

Drug Corner

Exploring Multi-dimensional Approach for Treating and Preventing Hair Loss with Nutraceuticals

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Although hair disorders are not life-threatening, there is no denying that they significantly influence social interactions and patients' psychological well-being. A sufficient and well-balanced nutritional intake is responsible for normal skin and hair function integrity. Dietary imbalance can disturb this equilibrium, whether it takes the form of an overall deficiency, a more specific shortage, or an excess of one component over another. Human skin and hair can be affected by nutritional factors, resulting in excessive hair shedding and hair loss. It is essential to separate those nutritional factors that directly affect the hair cycle and promote hair growth. One of the most emerging areas in dermatology is the role of nutraceuticals in hair loss without any side effects. However, with increasing awareness among patients, there has been a tremendous demand for natural hair care and treatment products. An effective combination of bioactive ingredients derived from natural sources is essential in hair growth stimulation and provides a therapeutic benefit in hair conditioning. When it comes to hair health, dietary supplements and nutraceuticals can be part of a plan to address a visible problem that impacts self-esteem and confidence in men and women.

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Hair loss is among the most frequent complaints among all patients who visit a dermatologist, which profoundly impacts social interactions and patients' psychological well-being. It can be temporary or long-lasting. Alopecia areata, which causes bald patches, has a visible hair loss pattern, whereas Telogen effluvium, which causes diffuse hair loss, has a more subtle pattern. As with most conditions, the physician begins the evaluation with a detailed history and physical examination. The diagnosis is a comprehensive clinical history, physical examination, clinical diagnostic tests, laboratory analysis, and, in some cases, a scalp biopsy. Infectious, nutritional, congenital, autoimmune, or environmental factors may all have a role in the pathophysiology of such disorders^{1,2}. Androgenic alopecia, telogen effluvium, and alopecia areata are the most common types of non-scarring alopecia. A cross-sectional study conducted on 393 men aged between 18-50 years in India showed that the total prevalence of hair fall was 60.4%, whereas female pattern hair loss accounts for 15.3 % of hair loss in women in India^{3,4}.

The demand for treatments for hair loss fuels a multi-billion-dollar industry. Despite this, most currently marketed products are ineffective, as evidenced by the

Editor's Comment :

- Various factors, including illness, poor nutrition, hormonal imbalances, and stress, can contribute to hair loss, which is associated with lowered self-esteem and decreased confidence.
- Nutraceuticals with bioactive properties are essential in promoting modest hair growth in men and women with different hair conditions and are safe and effective for long-term use.

fact that the FDA has approved only two treatments - Finasteride and Minoxidil for hair loss. Our awareness of molecules and pathways regulating hair follicle formation and hair growth has significantly advanced recently. One of the markets for beauty products with the fastest growth is nutricosmetics, an emerging product category. Among the most popular nutricosmetics are nutritional alternatives and supplements to treat hair loss. Many individuals who encounter hair loss turn to nutraceuticals since healthy hair demands more than just balanced nutrition. Natural supplements appeal to patients looking for safe and effective treatments for hair loss^{5,6}. This article highlights some of the most significant nutraceuticals having pharmacologic effects that can prevent hair loss and promote hair growth. While there is no magic bullet or single natural ingredient to address all of the mechanisms at play in the multiple forms of clinical hair loss, using the combination of bioactive nutraceuticals offers a promising approach for hair loss.

Physiology of Hair Growth :

Hair growth is cyclic, with phases of growth

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(anagen), involution (catagen), and rest (telogen). The cycles of active growth and rest are regulated by complex messages between the epithelium and the dermis. In a normal scalp, most follicles are growing (90 to 95 percent), a few are undergoing involution (less than 1 percent), and the remainder are resting (5 to 10 percent). At the end of telogen, hair is released and shed, and the next cycle is initiated (Fig 1). Each day, up to 100 hairs in telogen are shed from the head, and about the same number of follicles enter anagen⁷. The duration of anagen determines the length of hair, and the volume of the hair bulb determines the diameter. Hair follicles form during embryogenesis in humans, and no new hair follicles develop after birth. However, the character of individual follicles can change drastically over time. Thicker and darker hairs replace fine, lightly pigmented hairs in the beard at puberty. Conversely, thick scalp hairs convert into fine small hairs later in life. The hair shaft's size and length correspond to the hair follicle's size and the duration of the anagen^{8,9}.

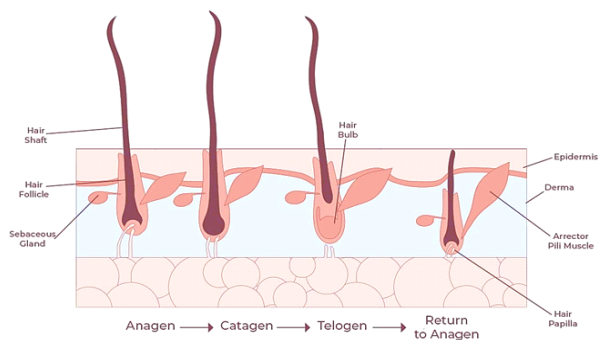


Fig 1 — Physiology of hair structure and its growth cycle¹⁰

Factors Affecting the Health of Hair :

With successive hair cycles, the duration of anagen shortens, and the follicles become smaller, producing shorter, more delicate hairs that cover the scalp poorly. Androgenetic alopecia is distinguished by these miniaturized hairs of varying lengths and diameters. Dihydrotestosterone (DHT) is formed by the peripheral conversion of testosterone by 5 α -reductase. Higher levels of 5-reductase, more androgen receptors, and lower levels of cytochrome P-450 aromatase are found in young men and women with androgenetic alopecia. Cytochrome P-450 aromatase converts testosterone to estradiol in hair follicles in the frontal region of the scalp than in the occipital region, which develops into androgenetic alopecia¹¹. Among these hair loss causes, other factors also affect the hair (Table 1).

Limitations of the Current Treatment :

Hair loss is often distressing and can have a significant effect on the patient's quality of life Different treatment options are available in the treatment of hair loss such as use of drugs such as minoxidil & finasteride. However, these drugs displays side effects such as irregular heartbeat, blurred vision, loss of libido etc.

Minoxidil :

Minoxidil promotes hair growth when it has been affected by various conditions, including androgenetic alopecia. Topical Minoxidil is now the most widely recommended and is available in 2% and 5% solutions for hair loss. However, Minoxidil can induce allergic contact dermatitis, and the most common complaint among users is scalp pruritus and scaling. In addition to irritant and allergic contact dermatitis, these

Table 1 — Factors affecting the hair quality

Stressors	Effect on hair
Emotional stress	Stress can exert profound hair growth-inhibitory catagen-inducing and hair-damaging pro-inflammatory effects ¹² .
Aging	Dermal papilla undergoes progressive cell loss and eventual miniaturization that contributes to impairment in hair follicles ¹³ .
Infections	Fungal infections like Tinea capitis cause hair loss that generally is associated with pruritis; Bacterial infections like <i>Staphylococcus</i> bacteria can produce scarring alopecia ¹⁴ .
Hormonal imbalance	An imbalance in the levels of Estrogen and progesterone slows down the hair growth, and hair becomes thinner. A decrease in these hormones also triggers an increase in the production of androgens that shrink hair follicles, resulting in hair loss ¹⁵ .
Pollutants	Nano-size suspended air particle matter causes oxidative stress apart from the biological interaction with the hair cells. Polycyclic aromatic hydrocarbons in the environment damage the hair due to skin penetration, transepidermally or through the hair follicles ¹⁶ .
UV radiation	Excessive sun exposure is the most frequent cause of hair shaft structural impairment and is responsible for hair protein loss and color changes. Absorption of radiation in hair produces free radicals, which affect keratin.
Nutritional deficiency	Hair loss in premenopausal women is due to nutritional deficiency of iron, Severe protein, caloric restriction, Vitamin D deficiency, zinc deficiency, and chronic starvation, which can induce diffuse telogen hair loss ¹⁷ .
Drugs	Anticoagulants, retinol, interferon, and antihyperlipidemic drugs have two different effects on anagen follicles: either they cause the follicles to enter an early stage of rest (telogen effluvium), or they cause the rapidly dividing hair matrix cells to abruptly stop mitosis ¹⁸ .

symptoms may be due to an exacerbation of seborrheic dermatitis. Topical Minoxidil can also induce hypertrichosis in different areas out of the scalp. It affects temples, forehead, and cheeks, which is the consequence of contamination of these areas. The fair or white-haired can become yellow or green after applying this drug. Postural hypotension/dizziness and increased heart rate by 6.5% were associated with oral minoxidil^{19,20}.

Finasteride :

Finasteride is a 5α reductase inhibitor that decreases the conversion of testosterone to the more potent androgen DHT used for treating male pattern hair loss. Many reports describe adverse effects in men during treatment, such as sexual dysfunction and mood alteration. This condition, termed post-finasteride syndrome, is characterized by sexual side effects (ie, low libido, erectile dysfunction, decreased arousal, and difficulty in achieving orgasm), Depression, Anxiety, and cognitive complaints that are still present despite drug withdrawal. Animal studies show external genital abnormalities in male fetuses exposed to Finasteride in utero. The drug is classified in FDA pregnancy category X and is contraindicated in women who are or may become pregnant^{21,22}.

Nutraceuticals for Hair Growth and Maintaining Healthy Hair :

Nutraceuticals include vitamins and minerals, herbs/botanicals, and probiotics, all of which are globally marketed as dietary supplements and do not require Food and Drug Administration (FDA) approval. According to the 2012 National Health Interview Survey, natural products are the most popular complementary and Alternative Medicine (CAM) approach for dermatologic conditions, used by 17.7% of Americans. Different clinical papers are available on the use of amino acids, caffeine, capsaicin, millet extract, wheat gum, soya protein isolate, vitamin B7 (biotin), vitamin D, vitamin E, and zinc to treat hair loss^{23,24}.

Millet Extract :

In dermatological research, millet (*Panicum miliaceum*) and its main component, miliacin, are of great interest, particularly for their capacity to promote tissue repair and wound healing. Miliacin, also called Panicol or Prosol, belongs to the class of organic compounds known as triterpenoids. Cellular studies using thymocyte and splenocyte cultures have revealed a protective effect of miliacin from DNA fragmentation and apoptosis²⁵. More recent studies focusing on miliacin have shown that it improved cellular renewal

and proliferation and promoted the process of hair growth²⁶. Ex vivo studies show that treating scalp fragments with miliacin alone significantly increased the number of proliferative cells in the hair bulb ($P < 0.01$) and in the outer root sheath. Moreover, there was an increase of 140% in the number of proliferative cells and keratinocytes mitotic index in the hair bulb. Another study with miliacin demonstrated a significant ($p < 0.01$) increase (20.8%) of collagen thickness in the connective tissue sheath of the hair in comparison with control scalps. Miliacin acts on dermal papilla where it stimulates growth factor production like IGF1 and increases the thickness of the extracellular matrix of the connective tissue sheaths. Moreover, it stimulates the renewal of keratinocytes in the hair bulb. In a placebo-controlled, randomized, double blind trial conducted on women with telogen effluvium, it was demonstrated that, in comparison with a placebo treatment, a 12-week supplementation of miliacin decreased telogen density ($P < 0.001$) and increased anagen density ($P < 0.001$) in subjects. In addition, scalp dryness was significantly reduced, and there was improved hair brightness and beauty for the miliacin group after 6 and 12 weeks of supplementation ($P < 0.001$). These studies confirm the role of millet extract in preventing hair loss and limiting telogen effluvium in women^{27,28}.

Wheat Germ Oil

Wheat germ is a by-product of wheat milling from which wheat germ oil (WGO) can be obtained. The WGO is rich in Phosphorus, Vitamins B and E, containing mainly phytosterol and tocopherol. The higher amount of vitamin E stabilizes cell membranes by protecting unsaturated fatty acids from peroxidase cleavage and reducing the incidence of reaction with peroxide radicals, which helps prevent hair loss²⁹. Plant pigments such as carotenoids are efficient antioxidants capable of eradicating singlet molecular oxygen and peroxy radicals. They can play an essential role in the antioxidant defense system in the human body as they establish synergistic relations with other antioxidants³⁰. Ceramides in WGO are associated with skin aging and can protect and moisten skin, with moisturizing and soothing effects on scalp skin. Ceramide protects the extracellular matrix against leukocyte proteinases which cause degradation by inhibiting this elastase, making it an excellent anti-inflammatory agent. Moreover, WGO stimulates the scalp's microcirculation and cures dystrophic cells in the hair bulb. It plays a vital role in hair loss prevention. It has also been shown to improve the texture of damaged hair^{31,32}.

Soya Protein Isolate :

Soya protein isolate found in soybeans contains large amounts of protein and amino acids, indicating that it has various pharmacological activities, including antioxidants, is essential for hair growth, and is also effective in preventing hair loss³³. Moreover, soya protein is rich in high-quality minerals (eg, Potassium, Calcium and Iron), Vitamin B groups, and Vitamin E, which can support smooth blood circulation, thus preventing hair loss and keeping hair healthy. Based on preclinical studies, soya protein is thought to effectively prevent hair loss by nourishing the hair roots through improved scalp blood circulation³⁴. It has long been used as a health food for hair loss prevention or as a raw material for herbal medicine prescriptions. One of the studies conducted by Sung HY, *et al* showed that after applying soya protein extract once a day for 12 weeks, there were significant changes in the number of lost hair, the diameter of the hair, hair condition, and satisfaction score of subjects. The application of soya protein extract to the scalp led to hair growth promotion, which is thought to result from activated breast papillary cells, expanded capillaries, and improved blood flow. Considering the excellent hair loss prevention and hair growth-promoting effects, soya protein isolate may be used for hair loss treatment³⁵.

Pantothenic Acid :

Pantothenic acid, a water-soluble Vitamin, also known as vitamin B5, is required for synthesizing CoA and for the metabolism of carbohydrates, proteins, and fats. The deficiency of Pantothenic acid affects the synthesis of CoA and results in alopecia and loss of hair pigment³⁶. Pantothenic acid dietary supplements are commonly used as over-the-counter products for hair loss treatment. It is used in cosmetics due to its anti-static and hair conditioning properties. Studies have reported that exogenous Calcium D -pantothenate could alter gene expressions to increase the synthesis of secreted proteins in human dermal fibroblasts (which regulate hair growth) and promote the proliferation and migration of human dermal fibroblasts. In vitro studies show that Pantothenic acid treatment promoted the proliferation and migration of dermal papilla cells and accelerated hair growth³⁷. In addition, it regulates the proliferation of several cells, including keratinocytes and fibroblasts³⁸.

Biotin :

Biotin (also known as Vitamin B7 or Vitamin H) is a water-soluble vitamin that is an essential cofactor for carboxylase enzymes in multiple metabolic pathways. Biotin has gained commercial popularity

for its claimed benefits on healthy hair and nail growth³⁹. Of the reported cases in the literature, all patients receiving biotin supplementation had some underlying pathology for either poor hair or nail growth. Moreover, all cases showed evidence of clinical improvement after receiving biotin. Cases reported with alopecia subsequently resolved after varying months of biotin supplementation. Additionally, there were reported cases of uncombable hair syndrome that all showed improvement in hair quality after a few months of treatment. In another case of low serum and urine levels of biotin, hair regrowth in the patient occurred after two months of biotin supplementation. The administration of the cofactor, biotin, positively changed the character of hair since the root strength increased, scaling disappeared, the growth rate accelerated, and the hair became pliant and more combable. Biotin's function in protein synthesis and, more specifically, in keratin production explains its contribution to healthy hair growth. Moreover, biotin improves strength by altering the matrix proteins rather than the keratin itself^{40,41}.

L-cysteine :

L-cysteine is an amino acid that is classified as semi-essential in humans. L-cysteine primarily contributes to the observed protection against endogenous oxidative stress. It must be considered a candidate when considering which nutrients could be used for improving hair growth. Treatment of telogen effluvium includes L-cysteine-containing oral combinations available on the market. L-cysteine plays an essential role in the protection against oxidative stress, along with a positive effect on proliferation. Studies on the impact of dietary supplements containing L-cysteine have shown improvements in the trichogram and hair tensile strength. Moreover, its effect has significant hair growth in healthy women with telogen effluvium^{42,43}. A study by Lengg N *et al*. demonstrated that L-cysteine in combination with pantothenic acid significantly improves mean anagen hair rate within six months of treatment ($p = 0.003$)⁴⁴. Additionally, L-cysteine promotes the repair of structural lesions, slows down hair loss experienced by patients affected by certain disorders (diffuse alopecia), and provides strength and rigidity to keratin⁴⁵.

Combination of Millet Extract, Wheat Germ Oil, Calcium Pantothenate and L-cysteine :

One of the studies evaluated the effects of a formula composed of millet extract, wheat germ oil, calcium pantothenate (Vitamin B5), and L-cysteine in women

with diffuse alopecia. The patients were given a capsule containing 140 mg millet extract, 271 mg wheat germ oil, 2 mg L-cysteine, and 10 mg calcium pantothenate three times a day for three months. There was a significant increase ($P < 0.05$) in anagen ratio and a parallel decrease in telogen ratio post-treatment in the frontal and occipital regions. In addition, A statistically significant difference was found between the pre-treatment hair pulling test and the post-treatment hair pulling test, and a decrease in the number of hair shedding per day after the treatment. After three months of treatment, 43.4% of the subjects had a positive response in the frontal region and 49.1% in the occipital region, which show that formulation consisting of L-cysteine, calcium pantothenate, wheat germ oil, and millet extract is effective in the treatment of telogen effluvium⁴⁶.

Conclusion :

Oral nutraceuticals have demonstrated efficacy in promoting modest hair growth in men and women with different hair conditions. As the popularity of nutraceuticals grows, dermatologists and physicians need to know the potential benefits of nutraceuticals and appropriately counsel patients seeking treatment for hair loss. Further randomized, controlled trials are required to investigate the efficacy of supplements to maintain healthy hair and those which promote hair growth. Moreover, nutraceuticals are coming up with natural constituents with bioactive properties which are safe and effective for long-term use.

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