J Cosmo Trichol
Volume 7:5, 2021

Journal of Cosmetology & Trichology

Research Article

Open Access

Double Blind, Randomized, Placebo-Controlled Assessment of the Efficacy of a Food Supplement in Reducing Hair Loss in Male Subjects

Vincenzo Nobile[1*], Enza Cestone[1], Gloria Roveda[1], Marta Pisati[1], Angela Michelotti[1] and Maurizia Dossena[2]

[1]*Complife Italia Srl, San Martino Siccomario, Pavia, Italy*

[2]*Department of Biology and Biotechnology "Lazzaro Spallanzani", University of Pavia, Pavia, Italy*

Abstract

Background: Hair loss is a not life-threatening dermatological condition with some physical effects but with more severe psychosocial consequences. Nutrition deficiencies have been associated to hair loss, opening the door for food supplement's use in decreasing hair loss.

Objective: The aim of this study was to investigate the efficacy and safety of a commercially available food supplement (Alline proMEN) containing a patented keratin (Keramax®), venus hair fern extract and a combination of 11 vitamins and two minerals.

Patients/Methods: Men with hair loss were randomized to receive a tablet per day of the active or the placebo product over a 3-months study period. Anagen, telogen and hair density were measured as primary endpoints; while hair mechanical properties, hair structure, hair radiance, clinical analysis and self-assessment were investigated as secondary endpoints.

Results: The mean change of the percentage of telogen hair over 1 month product use was -4.6%; while the mean change over 3 months product use was -13.2%. The hair breakage force and the hair elongation were statistically changed after 3 months of product use by +7.5 and 5.3%; while the hair radiance was improved both at 1 and 3 months. These effects were visible also on the clinical analysis, on the hair structure and by the subjects.

Conclusion: In conclusion, the oral supplementation with Alline proMEN for 3 months was effective in speeding up the resolution of the hair loss in men, in improving the hair physical and mechanical properties and was well-tolerated. The product is then a safe and effective way to address hair loss in men.

Keywords: Hair loss • Acute telogen effluvium • Food supplement • Telogen effluvium • Keratin • Venus hair fern extract

Introduction

Hair loss is a not life-threatening dermatological condition with some physical effects but with more severe psychosocial consequences. Hair symbolism has been and is still extensively researched by anthropologists, psychologists, and sociologists [1]. In 2005, Alfonso et al., surveyed 1536 European (Italy, Germany, France, Spain, and United Kingdom) men aged between 18 and 40 years old. Over 70% of these men reported hair as an important feature of image while 62% agreed that hair loss could affect self-esteem. Interestingly, even if in a small part of the interviewed, successful hair treatment resulted in psychosocial benefits [2]. For many people, hair is a central aspect of a daily grooming ritual and in contrast to other bodily transformations (e.g., weight loss, increase of muscle definition, face lift, etc.) does not require substantial time and effort [3]. The expressions "bad hair day" or "I have been tearing my hair out", are a testimony in the common parlance of the psychological importance of hair. Male hair loss starts in the 20s, but it takes 15 to 25 years to go bald [4,5]. According to the American Hair Loss Association, by the age of 35, two-thirds of American men will have some degree of appreciable hair loss, and by the age of 50, approximately 50 to 85% of men will have significant hair thinning [4,6]. The prevalence of male pattern hair loss has been evaluated by an Australian team [7]. Among the 396 men and women over 20 years old examined by dermatologists, 98,6% of the men showed some level of bitemporal recession. The etiologies of hair loss in men are various but the 2 most common are acute Telogen Effluvium (aTE) and Androgenic Alopecia (AGA). Acute Telogen Effluvium (aTE), is a transient condition characterized by excessive and diffuse hair shedding ("effluvium") for less than 6 months [8,9]. No racial predilections of telogen effluvium have been recognized. In subjects suffering from acute telogen effluvium, the hair shedding associated with the abrupt interruption of the anagen phase starts 2 to 3 months after the triggering event and lasts for less than 6 months (3 months average time). The identification of the triggering factor is difficult in one-third of the cases [10]. The triggering events of acute telogen effluvium include psychological causes, physical/emotional stress, and pharmacological therapy [11]. Among these, severe infection, major surgery, severe trauma, hypothyroidism, crash dieting, low protein intake, malnutrition, heavy metal ingestion, iron/zinc deficiency, and seasonal variation (July to October) are the most common conditions associated with acute telogen effluvium [12]. Androgenic alopecia affects 80% of Caucasian men [13,14]. According to Hamilton's study in 1951, by the age of 30 years the mean prevalence was 30%, 40% in mid-forties, and this rate rises to 50% by the age of 50 in Caucasian men [15]. In studies from the US, Italy, Norway, and Australia similar results to Hamilton's study were reported [16-18]. Different processes are involved in the pathogenesis of androgenic alopecia, including: microinflammation of the follicular bulge [19], abnormal sensitivity of follicules to androgens [20-23], dysregulation in arrector pili muscles [24-28] and genetics [29].

Interestingly there is mounting evidence that inflammation is central to the pathogenesis of all types of hair loss. Indeed, numerous triggers (genetic, hormonal, mental or nutritional) of hair loss induce inappropriate

***Address for Correspondence:** Vincenzo Nobile, Complife Italia Srl, San Martino Siccomario, Pavia, Italy; E-mail: vincenzo.nobile@complifegroup.com*

***Copyright:** © 2021 Nobile V, et al. This is an open-access article distributed under the terms of the creative commons attribution license which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.*

Received date: 05 October, 2021; **Accepted date:** 21 October, 2021; **Published date:** 28 October, 2021

inflammatory responses and chronic inflammation at the level of the follicle is common to all hair loss conditions [30]. Controlled production of cytokines (the mediators of inflammation) is involved in hair cycle regulation. However, in the event of inflammation, overproduced cytokines like IL-1 and TNFα are known to induce premature catagen, liberate Reactive Oxygen Species (ROS), cause apoptosis, and further propagate inflammation [31-33]. In recent years, evidence of the beneficial role of food supplements in subjects affected by hair loss (including acute telogen effluvium from various aetiology) is growing [34-39]. In a survey administered to 177 dermatologists attending a national dermatology conference in Riyadh (Saudi Arabia), 62% of the respondents recommended vitamins and minerals for acute telogen effluvium.

In this study we tested the efficacy of a food supplement (Alline proMEN) containing a patented keratin (Keramax®), venus hair fern extract and a combination of 11 vitamins and two minerals in reducing hair loss and restoring hair density in men. The composition of this supplement addresses two of the central pathogenic factors of hair disorders: nutritional deficiencies and inflammation. Indeed, beside the classic vitamin and minerals approach, there is increasing evidence of the role of keratin as an effective supplement for improving hair conditions [40]. The role of keratin (alone or in combination with vitamins) in improving hair conditions in subjects with acute telogen effluvium has also been investigated by our team (unpublished data). Adiantum Capillus-veneris means hair of Venus, the goddess of love named by the ancient Greeks because she has a beautiful mane, "capillus" means "hair" and "veneris" comes from Venus [41]. Given its content of phenolic flavonoid compounds, it is not surprising that the Venus capillary has anti-inflammatory and antioxidant effects [42]. Finally, the efficacy of a Venus capillary extract was established in a murine model of androgenic alopecia [43].

Methods

Clinical evaluation

This was a multicentric study (3 sites), double-blind, placebo-controlled, parallel-group (with 1:1 balanced randomization), conducted in Italy by Complife Italia srl. The study protocol and the informed consent form were approved by the 'Independent Ethical Committee for Non-Pharmacological Clinical trials' during its meeting on 09 September 2020. All subjects provided written informed consent before initiation of any study-related procedures. No changes to treatment regimen or to methods were necessary after study starting. The study is registered at ClinicalTrials.gov, number NCT04884347.

Participants

The study included a total of 100 subjects with acute telogen effluvium. Eligible participants were all adult (age range 25-55 years old) Caucasian male subjects showing the clinical signs of acute telogen effluvium. The subjects were of good general health, with all scalp and hair type, with acute telogen effluvium (due to seasonal change, stress, fatigue, imbalanced diet, pollution), with a proportion of hair in telogen phase over 20%, had no alimentary/eating disorders or known medical history of metabolic syndrome. Exclusion criteria were acute, chronic or progressive illness liable to interfere with the study data, diagnosed hair disorder or diseases related to hair cycle, and inflammatory skin disease or progressive skin lesion on the scalp. The study further excluded subjects under systemic treatment affecting the hair growth taken for more than 4 consecutive weeks during the last 24 weeks, excessive and/or fluctuating hair shedding for more than 6 months, radiotherapy or chemotherapy and scalp surgery at any time during the study period. The complete list of the inclusion and exclusion criteria is reported in Table 1.

Table 1. Inclusion and exclusion criteria.

	Inclusion criteria	Exclusion criteria
Criteria related to population	1. Male subjects; 2. Caucasian ethnicity; 3. Subjects aged between 25 and 55 years old included; 4. Subjects with all type of scalp; 5. Subjects with all type of hair; 6. Phototype I to IV included, according to Fitzpatrick classification; 7. Subjects registered with health social security or health social insurance; 8. Subjects having signed their written Informed Consent form (ICF) for their participation in the study and a photograph authorization; 9. Subjects certifying the truth of the personal information declared to the Investigator; 10. Subjects able to understand the language used in the investigation centre and the information given; 11. Subjects able to comply with the protocol and follow protocol's constraints and specific requirements	1. Subjects taking part or planning to participate to another clinical trial during the study in the same or another investigation centre; 2. Subjects deprived of freedom by administrative or legal decision or under guardianship; 3. Subjects not able to be contacted in case of emergency; Subjects admitted in a sanitary or social facility; 4. Subjects planning a hospitalization during the study; 5. Subjects belonging to the staff of the investigation centre; 6. Subjects who have participated in another clinical trial with anti-hair loss product or treatment within the last 12 weeks before the inclusion visit
Criteria related to subjects health	12. Subjects considered "healthy subject" by the Investigator; 13. If the subject is under systemic pharmacological treatment, this should be stable for at least one month before the study start and do not change over the study period, excluded the treatments specified in non-inclusion criteria"	Not applicable

Criteria related to hair loss disorders	14. Acute hair loss due to the following etiological reasons: season, stress, fatigue, imbalanced diet, pollution; 15. Proportion of hair in telogen phase superior or equal to 20% as assessed by phototricogram, 16; Subjects agreeing to preserve a length of hair longer than 10 cm during the study; 17. Subjects agreeing to have a zone of 1.8 cm² shaved on the scalp	7. i). Subjects who have any other diagnosed hair disorder or hair disease; ii). Subjects having excessive and/or fluctuating hair shedding for more than 6 months; 8 Subjects with Inflammatory skin disease or progressive skin lesion on the scalp (psoriasis, seborrhoeic dermatitis, severe erythema, severe excoriation, severe sunburn, etc.); 9. Subjects having a scalp lesion in relief which may be traumatized; 10. Subjects with history of hypersensitivity or intolerance to any of the following components applied by topical route: ethyl alcohol, components of the used hair dye, components of the studied product; 11. Subjects having systemic treatment affecting the hair growth taken for more than 4 consecutive weeks during the last 24 weeks before inclusion visit: Retinoids, Anti-mitotic, cytotoxic drugs other than antineoplastic, Anti- androgens (spironolactone, flutamide), androgens, Anti-epileptic agents, interferon alpha; 12. Subjects having systemic or local androgenetic alopecia treatment or product, taken or applied (Minoxidil, Aminexil, Finasteride, Dutasteride, cosmetic solution or capsules with vitamin B, zinc, caffeine…) for more than 4 consecutive weeks during the last 24 weeks before the inclusion visit; 13. Subjects having any other local treatment applied on the scalp (non-steroidal anti-inflammatory, ketoconazole…) within the last 2 weeks before the inclusion visit; 14. Subjects having any following hair care within the last 2 weeks before the inclusion visit or foreseen during the study (except for dying): dandruff shampoo, antifungal shampoo, dyeing, bleaching, perm ; 15. Subjects having any hair care product applied on the scalp between the last shampoo and the inclusion visit (e.g. gel, hairspray, wax, foam…); 16. Subjects under radiotherapy, chemotherapy at any time; 17. Subjects having scalp surgery (hair transplants, laser) at any time.

The study took place in Complife's Italia facilities (Biella, Milan, and Pavia) from October 2020 to February 2021. Complife Italia is an independent testing laboratory for safety and efficacy assessment of cosmetics, food supplements and medical devices.

The study took place in Complife's Italia facilities (Biella, Milan, and Pavia) from October 2020 to February 2021. Complife Italia is an independent testing laboratory for safety and efficacy assessment of cosmetics, food supplements and medical devices.

Intervention

Subjects were randomly assigned to receive a commercially available food supplement (Alline proMEN, Trenker Laboratoires, Thines Belgium) or a placebo product. The test food supplement contained a patented keratin (Keramax®), venus hair fern extract and a combination of 11 vitamins and two minerals; while the placebo product contained only excipients (Table 2). The frequency of product use was a tablet per day for a total period of use of 3 months. Subjects were asked to take the tablet during the meal with a glass of water. Both the active and placebo tablets were identical in appearance.

Outcomes

The primary end point with respect to efficacy in decreasing hair loss was the change from base-line of the number of hair in anagen and telogen phase (phototricogram) after 1 and 3 months product use. The secondary endpoints were hair radiance (colorimeter/spectrophotometer), hair mechanical properties (hair elongation and hair breakage force by dynamometer), and hair structure (SEM). Clinical evaluation (hair growth and hair radiance) and self-assessment were taken to integrate the instrumental measurements.

Table 2. Active (Alline proMEN) and placebo product composition

Active product	Placebo product
500 mg Keramax, 225 mg Inactive dried yeast rich in vitamin (containing 200 mg Saccharomyces cerevisiae 100% inactivated, 11.2-18.4 mg Vitamin B3, 6.8-7.2 mg Vitamin B5, 1.6-1.8 mg Vitamin B6, 1.6-1.8 mg Vitamin B2, 1.6 -1.8 mg Vitamin B1, 0.2-0.4 mg Vitamin B9, 0.2 mg Vitamin B8, 5.6 µg Vitamin B12), 150 mg Venus hair fern extract, 117.6 mg Iron gluconate (containing 14.7 mg Iron), 84.2 mg Sodium ascorbate coated, 76.8 mg Zinc gluconate (11 mg Zinc) 24 mg Beta carotene 20%, 14.8 mg Vitamin E, 256.3 mg Acacia gum, 100 mg Microcrystalline cellulose, 11.3 mg Magnesium stearate, 78 mg White coating (containing: 23.4-39 mg Hydroxypropylmethylcellulose (E464), 15.6-23.4 mg Calcium sulfate anhydrous (E516), 15.6-23.4 mg Magnesium carbonate, light (E504), 7.8-15.6 mg Hydroxypropylcellulose (E463), 3.9-11.7 mg Stearic acid (E570)	1095 mg Microcristalline cellulose, 5 mg Magnesium stearate, 55 mg White coating (containing: 16.5-27.5 mg Hydroxypropylmethylcellulose (E464), 11.0-16.5 mg Calcium sulfate anhydrous (E516), 11.0-16.5 mg Magnesium carbonate, light (E504), 5.5-11.0 mg Hydroxypropylcellulose (E463), 2.8-8.2 mg Stearic acid (E570).
Note: Way of use: 1 tablet per day to be taken with a glass of water, with a meal.	

Phototricogram : Phototricogram was carried out as recommended by TrichoScan® supplier. Pictures were taken 48 hours after shaving. The phototricogram procedure involves: i) clipping of a scalp area two fingers width away from the parting on the receding hairline of the fronto-temporal region or on the vertex. A template (Ø 1.8 cm) is used; ii) removal of the clipped hair with sticky tape; iii) application of dye on the clipped scalp region; iv) removal of dye remnants by means of a swab and an alcohol solution; v) photograph taking. Anagen, telogen and hair density are automatically calculated by TrichoScan® software [44].

Hair structure by SEM: Hair structure was assessed by mean of scanning electronic microscopy (SEM). Proximal (near the scalp) hair was analysed and clinically scored (improvement vs. baseline). The scoring system was as follows: 1 no variation vs. baseline, 2 mild variations vs. baseline, 3 moderate variations vs. baseline, 4 strong variation vs. baseline.

Hair radiance: Hair radiance (ability to reflect the light) was measured using a spectrophotometer/colorimeter CM 700D (Konica Minolta) by means of the 8° gloss value.

Clinical analysis: Hair growth and radiance were assessed by the investigator on a 7-point Likert scale from -3 (greatly decreased/improved) to +3 (greatly increased/worsened).

Hair mechanical properties: The force at which the hair breaks (breakage force) and their elongation (hair elasticity) was evaluated by means of dynamometer reading (Tensolab 2512A, Mesdan Lab). The dynamometer reading is done on a single hair fiber. In total 10 hair fibers were measured. Measurements were carried out according to UNI EN ISO 5079:1998.

Self-assessment questionnaire: Subjects were asked to reply to a self-assessment questionnaire and to fill a day-by-day alimentary diary.

Sample size

To detect a reduction of the percentage of anagen hair in 3 months with a two-sided 5% significance level and a power of 80%, a sample size of 50 patients per group was necessary, given an anticipated dropout rate of 10%. The recruitment and inclusion period were 1 month. Sample size was calculated using PASS11 statistical software (version 11.0.10 for Windows) running on Windows Server 2009 Standard 64-bit edition (Microsoft, USA). An official interim analysis (on December 4th, 2020) was performed after 1 month product use. The interim analysis was performed to monitor the product efficacy and safety. The outcomes analyzed in the interim analysis were: hair density, percentage anagen and telogen hair, hair radiance, and tolerability. No correction of the methods and/or to treatment regimen was performed after this interim analysis.

Randomization and blinding

Half of the test subjects were randomized to receive the test product and half of the test subjects were randomized to receive the placebo product. A restricted randomization list was created using PASS11 statistical software (version 11.0.10 for Windows) running on Windows Server 2009 Standard 64-bit edition (Microsoft, USA) by a biostatistician and stored in a safe place. The randomization sequence was stratified using "Efron's biased coin" algorithm with a 1:1 allocation ratio. The allocation sequence was concealed from the study director in sequentially numbered, opaque, and sealed envelopes, reporting the unblinded treatment allocation (based on subject entry number in the study). A masked allocation sequence was prepared for the staff delivering the intervention based on the subject entry number in the study. An independent technician dispensed either the active or the placebo products according to the masked allocation sequence. The study adhered to established procedures to maintain separation between the investigator and its collaborators and the staff that delivered the intervention. The investigator, the study staff who obtained outcome measurements and the subjects participating in the study were not informed on the (masked) product group assignment. Staff members who delivered the intervention did not take outcome measurements.

Statistical methods

All the calculations were done using a Microsoft® Office 365 ProPlus (vers. 1902; build 11328.20468; Microsoft, USA) worksheet running on Microsoft® Windows 10 Pro (vers. 1903; build 18362.476; Microsoft, USA). Intragroup (vs. baseline) statistical analysis on parametric data was carried out using two-ways Student's t-test for paired data; while intragroup statistical analysis on nonparametric data was carried out using Wilcoxon test. Intergroup (between treatments) statistical analysis on parametric data was carried out using two-way t test of Student for not paired data; while intergroup statistical analysis on nonparametric data was carried out using Mann-Whitney U test. Statistical analysis was carried out using NCSS10 statistical software (version 10.0.7 for Windows) running on Windows Server 2009 Standard 64-bit edition (Microsoft, USA). A $p<0.05$ was considered statistically significant. Statistical analysis output was reported as follows: *$p<0.05$, **$p<0.01$, and ***$p<0.001$.

Results

Participants, recruitment, and baseline characteristics

From October 2020 through February 2021, a total of 100 male subjects, meeting the inclusion criteria, were enrolled in three Complife's centers (Figure 1). Of the 100 subjects, 50 were randomly assigned to the active product and 50 to the placebo product. The study population's ethnicity

was Caucasian. Demographic and baseline characteristics (Table 3) were similar across treatment arms, indicating an unbiased randomisation and the absence of covariates.

Subjects attended clinic visits at the time of randomization (baseline) and after 1 and 3 months of product use. Data analysis was per protocol and involved all the subjects who were randomly assigned. Subjects' compliance to treatment was assessed by means of tablets count and was satisfactory. No deviations were observed in the treatment regimen. All the subjects were included in the safety analysis. Both the active and the placebo product were well-tolerated (neither objective or subjective tolerance reactions nor adverse events were reported).

Primary endpoints

The changes in hair count (hair density) are shown in Figure 2a. In the active treatment arm, the average number of baseline hair was 211.6 ± 2.5 hair/cm2, whereas the average number of hair was 220.7 ± 3.5 and 228.3 ± 2.8 after 1 and 3 months product use; respectively. The mean change over 3 months product use was +8.6%, which was statistically significant vs. baseline (p=0.004) and the placebo product (p=0.0195).

The changes in % telogen hair are shown in Figure 2b. In the active treatment arm, the average percentage of telogen hair was 25.2 ± 0.3, whereas the average percentage of telogen hair was 20.7 ± 0.6 and 12.0 ± 0.2 after 1- and 3-months product use; respectively. The mean change over 1 month product use was -4.6%; while the mean change over 3 months product use was -13.2%. The mean change of the percentage telogen hair was statistically significant both vs. baseline (p=0.0000 at 1 and 3 months) and the placebo product (p=0.0063 at 1 month and p=0.0000 at 3 months).

The changes in % anagen hair are shown in Figure 2c. In the active treatment arm, the average percentage of anagen hair was 74.8 ± 0.3, whereas the average percentage of anagen hair was 79.3 ± 0.6 and 88.0 ± 0.2 after 1- and 3-months product use; respectively. The mean change over 1 month product use was +4.6%; while the mean change over 3 months product use was +13.2%. The mean change of the percentage anagen hair was statistically significant both vs. baseline (p=0.0000 at 1 and 3 months) and the placebo product (p=0.0063 at 1 month and p=0.0000 at 3 months).

Secondary endpoints

The changes of the secondary endpoints are shown in Table 4. In the active treatment arm, hair radiance was improved by 15.4% and 24.0% after 1 and 3 months of product use. The variation of hair radiance was statistically significant both vs. baseline (p=0.0000) and the placebo product (p=0.0000) at 1 and 3 months. The hair breakage force and the hair elongation were statistically changed after 3 months of product use by +7.5 cN (p=0.0000 vs. baseline and placebo) and 5.3% (p=0.0000 vs. baseline and placebo); respectively. Clinical analysis confirmed a statistically significant improvement of hair growth, hair radiance and hair structure (Figure 3.), after 3 months product use, in the active treatment group vs placebo. The active product was perceived as effective by most of the subjects participating in the study (Figure 4).

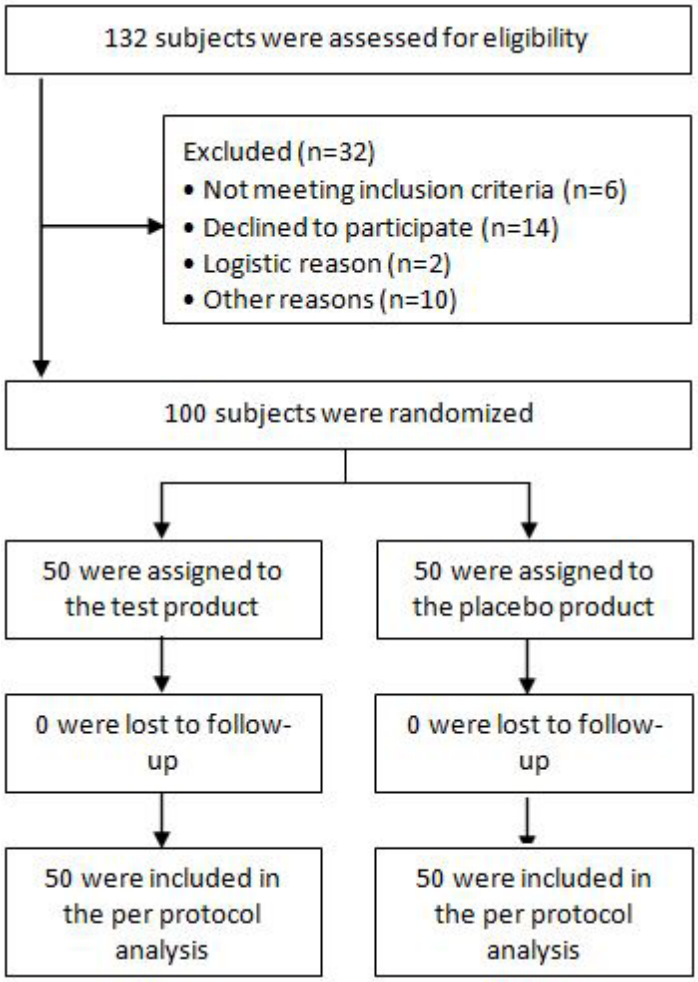

Figure 1. Study enrolment and randomization

Table 3. Subjects demographics and baseline characteristics. Data are mean ± SE.

	Active (n=50)	Placebo (n=50)
Sex		
Male	50	50
Female	0	0
Phototricogram		
Hair density (no.)	211.6 ± 2.5	212.8 ± 3.2
Anagen hair (%)	74.8 ± 0.3	75.1 ± 0.4
Telogen hair (%)	25.2 ± 0.3	24.9 ± 0.4
Hair radiance	9.0 ± 0.9	8.6 ± 0.8
Hair tensile properties		
Max elongation (%)	47.9 ± 0.5	48.4 ± 0.5
Breakage force (cN)	72.2 ± 1.1	72.7 ± 1.2

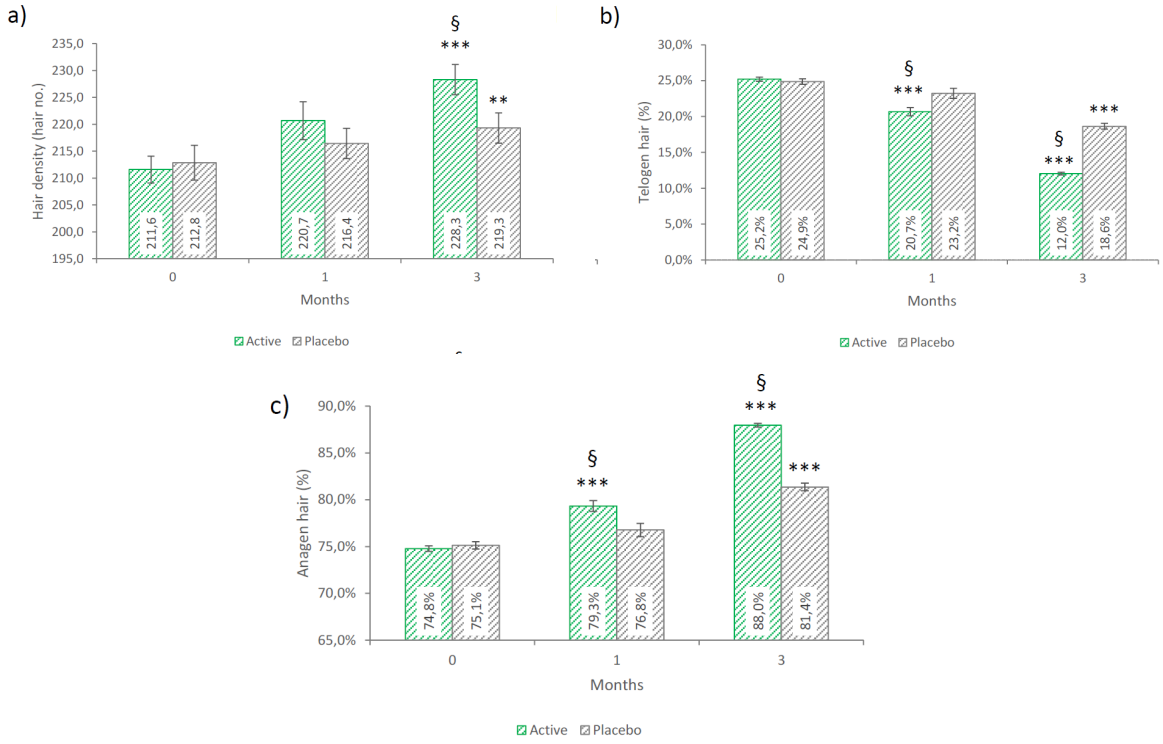

Figure 2. Phototricogram data. a) Hair density. b) % telogen hair. c) % anagen hair. Data are mean ± SE. Upon the bar is reported the intragroup statistical analysis (vs baseline). *p<0.05, **p<0.01, ***p<0.001.§ the variation is statistically significant vs. placebo (intergroup statistical analysis).

Table 4. Secondary endpoints. Data are means: ± SE. In brackets is reported the % variation vs. baseline. Near the raw data is reported the intragroup (vs. baseline) statistlcal analysis; while near the percentage variation is reported the intergroup (vs. plavebo) statistical analysis. *p<0.05, **p<0.01, ***p<0.001. § the variation is statistically significant vs. placebo (intergroup statistical analysis). •% of subjects showing an improvement.

	Active			Placebo		
	Baseline	1 month	3 months	baseline	1 month	3 months
Hair radiance	9.0 ± 0.9	10.1 ± 1.0*** (+15.4%)§	10.8 ± 1.0*** (+24.0%)§	8.6 ± 0.8	8.2 ± 0.8 (-3.2%)	8.6 ± 0.8 (+2.8%)
Hair tensile properties	47.9 ± 0.5	48.1 ± 0.5 (+0.2)	53.2 ± 0.5*** (+5.3)§	48.4 ± 0.5	48.5 ± 0.5 (+0.1)	48.8 ± 0.5*** (+0.4)
Max elongation (%)						
Breakage force (cN)	72.2 ± 1.1	72.8 ± 1.1 (+0.6)	79.7 ± 10*** (+7.5)§	72.7 ± 1.2	72.7 ± 1.2 (+0.1)	72.8 ± 1.2 (+0.1)
Clinical analysis		36	60		20	32
Hair growth (%•)		36	90		6	24
Hair radiance (%•)		16	72		10	18
Hair structure-SEM (%•)						

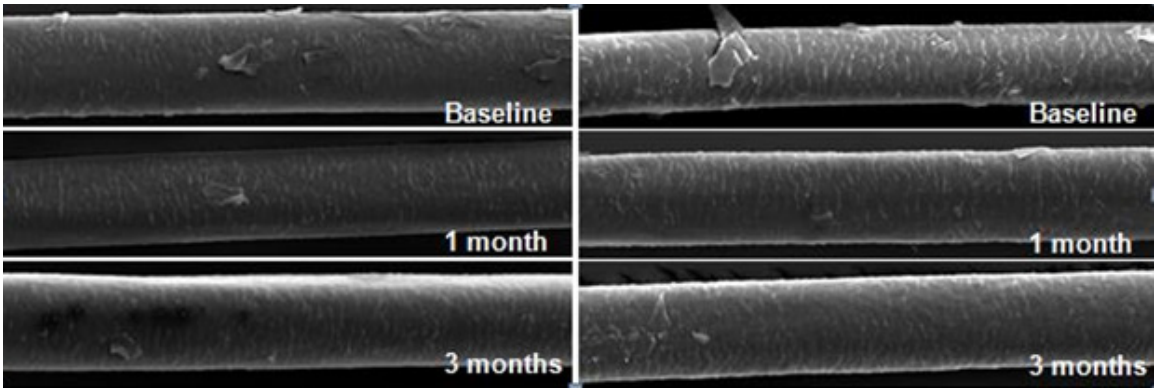

Figure 3. Representative SEM images of the hair structure (apical part of the hair) of two subject from the active treatment group showing the best effect.

Figure 4. Self-assessment questionnaire output. Data are reported as % of positive answers.

Discussion

It's nowadays clear that nutrition has an influence on hair loss [45-47]. This awareness fostered the food supplement industry in researching and developing products effectively helping the management of hair loss. In this trial we studied the efficacy of a commercially available food supplement (Alline proMEN) containing a patented keratin (Keramax®), venus hair fern extract and a combination of 11 vitamins and two minerals in men suffering from hair loss.

Conclusion

Although there is evidence in the literature of the efficacy for many of the ingredients used in the test product, to the best of our knowledge this is the first study reporting the benefits of their combined supplementation. While, most often, the food supplements efficacy is not investigated and their marketing claims relies on the literature on the ingredients, we preferred to test the finished product to give the real proof of product efficacy. In fact, ingredient claims referring to the properties of one or more specific ingredients shall not imply that the finished product has the same properties when the real product efficacy was not investigated. This is commendable and should be the preferred approach to avoid crowding the market with products of unknown efficacy.

Even in a reversible form of hair loss, the test product demonstrated to be effective in decreasing hair loss more quickly when compared to the placebo product. A quicker decrease of the percentage of telogen hair, in the real life, is related to a decrease of the time span in which subjects are worried about hair loss. Interestingly, the product was also effective in improving the hair mechanical properties and hair radiance. The improvement of these parameters was also correlated to an improvement of hair structure and was visible both to the investigator (clinical analysis) and to the subjects participating in the study (self-assessment questionnaire).

In conclusion the oral supplementation with Alline proMEN for 3 months was effective in speeding up the resolution of the hair loss in men, in improving the hair physical and mechanical properties and was well-tolerated. The product is then a safe and effective way to address hair loss in men.

References

1. Anthony, Synnott. "Shame and glory: A sociology of hair." British Journal of *Sociology* 38 (1987): 381-413.
2. Alfonso, Mariola, Richter-Appelt Hertha, Tosti Antonella and Viera Miguel Sanchez, et al. "The psychosocial impact of hair loss among men: a multinational European study." *Curr Med Res Opin* 21 (2005): 1829-1836.
3. Cash, Thomas F. "The psychology of hair loss and its implications for patient care." *Clin Dermatol* 19 (2001): 161-166.
4. Jaller, Jose A, MacQuhae Flor, Nichols Anna J. "Chapter 26 - Clinical Trials and Hair Loss." *Alopecia* (2019): 267-284.
5. Messenger, Andrew. "Male Androgenic Alopecia." Hair Growth and Disorders (2008): 159-170.
6. Rhodes, Thomas, Girman Cynthia J, Savin Ronald C and Kaufman Keith D, et al. "Prevalence of Male Pattern Hair Loss in 18–49 Year Old Men." *Dermatol Surg* 24(1998):1330-1332.
7. Gan, Desmond CC and Sinclair, Rodney D. "Prevalence of Male and Female Pattern Hair Loss in Maryborough" *J Investig Dermatol Symp Proc* 10(2005):184-189.
8. Grover, Chander and Khurana Ananta. "Telogen effluvium." Indian *J Dermatol Venereol Leprol* 79(2013):591-603.
9. Asghar, Fahham, Shamim Nazia, Farooque Umar and Sheikh Haris et al. "Telogen Effluvium: A Review of the Literature." *Cureus* 12(2020):e8320.

10. Shrivastava, Shyam Behari. "Diffuse hair loss in an adult female: approach to diagnosis and management." Indian *J Dermatol Venereol Leprol* 75(2009):20-27.

11. Mysore,Venkataram, Parthasaradhi Anchala, Kharkar RD and Ghoshal AK, et al. "Expert consensus on the management of Telogen Effluvium in India." *Int J Trichology* 11(2019):107-112.

12. Nobile, Vincenzo, Tursi Francesco, Cestone Enza and Sergheraert Renaud et al. "The effects of the oral supplementation with a natural keratin hydrolysate (Kera-Diet®) on hair and nails: Randomized, placebo and benchmark-controlled clinical trial on healthy females." *Trichol Cosmetol Open J* 1(2021): 27-36.

13. Martinez-Jacobo, Lizeth, Villarreal-Villarreal Cesar D, Ortiz-López Rocio and Ocampo-Candiani Jorge, et al. "Genetic and molecular aspects of androgenetic alopecia." *Indian J Dermatol Venereol Leprol* 84(2018):263-268.

14. Salman, Kubra Esen, Altunay Ilknur Kivanc, Kucukunal Nihal Asli and Cerman Asli Aksu. "Frequency, severity and related factors of androgenetic alopecia in dermatology outpatient clinic: hospital-based cross-sectional study in Turkey." *An Bras Dermatol* 92(2017):35-40.

15. Hamilton, James B. "Patterned loss of hair in man; types and incidence." *Ann N Y Acad Sci* 53(1951): 708-728.

16. Severi, Gianluca, Sinclair R, Hopper John L and English Dallas R. "Androgenetic alopecia in men aged 40-69 years: prevalence and risk factors." *Br J Dermatol* 149(2003):1207-1213.

17. DeMuro-Mercon, Carla, Rhodes Thomas, Girman Cynthia J and Vatten Lars. "Male-pattern hair loss in Norwegian men: a community-based study." *Dermatology* 200(2000):219-222.

18. Gan, Desmond CC and Sinclair Rodney D. "Prevalence of male and female pattern hair loss in Maryborough." *J Investig Dermatol Symp Proc* 10(2005):184-189.

19. Jaworsky, Christine, Kligman Albert M and Murphy GF. "Characterization of inflammatory infiltrates in male pattern alopecia: implications for pathogenesis." *Br J Dermatol* 127(1992):239-246.

20. Kaufman, Keith D. "Androgens and alopecia." *Mol Cell Endocrinol* 198(2002):89-95.

21. Liu, Shicheng and Yamauchi Hitoshi. "Different patterns of 5alpha-reductase expression, cellular distribution, and testosterone metabolism in human follicular dermal papilla cells." *Biochem Biophys Res Commun* 368(2008):858-864.

22. Sinclair, Rodney. "Male pattern androgenetic alopecia." *BMJ* 317(1998):865-869.

23. Randall, Valerie Anne. "Androgens and hair growth." *Dermatol Ther* 21(2008):314-328.

24. Poblet, Enrique, Jiménez Francisco and Ortega Francisco. "The contribution of the arrector pili muscle and sebaceous glands to the follicular unit structure." *J Am Acad Dermatol* 51(2004):217-222.

25. Torkamani, Niloufar, Rufaut Nicholas W, Jones Leslie and Sinclair Rodney. "Destruction of the arrector pili muscle and fat infiltration in androgenic alopecia." *Br J Dermatol* 170(2014):1291-1298.

26. Brack, AndrewS, Conboy Michael J, Roy Sudeep and Lee Mark. "Increased Wnt signaling during aging alters muscle stem cell fate and increases fibrosis." *Science* 317(2007):807-810.

27. Uezumi, Akiyoshi, Fukada So-ichiro, Yamamoto Naoki, Takeda Shin'ichi. "Mesenchymal progenitors distinct from satellite cells contribute to ectopic fat cell formation in skeletal muscle." *Nat Cell Biol* 12(2010):143-152.

28. Hugh Rushton, D, Norris Michael J and Van Neste Dominique. "Hair regrowth in male and female pattern hair loss does not involve the conversion of vellus hair to terminal hair." *Exp Dermatol* 25(2016):482-484.

29. Nyholt, Dale R, Gillespie Nathan A, Heath Andrew C and Martin Nicholas G. "Genetic basis of male pattern baldness." *J Invest Dermato*l 121(2003):1561-1564.

30. Sadick, Neil, Callender Valerie D, Kircik Leon H and Kogan Sophia. "New Insight Into the Pathophysiology of Hair Loss Trigger a Paradigm Shift in the Treatment Approach." *J Drugs Dermatol* 16(2017):s135-s140.

31. Trüeb, Ralph M. "Molecular mechanisms of androgenetic alopecia." *Exp Gerontol* 37(2002):981-990.

32. Piérard, Gerald E, Piérard-Franchimont C, Marks R and Elsner Peter. "EEMCO Guidance for the Assessment of Hair Shedding and Alopecia." *Skin Pharmacol Physiol* 17(2004):98-110.

33. Magro, Cynthia M, Rossi Anthony, Poe Jonathan, Manhas-Bhutani Suveena and Sadick Neil. "The Role of Inflammation and Immunity in the Pathogenesis of Androgenetic Alopecia." *J Drugs Dermatol* 10(2011):1404-1411

34. Addor, Flavia AS, Bombarda Patricia Camarano Pinto, Bombarda Júnior MS, Abreu FF. "Influence of nutritional supplementation in the treatment of telogen effluvium: Clinical and digital phototricogram evaluation in 60 patients" *Surg Cosmet Dermatol* 6(2014):131-136.

35. Sant'Anna Addor, Flávia Alvim, Donato Ludmila Coelho and Melo Camila Sirieiro Abreu. "Comparative evaluation between two nutritional supplements in the improvement of telogen effluvium." *Clin Cosmet Investig Dermatol* 11(2018):431-436.

36. Nistico, Steven, Tamburi Federica, Bennardo Luigi and Dastoli Stefano, et al. "Treatment of telogen effluvium using a dietary supplement containing Boswellia serrata, Curcuma longa, and Vitis vinifera: Results of an observational study." *Dermatol Ther* 32(2019): e12842.

37. Mubki, Thamer. "Use of Vitamins and Minerals in the Treatment of Hair Loss: A Cross-Sectional Survey among Dermatologists in Saudi Arabia." *J Cutan Med Surg* 18(2014):405-412.

38. Narda, Mridvika, Aladren Sonia, Cestone Enza and Nobile Vincenzo. "Efficacy and Safety of a Food Supplement Containing L-cystine, Serenoa repens Extract and Biotin for Hair Loss in Healthy Males and Females. A Prospective, Randomized, Double-blinded, Controlled Clinical Trial." *J Cosmo Trichol* 3(2017):127.

39. Hosking, Anna-Marie, Juhasz Margit and Atanaskova Mesinkovska Natasha. "Complementary and Alternative Treatments for Alopecia: A Comprehensive Review." *Skin Appendage Disord* 5(2019):72-89.

40. Beer, Christina, Wood Simon and Veghte Robert H. "A clinical trial to investigate the effect of Cynatine HNS on hair and nail parameters." *ScientificWorldJournal* 2014:641723.

41. Makbul, shaikh Ajij Ahmed. "Physicochemical and biological properties of adiantum capillus-veneris linn: an important drug of unani system of medicine." (2018).

42. Al-Snafi, Ali Esmail. "The chemical constituents and pharmacological effects of adiantum capillus-veneris - a review." *Asian J Pharm Sci Technol* 5(2015).

43. Noubarani, Maryam, Rostamkhani Hossein, Erfan Mohammad and Kamalinejad Mohammad, et al. "Effect of Adiantum Capillus veneris Linn on an Animal Model of Testosterone-Induced Hair Loss." *Iran J Pharm Res IJPR* 13(2014):113-118.

44. Hoffmann, Rolf. "TrichoScan: a novel tool for the analysis of hair growth *in vivo*." *J Investig Dermatol Symp Proc* 8(2003):109-115.

45. Rushton, D Hugh. "Nutritional factors and hair loss." *Clin Exp Dermatol* 27(2002): 396-404.

46. Haneke, E and Baran Robert. "Micronutrients for hairs and nails." *Nutrition for Healthy Skin* (2010):149-163.

47. Krutmann, Jean and Humbert, Philippe. " Nutrition for Helathy skin-Strategies forclinical and cosmetics practice." *Dermatology.*

How to cite this article: : Nobile, Vincenzo, Cestone Enza, Roveda Gloria and Pisati Marta, et al. "Double Blind, Randomized, Placebo-Controlled Assessment of the Efficacy of a Food Supplement in Reducing Hair Loss in Male Subjects" *J Cosmo Trichol* 7(2021): 171.