

Nutrients in Hair Supplements: Evaluation of their Function in Hair Loss Treatment

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ABSTRACT

Hair loss represents one of the most diffuse aesthetic issues among the worldwide population, with 50% of men and nearly 50% of women affected by pattern hair loss by age of 50. The loss of hair is not life-threatening, and it is a natural part of the ageing process. However, it can adversely affect the individual's quality of life. The integrity of normal hair function relies largely on an adequate and balanced nutritional intake, essential trace elements deficiency, genetic conditions, hormonal imbalance or stressful events, which can alter the hair growth cycle equilibrium. Dietary supplements, as well as the intake of specific nutrients, have traditionally been used to improve hair growth, even if the connection between the use of specific substances and the prevention or the treatment of hair loss not always is supported by scientific studies. Indeed, the use of specific vitamins and minerals for the treatment of hair loss is often based on popular traditions or commercial reasons, and several nutrients are part of the dietary supplements composition to adhere to the rule of "one size fits all". On the contrary, the non-pathological treatment of hair loss requires an in-depth analysis of the nutritional deficiencies of each individual in order to restore the biological functions of hair and to reach the normal physiological conditions. A review of the state of the art in hair loss and nutrients relationship was done, highlighting minerals and vitamins which may concretely contribute to prevent or treat this unpleasant event.

Keywords: Food supplements; Hair loss, Vitamins and minerals; Hair physiology; Hair treatments.

INTRODUCTION

Hair loss is one of the most common aesthetic problems among the world's population, with 50% of men and almost 50% of women over the age of 50 which suffering from this blemish [1]. Despite being part of the natural aging process, which also affects the scalp, it can negatively affect the quality of life of each individual, with situations that can lead to a state of psychological distress and demoralization.

It is important to understand whether hair loss falls within the normal physiological process, or otherwise, if it is an abnormal complication caused, for example, by problems related to the scalp or hair bulb. The classification of all forms of hair loss, baldness and alopecia, is always complex and reductive, since they are often the expression of multiple factors that contribute

to the onset of these pathologies [2]. Androgenetic alopecia is one of the most common causes of hair loss in men, which can be traced back to the action of the androgenic hormones and the malfunctioning of the enzyme 5-alpha-reductase, which leads to a growing weakness of the hair. In women, androgenetic alopecia is one of the main causes, but the incidence is extremely minor, due to the reduced presence of androgens [3]. Aggressive chemical and physical treatments that are applied to the women's scalp are responsible for the weakening of the hair, often resulting in hair loss. Conversely, the common causes that can be simultaneously associated in man and woman thinning hair are different, such as the so-called seasonal hair loss, in spring and autumn. Even this phenomenon, although temporary, should be kept under control, in order to not compromise any already critical situations. Other common

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causes that undermine the integrity of normal hair function are often related to inadequate and unbalanced nutritional intake, deficiencies of essential trace elements, genetic conditions, hormonal imbalances or stressful events, which can alter the balance of the hair growth cycle [2,4].

Traditional nutrients and several commercialized food supplements can help the patient to counteract and reduce hair loss, compensating for possible alterations and nutritional deficiencies that in the long run could accentuate or accelerate the loss of hair. Food supplements are often used to improve hair growth, although the link between the use of specific components and the prevention of hair loss is not always supported by scientific studies [4]. Indeed, the use of specific vitamins and minerals for the treatment of hair loss is often based on popular traditions or commercial reasons, and several nutrients are inserted into the dietary supplements composition to adhere to the rule of "one size fits all". Indeed, some elements are traditionally known to play an important role in the physiology of the hair, while others are often present in the composition of some food supplements without having enough scientific evidences to support their use. The non-pathological treatment of hair loss requires an in-depth analysis of the nutritional deficiencies of each individual in order to restore the biological functions of hair and to reach the normal physiological conditions.

The purpose of this work was therefore the evaluation of the possible relationships between hair loss and nutrients,

highlighting minerals, vitamins and other elements that can help to prevent and reduce hair loss.

METHODS

The choice of the elements was made by analyzing the ingredients of different food supplements marketed in Italy, collecting the most common substances normally present in the food supplements in order to individuate which nutrients can demonstrate a proven effectiveness in the treatment of hair loss. It is important to underline that often the formulations of food supplements contain plant extracts, phytocomplexes or trace elements that characterize the efficacy profile, but since they are present only in a specific food supplement, it would have been inappropriate and reductive describe them in this work. A deep analysis of scientific literature was carried out on the possible relationships between hair loss and nutrients. The scientific articles examined come from the main scientific databases such as PubMed, Scopus, MEDLINE and Google Scholar, in a time interval ranging from the 70s till today.

DISCUSSION

The nutrients evaluation shown below made it possible to highlight a correlation between the substances analyzed and the treatment of hair loss, based on scientific studies that through different *in vitro* or *in vivo* tests allowed to demonstrate tangible benefits (Table 1).

Table 1: Summary of nutrients and mechanisms related to hair loss and follicle biology.

Nutrient	Mechanism
Zinc	Zinc is involved in several metabolic pathways and cellular functions, moreover, it contributes to the production of keratin, which represents the 95% of the hair structure. Zinc is a potent inhibitor of hair follicle regression and accelerates hair follicle recovery. [6]
Copper	The role of copper in hair biology is not well clarified. It has an important enzymatic role in the production of crosslinks in elastin and collagen fibers in the dermis, post-translational formation of di-sulfide bonds between cysteine molecules in cytoskeletal proteins of cortical and cuticle proteins. [7]
Selenium	Selenium is an essential trace element that plays a role in protection from oxidative damage as well as hair follicle morphogenesis. [8]
Cysteine and Methionine	Cysteine, along with methionine, is one of the main constituents of hair, contributing to the formation of keratin for a quarter of the total. The use these amino acids promotes the repair of structural lesions and slows down hair loss. Moreover, they contribute to the normal processes of contrast to the oxidative stress that can lead to hair loss, favoring the production of natural antioxidants such as glutathione. [9,10]
Vitamin C	Vitamin C is an essential cofactor in the enzymatic step forming collagen and in supporting the cross-linking of keratin fibers. Moreover, it is a potent water-soluble antioxidant, helpful in contrasting the oxidative stress responsible of the hair follicles degeneration. [11,12]
Vitamin B5	The role of vitamin B5 in hair loss is not clear. Probably, like the rest of the B vitamins, an improvement in cellular metabolism can also benefit hair.[13]
Vitamin B6	Vitamin B6 is an important nutrient, acting as a cofactor for several enzymes. It plays a key role in skin development and maintenance, and more important it contributes in cysteine incorporation in hair cells.[14]

Biotin	Biotin is an important cofactor that contributes to the normal functioning of enzymes responsible for carboxylation. It has been shown that its deficiency can lead to skin rashes, conjunctivitis and alopecia. Its deficiency is rare, since intestinal bacteria can produce an adequate amount of biotin.[15]
Niacin	Niacin is an essential component for the body, contributes to the production of ATP and therefore to the correct energy support for the cells. Its deficiency leads to pellagra, with phenomena such as dermatitis, hyperpigmentation, diarrhea, weakness and hair loss.[4]
Taurine	Taurine is a beta-amino acid that, in addition to having an important role in the proper functioning and maintenance of our nervous system and muscle structure, seems to be able to counter androgenetic alopecia, limiting the process of follicular atrophy.[16]
Folic Acid	Folate is a water-soluble B vitamin and includes naturally occurring food folate and folic acid (fully oxidized monoglutamate). Folate is a coenzyme in the synthesis of nucleic acids and in amino acid metabolism.[17]
B Group Vitamins	Other B group vitamins include thiamine (B1), riboflavin (B2) and vitamin B12, which in general, help to keep hair healthy. There are no scientific studies that directly correlate these vitamins with the reduction of hair loss, but it is reasonable to assume that, given their extreme importance in terms of numerous biochemical processes, these may have, albeit to a lesser extent, a role also in growth and hair care. [18]

Iron. Widespread and chronic hair loss has been shown to be related to iron deficiencies and therefore anemia. In particular, a report by Trost and collaborators in 2001 gathered together a series of studies that suggested how serum iron deficiencies in women between the ages of 18 and 79 could be associated with diseases such as aerated alopecia and androgenetic alopecia [19]. In one of the six studies examined it was shown that by supplementing with iron (72 mg / day) the diet of women with severe deficiency, it was possible to observe clear improvements in hair loss compared to the control group of patients (31% less hair loss than the 9% reduction in the control group) [2].

Kantor et al. compared serum ferritin levels of women with different pattern of hair loss with a healthy control group, concluding that ferritin levels were reduced in women with androgenic alopecia and alopecia aerata as compared with healthy control patients [20].

On the contrary, Olsen et al. performed a controlled study on 381 women to determine if iron deficiency may play a role in female pattern hair loss. The results showed that iron deficiency is common in females, but the relationship with hair loss was not completely demonstrated, indicating that more studies need to be assessed to better clarify the role of the iron in the treatment and prevention of hair loss [21].

Zinc. Zinc contributes to the production of keratin, which represents the 95% of the hair structure. Statistically lower concentrations of serum zinc have been observed in patients with hair loss disorders. In particular, in 2009 Park et al. studied the contribution that an external supplementation of zinc could have in individuals who presented phenomena of alopecia aerata [22]. It was found that the administration of 50 mg zinc per day over a prolonged period improved the clinical frame of the patients involved in the study. Therefore, the high concentration administered was calculated based on a compensation of low serum levels, which however effectively contributed to the reduction of hair loss in treated patients.

Kil et al. performed a study involving 312 patients with male or female pattern hair loss and 30 healthy individual, evaluating

the zinc serum concentration in both the examined group [6]. Results showed that in all of the hair loss patients, the mean serum zinc was significantly lower than the control group (84.33 µg/dL and 97.94 µg/dl, respectively), concluding that zinc metabolism imbalance could play a key role in hair loss.

Copper. Copper is one of those controversial elements, since it is present in many formulations among the best-selling food supplements, but which requires further scientific studies to demonstrate a direct action for combating hair loss. In particular, in a 2013 study by Kil and collaborators, serum levels of zinc and copper were evaluated as a possible correlation to hair problems [6]. Serum levels of zinc and copper were measured in patients with diseases related to hair loss and in a healthy control group. While it was seen that serum zinc levels were significantly lower in the group of patients with pathology, serum copper levels were not significantly different. The conclusion of the study therefore confirmed on the one hand the key role of zinc, but it did not clarify whether copper could be implicated for the benefit of hair pathologies, making further studies necessary.

Selenium. Selenium is a micronutrient with several properties, performing numerous functions within the body. Its presence in hair food supplements is also justified by the fact that it contributes in an essential way to the mechanisms of protection from oxidative stress and free radicals, elements that can negatively influence the morphogenesis of the hair follicle [8]. In the specific case of hair physiology, scientific studies have shown as selenoprotein knockout mice presented progressive loss of coat since birth. In particular, the lack of these selenium-dependent proteins in epidermal cells led to the development of hyperplastic epidermis and aberrant hair follicle morphogenesis, accompanied by progressive alopecia after birth [23]. Thus, this study links selenoprotein and selenium deficiency to abnormalities in skin and hair.

Masumoto et al. have focused on the physiological effects of selenium supplementation in six infants during a period of long-term nutritional support. After starting the therapy, selenium

serum levels returned to the normal range and alopecia and pseudoalbinism, some of the physiological issues found in the children, sensibly improved [24].

Cysteine. Cysteine, along with methionine, is one of the main constituents of hair, contributing to the formation of keratin for a quarter of the total [11, 12]. Already in 1989 Hertel and colleagues pointed out that a combination of cysteine and retinol was able to attenuate hair loss. The pilot study was conducted on 36 subjects. After treatment with cysteine and retinol, patients reported an increment of 11% in hair in the anagen phase, along with a reduction in hair in the telogen phase of 8.3% [25-27]. A more recent German study shows that a specific combination of Cysteine and two other elements can reverse hair loss. The group of women who received cysteine in combination showed a return to normal levels of hair growth [28].

D'Agostini et al. evaluated whether L-cystine, the oxidized form of L-cysteine, may have a role in inhibiting an alopecia induced by smoke in mice. Groups of mice received different concentrations of cystine in combination with vitamin B6, which plays a role in cystine incorporation in hair cells. The effects on alopecia and atrophy of hair bulb cells were evaluated after 6 months of treatment, and the results showed that the combination of L-Cystine and vitamin B6 inhibited alopecia in a dose-dependent manner [14].

Methionine. Methionine is an essential amino acid, an excellent source of sulfur, and as mentioned above, it is one of the main constituents of hair. It can prevent premature hair loss by providing sulfur to hair bulbs and connective tissues, thus improving resistance and normal growth as well as the appearance of hair [26]. Moreover, together with cysteine, it contributes to the normal processes of contrast to the oxidative stress that can lead to hair loss, favoring the production of natural antioxidants such as glutathione [29].

Borowczyk et al. demonstrated *in vitro* that the demethylation of methionine residues contributes to keratin damage in human hair, indicating that an appropriate intake of this amino acid with diet or food supplement is necessary to reduce the protein damage [30].

Vitamin C. Vitamin C, besides being a powerful antioxidant, plays an important role in collagen synthesis and in supporting the cross-linking of keratin fibers [11]. Because of this dual role it could be an important element for hair regeneration, helping in optimal preservation of the scalp and more generally of the whole organism. In the right quantities it can be of great help for maintaining optimal state of health of the scalp [12].

Vitamin E. Vitamin E shows good antioxidant properties and it is important for the proper functioning of the organism. Its properties could help to repair damaged hair follicles and prevent tissue oxidative stress, encouraging healthy hair growth. In a study of 2010, it was seen how the administration of vitamin E reduced hair loss by 30% compared to a control group, demonstrating how oxidative stress could be connected to different types of alopecia [31]. We must also consider how vitamin E plays a very important role in counteracting phenomena of oxidative stress especially at the level of the skin,

and therefore indirectly to guarantee a certain protection to the hair [32].

Vitamin B5. In 2001, a study showed that vitamin B5 and vitamin B6 can improve the trichogram of women with significant hair loss. The results were a marked improvement in hair loss, particularly towards the telogen effluvium [33]. However, the role of vitamin B5 in hair loss is not clear. Probably, like the rest of the B vitamins, an improvement in cellular metabolism can also benefit hair [13].

Vitamin B6. The importance of Vitamin B6 in promoting hair growth emerged also from the previous study [33]. Since this vitamin is involved in protein metabolism, the production of keratin at the level of the hair follicle is also increased and improved. D'Agostini et al. in 2007 demonstrated how the combination of vitamin B6 and L-cysteine was able to prevent the loss of hair from mice exposed to smoke, probably thanks to an antioxidant effect that prevents damage to the hair bulbs [14]. Furthermore, a study published by the same authors in 2013 showed that high doses of vitamin B6 always associated with L-cysteine helped to prevent hair loss during chemotherapy treatment in mice, confirming that the vitamin can play an important role not only in the development and maintenance of the skin, but also in the reduction of hair loss [34].

Biotin. Biotin is an important cofactor that contributes to the normal functioning of enzymes responsible for carboxylation. It has been shown that its deficiency can lead to skin rashes, conjunctivitis and alopecia [15]. Its deficiency is rare, since intestinal bacteria can produce an adequate amount of biotin. Khalidi et al. reported a beneficial effect after 5 days of treatment with biotin at 60 µg / dose on patients with alopecia and who had short bowel syndrome [35]. So although there are no clinical studies on healthy patients suffering from hair-related diseases, the use of biotin in different hair supplements is very common, encouraged also by the positive results found in other phenomena of keratinization related to onychoschizia and other nail diseases [1].

Niacin. Niacin is an essential component for the body, contributes to the production of ATP and therefore to the correct energy support for the cells. Its deficiency leads to pellagra, with phenomena such as dermatitis, hyperpigmentation, diarrhea, weakness and hair loss. There are still no studies linking its lack with hair loss, although some reviews mention it among the components that could affect hair-related diseases due to its contribution to energy production, and therefore also to an increase in trophism of the hair bulb [4].

Taurine. Taurine is a beta-amino acid that, in addition to having an important role in the proper functioning and maintenance of our nervous system and muscle structure, seems to be able to counter androgenetic alopecia, limiting the process of follicular atrophy. *In vitro* studies have shown that taurine can increase the survival of follicular cells [16]. However, human studies have never been carried out regarding its real effectiveness in combating hair loss.

Folic Acid. Folate is a water-soluble B vitamin and includes naturally occurring food folate and folic acid (fully oxidized

monoglutamate). Folate is a coenzyme in the synthesis of nucleic acids and in amino acid metabolism. In a 2006 review, Trost and collaborators put together various data on the correlation between iron / folate deficiency and hair loss [19]. They noted that a lack of folate could accentuate anemic episodes, which then increased the potential hair loss especially in women.

Yousefi et al. examined red blood cell folate concentration in 29 patients with alopecia aerata, showing that in this group the concentration was significantly lower than the control group and significantly lower in patients with alopecia totalis/alopecia universalis than in patients with patchy hair loss [36].

Other B Vitamins. Other B group vitamins include thiamine (B1), riboflavin (B2) and vitamin B12, which in general, help to keep hair healthy. There are no scientific studies that directly correlate these vitamins with the reduction of hair loss, but it is reasonable to think that, given their extreme importance in terms of numerous biochemical processes, these may have, albeit to a lesser extent, a role also in growth and hair care. In fact, they perform different functions in the organism, they intervene in numerous metabolic reactions that involve digestion, the nervous system and the metabolism of nutrients [37–39]. In particular, although some of these reactions are also the basis of the growth and repair of the tissues that make up skin, nails and hair, it is not usual to include all the B group vitamins among the "essential" ones for hair care [18].

CONCLUSIONS

The use of food supplements or the normal intake of vitamins and minerals, together with a healthy lifestyle and a balanced diet, can contribute to the well-being of everyone. These recommendations are essential in the treatment of important pathologies, and at the same time they are important for dealing with minor pathologies such as hair loss. Stress and unhealthy lifestyles, combined with genetic conditions, hormonal imbalances and other types of diseases play an important role in the physiology of the hair and imperfections related to the scalp. When imbalances occur in the delicate biological mechanisms that characterize the trophism of hair, it becomes clear how a targeted and complete food supplementation can give concrete help to the rebalancing and maintenance of the hair physiology. Such deficiencies often have turned into a busy life, food shortages, or physiological deficiencies of the individual. It is good to know which elements are important for hair growth, and therefore able to counteract hair fall.

The analysis carried out has shown that several nutrients present in the composition of hair supplements demonstrate a proven effectiveness. However, it is possible to identify these substances among the components of numerous hair products, or it is possible that these essential vitamins and minerals are completely absent. One of the reasons could be formulate food supplements that are suitable for many consumers as possible, leading to a generalization of the product that too often can mislead the consumer, the so-called "one size fits all" rule. See a long list of components or the indication for multipurpose treatments can give the idea of a better food supplement, but often this is not entirely true. Only a targeted formulation and a careful evaluation of the elements will allow the creation of a

food supplement capable to effectively combating hair loss. The knowledge of the properties of each component, together with the advice of the physician or the pharmacist, will allow the identification of the best product for the specific needs of the consumer.

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