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Nutrafol: A Redefined Approach To Thinning Hair

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Abstract Hair loss is a complex problem that affects millions of men and women of all ages and ethnicities, impacting appearance, social interactions, and psycho-emotional well-being. Patients seeking medical treatment for hair loss have limited options that are difficult to incorporate into their daily routine and may carry risks of potential side effects. To complicate matters even further, other treatment options can be invasive with frequently required repetition. There is increasing patient interest in natural treatments for hair thinning, however, basic nutritional vitamin supplements lack standardization, regulation, and clinical efficacy. Recent research has identified that hair loss is the result of multiple causative factors that include inflammation, oxidative damage, environmental assaults, aging, psycho-emotional stress, and hormonal imbalances that span beyond the previously studied and known factors like androgens and nutrition. Based on this current understanding of the pathogenesis of hair loss, a multi-modal solution is required and therapies targeting only singular mechanisms or pathways may be less than ideal or result in less than optimal effectiveness. While supplements addressing one factor of hair loss and thinning, like nutrition, have been popular in the dermatologic community, a clinically studied nutraceutical that is able to target multiple pathways tied to hair growth may be the key to providing an effective intervention. Several key publications have highlighted Nutrafol® (Nutraceutical Wellness Inc, New York, NY), a nutraceutical containing a blend of highly purified, standardized, bio-optimized, and bioavailable extracts with clinical efficacy in targeting key pathways that compromise hair growth.

Introduction

Hair loss is chronic and progressive without treatment, affecting at least 50% of women by age 50 and 40% of men by age 45, progressing to up to 70% by later life.[1] Hair is an important part of our appearance, social interactions, and psycho-emotional well-being, and its loss is associated with significant psychological trauma resulting in symptoms of depression and diminished quality of life.[2] The current medical interventions for hair loss are limited — FDA approved finasteride and topical minoxidil. While these treatments are backed by research and long-term clinical use, they can be difficult to incorporate into daily use and carry risks of potential side effects including in some cases sexual dysfunction, allergic contact dermatitis, and/or growth of unwanted hair. The medications may also need to be used indefinitely.[1,2,3]

Traditionally in dermatology, hair loss has been segmented to reflect etiology and morphology, inflammatory vs non-inflammatory, hereditary vs acquired, inflammatory vs non-inflammatory. This view has led to the development of drugs that target specific pathways within the complex biology of hair growth, with variable success. As a result, the only available therapeutics address singular targets, as exemplified by anti-androgen therapies like finasteride that inhibits DHT.[1] However, recent research published by Sadick et al and others has clarified that hair loss is multifactorial, pointing to numerous external and internal contributing factors and to similar dysregulation of intrinsic signaling pathways within the follicle physiology that span the hair loss disorder spectrum.[1] Further, a common immune and micro-inflammatory component is identified in most hair loss pathogenesis, including that of androgenetic alopecia (AGA), which was traditionally seen as non-inflammatory in nature.[4]

Thus, hair loss is not the result of one singular pathway and androgens are not the sole player in this much larger picture. Therefore, when it comes to drugs or supplements, targeting singular pathways is not ideal. Most medical therapies focus on singular targets, without considering the downstream effectors, dysregulation of immune signaling, or inflammatory cascades. Most basic vitamin and mineral supplements provide nutritional support, thus also targeting a singular potential cause for hair thinning. Although biotin supplementation alone has been used in the past by the dermatology community, its efficacy for hair growth and quality improvement remains largely unsubstantiated in scientific literature. In a recent article (Soleymani et al) and letter to the editor (Callender et al), authors conclude that apart from instances of frank hereditary and very rarely acquired biotin deficiencies, there is no evidence validating clinical efficacy to support the use of biotin supplementation alone for hair loss.[5,6] However, biotin, in combination with standardized multi-targeting botanical nutraceuticals and other nutritional ingredients, has shown efficacy in successfully improving hair growth.[2,3]

The development of sustained, comprehensive, efficacious, and side-effect-free therapies takes into account the impact and interplay of multiple factors that disrupt immune and signaling pathways of tightly regulated follicle biology. Dermatologists are now interested in offering a multi-targeted approach that addresses a variety of these complex factors. A novel nutraceutical supplement, Nutrafol® (Nutraceutical Wellness Inc, New York, NY) has gained much interest among dermatologists for its clinical efficacy and multi-targeted mechanism of action. Nutrafol® attributes its efficacy to the isolation and standardization of specific phytocompounds that have clinically studied and proven therapeutic effects and may help restore balance to the sensitive microenvironment of the hair follicle.

Hair Follicle Biology

New knowledge about hair follicle biology reveals a common thread within all hair disorders, the dysregulation of follicle homeostasis. It is increasingly apparent that multiple immune-driven pathways are involved in the normal physiology of the follicle, as well as in the pathophysiology of hair loss, when disrupted. Intrinsic and extrinsic factors including hormonal fluctuations, genetics, diet, oxidative damage, aging, and environmental aggressors such as UV light, overstyling, and pollutants, as well as mediators of psycho-emotional stress such as cortisol and corticotropin releasing hormone, can affect the complex microenvironment of the hair follicle. Compounded, these factors lead to a dysregulation of complex follicle immunology and biology, affecting the follicle through stimulation of pro-apoptotic and pro-inflammatory cytokines, perifollicular micro-inflammation, and release of reactive oxygen species (ROS).

Restoring hair follicles to a state of homeostasis requires embracing a new outlook in terms of therapeutics. Any interference of the normal hair growth cycle phases can influence the health of the hair follicle and result in hair loss. Within the intrinsic follicular environment, multiple cytokines, growth, and transcription factors signal the follicle to go into the anagen or catagen phase, which, under normal conditions, ensures that shedding is followed by new growth. In the event of micro-inflammation, overproduced cytokines like IL-1 and TNF-α are known to induce premature catagen, delay return to anagen, liberate ROS, cause apoptosis, and further propagate inflammation.[4,7] Likewise, factors like DHT-

induced TGF-β are prominently overproduced by dermal papilla cells in the presence of androgens and signal growth arrest, as well as play a role in perifollicular fibrosis and miniaturization. Preventing the hair follicle from premature entry into the catagen phase is vital for considering therapeutics. Any therapy designed to comprehensively treat hair loss must address growth arrest triggering factors such as androgens or cortisol overexpression and their downstream signaling cascades, as well as mitigate the inflammatory response.

Bio-Optimized Phytocompounds To Treat Hair Loss

The scientifically based ingredients in Nutrafol® have antioxidant and anti-inflammatory benefits to counter the effects of an inflammatory cascade caused by intrinsic and extrinsic factors. Advances in biotechnology have made way for bio-optimizing to improve absorption and bioavailability of these ingredients in the body. Select standardized phytoactives with stress-adaptogenic properties have been shown to lower elevated cortisol levels and stabilize the metabolic process that confer greater resilience to stress. The ingredients in this nutraceutical supplement provide benefits at multiple steps in the hair growth cycle and can potentially restore natural balance to the sensitive microenvironment of the hair follicle.

Multi-Modal Activity

Botanicals in the Synergen Complex provide a unique therapeutic value because of their multi-modal clinical biological activity against these multiple molecular and environmental causative factors of hair loss. Their advanced patented extraction technology is improved for bio-optimization, standardization, and bioavailability.[3,8-10] Standardized ingredients like curcumin and ashwagandha have been clinically shown to lower inflammatory bio-markers such as C-reactive protein (CRP) in human subjects.[11,12] Curcumin inhibits factor NF-kB, decreasing the inflammatory pro-apoptotic cytokines, TNF-α, and interleukin 1 that induce catagen and follicular regression.[11,12] Curcumin has also been shown to have efficacy against androgens and androgen-induced downstream TGF-β signaling that is implicated in follicular miniaturization and fibrosis.[13-15] This complements the documented anti-androgenic effects of saw palmetto in hair loss, which is shown in numerous hair loss studies to effectively inhibit 5-α-reductase enzyme and prevent conversion of testosterone into DHT.[8] Patients with alopecia have been shown to have lower levels of antioxidants such as GSH and GSH-Px and an increase in reactive oxygen species. Curcumin up-regulates transcription factor nuclear factor erythroid-like-2 (Nrf-2), which increases synthesis of endogenous antioxidants like glutathione and hemoxygenase-1, improving cellular defenses against oxidative stress, in addition to another ingredient, tocotrienols.[1] Tocotrienols are superior at preventing lipid peroxidation and have been clinically shown to promote hair growth by reducing oxidative stress in the scalp.

Ashwagandha, used in Ayurvedic medicine to build resistance to stress, contains steroidal lactones (withanolides) and other alkaloids that can mimic certain corticosteroids, interact with steroid receptors, and modulate cortisol levels, thereby improving the stress response.[17] Daily administration of the standardized ashwagandha in the Synergen Complex was shown to significantly reduce cortisol levels in chronically stressed adults[18] – providing the only available potential option for addressing the impact of psycho-emotional stress in hair loss (Figure 1).

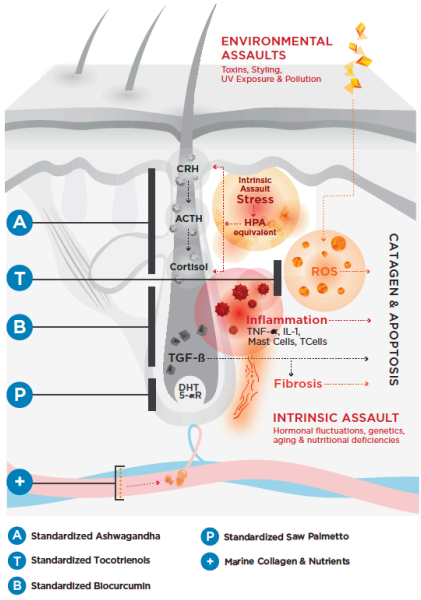

Figure 1. Proposed synergetic mechanism of action of standardized nutraceutical ingredients against the triggers of hair loss.

Nutrafol Efficacy

In Ablon's recent randomized, double-blind, placebo-controlled study, the ability of daily intake of Nutrafol® (Nutrafol® Women's Capsules) to strengthen and promote the growth of hair in adult women with self-perceived thinning hair was assessed. Enrolled subjects were randomized to receive active treatment (n=26) or placebo (n=14). The primary endpoint in this study was a statistically significant increase in the number of terminal and vellus hairs based on phototrichograms obtained through macrophotography analysis. The secondary endpoints were improved grading on blinded Investigator Global Hair Assessments for hair growth and hair quality, changes in terminal hair diameter and bundle measurements, and responses on subject Self-Assessment, Ease of Use, and Quality of Life questionnaires.

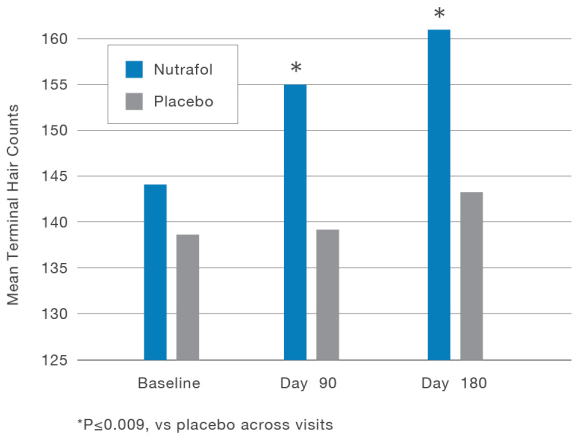

Figure 2. Active treatment resulted in significant improvement in the growth of terminal hairs, as indicated by mean target area terminal hair counts increasing from 141.7 at Baseline to 151.4 at Day 90 and 156.4 at Day 180.

Daily intake of the nutraceutical supplement resulted in a significant increase in the number of terminal and vellus hairs in the target area at Day 90 and Day 180 vs placebo (P<0.009; Figure 2). Blinded Investigator Global Hair Assessments revealed significant improvements in hair growth (P=0.016) and overall hair quality (P=0.005; Figure 3).

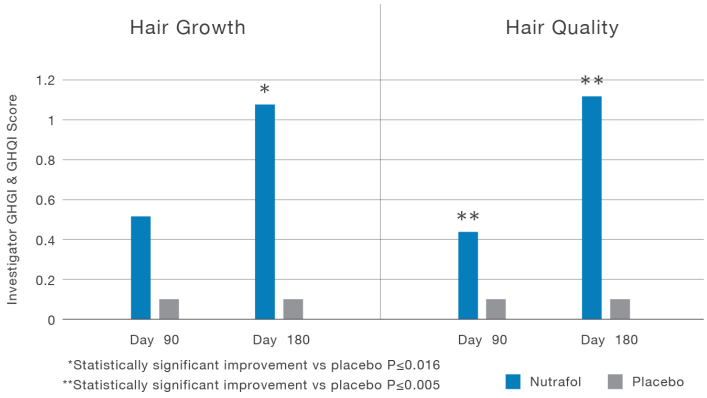

Figure 3. Investigator Global Hair Growth Improvement and Global Hair Quality Improvement Scale Scores significantly improved for subjects treated with active product vs placebo at Day 90 and Day 180.

A significant percentage of subjects receiving active treatment also reported improvement in hair growth, volume, thickness, and hair growth rate (Figure 4).

Additionally, there was a significant improvement in wellness measures, such as anxiety levels, stress, and overall well-being. A significant percent also reported improvements on 5 of 15 quality of life items, indicating improvement in feelings of self-consciousness, attractiveness, and self-esteem. Additionally, in several published case studies on supplementation with Nutrafol® as monotherapy, patient's results were associated with a high degree of improvement in hair growth and a favorable safety profile.[3]

The stress of hair loss is further compounded by lack of available treatment options. In the abovementioned study, the overwhelming majority of subjects taking the active product not only found it to be more convenient to incorporate into their daily routine over using a topical application, but also preferred taking a natural alternative – underscoring the increasing interest of patients turning to nutritional vitamins. This further emphasizes the importance of both physicians and patients to be cautious, selective, and knowledgeable about using supplements that have clinical data on phytoactive activity, bioavailability, standardized dosing, and potency.

Conclusion

Today's dermatologists are able to draw upon a host of different modalities including medications, LLLT, PRP, and nutraceuticals as therapeutics for hair loss and thinning. Nutraceuticals represent a new set of therapies with their multi-modal approach by focusing on multiple signaling cascades and disrupted pathways involved in thinning hair. They offer an innovative solution for dermatologists with the ability to be used standalone or in combination with other therapies without compromising efficacy.

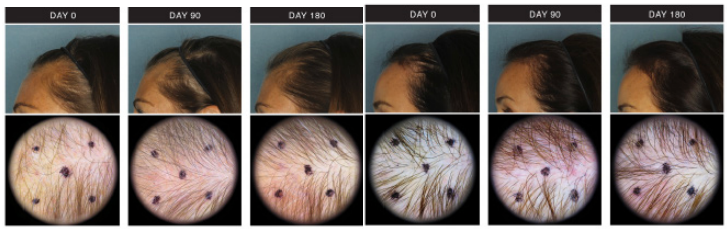

Figure 4. Improvement in hair growth for 2 representative subjects treated with the active product.

Nutraceuticals contain potent botanicals with antioxidant and anti-inflammatory benefits able to combat the effects of intrinsically and extrinsically mediated inflammatory cytokines and ROS formation, in addition to targeting androgens and cortisol. The ability to address multiple factors in a patient's healthy hair growth cycle without the need for invasive or cumbersome daily routines, make nutraceuticals a useful addition to dermatologist strategies.

Nutrafol®, with its combination of clinically tested, bio-optimized vitamins and botanicals, shows its ability to promote hair growth in women with self-perceived thinning hair, promising a multi-targeting approach that combats the intrinsic and extrinsic factors that compromise the hair follicle. Further, it provides breakthrough ingredients that address the impact of psycho-emotional stress. As evidenced by clinical trial data and case studies, Nutrafol® is well-tolerated, easily incorporated into patients' lifestyles, and has shown to improve quality of life measures in its subjects.

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