



# Nutraceuticals for Androgenetic Alopecia

by CHRISTINA RING, MD; KERRY HEITMILLER, MD; EMILY CORREIA, BS; ZENA GABRIEL, MD; and NAZANIN SAEDI, MD

All authors are with the Department of Dermatology and Cutaneous Biology at Thomas Jefferson University in Philadelphia, Pennsylvania.

*J Clin Aesthet Dermatol.* 2022;15(3):26–29.

**BACKGROUND:** Several oral nutraceuticals have recently emerged as products marketed to increase hair growth and thickness. However, these supplements typically lack the rigorous testing and statistically significant data that apply to pharmaceuticals. Therefore, the potential benefits of oral nutraceuticals for conditions of hair loss, such as androgenetic alopecia, have yet to be fully understood by dermatologists.

**OBJECTIVE:** The purpose of this article is to evaluate current studies in the literature to assess the efficacy of popular oral nutraceuticals marketed for hair growth in subjects with androgenetic alopecia. **METHODS:** This article reviews the currently available literature on the nutraceuticals Nutrafol® and Viviscal® for hair growth and describes and evaluates the results observed. **RESULTS:** Oral nutraceuticals are effective to a modest degree in promoting hair growth in men and women with androgenetic alopecia. **CONCLUSION:** Oral nutraceuticals have demonstrated efficacy in promoting modest hair growth in men and women with androgenetic alopecia and may serve as useful adjuncts to current treatments. As the popularity of nutraceuticals grows, it is important for dermatologists to be knowledgeable of the potential benefits and pitfalls of these supplements to appropriately counsel patients seeking treatment for hair loss. **KEYWORDS:** Alopecia, androgenetic alopecia, hair growth, hair, supplements

Androgenetic alopecia (AGA) is a common, distressing condition that is estimated to affect up to 85 percent of men by the age of 50 and 50 percent of women by age 60.<sup>1</sup> Thick, full hair is associated with youth, beauty, health, and success in many cultures. Therefore, hair loss can be a source of significant psychological distress among both men and women.<sup>2</sup> As of 2020, the hair loss treatment industry is estimated at \$3.8 billion, which is projected to increase to \$5.3 billion by 2027.<sup>3</sup> Topical minoxidil is currently the only treatment approved by the United States Food and Drug Administration (FDA) for both male and female patterned hair loss, but has variable efficacy, requires life-long treatment adherence, and has several side effects, including unwanted hypertrichosis and contact dermatitis that might lead to discontinuation. Oral finasteride, a type II 5-alpha reductase inhibitor, is FDA-approved for male pattern hair loss, however potential side effects including sexual dysfunction may be a deterrent to use. Therefore, alternative treatment options for both male and female pattern hair loss are of particular interest.<sup>4</sup>

Nutraceuticals are an emerging category of health and beauty products due to growing acceptance of an "inside-out" approach to health.<sup>5</sup> Many nutraceutical products contain phytochemicals, which are naturally derived, biologically active compounds that are increasingly being studied and advertised to promote health. Several studies have already demonstrated benefit of various products including vitamins, omega

fatty acids and antioxidants in improving hair growth.<sup>6–9</sup> These products are regulated by the FDA but are not subjected to rigorous testing and standards that apply to pharmaceuticals. As such, some products may lack pure, potent, and bioavailable ingredients leading to inefficacy or adverse effects.<sup>5</sup> As popularity of nutraceuticals grows, it is important for dermatologists to be knowledgeable about these products to appropriately guide and counsel their patients on nutraceutical use. This article will review the currently available data evaluating the efficacy of popular hair loss supplement brands Nutrafol® (Nutraceutical Wellness Inc.; New York, New York) and Viviscal® (Viviscal Limited; Ewing, New Jersey).

**Nutrafol.** Nutrafol launched in 2016 and is currently the fastest growing nutraceutical supplement for hair growth on the market. It is composed of 21 ingredients, including a proprietary Synergen Complex®, which includes standardized phytoactives with clinically tested anti-inflammatory, stress-adaptogenic, antioxidant and dihydrotestosterone-inhibiting properties.<sup>10</sup> The phytochemicals in this complex include curcumin, piperine, ashwagandha, saw palmetto, and tocotrienols.<sup>11</sup> Curcumin is a potent anti-inflammatory and immunomodulating agent that has been shown to inhibit NF-kb and decrease tumor necrosis factor (TNF)-alpha and interleukin (IL)-1, inflammatory cytokines involved in follicular regression.<sup>5</sup> Curcumin also inhibits androgen receptor expression, which is known to be overexpressed in follicles in androgenetic

**FUNDING:** No funding was provided for this article.

**DISCLOSURES:** The authors report no conflicts of interest relevant to the content of this article.

**CORRESPONDENCE:** Christina Ring, MD; Email: ring.christina@gmail.com

alopecia.<sup>5,12,13</sup> Co-administration with botanical piperine, found in black pepper and long pepper, enhances curcumin bioavailability and has been shown to increase plasma levels up to 154 percent after ingestion.<sup>5,14</sup> The stress response is known to play an important role in hair loss pathology and is intrinsically linked to alopecia areata and telogen effluvium, with recent studies indicating that cortisol and micro-inflammation at the level of the hair follicle also plays a role in AGA.<sup>5,15,16</sup>

Ashwagandha is a botanical that contains steroidal lactones which modulate and reduce cortisol levels. In a randomized, double-blind, placebo-controlled study of 98 patients, daily supplementation with 10% withanolide ashwagandha showed statistically significant reductions in serum cortisol, serum C-reactive protein, blood pressure, and subjective feelings of stress compared to placebo.<sup>16</sup> Saw palmetto extract is a natural inhibitor of both types I and II 5-alpha reductase which prevents conversion of testosterone to active DHT. A study of 100 men with mild to moderate AGA who were treated with either 320mg of saw palmetto or 1mg of finasteride daily for two years revealed a significant improvement in 38 percent of patients taking saw palmetto and 68 percent of patients taking finasteride.<sup>17</sup> Despite the increased efficacy of finasteride, saw palmetto might be a desirable alternative to avoid side effects of erectile dysfunction and falsely reducing prostate specific antigen (PSA) levels.<sup>5</sup> While there are no reports of teratogenicity, saw palmetto is considered functionally related to finasteride, and therefore, it is considered unsafe in pregnancy. Vitamin E isoforms consist of four tocopherols and four tocotrienols, which are potent free radical scavengers.<sup>5</sup> A randomized, placebo-controlled study of 38 patients with hair loss showed a statistically significant increase in hair counts of 38 percent from baseline compared to placebo.<sup>19</sup> The authors concluded that the effect was most likely due to antioxidant activity, inhibition of lipid peroxidation, and oxidative stress in the scalp.<sup>5,18,19</sup>

In addition to the components detailed above, Nutrafol contains amino acids, marine collagen, hyaluronic acid, organic kelp, and vitamins and minerals that have been identified to play a role in the stress response as well as gut, thyroid and hair health.<sup>5</sup> There are currently four formulations available: Nutrafol Women,

Nutrafol Women's Balance, Nutrafol Postpartum, and Nutrafol Men, which has a higher concentration of saw palmetto.

The efficacy of Nutrafol to promote hair growth was studied in a six-month randomized, double-blind, placebo-controlled trial. Forty healthy women between the ages of 21 and 65 years old with self-perceived hair thinning were randomized into two groups, with 26 subjects receiving four capsules of Nutrafol daily and 14 subjects receiving placebo. The number of terminal and vellus hairs was analyzed based on phototrichograms of a 1cm<sup>2</sup> area along the frontalis bone at Day 0, Day 90, and Day 180. Subjects taking Nutrafol showed an increased terminal hair count of 6.8 percent and 10.4 percent at 90 and 180 days, respectively, compared to 0.07 percent and 3.5 percent in the placebo group.<sup>5</sup> Vellus hair counts increased by 10.1 percent and 15.7 percent at days 90 and 180 in the Nutrafol group compared to a decrease in vellus hair counts of 2.9 percent and 2.2 percent at days 90 and 180 in the placebo group.<sup>11</sup> There was no statistically significant difference in mean hair shaft diameter between treatment and placebo groups at any point in the study.<sup>11</sup> Investigator scores for hair growth and hair quality increased significantly from baseline to day 180. Eighty percent of subjects in the Nutrafol group reported a significant improvement in hair growth compared with 46.2 percent of placebo-treated subjects. Subjects taking Nutrafol also reported improvement in overall hair volume, noticeable new hair, hair growth rate, stress and anxiety levels, sleep quality, skin smoothness and skin health (all  $p < 0.05$ ). The majority of subjects taking Nutrafol (73.1%) would recommend it to friends with hair loss.

A recent case series demonstrated clinical improvement in four subjects taking Nutrafol as a monotherapy.<sup>5</sup> A 52-year-old woman who had previously failed a several month course of topical minoxidil showed increased hair density after seven months. A 45-year-old woman with early signs of diffuse pattern hair loss showed improved hair density after four months. A 37-year-old man with early pattern hair loss and a strong family history of hair loss who had previously failed minoxidil showed improved hair growth and decreased shedding. Lastly, a 38-year-old woman with early diffuse thinning of the temple areas experienced increased density after three months of daily Nutrafol use.

No patient reported any side effects, and all were satisfied with their improvement.

**Viviscal.** Viviscal<sup>®</sup> is an oral supplement based on a novel marine complex formulation designed to promote hair growth in both men and women.<sup>1,20</sup> The key ingredients include a proprietary blend of shark and mollusk powder derived from sustainable marine sources (AminoMar<sup>®</sup> C marine complex), *Equisteum arvense* (natural occurring form of silica), *Malpighia glabra* (acerola cherry providing vitamin C), biotin, and zinc. Other ingredients include calcium, iron, horsetail stem extract, millet seed extract, flaxseed extract, procyanidin B-2 (i.e., apple fruit extract), L-cystine and L-methionine, depending on the formulation. In addition to the original formulation, other formulations include Viviscal<sup>®</sup> Professional Strength and Viviscal<sup>®</sup> Man. Early studies evaluating a similar oral formulation of marine extracts in women with photodamaged skin demonstrated improvements in skin thickness, elasticity and erythema, as well as improvements in hair and nail brittleness after 90 days of treatment.<sup>21,23</sup> Following an initial open-label pilot study, several randomized, placebo-controlled trials have demonstrated the current oral marine complex supplement to be effective in promoting hair growth in both men and women.<sup>20, 24-28</sup>

In the first randomized-controlled trial, 15 healthy women with Fitzpatrick Skin Types I to IV and self-perceived hair thinning were randomized to receive the Viviscal<sup>®</sup> Maximum Strength oral supplement or placebo twice daily for 180 days.<sup>25</sup> A 2-cm<sup>2</sup> area of the scalp was selected for hair counts, which were performed at baseline and after 90 and 180 days of treatment. Mean number of terminal hairs in the treatment group increased from 271.0 to 571 and 609.6 at 90 and 180 days, respectively. In contrast, the mean number of terminal hairs in the placebo group decreased at 90 and 180 days. The mean number of vellus hairs did not significantly change in either group. After 90 days, more subjects in the treatment group reported improvements in overall hair volume, scalp coverage and hair thickness. Additional improvements noted at 180 days in the treatment group included increased hair shine, skin moisture retention, and skin smoothness. No adverse events were reported.

In another double-blind, placebo-controlled trial, 60 healthy women with Fitzpatrick Skin

Types I to IV with self-perceived hair thinning were randomized to receive either the Viviscal® Extra Strength oral supplement or placebo twice daily for 90 days.<sup>20</sup> Similar to the prior study, a predesignated 4-cm<sup>2</sup> area of the scalp was selected for evaluation at baseline and after 90 days. Additionally, ten terminal hairs in the target area were chosen and cut at the surface of the scalp to evaluate hair growth. Digital photographs were obtained to measure hair diameter and the diameter for ten hairs was used to obtain the mean hair diameter within the target area. At 90 days, there was a significant increase in mean number of terminal hairs from 178.3 to 235.8 in the treatment group compared to a smaller increase of 178.2 to 180.9 in the placebo group. The number of vellus hairs also increased in the treatment group from 19.6 to 21.2 compared to 19.8 to 19.9 in the placebo group. A significant decrease in the mean number of shed hairs from 27.1 to 16.5 was also observed in the treatment group (vs. 23.4 to 21.9 in the placebo group). No significant change in terminal hair diameter was observed in either group. In addition to the improvements in objective measures observed, subjects in the treatment group also had higher scores on a self-assessment questionnaire that rated overall hair quality including hair growth, hair volume, hair thickness, hair strength, eyebrow hair growth and scalp coverage as well as overall skin health. No adverse events were reported.

A subsequent double-blind, placebo-controlled trial evaluated the efficacy of the Viviscal® Professional Strength Oral Tablets, an oral formulation of the marine supplement containing procyanidin B-2 (i.e., apple fruit extract), L-cystine and L-methionine for the treatment of hair loss in women.<sup>26</sup> Forty healthy women with Fitzpatrick Skin Types I to IV and with self-perceived hair thinning were randomly assigned to receive either the oral supplement or placebo twice daily for 180 days.<sup>26</sup> A predesignated target area on the scalp was assessed using phototrichogram analysis to determine change in number of terminal and vellus hairs at 180 days. Terminal hair diameter and response scores to quality of life and self-assessment questionnaires were also evaluated. In the treatment group, the mean number of terminal hairs increased from 189.9 to 297.4 and 341.0 at 90 and 180 days, respectively, and mean number of vellus hairs increased from 19.9 to 20.2 and 22.8 at 90 and

180 days, respectively. Mean hair diameter also significantly improved in the treatment group from 0.06 mm to 0.07mm and 0.067mm at 90 and 180 days, respectively, which had not been found in previous studies of the prior formulation. There were no significant improvements in any of these parameters in the placebo group. Subjects in the treatment group reported greater scores on the quality of life and self-assessment questionnaires compared to the placebo group, indicating greater improvements in overall hair volume, scalp coverage, hair strength, nail strength, eyelash growth, skin smoothness, and overall skin health.

In another study, 96 healthy women with Fitzpatrick Skin Types I to III and self-perceived hair thinning were randomly assigned to receive the Viviscal® Oral Supplement or placebo three times daily for 180 days.<sup>27</sup> The aim of this study was to add to the results of the initial double-blind, placebo-controlled trial by evaluating shed hair count analysis and hair diameter analysis using a phototrichogram. A predesignated area of the scalp was selected for two-dimensional digital images and trichoanalysis, which was performed at baseline, 90 days and 180 days. Shed hair was collected during shampooing and counted at each visit. Overall, mean hair shedding was significantly reduced in the treatment group from 52.1 to 42.6 and 42.7 at 90 and 180 days, respectively. In the placebo group, an initial increase in mean hair shedding was seen at 90 days, followed by a small decrease at 180 days. Mean vellus hair diameter showed a small but significant increase in the treatment group at 90 and 180 days, but no change was observed in the placebo group at either time point.

The studies discussed thus far consistently demonstrated the effectiveness of Viviscal® in promoting hair growth in women with self-perceived hair thinning. However, the efficacy of the oral supplement in men with hair loss had not yet been evaluated. In a double-blind, placebo-controlled trial, Ablon<sup>28</sup> evaluated the efficacy of Viviscal® Man, a reformulation of the original marine complex supplement for use in men. Sixty healthy men with clinically diagnosed male pattern hair loss were randomized to receive the reformulated supplement or placebo twice daily for 180 days. A predesignated target area on the midline scalp was chosen for two-dimensional digital images and trichoanalysis at baseline, 90 days and 180 days. A hair pull

test on the right and left parietal, frontal and occipital scalp was also performed at baseline and 180 days. After treatment, subjects in the treatment group experienced significant improvement in all efficacy measures. Mean total hair increased from 162.2 to 169.1 and 174.9 at 90 and 180 days, respectively, total hair density increased from 159.7 to 166.5 and 172.2 at 90 and 180 days, respectively, and terminal hair density increased from 121.9 to 127.7 and 130.3 at 90 and 180 days, respectively. The hair pull test was also significantly improved in the treatment group at 180 days. No improvements in any of these parameters were observed in the placebo group. Subjects in the treatment group also reported significant improvements in several quality of life measures and self-assessment items including overall hair growth, hair volume, hair and nail strength, and overall skin health. No adverse events were reported.

Based on the current literature, Viviscal® appears to be effective in promoting hair growth and decreasing hair shedding in both men and women.<sup>20,24-26,28</sup> Studies have also demonstrated that Viviscal® may offer the additional benefit of subjective improvements in the appearance and quality of the skin, nails and eyebrows.<sup>25,26,28</sup> Theories behind the benefit of Viviscal® primarily involve providing adequate nutrition and vitamins that promote hair growth, as inadequate nutrition and various vitamin deficiencies have been associated with hair loss.<sup>1</sup> As previously mentioned, several prior studies have demonstrated vitamins, omega fatty acids, and antioxidants to also promote hair growth, suggesting a role of adequate nutrition in hair growth and supporting the use of dietary supplements for hair loss.<sup>6,7,9</sup> Advantages of Viviscal over current pharmaceutical therapies, such as topical minoxidil and oral finasteride, include additional improvements to skin and nail health and a more favorable side effect profile. In all of the studies performed thus far, no significant adverse events associated with the oral supplement have been reported. Therefore, Viviscal would likely be appropriate to use in the majority of patients. This is in contrast to many of the current pharmaceutical treatments for hair loss, such as topical minoxidil, which may cause local irritation at the application site, or oral finasteride, which has been associated in rare instances with sexual dysfunction in men and is often not favorable to use in women. Several Viviscal formulations contain biotin,

which may be a cause for concern. Recently, the FDA issued a warning that biotin might interfere with certain laboratory testing results, including endocrine and cardiovascular laboratory tests. Given this warning, patients taking Viviscal® regularly should be aware of this possibility and dermatologists should counsel patients appropriately. However, this supplement contains about 100 to 240 micrograms of biotin compared to 5,000 micrograms found in most biotin supplements, which might have a smaller impact on laboratory tests compared to supplements containing higher amounts of biotin. Of note, the formulation for men does not contain any biotin.

## CONCLUSION

While prior studies have demonstrated the efficacy of Nutrafol® and Viviscal® as monotherapy in promoting hair growth in men and women, optimal improvements would likely be achieved when used as an adjunct/in combination with pharmaceutical or office-based treatments including topical minoxidil, autologous platelet rich plasma injections and hair transplantation. Patients should also be counseled on maintaining proper nutrition and a well-balanced diet. Nutraceuticals continue to emerge as adjuncts or alternatives to standard pharmaceutical therapies for hair loss and it is important for dermatologists to be up-to-date on the currently available products to appropriately counsel patients seeking treatment for hair loss.

## REFERENCES

- Hornfeldt CS. Growing evidence of the beneficial effects of a marine protein-based dietary supplement for treating hair loss. *J Cosmet Dermatol* 2018; 17:209-213.
- Kanti V, Messenger A, Dobos G, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men - short version. *J Eur Acad Dermatol Venereol*. 2018; 32:11-22.
- Alopecia Market Size, Share, Trends: Global Industry Report 2020-2027 (2020). Available from: [www.grandviewresearch.com/industry-analysis/alopecia-market](http://www.grandviewresearch.com/industry-analysis/alopecia-market).
- Blumeyer A, Tosti A, Messenger A et al. (2011) Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. European Dermatology Forum (EDF). *Journal of the German Society of Dermatology Supplement* 6: S1-57.
- Farris PK, Rogers N, McMichael A, et al. A Novel Multi-Targeting Approach to Treating Hair Loss, Using Standardized Nutraceuticals. *J Drugs Dermatol*. 2017; 16:s141-s148.
- Trueb RM. Diffuse hair loss. In: Blume-Peytavi UTA, Whiting DA, Treub R, eds. *Hair Growth and Disorders*. Berlin Heidelberg: Springer-Verlag; 2008.
- Le FC, Cheniti A, Connetable S, Piccardi N, Vincenzi C, Tosti A. Effect of a nutritional supplement on hair loss in women. *J Cosmet Dermatol* 2015; 14:76-82.
- Leng N, Heidecker B, Seifert B, Trueb RM. Dietary supplement increases anagen hair rate in women with telogen effluvium: results of a double-blind, placebo-controlled trial. *Therapy*. 2007; 4:59-65.
- Almohanna H, Azhar A, Tsatalis JP, Tosti A. The Role of Vitamins and Minerals in Hair Loss: A Review. 2019;9:51-70.
- Hunt N, McHale S. The psychological impact of alopecia. *BMJ*. 2005;331(7522):951-953.
- Ablon G, Kogan S: A Six-Month, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of a Nutraceutical Supplement for Promoting Hair Growth in Women With Self-Perceived Thinning Hair. *J Drugs Dermatol* 2018, 17(5):558-565
- Nakamura K, Yasunaga Y, Segawa T, et al. Curcumin down-regulates AR gene expression and activation in prostate cancer cell lines. *Int J Oncol*. 2002; 21:825-830.
- Shishodia S. Molecular mechanisms of curcumin action: gene expression. *Biofactors*. 2013;39(1):37-55.
- Shoba G, Joy D, Joseph T, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Med*. 1998; 64:353-356.
- Thom E. Stress and the Hair Growth Cycle: Cortisol-Induced Hair Growth Disruption. *J Drug Dermatol*. 2016;15(8):1001-1004.
- Auddy B, Hazra J, Mitra A, et al. A Standardized Withania Somnifera Extract Significantly Reduces Stress-Related Parameters in Chronically Stressed Humans: A Double-Blind, Randomized, Placebo-Controlled Study. *Journal of American Nutraceutical Association*. 2008; 11:50-56.
- Rossi A, Mari E, Scarno M, et al. Comparative effectiveness of finasteride vs Serenoa repens in male androgenetic alopecia: a two-year study. *Int J Immunopathol Pharmacol*. 2012; 25:1167-1173.
- Beoy LA, Woei WJ, Hay YK. Effects of tocotrienol supplementation on hair growth in human volunteers. *Trop Life Sci Res*. 2010; 21:91-99.
- Wang Y, Park NY, Jang Y, Ma A, Jiang Q. Vitamin E gamma-Tocotrienol Inhibits Cytokine-Stimulated NF-kappaB Activation by Induction of Anti-Inflammatory A20 via Stress Adaptive Response Due to Modulation of Sphingolipids. *J Immunol*. 2015;195(1):126-133.
- Ablon G. A 3-month, randomized, double-blind, placebo-controlled study evaluating the ability of an extra-strength marine protein supplement to promote hair growth and decrease shedding in women with self-perceived thinning hair. *Dermatol Res Pract*. 2015; 2015:841570.
- Lassus A, Jeskanen L, Happonen HP, Santalahti J. Imdeen for the treatment of degenerated skin in females. *J Int Med Res*. 1991; 19:147-152.
- Eskelinin A, Santalahti J. Special natural cartilage polysaccharides for the treatment of sun-damaged skin in females. *J Int Med Res*. 1992; 20:99-105.
- Costa A, Pereira ESP, Favaro R, et al. Treating cutaneous photoaging in women with an oral supplement based on marine protein, concentrated acerola, grape seed extract and tomato extract, for 360 days. *Surg Cosmet Dermatol*. 2011; 3:302-311.
- Thomas J. Stephens & Associates, Inc. A 10-week pilot consumer perception test to evaluate the overall acceptability of a Viviscal oral supplement when used by females with self-perceived thinning hair. <http://www.viviscal.com/media/cms/docs/pilot-study.pdf>. August 8, 2017.
- Ablon G. A Double-blind, Placebo-controlled Study Evaluating the Efficacy of an Oral Supplement in Women with Self-perceived Thinning Hair. *J Clin Aesthet Dermatol*. 2012;5(11):28-34.
- Ablon G, Dayan S. A randomized, double-blind, placebo-controlled, multi-center, extension trial evaluating the efficacy of a new oral supplement in women with self-perceived thinning hair. *J Clin Aesthet Dermatol*. 2015; 8:15-21.
- Rizer RL, Stephens TJ, Herndon JH, Sperber BR, Murphy J, Ablon GR. A marine protein-based dietary supplement for subclinical hair thinning/loss: results of a multisite, double-blind, placebo-controlled clinical trial. *Int J Trichology*. 2015; 7:156-166.
- Ablon G. A 6-month, randomized, double-blind, placebo-controlled study evaluating the ability of a marine complex supplement to promote hair growth in men with thinning hair. *J Cosmet Dermatol*. 2016; 15:358-366. **JCAD**