ORIGINAL RESEARCH

A Randomized, Placebo-controlled Clinical Study Evaluating a Dietary Supplement for Hair Growth

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OBJECTIVE: The desire for improved hair appearance, hair growth and strength are common drivers of supplementation for women experiencing thinning hair. This study examined the effect and safety of a gummy supplement containing B vitamins, zinc and botanical ingredients to improve hair growth, strength and perceived hair quality outcomes. **METHODS:** Healthy females (n=65) ages 18 to 60 with thinning hair were enrolled. After obtaining consent, subjects were evaluated for hair density and tensile strength, then randomized to either a placebo or test product. The test product consisted of two gummies consumed daily. Subjects returned after six months and were again evaluated using phototrichogram for hair density and tensile strength assessment and completed a Self-Assessment Questionnaire reporting hair quality outcomes. **RESULTS:** Subjects who consumed the test product showed increased hair density between baseline and 6 months (10.1% increase, $p<0.001$) as well as compared to placebo (2% decrease) ($p<0.001$). Hair strength tensile measurements were improved in the test group from baseline (10.2% improvement, $p<0.002$) compared to placebo (9.3% improvement), yet the difference was not statistically significant between groups. Self-assessed improvements in shedding, strength, breakage and brightness were noted compared to the placebo group ($p<0.05$). There were no adverse events or reactions. **LIMITATIONS:** This study did not assess hair for longer than a six-month period and utilized subject perception for outcomes that differ from clinical assessments. **CONCLUSION:** Daily use of a dietary supplement gummy was associated with significant improvement in hair growth as well as self-assessed improvements in hair strength, shedding, and appearance. **KEYWORDS:** Hair growth, hair strength, supplement, vitamin, gummy

Hair thinning and quality concerns can have wide ranging impacts on quality of life and cause distress to affected individuals.[1,2] An array of factors have been shown to influence hair loss, including but not limited to stress, nutritional deficiencies, illness, hormonal imbalances, and drugs.[3–5] Telogen effluvium causes premature entry into the resting phase, resulting in excessive shedding and thinning.[3,6] The appropriate operation of cell metabolism during the phases of hair growth increases the resistance of the hair to new external insults, and also stimulates healthy hair growth.[7]

Nutritional status contributes to hair quality at each phase and can affect the anagen to telogen transition as well as telogen to anagen (ie, new growth) with energy deficiency or other nutritional deficiencies known to impact hair structure, loss, and growth.[8] The global market for hair growth supplements to target nutritional considerations has been growing and is projected to have a $2.86 billion USD value by 2031.[9]

Biotin (vitamin B7) is commonly found in hair growth dietary supplements as it is an essential nutrient that functions as a cofactor required for biotin-dependent carboxylases that act as catalysts in metabolic processes including amino acid catabolism.[10] Its function in protein synthesis and keratin production contribute to hair shaft strength.[11,12] While rare, biotin deficiency manifests in part as thinning and progressive hair loss.[8] Similarly, folate deficiency can cause changes to hair, skin and nails with folate acting as a coenzyme in synthesis of nucleic acids and amino acid metabolism.[10] Zinc is an essential nutrient cofactor for enzymes involved in hair growth, and hair loss is a well-established sign of zinc deficiency with regrowth occurring with supplementation.[13] Vitamin B12 is another nutrient involved in nucleic acid production that appears to play a role in hair protein production.[10]

This study aimed to evaluate the effectiveness and tolerability of a novel dietary supplement, Hair Strong Gummies (HUM Nutrition Inc., Los Angeles, California) that contains a blend of B vitamins, zinc, and botanicals in healthy women with self-reported thinning hair.

METHODS

Design. This was a single center, double-blind, randomized, placebo-controlled clinical study in an ambulatory setting. The study was conducted in Brazil in accordance with the Declaration of Helsinki Good Clinical Practices and to the Resolution CNS n° 466/12 (National Health Council, 2013) and in conformity with the Standard Operating Procedures of the Institute. The study was approved by the Independent Ethics Committee of Investiga- Instituto de Pesquisas and registered by the National Research Ethics Commission (Comissão National de Ética em Pesquis) for written approval.

Subjects. Study subjects (N=65) were healthy women aged 18 to 60 years with self-reported hair loss, less voluminous hair, and lack of hair shine, as well as diffuse hair thinning with telogen effluvium assessed by a

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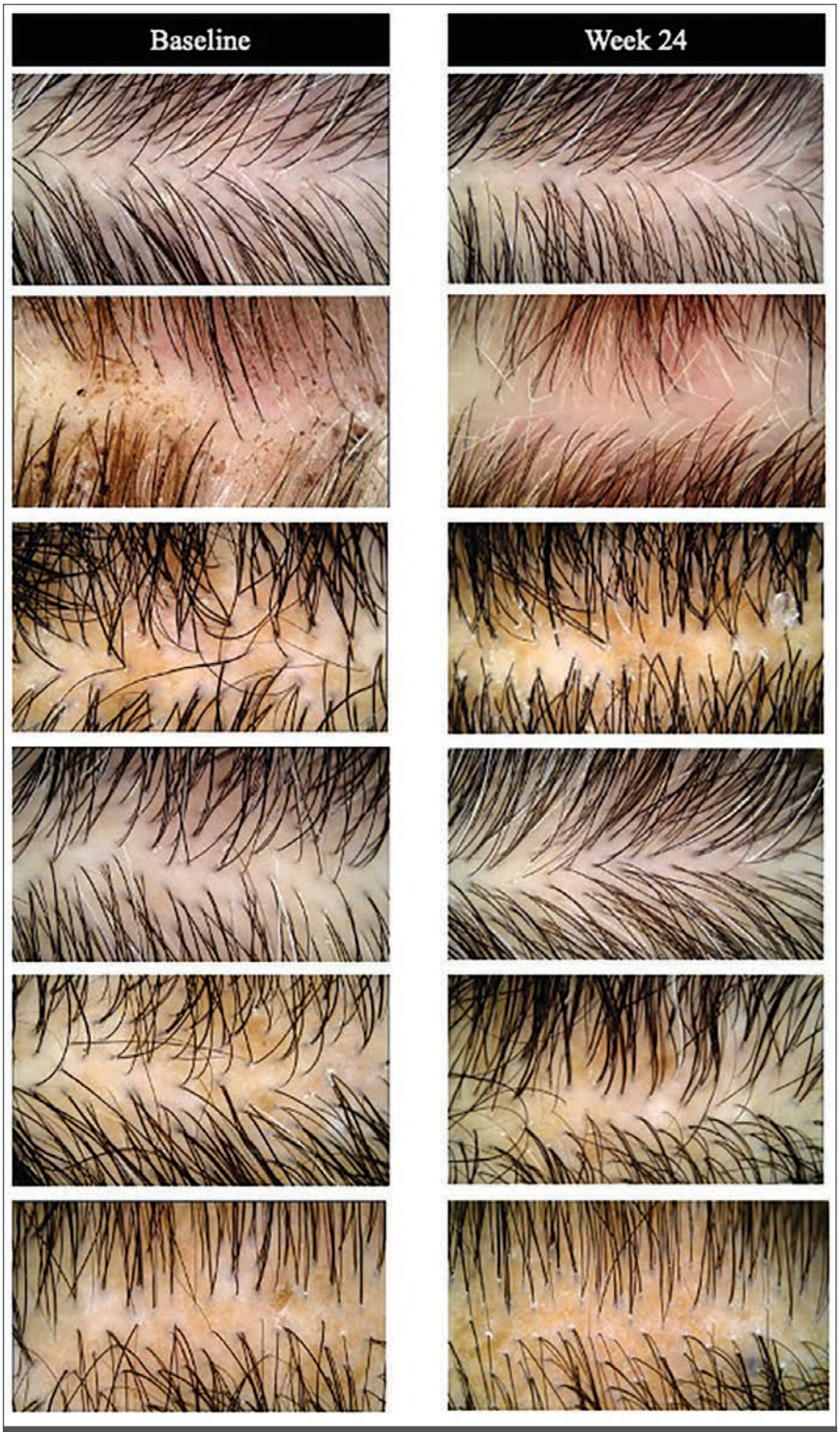

FIGURE 1. Matched before and after trichogram images of select test group participants at baseline (left) and Week 24 (right)

dermatologist.

Exclusion criteria included pregnancy and breastfeeding, subjects diagnosed with cicatricial alopecia, moderate dandruff, more than 50-percent grey hair, very light or blonde hair through more than 50 percent of their hair), moles, tattoos, scars, irritated skin or other irregularities on the test sites that could influence assessments or measures. Additional exclusions included subjects with pathological hair loss (ie, alopecia universalis or totalis), treatment with chemotherapy, skin pathology on the area of evaluation, diabetes diagnosis, use of systemic corticosteroids or immunosuppressant drugs, and skin diseases such as vitiligo, psoriasis, and atopic dermatitis. Study subjects were required to maintain hair length of at least 10cm, not change hair dyeing routine during the study, not perform any chemical treatments on the hair or use any hair treatments for hair loss, dietary supplements, or dandruff prevention treatments. Subjects were included who met all inclusion criteria, agreed to the study stipulations, and completed informed consent and image release.

Study procedures. Participants visited the study on two separate occasions. At the initial study visit, subjects were consented and then assessed by a dermatologist to verify inclusion and non-inclusion criteria and clinical safety assessment. An area of 1.7cm^2 was selected on the top of the scalp for phototrichogram analysis (scalp micrographs). Subjects were seated with their head slightly angled down and hair was parted in the middle using clips and Transpore® tapes and a ruler to mark the area of assessment. A trained technician captured images using the FotoFinder Leviacam®. Technicians then pulled at least 30 hair threads from each subject for assessment of hair resistance using the Instron® 5565 device.

After 168±2 days of product use, subjects returned for the second assessment visit. The dermatologist performed a clinical safety assessment and a new image acquisition for phototrichogram analysis was obtained on the same area of 1.7cm^2 determined on the first visit. Subjects again submitted manual hair thread collection for assessment of hair resistance. An 8-item Self-Assessment questionnaire was also completed by each subject to assess agreement on a 5-point Likert-type scale evaluating hair shedding, fullness, new growth, growth speed, volume, broken

TABLE 1. Hair growth density measures

TREATMENT	STATISTICS	BASELINE	DAY 168	CHANGE
Test Product	Mean (count)	148.43	163.46	15.03
	Std. Error	3.98	5.27	3.67
	% improvement			10.1
	% of subjects with improvement			80.0
	p-value			<0.001*
Placebo	Mean (count)	174.57	171.07	-3.50
	Std. Error	5.64	5.89	3.42
	% improvement			-2.0
	% of subjects with improvement			46.7
	p-value			0.797
Test vs Placebo	*p*-value (treatments)			<0.001*

* $p<0.05$

TABLE 2. Hair strength tensile measures

GROUP	STATISTICS	BASELINE	DAY 168	CHANGE
Test Product	Mean (MPa)	276.69	305.05	28.36
	Std. Error	9.19	7.52	9.2
	% improvement			10.2
	% of subjects with improvement			65.7
	p-value			0.002*
Placebo	Mean (MPa)	270.25	295.36	25.12
	Std. Error	11.24	7.33	8.02
	% improvement			9.3
	% of subjects with improvement			73.3
	p-value			0.002*
Test vs Placebo	*p*-value (treatments)			0.396

* $p<0.05$

hairs, and brightness. During all visits, subjects were under acclimatization of controlled temperature and humidity for 30 minutes before assessments (20°C±2°C) and (50%±5 RH).

The test product consisted of two gummies containing 300mcg folic acid, 5000mcg biotin, 850mcg vitamin B12, 20mg zinc citrate, 15mg para-aminobenzoic acid, 10mg Fo-ti (*Polygonum multiflorum*) root extract in a pectin-based gummy. The placebo was a gummy similar in appearance and taste to the study product but with no active ingredients (ie, no added vitamins, minerals, or botanical ingredients).

Statistical methods. Exploratory data analysis was performed using means, standard error, percentage of improvement on the mean and percentage of subjects with improvement. For Instron® 5565 evaluation, comparison between time-points and treatments were performed using Student's t test (one-sided). For FotoFinder leviacam® evaluation, comparison between time-points were performed using Student's t test or Wilcoxon non-parametric test and comparison between treatments was performed with Mann-Whitney test (one-sided). The normality was verified by Shapiro-Wilks test. For Self-Assessment, comparison between treatments was performed by z test for two proportions (one-sided). Detailed description of the treatment applied to the data is presented in the table below. Analyses were performed with XLSTAT 2021 and Minitab 14 and confidence level were set at 95 percent.

RESULTS

The final sample of 65 female participants were included in the analysis, with 35 randomized to the test product group and 30 to the placebo group. There was a statistically significant improvement in hair growth density after 168 days from baseline as assessed by phototrichogram as well as significantly more hair growth compared to the placebo (see Table 1). Subjects who consumed the test product increased hair growth density by 10.1 percent ($p<0.001$), with subjects in the placebo group having a decrease of two percent in hair density. The difference between the two groups was statistically significant ($p<0.001$).

A statistically significant increase in maximum stress parameter was observed from baseline to Day 168 in the test product group. There was also, however, an improvement in strength noted in the placebo group, although the percent improvement was greater in the test group, there was no statistically significant difference between test and placebo (10.2% vs 9.3%, $p=0.396$) (see Table 2).

Subjects in the test product group reported statistically significantly higher agreement (responded "agree" or "strongly agree") that the test product decreased shedding of hair, improved strength of hair, hair was less broken, and hair was brighter on a self-assessment questionnaire (see Table 3).

No adverse events or reactions to the test product or placebo were reported by participants or noted by the supervisory dermatologist.

TABLE 3. Self-assessment questionnaire results

ATTRIBUTE	% OF SUBJECTS IN AGREEMENT WITH IMPROVEMENT
Decreases shedding	91.4%*
Improved strength	94.3%*
Increased fullness	85.7%
More growth	88.6%
Increased growth rate	88.6%
More voluminous	82.9%
Less broken	88.6%*
Brighter	91.4%*

*Statistically significant improvement $p<0.05$

DISCUSSION

The results of this study show that the use of a unique blend of nutrients and botanicals in the evaluated dietary supplement taken daily was effective and well tolerated in women with thinning hair. A significant increase in hair density compared to placebo was reflected in self-assessments with improvements observed in hair growth, strength, less breakage and more shine. There were improvements in hair tensile strength, but not significantly different from the placebo, however self-assessment found that participants taking the test product reported stronger hair and less breakage compared to the placebo group ($p<0.05$). Perception of hair loss and quality have been shown to be distinct from clinical diagnosis and physician observation in other clinical trials, with patients rating hair loss and quality more severely than expert assessments.[2,14,15]

The complex etiology of hair growth and nutritional strategies has yielded little success in supplementation with individual ingredients,[8,12] yet provision of supplements that contain a combination of ingredients and nutrients appear to have synergistic effects to positively affect hair growth outcomes.

Biotin is included in numerous dietary

supplements for hair health due to its deficiency being associated with alopecia and brittle nails.[8] The overall self-reported prevalence of use of a biotin dietary supplement of 1mg/day or more was 2.8 percent in the general population in 2015–2016, increased from 0.1 percent in 1999–2000.[16] Deficiency of biotin was found in 38 percent of women complaining of hair loss,[17] yet supplementation of biotin alone shows mixed results in efficacy to grow or strengthen hair outside of specific pathologies or deficiencies.[12]

Water soluble vitamins B12 and folate have important roles in hair follicles and have been evaluated with mixed outcomes in hair growth and loss. In a study of subjects presenting with TE, vitamin B12 and folate serum levels were significantly lower than those in the control group.[18] Another retrospective, cross-sectional study showed 2.6 percent of subjects with TE to be vitamin B12 deficient but none had folate deficiency.[13] Another showed no significant difference in vitamin B12 and folate levels and hair loss.[19] Folate and B12 may have an effect on hair color, as a case-control study of 52 subjects in India with premature greying (defined as greying occurring before the age of 20) had significantly lower serum levels of B12, folic acid, and biotin.[20] Despite these mixed associations, no clinical trial that could be located has evaluated supplemental vitamin B12 or folate alone on outcomes of hair growth or strength.

Zinc supplementation was explored in an in-vivo examination with the C57BL/6 mouse model for hair research given high doses of oral zinc, appears to inhibit hair follicle regression and accelerate hair follicle recovery.[21] A study of patients with hair loss, including telogen effluvium hair loss showed significantly lower serum zinc concentrations in subjects with TE and androgenic alopecia.[22] A known sign of zinc deficiency in children is alopecia, with regrowth occurring with supplementation.[23,24] A clinical trial supplemented 50mg of zinc gluconate daily in deficient subjects with androgenic alopecia who experienced increase in serum zinc concentration and clinically therapeutic effects seen after 12 weeks.[25]

Fo-ti (*Polygonum multiflorum*), also known as He-Shou-Wu, is an herbal remedy that is commonly used in Traditional Chinese Medicine to treat a variety of ailments, including hair loss and premature hair greying.[26,27] In an *in vitro* assay, a Fo-ti extract applied to cultured human dermal papillar cells stimulated proliferation and mitochrondrial activity, as well as decreased expression of catagen inducing protein.[28] This points to the potential role of fo-ti promoting hair growth via inhibition of entering the catagen phase and/or ability to prolong the anagen phase. Both oral and topical administration of Fo-ti extract have been shown to increase hair growth in a C57BL/6J mouse model.[29]

The organic compound para-aminobenzoic acid (PABA) is considered part of the vitamin B complex and is found in various foods and also synthesized by bacteria in the gut. Clinical and case studies from the 1940s and 1950s showed doses of 200mg to 24 grams to be effective to promote hair regrowth and darkening of grey hair.[30–32]

While there has been limited human clinical research evaluating the efficacy of the individual nutrients and botanical ingredients to improve hair growth and quality outcomes, the dietary supplement studied there targets various root causes of hair growth cycle disruption is effective in promoting hair growth. This study also showed positive self-perceptions from study subjects compared to device assessment (Table 3). Other clinical trials of combinations of ingredients that target hair cycle have shown varying degree of efficacy with regard to hair growth.[33]

This research is novel in its evaluation of a gummy format dietary supplement. Gummy supplements have been growing in popularity. According to a recent report, 47 percent of supplement users stated that gummies were their preferred format when they started a supplement regimen.[34] The evaluated hair supplement was able to provide statistically significant and noticeable differences to users compared to a placebo, supporting the use of carefully formulated dietary supplements in gummy formats for consumers who may prefer them over other formats.

Limitations. This study did not assess hair longer for than a six-month period and utilized subject perception for outcomes that differ from clinical assessments.

CONCLUSION

The dietary supplement evaluated there, taken daily for six months, significantly increased hair density assessments compared to placebo and resulted in positive subject self-assessment of hair appearance and quality. There appears to be a synergistic effect of ingredients in the novel supplement formulation to positively affect hair growth and subjective evaluation with no adverse reactions.

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