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Physiological Importance of the Vitaminoid Thiocyanate and Its Influence on Hair Growth

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Abstract

Thiocyanate is a physiologically and biochemically active metabolite that is not sufficiently formed by endogenous synthesis in the case of diseases, stress, malnutrition, infection, toxic influences or loss through washing out during hair washing. In these siuations, alimentary supplementation or local application become necessary depending on the objective. An important effect of thiocyanate is the stimulation of new cell formation, initially proven in cell culture and in plants by the increase in yield, later also in the animal species mink (improved coat quality), sheep (increased wool yield) and guinea pigs (stimulation of the anagen phase of hair formation). Therapeutic efficacy was even demonstrated in human alopecia areata, with 51% showing complete to good remission 12 months after completion of treatment. The growth-promoting effect was confirmed in the trichogram. The biological activity of the vitaminoid is not based on a uniform mechanism of action but is to be understood as the sum of various partial effects.

However, the current state of knowledge focuses on the prophylactic use of thiocyanate to prevent the side effects on head-hair that are related to the modern lifestyle. Hair washing is the greatest burden, because the thiocyanate is washed out of the scalp and hair due to its water solubility. A constant thiocyanate concentration in the hair is only achieved if the hair is washed only about every 2 weeks. If the hair is washed more frequently, the loss cannot be compensated by nutrition and common body care, so that the substitution of lost thiocyanate by wetting the scalp and hair is recommended with a thiocyanate liquid after each hair washing.

Keywords: Thiocyanate; Vitaminoid; Physiological Importance; Biochemical Importance; Stimulation hair growth; Mode of action

Physiological and Biochemical Importance of the Vitaminoid Thiocyanate

Thiocyanate is a bioactive metabolite which, in contrast to vitamins, does not need to be taken as a supplement, as it can be synthesized in sufficient quantities in the metabolism. However, in case of diseases, stress, malnutrition, infection, toxic influences, or loss through washing out of the hair, the amount synthesized by the body can be below the necessary daily requirement, so that an additional exogenous supply via food or as a local application becomes necessary.

The anion consisting of carbon, hydrogen, and nitrogen (Figure 1) is one of the oldest molecules on Earth and was already present in prebiotic chemical evolution, because it was formed abiotically from carbon disulphide and ammonia under pressure and elevated temperature (110˚C) [1].

Thiocyanate was first detected in saliva by Tiedemann and Gmelin in 1826 [2]. The investigations performed by Hofmeister in 1888 were the beginning of the targeted investigation of the influence of thiocyanate and other physiological anions occurring in the organism during physiological processes [2].

About 2/3 of thiocyanate is formed enzymatically in the organism and about 1/3 is ingested with food. The formation takes place in the thiocyanate-cyanide cycle, in which an equilibrium to cyanide (CN-) is shifted towards thiocyanate [3]. Lacto-vegetarian diets, especially with dairy products, different types of cabbage, chickpeas, sweet potatoes and cress, increase the thiocyanate level. The intake of cyanogenic glycosides (e.g., maize, linseed, millet) and the detoxification of cyanide produce about 2/3 of the total thiocyanate balance. When the thiocyanate serum level drops,

metabolic activation occurs. Three enzymes, thiosulphate: cyanide sulfurtransferase, 3-mercaptopyruvate cyanide sulfurtransferase, and thiosulfate reductase are involved in its formation [3]. Thiocyanate is mainly formed in the liver via sulfur-transferase enzymes. In addition, thiocyanate and hydrogen peroxide react by means of three other enzymes to form antimicrobially active hypothiocyanite and higher oxidation products [4].

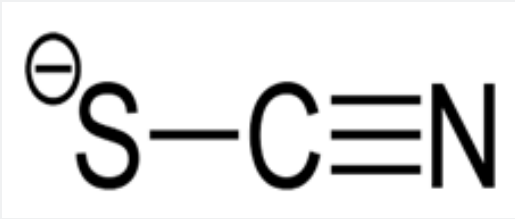

Figure 1: Thiocyanate anion (SCN-).

For decades, thiocyanate was only considered a detoxification product of cyanide without any physiological or biochemical significance. It was only in the middle of the 20th century that intensive research into the physiological and biochemical significance of thiocyanate began with the following findings. Thiocyanate is present in all cells and body fluids of humans, mammals and partly in plants. In the human organism, serum levels change reactively, e.g., in the case of toxic stress, UV radiation, certain diseases [5] and stress [6]. Any form of immunization [7] leads to an increase in the thiocyanate level in the blood. In 1968, the stimulation of the humoral immune response was proven [8]. Thereafter, the following further effects were confirmed at physiological doses within the physiological regulatory range: stimulation of wound and bone healing [9-12], phagocytosis [13], spermiogenesis [14], interferon production [5] and chemo fusion in protoplasts [5]. The stimulation is particularly pronounced in the case of thiocyanate deficiency or increased demand. Additionally, thiocyanate has an antiphlogistic and protective effect in infectious, allergic, toxic, irritative and mutagenic exposure [5]. The anti-infective protective effect is based both on the promotion of colonization resistance and indirectly on the formation of hypothiocyanite. The latter is essential for the body's own defense against pathogens, especially in the oral cavity, respiratory tract, lacrimal fluid, milk, gastrointestinal tract, and vaginal secretions. Adding it to toothpaste as potassium thiocyanate significantly inhibits plaque formation and significantly improves gingivitis [15,16]. In plants, vegetative development, yield, and resistance to microorganisms are promoted [17,18] and a protective effect against toxic stress is achieved [19]. In sum, thiocyanate is a vitaminoid of essential importance.

Besides its exogenous and endogenous presence during the evolution of life, the importance of thiocyanate in cell metabolism is probably due to the variety of arrangement and distribution possibilities of the 16 electrons of the anion. In addition to ionic interactions, they can form coordinate covalent bonds via N-S ligator atoms in the form of one- to five-dentate linkages as well as covalent or coordinate fixation to receptors and binding partners [20]. Thiocyanate changes the conformation of conformationally labile proteins, depending on the type of ligand of the iron porphyrins. The activity-increasing effect of physiological thiocyanate concentrations on several drug-metabolizing and other enzymes, e.g., collagenase, lysozyme, Na^+, K^+, Mg^{2+} and anion-sensitive ATPase, myelo- and lactoperoxidase and phosphodiesterase, is apparently also based on a conformational change. Via the conformational change, thiocyanate can influence growth and division processes through the second messenger cAMP. Further effects at the molecular level include the shift of thermodynamic equilibria, the protection of SH groups, the loosening of H-bridge bonds with an increase in entropy, the influence on hydration and affinity of biomacromolecules (e.g., antibodies and hormone receptors), the influence of cation and anion transport processes, the increase in transmembrane potential with associated stabilization of the cell membrane and modulation of transport processes, the inhibition of formation of free radicals, the stabilization of DNA and the inhibition of oxidative metabolism [21]. Through interactions with the hydrogen peroxide-peroxidase systems, thiocyanate is involved in physiological cycling processes with different effects depending on concentration, e.g., influencing glycolysis and glucose transport, immune regulation, cytolytic lymphocyte activity with inhibition of inflammatory reactions and reduction of DR antigens on the cell surface. In vitro, thiocyanate ions have significant effects on glucocorticoid receptors. Apparently, the biological activity of thiocyanate ions is not based on a uniform mechanism of action but is to be understood as the sum of various partial effects [2].

Influence of Thiocyanate on Hair Growth

The stimulation of hair growth by thiocyanate was noticed as a surprising effect when investigating whether thiocyanate

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could attenuate the side effects of the cytostatic agent cyclophosphamide [22]. The study showed that mice that had received oral thiocyanate exhibited fewer toxic side effects. At the same time, the animals showed no or only slight hair loss, whereas when given cyclophosphamide without simultaneous thiocyanate intake, the animals initially showed a shaggy coat with subsequent hair loss.

Following this observation, we investigated the influence of thiocyanate on hair growth and coat properties in mink and sheep through alimentary supplements and in guinea pigs through external application by saturating the coat. In mink, the coat quality was improved [23], in sheep the wool mass and body weight increased [24]. In guinea pigs, there was a significant increase in anagen hair and an improvement in the hair root status in favour of the anagen phase [25]. These results were pointed to possible application in humans, as hair development in guinea pigs proceeds as a mosaic moult and represents a valid model for the hair development cycle in humans. The increase of hair in the anagen phase indicates that thiocyanate stimulates cell division in dormant or only partially active hair follicles. This agrees with findings that thiocyanate significantly stimulates the proliferation of human skin fibroblasts by 14% *in vitro* [19].

Analogously, hair properties are improved in humans and hair growth is promoted [26,27]. In a double-blind, placebo-controlled parallel group study in patients with alopecia areata, initial success was already visible after eight days of application of the aqueous solution of sodium thiocyanate. After 12 months, complete to good remission of alopecia was achieved in 51% at the end of treatment. In contrast, an increasing deterioration of hair growth was observed in the placebo group. Already after 6 months, no hair growth was observed in half of the placebo patients. This remained unchanged until the end of the follow-up. The trichogram confirmed the growth-promoting effect of thiocyanate. With a mean increase of 20%, the proportion of anagen hair roots increased to an average of 62%. 24% of the patients in the verum group showed normal values with an anagen percentage above 80%. The responder rate was high with 24% of patients for the anagen phase and in 26% patients the telogen phase decreased. With an overall responder rate of 87%, the therapy was effective for all forms of alopecia areata [26]. Since furry animals perform their grooming by licking and saliva is the bodily secretion in the human body with the highest thiocyanate content, its concentration in humans was used as basis in this and following studies. In cases of complete loss of scalp hair resulting from cancer chemotherapy, regular application of thiocyanate stimulated hair growth to such an extent (2-3 cm) that it was no longer necessary to wear a wig [Kramer pers. comm.].

Given the current state of knowledge, the focus is on the preventive use of thiocyanate to prevent the side effects on hair that are associated with the modern lifestyle. Every time the hair is washed, thiocyanate is washed out of the scalp and hair due to its water solubility. The more often the hair is washed, the more thiocyanate is lost. A constant thiocyanate concentration in the hair is only achieved if the hair is washed only about every 2 weeks. If the hair is washed more frequently, the loss cannot be compensated by diet and body care, since the diet is not sufficiently lacto-vegetarian and conventional body-care products do not contain thiocyanate; thus, common hair care today might as well be no care at all, compared to the care animals give their hair by licking it [28]. Additionally, the hair may be stressed by blow-drying or dyeing. Another reason for hair loss can be insufficient activity of the thiocyanate-forming enzymes in cases of hereditary predisposition. Also, among smokers, for example, one of the enzymes responsible for endogenous thiocyanate formation is inhibited by cyanide released during smoking, which hinders the formation of thiocyanate. People who are malnourished or on a strict diet are also deficient in thiocyanate [29]. Stress initially increases thiocyanate serum levels, followed by a massive drop [6]. After discontinuing hormonal contraceptives, there is sometimes considerable hair loss. Finally, the hair is exposed to negative environmental influences. Therefore, the substitution of thiocyanate loss is recommended after every hair wash. It should be noted that some users experience increased hair loss at the beginning because the telogenic hairs are initially shed, known as shedding effect. After about four weeks, however, users feel that the hair structure becomes stronger due to stimulation of the anagen hairs. After four to five months, the imbalance normalizes, and the hair grows back to more than it was before.

It can be assumed that the influence of thiocyanate on the maintenance of healthy hair growth is based on different effects in hair roots. Supplementary administration of thiocyanate relieves the deficiency situation, detoxifies accumulated radicals [19], and promotes regeneration and regulation of the natural hair cycle.

Conclusion

It can be deduced that thiocyanate stimulates the radix pili to form new hairs when applied topically to intact hair roots and that its loss due to hair washing should ideally be replaced preventively after each hair wash by applying a solution of sodium thiocyanate to the scalp and wetting the hair. Important for the local application is the high affinity of the skin organ to thiocyanate. In guinea pigs, the thiocyanate content in the skin increased up to 8.5-fold after balneological application of thiocyanate in physiological concentration. Since thiocyanate is not absorbed dermally in measurable amounts [30], no side effects have become known or are to be expected with local application within the physiological concentration range of saliva. Furthermore, thiocyanate can therapeutically be used to stop effluvium and alopecia.

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