The multi-targeted approach to hair loss expands to a systems-wide and personalized view of hair health, leveraging the functional medicine framework.
Executive Summary

Hair loss is an increasingly common condition that will impact over 50% of both men and women at some point in their lives. Although not life-threatening, it is frequently seen as destructive to self-image and emotional well-being, leading to significant psychological impact. Globally, upwards of three billion US dollars are spent by individuals trying to find solutions. Treatments to date are limited and have relied mainly on modern medicine's reductionist approach—narrowly focusing on singular targets and pathways, as exemplified by Finasteride addressing the androgen pathway. Amongst the few FDA approved solutions available, many carry associated side effects, application and compliance issues and provide variable success.

New research has revealed that a multitude of signaling pathways, as well as internal and external triggers underlie hair loss pathophysiology. Reflecting these new findings, the scientists behind Nutrafol put forth several research publications, including a previous White Paper (2015) addressing the multi-factorial nature of hair loss with its multi-targeted Core formulations. In a 2017 Journal of Drugs in Dermatology (JDD) article, Nutrafol scientists in collaboration with key hair loss experts in dermatology, put forth this research introducing a paradigm shift in the treatment of hair loss—from mono-targeting to multi-targeting interventions. Nutrafol Core products were developed with these concepts in mind, leveraging the power of standardized nutraceuticals to multi-target the numerous triggers that compromise hair health at the follicle level: micro-inflammation, stress, hormonal imbalances and oxidative damage. In a 2018 double-blind, placebo-controlled, randomized clinical study published in JDD, these core formulations were demonstrated to safely and effectively promote hair growth in subjects with hair loss and thinning.

As research in medicine continues to evolve, Nutrafol is once again poised to partake in this evolution. Contrary to modern medicine practices that approach disorders via localized treatment targeting singular organs, recent advances in genomics and systems biology offer insight into new approaches to treat disease. It’s been demonstrated that most chronic diseases stem from dysfunction and dysregulation in multiple organ systems and their complex interactions, as well as cumulative environmental influences and genetic predispositions.

In addition to multi-targeting triggers at the follicle level, a systems-wide perspective has made it important to view the hair follicle as an organ which is impacted by all other organ systems in the body. Accordingly, poor hair health and subsequent hair loss is influenced by different combinations of dysfunction and/or dysregulation of associated biological systems based on environmental and genetic predisposition. The allostatic load—the wear and tear on each organ system as they attempt to adapt to cumulative stressors and demands over time—is considered a critical factor in assessing system dysfunction. In any given individual, the combination of unique biochemical, genetic and environmental influences dictates which organ systems will become compromised as a result. Different organ systems can present with different levels of wear and tear, thus increasing the need for more robust and personalized support of those particular organ systems. It is this expanded research that is driving a systems-wide, personalized approach to hair health which leverages the concept of systems biology.

Research has identified how the complex array of biological systems defines one’s biology pertaining to hair health. The identified key biological systems, and the mechanisms by which they affect hair health, include:
Stress Response System
Stress, including psycho-emotional stress, impacts the body on a physiological level. There are distinct and interconnected stress-induced, inflammatory and neuronal mediators (e.g. cortisol, CRH, SP, TNF-α, etc.) that produce a cascade of multiple mechanisms which directly disrupt hair health. Examples of resulting disruptions can include compromising hair follicle immune privilege and induction of catagen, thus exacerbating hair loss. Similar stress-induced cascades affect dysfunctions of all other organ systems, such as proper nutrient assimilation in the gut which is necessary to support hair growth.

Digestive System
In addition to nutrients assimilation and elimination pathways, the gut contains an abundant and diverse community of microbes essential to the health of multiple systems and the body as a whole. Disruptive events to gut health include stress, antibiotic use, poor diet, environmental exposure and other causes. Manifestations of these disruptions can result in:
- Increased gut permeability allowing exposure of the hair follicle to antigenic and immune damage,
- System-wide increase of low-grade inflammation, and subsequent elevation of inflammatory mediators implicated in hair loss, and
- Suppressed breakdown and/or absorption of nutrients that support follicular metabolic processes.

Detoxification System
Environmental toxins are key stressors impacting multiple body systems (including hair). Heavy metals disrupt mitochondrial function and cause substantial oxidative damage and subsequent poor cellular health and turnover. Xenobiotics (chemicals foreign to the body) disrupt the endocrine system and add to the allostatic load. The result is dysfunction of proper cell signaling—including those required by follicular cells. Normally, toxins are extricated by the liver; however, chronic and repeated exposure can overtax the liver and reduce functionality.

Metabolic System
Glucose dysregulation and insulin resistance are correlated with poor hair health and subsequent hair loss. Follicular cells cycle very quickly, requiring a continuous supply of energy and nutrients. Elevated blood glucose and insulin, due to combinations of genetics and life style choices, drive several counterproductive mechanisms:
- Extreme fluctuations in glucose homeostasis negatively impact small blood vessel function, which can reduce blood flow to the hair follicle and compromise energy and nutrient supply.
- Elevated insulin and insulin resistance increase the production of dihydrotestosterone (DHT), the presence of which leads to miniaturization of the follicle and fibrosis.
- Proper thyroid function is necessary for metabolic signaling within hair cells for growth and differentiation; altered signaling has been correlated to hair loss.

Endocrine System (reproductive hormones)
Local and systemic sex hormones strongly influence the hair follicle; either deficit or surplus can affect hair growth. Excess conversion of testosterone to DHT as well as increased affinity of follicular androgen receptors (due to genetics and environmental pathways) can predispose an individual to hair loss. Further, hormone imbalance can result in impairment of stem cell differentiation and dysregulation of follicle immune pathways. Age-related hormone imbalance shifts have implications for more severe hair loss later in life, especially in post-menopausal women.
This multi-factorial and systems-wide perspective is driving new study, innovation and treatment in hair loss. Nutraceutical Wellness Inc. endeavors to lead the industry in hair loss innovation through the introduction of the NUTRAFOL® GrowthPlan™, a multi-targeted, systems biology driven and personalized approach to improving hair health. NUTRAFOL® Core formulations are designed to approach hair health at the follicle level, by multi-targeting the multiple disrupted pathways involved in hair loss. Further, NUTRAFOL® Targeted Booster formulations focus on supporting the specific organ systems which foster hair follicle health and may be presented with exceptional cumulative stress in an individual.

(1) NUTRAFOL® Core: Multi-targeting the key triggers of hair loss
Designed to serve as the backbone of an individual’s hair health regimen. These formulations leverage botanicals and phytoactives that have been carefully selected to target the dysregulation of the hair follicle, based on the aging and hormonal needs of men and women. Each supports proper regulation of stress hormones, DHT, inflammation, oxidative stress, and corrects for insufficient or inappropriate nutrition.

- NUTRAFOL® Core for Men
- NUTRAFOL® Core for Women
- NUTRAFOL® Core for Women Plus

(2) NUTRAFOL® Targeted Boosters: Systems-wide support based on personalized needs for hair health
Recognizing each individual's differences regarding their sources of stress, the cumulative demands put on their biological systems, and each system's ability to adapt to said stress, adjunct interventions were designed. These Targeted Boosters provide more robust support in those systems that see high levels of allostatic load and reduced ability to properly adapt. Access to the entire line of formulations enables greater personalization to meet the precise needs of the individual as defined by their specific combination of biology and stressors.

- NUTRAFOL® Vitamin B-Booster
- NUTRAFOL® Stress Adaptogen
- NUTRAFOL® Liver Support
- NUTRAFOL® Sugar Balance
- NUTRAFOL® Hairbiotic
- NUTRAFOL® Digestive Enzyme
- NUTRAFOL® DHT Inhibitor

The NUTRAFOL® GrowthPlan reflects new research, providing an opportunity to treat the individual as a whole—rather than treating a condition in isolation. This innovation in health care has enabled a paradigm shift in how hair health is perceived and treated.

Please email sales@nutrafol.com for the full content of the white paper if interested.
Biological Individuality. No two individuals are alike in what stressors they encounter, which of their biological systems are affected, or how well they can adapt—calling for a systems-wide, personalized approach to addressing hair loss.
**NUTRAFOL® Core** and **Targeted Boosters**, make up the **NUTRAFOL® GrowthPlan**, a multi-targeted, systems-biology driven and personalized approach to addressing hair loss and hair health at the follicle and systems-wide.

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**Personalization of the Systems-wide, Multitargeted Approach to Hair Loss Therapy.** A multi-targeted approach to hair loss is optimized when expanded to personalized and systems-wide application. The Nutrafol® GrowthPlan™ addresses the multiple triggers that affect the follicle in men and women, as well as the specific systems impacted by allostatic load in an individual.