

Trace elements – tiny helpers for a healthy life

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They only occur in minute amounts in the human body. Nevertheless, a decline in trace element concentration causes severe deficiency symptoms. Read more about their function, effects and their significance in the cosmetic field in the following.

In the human body, trace elements occur in minute concentrations even so they are as essential as vitamins. Trace elements are:

- chromium (Cr)
- cobalt (Co)
- iron (Fe)
- fluorine (F)
- iodine (I)
- copper (Cu)
- manganese (Mn)
- molybdenum (Mo)
- selenium (Se)
- silicon (Si)
- zinc (Zn)

Further elements are assumed to be of vital importance for the human body, but not yet proven. With exception of silicon, fluorine and iodine, all the trace elements are of importance for biological redox reactions – the oxidation and reduction of organic compounds. Some of these elements are evenly balanced in the body and influence each other. Thus, a high copper concentration reduces the availability of zinc and vice versa. In other words, a surplus of the one element automatically involves a deficit of the other. In one way or another, almost all the elements play a role for the functionality of the skin.

Oral or topical application?

Trace elements are assimilated with the daily nutrition, mostly with vegetables, nuts, cereal seeds or algae (iodine), others mainly are ingested with meat or giblets. They are then integrated into the respective enzymes or hormones and distributed all over the body, correspondent to their function. With a few exceptions only, the topical application is limited to enzymes or organic compounds such as copper peptide for example. Basic salts are not very common; exceptions here are the salts of copper or zinc. Salts of other trace elements can have counterproductive effects. Thus, under the influence of UV light, free iron and cobalt salts catalytically support the formation of free radicals in the skin but also in cosmetic

products. As iron and cobalt compounds cannot be completely ruled out in raw materials or appear with the contaminations involved with the use of jar products, various cosmetic products contain additives to complex these elements or to render them harmless. Typical representatives here are citric acid (citrates) phosphoric acid (phosphates) or EDTA.

Functions and side effects

Chromium is an essential element of the glucose metabolism.

The toxicity of chromium compounds depends on the oxidation level. While Chromium-III-compounds (Cr^{3+}) only show low toxicity, Cr^{6+} (Chromium-VI: chromates, dichromates) is famous for its allergenic and carcinogenic effects in minute amounts already. Chromium compound induced diseases, particularly in the construction sector belong to the occupational diseases.

Chromium oxide is used as a green pigment; however the German Cosmetic Regulation (KVO) stipulates that it has to be free of chromate ions. Water soluble chromium salts are generally banned in cosmetic products.

Cobalt is the key atom in vitamin B_{12} , a preliminary stage of coenzyme B_{12} that catalyzes rearrangement reactions. Vitamin B_{12} is able to absorb nitrogen oxide radicals.

Cobalt (Co^{2+}) has carcinogenic effects¹. That is why metal-working plants have strict requirements regarding cobalt contaminations in working fluids, such as grinding coolants or inhalable dusts.

The use of cobalt salts, as e.g. cobalt chloride and cobalt sulfate is explicitly banned in cosmetic products.

Iron is a component of hemoglobin (blood pigment) and myoglobin. Both proteins transport oxygen. Myoglobin controls the intracellular oxygen transport. Iron is involved in enzymes that, among others degrade peroxides

¹ Source: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (baua)

(peroxidases, catalase), and vice versa also can form hydrogen peroxide. Peroxidases can oxidize iodide into iodine which is the key substance for the iodine-containing thyroxines of the thyroid gland. Ferrous hemoproteins, such as cytochrome P450, hydroxylate organic compounds with molecular oxygen. In the presence of hydrogen peroxide, endogenic as well as exogenous iron salts (Fe^{2+}) can generate highly reactive hydroxy radicals ($\text{HO}\bullet$) which unselectively attack organic compounds and form radicals and Fe^{3+} (Fenton reaction). In biological systems Fe^{3+} again is reduced to Fe^{2+} so that the process will re-start in presence of hydrogen peroxide².

In the form of its soluble salts, orally applied iron has no or only minor toxicity.

Iron oxide, iron hydroxide and iron hexacyanoferrate serve as yellow, orange, red, brown, blue or black pigments. Iron salts are not used in cosmetic products due to their specific property of triggering autoxidative processes.

Fluorine is important for the hardness of the tooth enamel.

Due to its tooth conserving characteristics and its low toxicity, the fluoridation of drinking water has been discussed again and again.

Fluorine in the form of precisely defined salts (fluorides) and in strictly limited dosage is licensed for the use in dental care products.

Iodine occurs in L-thyroxin and tri-iodine thyroxin. Both are hormones of the thyroid gland which controls a whole number of growth and metabolism processes in the human body. Among them are the formation of nerve cells, the control of cardiovascular functions and the gene expression.

Iodine salts (iodides) occur in sea water and are only slightly toxic.

In cosmetic applications, only iodine propinyl butylcarbamate is used as a preservative.

Copper is contained in oxidoreductases, among others in the tyrosinase which is responsible for the melanin formation, or in the superoxide dismutase (SOD, see zinc). Analogous to the Fenton reaction (see Fe^{2+}), copper ions (Cu^+) form aggressive hydroxyl radicals in the presence of hydrogen peroxide.

Similar to silver salts, copper salts have antibacterial effects. Higher dosages of copper sulfate cause nausea.

With the exception of copper chlorophyll compounds, copper containing pigments are banned from cosmetic products. The natural

copper tripeptide-1 (INCI denomination) of the body is used in facial creams: it enhances the collagen formation of radiation-damaged skin and reduces wrinkles³. Another frequently used salt is copper gluconate.

Manganese is a component of the pyruvate carboxylase, the manganese superoxide dismutase (SOD) of the mitochondria and many other enzymes. Manganese can activate other enzymes. In combination with a narrow band UVB therapy (311 nm), manganese salts (Mn^{2+}) can stimulate a repigmentation of the vitiligo-affected skin⁴. The effect practically corresponds with the catalase with intermediary Mn^{3+} -ions reacting with cellular hydrogen peroxide into Mn^{2+} and free oxygen. The catalytic decomposition of hydrogen peroxide with manganese dioxide (pyrolusite) is familiar from inorganic chemistry.

Manganese compounds are slightly toxic only. While manganese ammonium diphosphate is a violet pigment, manganese phosphate hydrate serves as a red pigment.

Molybdenum, as molybdenum cofactor, catalyzes the degradation of aldehydes by means of the aldehyde hydroxidase, and the oxidation of xanthenes into uric acid through xanthine oxidase (= xanthine dehydrogenase).

Whatever their oxidation level, molybdenum compounds generally are well tolerated.

The trace element is not used in cosmetic products.

Selenium is a component of the glutathione peroxidases⁵, a widely spread family of enzymes that reduce peroxide anions (O_2^{2-}) into water. Hence, they protect oxygen-sensitive structures such as cell membranes and essential fatty acids against the attacks of aggressive oxygen compounds and inhibit a formation of radicals.

Inorganic selenium compounds are extremely toxic whereas many of the organic compounds show an extremely high lethal dosage. Ebselen (2-Phenyl-1,2-benzisoxaselenazol-3-on) is absolutely non-toxic and can destroy hydrogen peroxide and organic peroxides analogous to

³ Pickart L, The human tri-peptide GHK and tissue remodeling, J. Biomater. Sci. Polymer Edn. 2008;19;8:969-988

⁴ Schallreuter KU, Salem MMAEL, Vitiligo – Was ist neu? Hautarzt 2010;61:578-585

⁵ Battin EE, Brumaghim JL, Antioxidant Activity of Sulfur and Selenium: A Review of Reactive Oxygen Species Scavenging, Glutathione Peroxidase, and Metal-Binding Antioxidant Mechanisms, Cell Biochemistry and Biophysics 2009;55;1:1-23

² Belitz HD, Grosch W, Schieberle P, Lehrbuch der Lebensmittelchemie, Springer Verlag, Berlin 2008:205

the glutathione peroxidase; it also reacts with peroxinitrite^{6 7}.

Selenium disulfide is licensed as an ingredient of anti-dandruff shampoo in concentrations up to 1 per cent (health warning: "contains selenium disulfide - avoid eye contact and irritated skin"). The use of other selenium compounds is banned.

Silicon occurs in the connective tissue.

As a widely spread element in natural surroundings, it is only toxic in the form of respirable and non-degradable silica and silicate dusts (mineral wool, asbestos) or fibers.

Talcum powders for children under 3 years consisting of magnesium silicate have to be labelled with the health warning "Keep off nose and mouth of children". Aluminum silicates serve as a white pigment. Siliceous horsetail extract has astringent effects and is an ingredient of toning lotions.

Zinc is a component of many enzymes particularly of dehydrogenases and several peptidases. The zinc and copper-containing superoxide dismutase (SOD) reduces superoxide anions (O_2^-) into peroxide anions (O_2^{2-}).

High concentrations of zinc are toxic for humans.

The European Cosmetic Regulation has limited the dosage of water soluble zinc salts to 1 % of zinc. Zinc oxide is licensed as a pigment however in the form of micro-fine coated zinc oxide as a UV filter it was allowed up to 1.1.2011; an extension of the licence has been applied⁸. Zinc phenol sulfonate and zinc ricinoleate are deodorizing agents in antiperspirants and astringent lotions. Zinc pyrithione has antifungal and antibacterial effects and is contained in anti-dandruff products. The maximum concentration in rinse-off products amounts to 1 % and to 0.1 % in products that remain on the skin. Non-soluble zinc soaps, such as zinc stearate for instance are practically non-toxic and used in W/O emulsions, oleogels and powders as a stabilizing agent, consistency

agent and pigment analogous to magnesium stearate.

Acne patients often have reduced zinc values. It is assumed that zinc influences the hormone metabolism. That is why the oral medication with zinc reduces acne symptoms. It has to be mentioned though, that the treatment takes at least four weeks before first results become visible⁹. Zinc gluconate is contained in acne sticks.

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⁶ Schewe T, Molecular actions of ebselen – an antiinflammatory antioxidant, Gen Pharmacol 1996;26;6:1153-1169

⁷ Zhao R, Holmgren A, A Novel Antioxidant Mechanism of Ebselen Involving Ebselen Diselenide, a Substrate of Mammalian Thioredoxin and Thioredoxin Reductase, Journal of Biological Chemistry 2002;277;42:39456-39462

⁸ Sonnenschutzmittel: Zinkoxid als UV-Filter ist nach derzeitigem Kenntnisstand gesundheitlich unbedenklich, Stellungnahme 037/2010 des deutschen Bundesinstituts für Risikobewertung (BfR) vom 18. Juni 2010

⁹ Meyer EA, Zink als interessante Therapieoption, Pharmazeutische Zeitung 2011;13;PTA-Forum 4:42-44