few ingredients were demonstrated to be effective in the treatment of aTE,[18–24] highlighting the need to investigate the efficacy of new ingredients with a safe profile of use and validated claims.

Lipids are bound to both the hair shaft (cuticle, cortex and medulla) and the hair follicle. In the hair shaft, lipids are involved in the hydration, strength and texture of the hair; while in the hair follicle they function as a hair barrier similar to the skin barrier.[25,26] The major components constituents of this barrier, mainly located in the inner root sheath (IRS), are fatty acids, phytosphingosine, ceramide, cholesterol and cholesterol sulfate in decreasing order[26] and are tightly associated with IRS in such a way to be resistant to solvent extraction. The hair lipids metabolism is thought to play an essential role in hair development and function as demonstrated by the altered hair growth in animal models having genetic errors in lipid metabolism.[27–30] Interestingly, Wan et al and Karnik et al reported that the altered hair phenotype (ie hair shaft distortion, distal follicle ectasia, and dystrophic catagen/telogen forms) is dramatically reversible under the proper rescue treatment.[31,32] Even if the precise mechanism behind the altered hair phenotype remains unclear, a possible role for inflammation induced by proinflammatory lipids or sterols seems to play a role.[33] The knowledge of lipid metabolism can then give new opportunities for the development of targeted treatments for hair loss, including aTE.[34]

WPLC is a wheat (*Triticum aestivum*) polar lipid complex, mainly composed of sphingolipids, among which glucosylceramides, and digalactosyl diglycerides (DGDG). In previous studies, this ingredient was demonstrated to be effective in reducing the skin aging signs, specifically improving skin barrier and moisturization.[35,36] Like the skin's outer layer, hair cuticles rely on ceramides within their intercellular lipids to create a protective barrier against external damage.[26] Thus, oral ceramide supplementation is likely to exert a positive influence on hair health. In a pilot preliminary study, WPLC in powder form was demonstrated to be effective in reducing excessive hair shedding.[37] The present study therefore aimed to investigate and compare the efficacy of WPLC in its oil (WPLC–O) and powder form (WPLC–P), providing equal amounts of sphingolipids and DGDG, in women with aTE.

Materials and Methods

Trial Design

This was a multi-center, randomized, placebo-controlled clinical trial carried out in Italy at Complife Italian facilities (Pavia, Milano and Rende) between September and December 2023. Subjects attended a screening visit, a baseline visit (D0) and two follow-up visits after 56 (D56) and 84 (D84) days of product use. During the screening visit, a board-certified dermatologist evaluated the aTE condition by an accurate collection of the subject's medical condition relevant for the diagnosis of aTE.

The study protocol (ref. no. H.E.HU.TE.NHL00.090.10.00_IT0003622/23) was approved by the "Comitato Etico Indipendente per le Indagini Cliniche Non Farmacologiche" (Genova, Italy) on 2 August 2023 (ref. no. 2023/09). All the study procedures were carried out in full accordance with the principles of the Declaration of Helsinki and its amendments, and informed consent was obtained from all subjects involved in the study. The clinical trial was registered at www.clinicaltrials.gov (NCT06028295).

Interventions and Randomization

The active treatment arms (WPLC–O and WPLC–P) received 2 capsules per day (in the evening before to go to sleep) of a food supplement containing either 35 mg of the oil wheat extract (Ceramosides^{TM} oil, Seppic, France) or 15 mg of the powder wheat extract (Ceramosides^{TM} powder, Seppic, France) for 84 days. Each active treatment provided an equal amount of sphingolipids and DGDG. Both WPLC–O and WPLC–P are obtained from wheat (*Triticum aestivum*) endosperm flour, as described by Bizot et al.[35]

The placebo (PL) treatment arm received two capsules per day containing maltodextrin and excipients. The complete capsule composition is reported in Table 1.

Table 1 Capsule Composition

Ingredients	Quantity (mg) Per Capsule		
	WPLC-O	WPLC-P	PL
Maltodextrin	210	230	245
Dicalcium phosphate	100	100	100
Magnesium carbonate	50	50	50
Silica	30	30	30
Magnesium stearate	5	5	5
Ceramosides™ oil	35	–	–
Ceramosides™ powder	–	15	–
Total net weight (mg)	430	430	430

During all the study period subjects were asked to use their shampoo and conditioner and to not change their hair care cosmetological routine.

Subjects were randomized to receive WPLC–O, WPLC–P or PL by a computer-generated (PASS 11, version 11.0.8, PASS, LLC, Kaysville, UT, USA) restricted and balanced (1:1:1) randomization list using the "Wey's urn". The actives and placebo products were identical in shape and size and were numbered. The randomization list was concealed in sequentially numbered, sealed, opaque envelopes. Separation between the investigators and the study staff that delivered the interventions was implemented to ensure the blind conditions.

Participants and Compliance with Treatment

Eligible participants were all the adult (age between 18 and 65 years old) female Caucasians showing acute (lasting less than 6 months) hair shedding due to fatigue, seasonal change, deficiency of vitamins and minerals, stress, change or imbalance of normal daily routine, or emotional stress. Acute TE was confirmed by a positive hair pull test (see description below) and a proportion of hairs in the telogen phase exceeding 15%, as determined by phototrichogram evaluation (see description below). All participants were also complaining about brittle and thin hairs. Exclusion criteria were concomitant participation in other clinical trials, treatment with anti-hair loss products 3 months before the screening visit, pregnancy or breastfeeding (for women of childbearing age), starting or variation of oestrogen-progesterone contraception or hormonal treatment products 3 months before the screening visit, excessive and/or fluctuating hair shedding for more than 6 months. The complete inclusion and exclusion list is reported in the Supplementary Materials (Table S1).

During all the study period subjects were asked to write a journal about their food and drink consumption to ensure the stability of their alimentary habits, and to report the appearance of any adverse event. They were also asked to not wash their hair 48 hours before each visit. Any hair care procedures (eg antidandruff shampoo, antifungal shampoo, dyeing, bleaching, perm) were prohibited 2 weeks before each visit.

The compliance with treatment was assessed by counting and recording the remaining capsules in each bottle after 56 and 84 days of treatment. The threshold value for compliance with treatment was set at $\geq$ 80%.

Primary and Secondary Efficacy Endpoints and Outcome Measures

The primary endpoint was the assessment of the efficacy of WPLC-O and WPLC-P in reducing hair shedding (anagen/telogen ratio, anagen and telogen hair density and proportion, pull test). The secondary endpoints included the improvement of hair shaft mechanical properties (hair elongation/elasticity) and hair growth, as well as the products acceptability and the subjects perceived efficacy (self-assessment questionnaire).

The outcome measures were taken in standard temperature (T = 22 ± 4 °C) and humidity (RH = 50 ± 10%) conditions after an acclimation period of 15–20 min to T/RH ambient conditions.

Assessment of Hair Growth Cycle Related Parameters by Phototrichogram

The proportion and density of hair were assessed by the phototrichogram technique using the TrichoScan (vers. 4.0.10.102; Tricholog GmbH & Datinf GmbH, Germany) automated digital images analysis.[38,39] All the procedures were carried out as recommended by the TrichoScan software supplier. Briefly, hair in the mid vertex were clipped at each visit. After 48 hours, hair in the clipped region were dyed with a black hair dye to enhance the hair contrast over the scalp area, the hair dye was removed with an alcoholic solution and then a picture was taken using DermoGenius (DermoScan GmbH, Regensburg, Germany). The clipping area was chosen to allow the hair in close vicinity to be combed over the clipped area. The following parameters related to the hair growth cycle were measured: anagen hair density and proportion, telogen hair density and proportion, anagen to telogen ratio.

Hair Pull Test

The hair pull test was performed by the dermatologist, selecting 50 to 60 hairs and holding the bundle close to the scalp between the thumb, index and long finger. The clinician then firmly pulled on the bundle using slow traction. The hair pulls were performed at the frontal, temporal and occipital area. The pull test was considered positive for aTE if more than 9 hairs were removed from the pulled scalp areas. Any broken hair that was extracted from the bundle was discarded.[40,41] The subjects were asked not to wash their hair in the previous 48 hours.

Hair Elongation

At each time point 15 hairs were collected for the evaluation of the hair elongation at break. Hair elongation was measured using a dynamometer (Tensolab 2512A, Mesdan Lab, Brescia, Italy) in accordance with UNI EN ISO 5079:2020 standard procedure.[42] The measurement was performed in calibrated conditions (T = 20 ± 2°C and RH 65 ± 4%). The pretension applied to each sample was 1 centinewton (cN) while the (constant) rate of extension (mm/min) was 1.5-fold the hair sample length.

Hair Growth

Hair in the mid vertex was clipped at baseline, in an area near the one chosen for phototrichogram analysis. After 84 days of product intake, the hair growth was measured.

Self-Assessment Questionnaire

At the end of the study, subjects were asked to give their opinion answering a self-assessment questionnaire. The items of the questionnaire focused on the products perceived efficacy (ie growth, shedding, density, volume and breakage), the hair cosmetic characteristics (ie brightness, softness, dryness, oiliness, styling properties and overall hair quality) tolerability and the overall treatment satisfaction. The questionnaire was taken before any outcome measurement so as not to influence the participants' answers. Possible answers were "completely agree", "agree", "disagree", or "completely disagree". "Completely agree" and "agree" were considered in the calculation of the responders.

Statistical Analysis

Intra-group statistical comparisons were performed on raw data using one-way repeated measures analysis of variance (RM-ANOVA), followed by post-hoc Dunnett's test for multiple comparisons to the control (D0), when data followed a normal distribution. Otherwise, Friedman test was applied, followed by Dunn's test for pairwise multiple comparisons of the ranked data. Intra-group comparison of hair elongation between D0 and D84 was assessed using paired *t*-test or Wilcoxon matched-pairs signed rank test.

Inter-group statistical comparisons were performed on the percentages of variation versus D0 using one-way analysis of variance (ANOVA), followed by post-hoc Šidák's correction for multiple comparisons, when data were normally distributed. Otherwise, Kruskal–Wallis test was applied, followed by Dunn's test for pairwise comparisons. Inter-group statistical comparison of the variation of hair elongation between D0 and D84 was performed using unpaired *t*-test. Hair growth, measured at the end of the supplementation period, was compared between the two groups using unpaired *t*-test.

Variations were considered statistically significant when p value was < 0.05. All statistical analyses were performed using GraphPad Prism 9.5.0 software (GraphPad Software, Boston, MA, USA).

Results

Participants, Tolerability, and Compliance with Treatment

The study screened 131 subjects of whom 25 did not meet the inclusion criteria and 7 declined to participate. The trial successfully randomized a total of ninety-nine (n = 99) subjects divided in each of the three treatment arms (33 subjects per treatment arm). The per protocol (PP) population consisted of 98 subjects since one subject in the PL treatment arm dropped out after the baseline visit. The reason for the drop out was not related to product use. The participants flow chart is shown in Figure 1. The study enrolled Caucasian women aged between 18 and 65 years old (WPLC–O: 46.2 ± 2.3; WPLC–P: 47.6 ± 1.8; PL: 46.8 ± 2.2) with aTE and all hair types (oily, normal, and dry). Additional demographics at baseline are shown in Table 2 and clearly indicate the homogeneity of WPLC–O, WPLC–P and PL groups.

WPLC–O, WPLC–P and PL products were well tolerated. No adverse effects were reported by the investigator during the entire study period. The overall tolerability was confirmed by 100% of the participants. The alimentary habits were unchanged during the study period and did not represent a covariate between groups. Compliance with treatment was 96% in each group (min. 86%, max. 100%).

Hair Growth Cycle Related Parameters (Phototrichogram)

The treatment with both WPLC–O and WPLC–P significantly decreased the density of telogen hair both at D56 and D84. The decrease in the telogen density in the WPLC–O group was by 23.0% ($p < 0.001$) and 26.9% ($p < 0.001$) at D56 and D84, respectively (Table 3). Similar results were obtained in the WPLC–P group where the telogen density was decreased by 17.6% ($p < 0.001$) and 24.2% ($p < 0.001$) at D56 and D84, respectively. The decrease in the telogen density was associated with a decrease in the telogen hair proportion that was indicative of normal conditions (% telogen ≤ 15%) starting from D56. In the placebo group the maximum telogen density decrease (−11.0%; $p < 0.01$) was seen at D84 with a proportion of telogen hair borderline (15.2 ± 0.5%) for aTE. The variation of both the density and the proportion of telogen hair between the active groups and the placebo group was statistically different at all the time points.

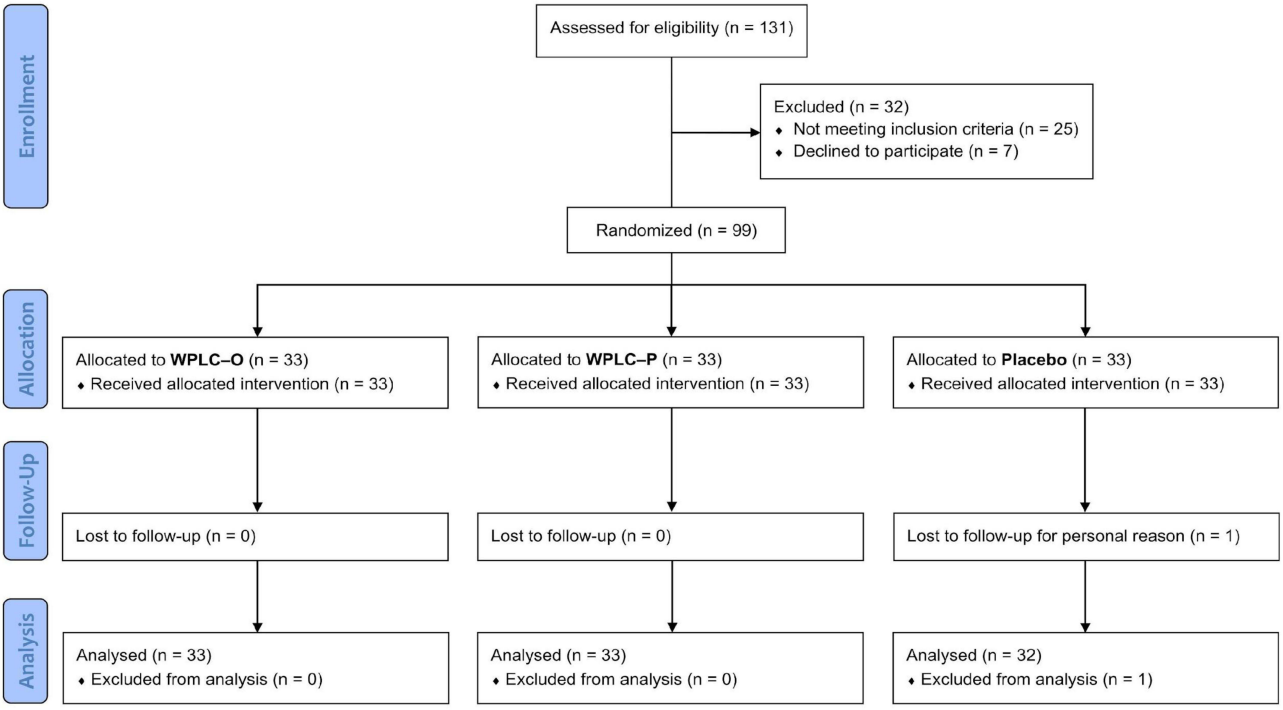

Figure 1 Participants flow diagram.

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Table 2 Demographics and Baseline Characteristics of Study Participants

	WPLC-O (n = 33)	WPLC-P (n = 33)	PL (n = 32)	Units
Age	46.2 ± 2.3	47.6 ± 1.8	46.8 ± 2.2	Years
Postmenopausal population	33.3% (11)	36.4% (12)	40.6% (13)	% (no.)
Hair type				
Oily	33.3% (11)	45.5% (15)	46.9% (15)	% (no.)
Normal	45.5% (15)	36.3% (12)	31.2% (10)	% (no.)
Dry	21.2% (7)	18.2% (6)	21.9% (7)	% (no.)
Phototrichogram				
Telogen hair density	33.4 ± 1.0	32.0 ± 1.0	31.6 ± 1.0	no./cm²
Telogen hair proportion	18.5 ± 0.4	17.7 ± 0.4	17.5 ± 0.4	%
Anagen hair density	147.5 ± 3.5	149.3 ± 3.6	148.9 ± 3.1	no./cm²
Anagen hair proportion	81.5 ± 0.4	82.3 ± 0.4	82.5 ± 0.4	%
Anagen/telogen ratio	4.5 ± 0.1	4.7 ± 0.1	4.8 ± 0.1	a.u.
Pulled hair	13.5 ± 0.6	13.8 ± 0.5	13.9 ± 0.5	no.
Hair elongation at break	43.5 ± 0.5	43.0 ± 0.6	45.1 ± 1.0	%

Notes: Continuous data are expressed as mean ± SEM; categorical data are expressed as counts and percentages.

Table 3 Phototrichogram, Pull Testing and Hair Elongation at Break Results

		D0	D56	D84
Telogen density (hair/cm²)	WPLC–O (n = 33)	33.4 ± 1.0	25.6 ± 1.1*** (−23.0%)###	24.3 ± 1.1*** (−26.9%)###
	WPLC–P (n=33)	32.0 ± 1.0	26.5 ± 1.5*** (−17.6%)#	24.1 ± 1.1*** (−24.2%)##
	PL (n = 32)	31.6 ± 1.0	29.5 ± 1.5 (−6.9%)	28.1 ± 1.2** (−11.0%)
Telogen proportion (%)	WPLC–O (n = 33)	18.5 ± 0.4	14.1 ± 0.6*** (−23.7%)###	13.1 ± 0.6*** (−29.1%)###
	WPLC–P (n=33)	17.7 ± 0.4	14.5 ± 0.7*** (−18.3%)##	12.7 ± 0.5*** (−27.5%)##
	PL (n = 32)	17.5 ± 0.4	16.4 ± 0.7 (−5.8%)	15.2 ± 0.5*** (−13.1%)
Anagen density (hair/cm²)	WPLC–O (n = 33)	147.5 ± 3.5	156.8 ± 4.3*** (+6.2%)#	162.7 ± 4.6*** (+10.3%)#
	WPLC–P (n=33)	149.3 ± 3.6	156.9 ± 4.5*** (+4.9%)#	165.5 ± 4.4*** (+10.8%)#
	PL (n = 32)	148.9 ± 3.1	149.4 ± 3.5 (+0.5%)	156.5 ± 3.3** (+5.4%)
Anagen proportion (%)	WPLC–O (n = 33)	81.5 ± 0.4	85.9 ± 0.6*** (+5.3%)###	86.9 ± 0.6*** (+6.6%)###
	WPLC–P (n=33)	82.3 ± 0.4	85.5 ± 0.7*** (+3.8%)#	87.3 ± 0.5*** (+6.0%)##
	PL (n = 32)	82.5 ± 0.4	83.6 ± 0.7 (+1.3%)	84.8 ± 0.5*** (+2.9%)

(*Continued*)

Table 3 (Continued).

		D0	D56	D84
Pulled hair (no.)	WPLC–O (n = 33)	13.5 ± 0.6	11.5 ± 0.7** (−15.4%)	7.9 ± 0.6*** (−41.2%)#
	WPLC–P (n=33)	13.8 ± 0.5	11.5 ± 0.6*** (−16.7%)	7.5 ± 0.4*** (−44.4%)##
	PL (n = 32)	13.9 ± 0.5	13.1 ± 0.6* (−6.7%)	9.8 ± 0.6*** (−29.1%)
Hair elongation (%)	WPLC–O (n = 33)	43.5 ± 0.5	n.d.[b]	44.9 ± 0.6* (+3.2%)
	WPLC–P (n=33)	43.0 ± 0.6	n.d.[b]	44.9 ± 0.8* (+4.6%)
	PL (n = 30)[a]	45.1 ± 1.0	n.d.[b]	46.3 ± 0.9 (+3.1%)

Notes: Data are mean ± SEM. The intragroup (vs baseline) statistical analysis is denoted by the symbol *, while the intergroup (WPLC–O vs PL and WPLC–P vs PL) statistical analysis is denoted by the symbol #, as follows: */#$p < 0.05$, **/##$p < 0.01$, ***/###$p < 0.001$. [a]For technical issue, two hair samples were not analyzed; [b]Not determined.

A similar trend was observed for the anagen hair density and proportion (Table 3). The anagen proportion at baseline was 81.5 ± 0.4% for WPLC–O, 82.3 ± 0.4% for WPLC-P and 82.5 ± 0.4% for PL. This proportion was increased at D56 and further increased at D84 both in the WPLC–O (+6.6%) and WPLC–P (+6.0%) groups (Figure 2). This variation corresponded to an increase in the anagen hair density by +6.2% ($p < 0.001$) and +4.9% ($p < 0.001$) at D56 and by +10.3% ($p < 0.001$) and +10.8% ($p < 0.001$) at D84, for WPLC–O and WPLC–P, respectively. In the placebo group both the anagen density and proportion were slightly increased with a maximum variation by +2.9% ($p < 0.001$) for anagen proportion and +5.4% ($p < 0.01$) for the anagen density at D84. The variation of both parameters between the active groups and the placebo group was statistically different at all the time points.

The anagen to telogen (A/T) ratio was shifted toward anagen (Figure 3). The increase of the A/T ratio in the WPLC–O group was +42.6% ($p < 0.001$) and +62.2% ($p < 0.001$) after 56 and 84 days, respectively. In the WPLC–P group the A/T

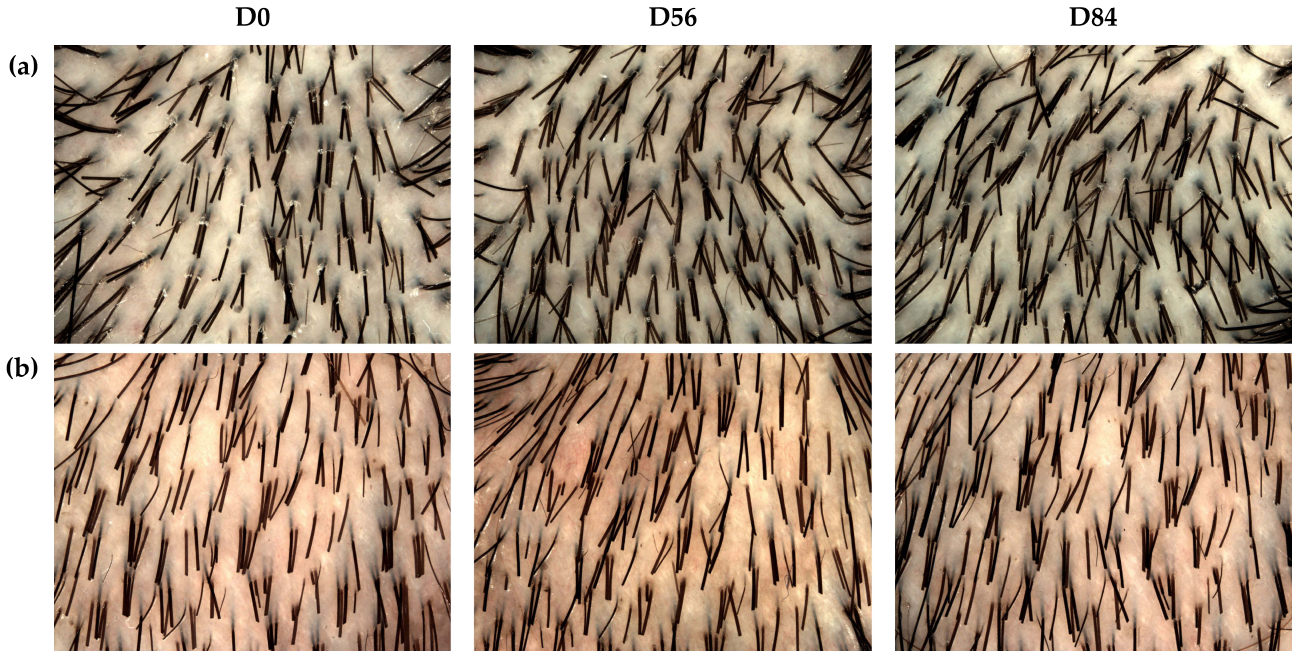

Figure 2 Images of the scalp of volunteers in the active groups at baseline (D0) and at the different timepoints. (**a**) WPLC–O. (**b**) WPLC–P.

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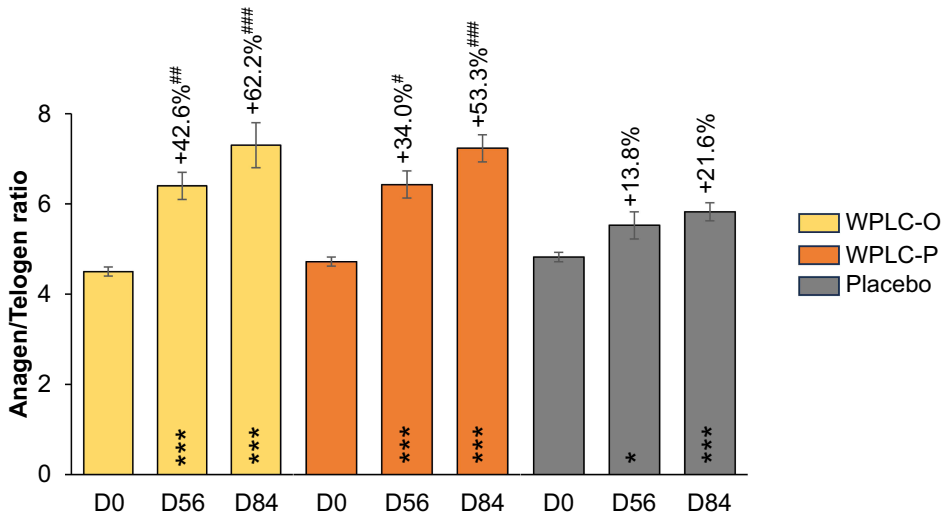

Figure 3 Anagen/telogen ratio. Data are mean ± SEM. The intragroup (vs baseline) statistical analysis is denoted by the symbol *, while the intergroup (WPLC–O vs PL and WPLC–P vs PL) statistical analysis is denoted by the symbol #, as follows: $^{*/\#}p < 0.05$, $^{\#\#}p < 0.01$, $^{***/\#\#\#}p < 0.001$.

ratio was increased by +34.0% ($p < 0.001$) and +53.3% ($p < 0.001$) after 56 and 84 days. Compared to the placebo, the increase of the A/T ratio for WPLC–O and WPLC–P was 2.5–3-fold higher indicating a hair shedding reversal 2.5–3 times quicker. The A/T ratio variation between the active groups and the placebo group was statistically different at all the time points. It should be noted that no significant difference was observed between WPLC-O and WPLC-P regarding the variation of both the density and the proportion of anagen and telogen hair.

Hair Pull Test

The number of pulled hairs was decreased at each time point for both WPLC–O and WPLC–P treatments (Table 3). The total number of pulled hairs was decreased by 41.2% ($p < 0.001$) at D84 in the WPLC-O and by 44.4% ($p < 0.001$) in the WPLC-P groups with the absolute number of pulled hairs (WPLC–O: 7.9 ± 0.6; WPLC–P: 7.5 ± 0.4) negative for aTE (ie number of pulled hair less ≤ 9 hairs). In the placebo group, the number of pulled hairs was decreased at each time point, even if the number of pulled hairs at D84 is still positive for aTE. The variation between the active groups and the placebo group was statistically different at all the time points, and no significant difference was observed between the two active groups.

Hair Growth

The hair growth at D84 was significantly higher in WPLC-O and WPLC-P groups when compared to the PL group (+16.7% vs PL, $p < 0.001$ and +11.3% vs PL, $p < 0.01$ respectively, Figure 4). No significant difference was observed between WPLC-O and WPLC-P.

Hair Elongation at Break

The hair elongation at baseline was 43.5 ± 0.5% in the WPLC–O group, 43.0 ± 0.6% in the WPLC–P group and 45.1 ± 1.0% in the PL group. At D84 this parameter was increased by 3.2% ($p < 0.05$) in the WPLC–O group, 4.6% in the WPLC–P group ($p < 0.05$) and 3.1% in the PL group (Table 3). The variation between the active groups and the placebo group at D84 did not reach statistical significance, and no significant difference was observed between the two active groups.

Self-Assessment Questionnaire

The percentage of subjects giving positive answers to each item of the self-assessment questionnaire was higher in the WPLC–O and WPLC–P active groups when compared to the PL group (Supplementary Table S2). In particular, the

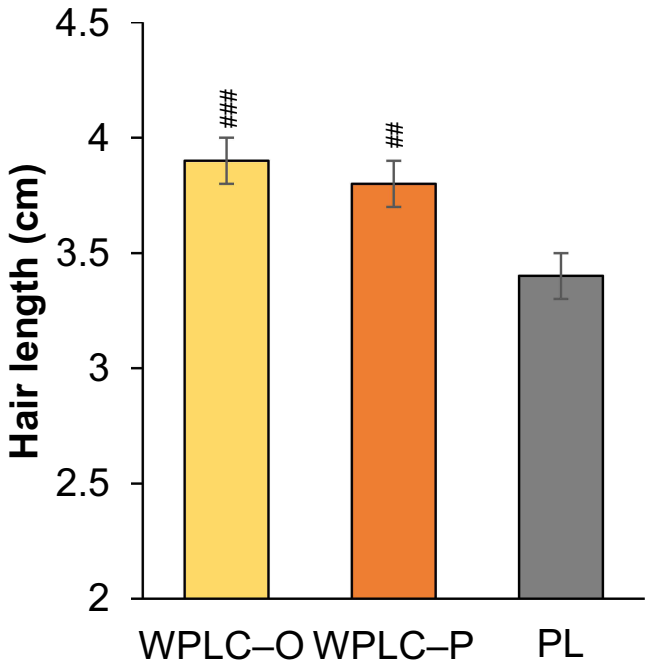

Figure 4 Hair length at D84. Data are expressed as mean ± SEM. The intergroup (WPLC–O vs PL and WPLC–P vs PL) statistical analysis is denoted by the symbol #, as follows: ##p < 0.01, ####p < 0.001.

volunteers from the active groups felt they lost less hair and that their scalp was more covered (93.9% and 97.0% for WPLC-O and WPLC-P respectively, for each item). An example of the clinical improvement in the WPLC–O and WPLC–P active groups is shown in Figure 5.

Subanalysis on Postmenopausal Women

A post hoc analysis carried out on the postmenopausal subpopulation (WPLC–O: n = 11, WPLC–P: n = 12, PL: n = 13) demonstrated a similar variation for the A/T ratio and the hair growth in comparison with the whole cohort. The

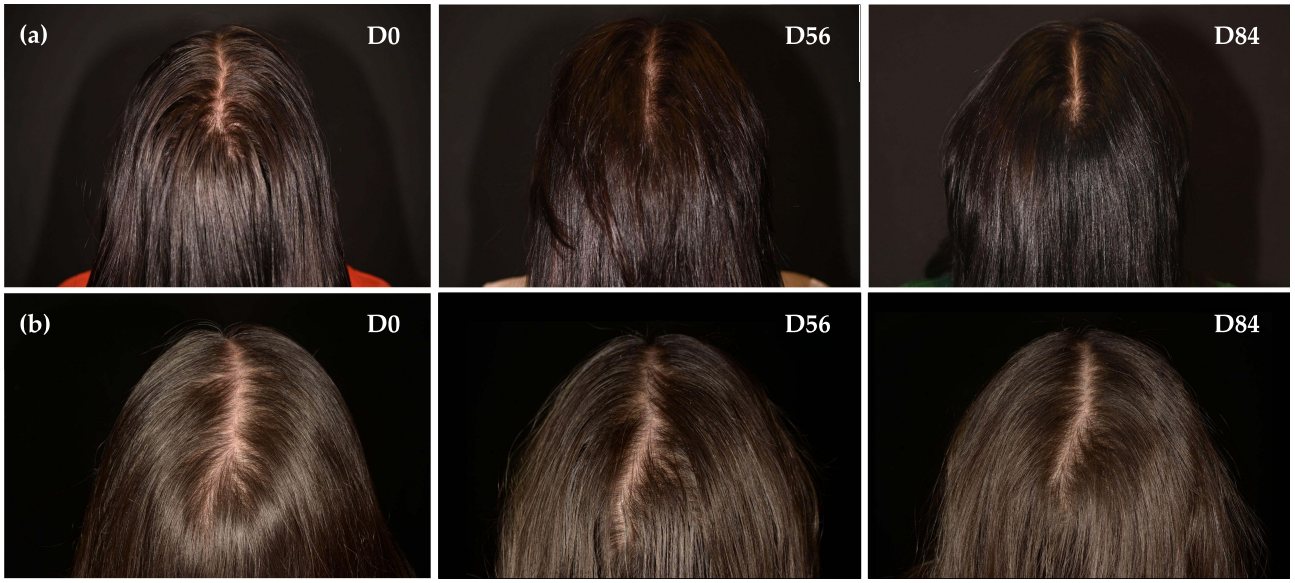

Figure 5 Example of clinical improvement in the active groups at baseline (D0) and at the different timepoints. (**a**) WPLC–O. (**b**) WPLC–P.

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variations between the WPLC–O and WPLC–P active groups and the PL group were statistically significant, as shown in the Supplementary Materials (Figure S1).

Discussion

In human beings, hair is more than a mechanism of evolutionary strategy – it is a powerful statement of personal identity central to the self-expression of both male and female beauty. From a psychological point of view, hair has a significant implication on well-being, self-esteem, quality of life and even on social competitiveness.[43] Even if hair loss is frequently diffuse and temporary, it not only affects the aesthetics but also imposes a psychological burden on those affected.[44,45] Acute telogen effluvium (aTE) is a transient and reversible non-pathological form of hair loss characterized by an early entry of the hair into the telogen phase. Such a condition is triggered by emotional or physiological stress.[17] In particular, inadequate consumption of nutrients, like essential fatty acids, has been proposed as a possible cause.

In this study we demonstrated the efficacy of a wheat (*Triticum aestivum*) polar lipid complex (WPLC) in its oil (WPLC–O) and powder form (WPLC–P) on hair shedding. Both WPLC–O and WPLC–P increased the A/T ratio 2.5–3 folds more than the PL. An increase of the A/T ratio in a shorter time indicates a quicker reversal time. Based on the results obtained we can postulate a decrease of the hair shedding reversion time by about 30–45 days when compared to the physiological reversion time. The evidence of a quicker reversal of the hair shedding was also confirmed by the hair pull test. At D56 the number of subjects with a pull test negative for aTE in both WPLC–O and WPLC–P active groups was 2.0–2.5-fold higher than in the PL group. Moreover, the pull test at D84 in the active groups was negative for aTE while it was still positive in the PL group. Also, hair growth was improved in both active groups when compared to the placebo. The improvement of the hair growth cycle related parameters was also associated with a slight improvement of the mechanical properties (elongation at break) of the new anagen hair, while the difference between the active groups and the placebo group did not reach statistical significance. While the anti-hair loss efficacy of WPLC-P was previously explored in a pilot clinical study,[37] the present trial extends the findings and brought out the similar beneficial effects of WPLC-O, which suggests a comparable bioavailability of the ingredient in its oil and powder form. While the delivery form of food ingredients is known to significantly impacts their bioavailability and subsequent bioefficacy,[46] the present clinical trial demonstrated that both the administration of WPLC bioactives (ie sphingolipids and DGDG) in oil or powder form lead to a comparable anti-hair loss efficacy.

The mechanism of action beside the anti-hair loss efficacy of WPLC is still under investigation. Sphingolipids have been reported to be essential to maintain the structure, tension and fluidity of the plasma membrane in mammalian cells.[47] These compounds are also involved in intracellular signal transduction, cell differentiation and migration, resistance to various stresses, and, eventually, in controlling programmed cell death.[47] We can therefore hypothesize that the beneficial effect of WPLC on hair cycle regulation could be partially mediated through a stimulation of the proliferation of hair dermal papilla cells, leading to the promotion of the anagen phase while delaying the onset of the telogen phase.

A variety of evidence derived from animal research suggests that glucosylceramides from food origin undergo metabolism in the gastrointestinal tract and subsequently enter the circulatory system, enabling their distribution to multiple organs such as the skin, where they act as precursors for ceramides.[48,49] Similar to what is observed in the skin, where ceramides are involved in structure and barrier function, they are essential components of the hair shaft (cuticle, cortex and medulla) and the hair follicle, and are thought to exert a barrier function for hair against various external damages.[25,26] Additionally, animal models with genetic errors in lipid metabolism were demonstrated to present an alteration of the hair phenotype, highlighting the fundamental role of lipids in hair structure and function.[27–30] Indeed, the lipids in the hair shaft have been reported to be involved in the elastic and tensile properties of hair,[25] which supports the results observed for the hair elongation at break parameter.

An alteration of hair lipids was reported during aging (reduced levels of hair lipids, disordered structure of the lipid bilayers, and increase of oxidative stress in scalp skin due to lipid oxidation).[50,51] Moreover, lipid peroxidation induces inflammation in the scalp and has been associated with alopecia areata in humans and to the early onset of the catagen phase in a murine model.[52,53] The supplementation with lipids, especially sphingolipids, is then a promising strategy to

decrease hair loss and thinning during aging, as demonstrated by the improvement of A/T ratio and hair growth not only in the general population but also in the postmenopausal women.

Conclusion

Our results highlight the efficacy of both WPLC–O and WPLC–P in accelerating the reversal of hair shedding in a clinical model of temporary hair loss (aTE). WPLC in both forms not only reduced excessive hair shedding but also stimulated the appearance and growth of new hairs. These effects were observed not only in the general population but also in the postmenopausal women. Oral supplementation with WPLC can be then a nutritional strategy to accelerate the reversal of transient hair shedding and to prevent hair loss due to aging.

Data Sharing Statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available since they are the property of the sponsor of the study (Seppic, France).

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Disclosure

SD, CK, and CG are full-time employees of Seppic Research and Innovation. SD and CK report a patent WO24231159 pending to Seppic, a patent WO24231160 pending to Seppic, a patent WO24231161 pending to Seppic, the sponsor of the clinical research described in the paper. The other authors declare no conflicts of interest.

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