ZINC: A CRITICAL IMPORTANCE ELEMENT IN COSMETOLOGY

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Received: *February 2004 - Presented at the "All for Cosmetics Conference", Warsaw 19-20 November, 2003*

Key words: *Zinc; Skin; Cosmetics;*

Summary

Zinc is one of the most important microelements in human body. It is a constituent of a great number of enzymes. It influences on many metabolic processes and provides proper functioning of all body as well as the skin. Zinc protects from free radicals and UV radiation, regulates keratinization and fibroblast proliferation. Zinc is also involved in melanogenesis, fatty acids and vitamin A and E metabolism. Topically applied zinc fastens wound healing, regulates sebum secretion, and exhibits antiseptic and antibacterial activity.
Zinc compounds are cosmetic ingredients of frequent use. They can be found in nearly every type of cosmetic products exhibiting a wide range of properties.

Riassunto

Lo zinco è uno dei più importanti microelementi del corpo umano. E' un costituente di un gran numero di enzimi, influenza molti processi metabolici e garantisce il corretto funzionamento del corpo e della pelle. Lo zinco protegge dai radicali liberi e dalle radiazioni UV, regola la cheratinizzazione e la proliferazione dei fibroblasti ed è inoltre coinvolto nel processo di melanogenesi e nel metabolismo degli acidi grassi e delle vitamine A ed E.
Applicato topicamente, lo zinco accelera il processo di cicatrizzazione, regola la secrezione sebacea ed esplica un'attività antisettica ed antibatterica.
I composti dello zinco sono frequentemente utilizzati in quasi tutte le preparazioni cosmetiche perché in grado di espletare una vasta gamma di attività.

INTRODUCTION

Zinc is one of the most abundant trace elements in human body. It takes part in over 200 enzymatic processes. Thus, it influences various metabolic pathways and decides of the proper functioning of the whole body. Zinc is a cofactor of a large group of different enzymes, including oxidoreductases (alcohol dehydrogenase), hydrolases (carboxypeptidase), liases (carbonic anhydrase) and others.

About 2g of zinc are present in all organs, tissues and fluids of the body. Of the total amount of this metal, about 60% are present in skeletal muscles, about 30% in bone and about 6% in the skin [1]. There are several publications regarding zinc concentration in various layers of the skin. Quite sizeable divergence in measurements indicates the difficulty of the proper estimation of zinc level in the skin. It is usually assumed that there is six times more zinc in the epidermis than in lower dermis. Michaelsson et al. evaluated that mean concentration of zinc in epidermis is about 62±15 mg/ g dry weight, and it decreases progressively in the papillary (40±10 mg/g) and reticular dermis (10±1 mg/g) [2]. Histochemical studies of normal cutaneous tissue demonstrated that zinc accumulates mainly in hair shafts and follicles, and in the subcutaneous muscles layer [1].

Zinc concentration in the skin changes with ageing. Studies with two groups of healthy subject (the first group aged less than 35 years and the second one aged above 65 years) showed much less zinc in the epidermis of elderly people [3]. However, there was no significant difference in plasma zinc level in two groups. These results confirm the absence of relationships between epidermal zinc and its reserves in the whole body. Such low concentration of zinc in epidermis observed in older people may be the result of aging-induced lower activity of epidermal enzymes. Conversely, zinc deficiency can retard the activity of other enzymes leading to the intensification of aging processes [3].

ROLE OF ZINC IN THE SKIN

Regulation of cellular division, DNA transcription and proteins synthesis.

Zinc is necessary for the proper cell division, tissue growth and regeneration. As a functionally important constituent of transferases (e.g. DNA and RNA polymerases and reverse transcriptase), zinc plays an essential role in proteins and nucleic acids synthesis. Thus, it is a great importance factor, which determines fibroblast proliferation and is responsible for the course of keratinization. Zinc also takes part in formation of eicosanoids- tissue hormones that regulate excretion processes in the skin [4,5].

Regulation of immune system processes

Zinc strengthens the immune system providing protection from the attacks of different external pathogens. Zinc deficiency depresses cell-mediated immunity through thymus atrophy, that is, the organ responsible for the most important element of immune system – T lymphocytes. Thymus atrophy follows decrease of T lymphocytes and antigen presentation by Langerhans cells. This can result in failure to induce contact sensitivity. It was confirmed in studies with zinc-deficient rats and mice, which showed a severely reduced response to cutaneous sensitisation with standard allergens such as dinitrochlorobenzene and dintrofluorobenzene. [4].

Zinc stimulates excretion and activity of cytokines: TNF, INF-γ (interferon gamma), INF-α, interleukines (IL-1, IL-2, IL-3, IL-4, IL-6) – factors affecting immune response [5]. It also inhibits histamine release from dermal mast cell [6], and virus replication (e.g. herpes simplex virus) as well.

Antiradical protection

One of the most important functions of zinc is UV radiation and antiradical protection. It is widely known that the radical activity causes serious changes in various cellular structures, including DNA damage, and can lead to cancerous lesions. When human fibroblasts used, the *in vitro* laboratory tests demonstrated that the addition of zinc (6,5 mg/L) as a zinc chloride to the cultured medium significantly decreases UVA-induced strand breaks and apoptosis processes [7].

There are several mechanisms of antiradical zinc activity:

1. Zinc (together with copper) is a constituent of superoxide dysmutase (Cu_2Zn_2SOD) – an antioxidant metalloenzyme that catalyses disproportionation (dismutation) of superoxide anion radical to hydrogen peroxide and oxygen, according to the equation:

$$2O_2^{\bullet -} + 2H^+ \longrightarrow H_2O_2 + O_2$$

   Hydrogen peroxide is a harmful product of the reaction. It is next decomposed by another enzyme called catalase. Co-operation of these two enzymes prevents the formation of harmful by-products in metabolic processes of oxygen. The role of zinc in SOD is not totally clear. One hypothesis is that zinc Zn (II) facilitates to generate the electrostatic potential between the positive active site of the enzyme and superoxide anion radical. This fact makes disproportionation reaction possible to occur [8].

   Probably zinc increases the thermal stability of the protein. Some studies demonstrated high thermal stability of Cu-Zn superoxide dysmutase, which decreases when the metals are removed.

2. Zinc can stimulate metallothionein synthesis [9]. Metallothionein are specific sulfhydryl-rich proteins. Maintenance of homeostatic equilibrium of essential metal ions (e.g. Zn, Cu) and removing toxic heavy metals (e.g. Cd, Hg, Pb) are the main functions of the molecules in human body. However, they are also capable of neutralizing reactive oxygen species providing protection for various cellular structures.

   Zn^{2+} can induce metallothionein synthesis forming a zinc-thiolate moiety that becomes preferred sacrificial site for free radical attacks and acts as a shield for surrounding cell structures [9].

3. Zinc ions may replace redox active molecules of copper or iron at critical sites in cell membranes and proteins [9]. Free copper (Cu^+) or iron (Fe^{2+}) ions don't usually exist in vivo, since they are bound strongly to respective binding proteins. However, they can be present in ligand binding to DNA or cell membranes. Then, they are capable of electron transferring and free radicals generating. In the presence of H_2O_2, the highly destructive hydroxyl radical HO· may be produced due to Fe^{2+} ion:

$$Fe^{2+}\text{-ligand} + H_2O_2 \longrightarrow Fe^{3+}\text{-ligand} + OH^- + HO^{\bullet}$$

   When Fe^{2+} ion is replaced by physiologically redox stable Zn^{2+} the reaction above is precluded. The resulted free ion is bound to the respective protein (ferritin or transferrin in case of Fe^{2+} ions) [9].

$$Fe^{2+}\text{-ligand} + Zn^{2+} \longrightarrow Zn^{2+}\text{-ligand} + Fe^{2+}$$

$$Fe^{2+} + \text{ferritin, transferrin} \longrightarrow \text{Fe-ferritin, -transferrin}$$

Regulation of vitamin A and E metabolism

There is no doubt that vitamins A and E are critical for skin health. Vitamin E is known for its antioxidative activity. Vitamin A is an important factor, which stimulates skin tissue regeneration. Zinc is involved in transport processes of these substances. It influences the chylomicrones (lipoproteins responsible for lipids' transport) formation in enterocytes. Thus, various lipids soluble substances, including vitamin A and E, can be provide to all cells and tissues in the needed extent. Zinc deficiency will lead to impaired vitamin A and E absorption and their low concentration in different parts of the body, despite their proper dietary level. In case of vitamin A, zinc also induces *retinol binding protein* (RBP) synthesis [10]. Moreover, it is a constituent of alcohol dehydrogenase which catalyses the transformation of retinol into retinal. This is the crucial step in retinoic acid synthesis, that is the most active form of vitamin A.

Regulation of fatty acids metabolism

Zinc may affects fatty acids metabolism through the regulation of Δ6 and Δ5 desaturases. Δ6 desaturase converts linoleic acid (18:2, n-6) into γ-linolenic acid (18:3, n-6) and α-linolenic acid (18:3, n-3) into octadecatetraenoic acid (18:4, n-3). After an elongation step, Δ5 desaturase forms the biological more important acids: arachidonic acid (20:4, n-6) and eicosapentaenoic acid (20:5, n-3). Those fatty acids serve as precursors for eicosanoids (tissue hormones and neurotransmitters) and are of primary importance as constituents of biological membranes. Zinc helps polyunsaturated fatty acids to incorporate into phospholipids, so that it can regulate cell membrane composition and alter its properties: fluidity, permeability and activity of membrane bound enzymes [11].

Inhibition of 5-α-reductase

Regulation of sebum secretion is the next beneficial zinc effect on the skin. It is very important in case of oily and acne skin. Dihydrotestosterone (DHT) is a product of testosterone reduction by the enzyme 5-α-reductase and is generally considered responsible for the stimulating of the sebaceous gland. Any other irritants also may increase the sebaceous gland activity. These could be free fatty acids or their oxidation products.

Zinc may inhibit 5-α-reductase activity. At high concentration, the enzyme could be totally deactivated. There is evidence that zinc also inhibits bacterial lipase catalysing decomposition of sebum triglicerides to free fatty acids [4, 5].

Regulation of melanogenesis

As high concentrations of zinc are frequently present in pigmented tissues, it seemed likely that it functions in the synthesis of melanin. In fact, some studies confirmed that, apart from copper, other metals (including zinc) are implicated in this process as well. The full mechanism is not understood but it is probable that zinc acts as an enzyme cofactor in tyrosine metabolism and its oxidation and subsequent conversion to melanins [5,12].

Regarding the number of biological processes that zinc is involved in, there is no surprise why it is believed to be the element of critical importance in human nutrition. However, there are the effects of zinc deficiency, which let us realise its significance for the organism. Tables I and II shows the most usual manifestations accompanying zinc deficiency in the whole body and the skin [6].

Table I

Consequences of zinc deficiency in the body

Growth retardation, dwarfism
Lack of appetite, weight loss, anorexia,
Altered immune response, number of lymphocytes decrease, intercurrent infectious,
Ocular and smell abnormalities, dysguesia Pregnancy and postnatal complications, increase abortion risk, neural tube defects of fetus
Vitality decrease, tiredness, weakness, emotional disorders (irritability, mental lethargy, depression)
Hepatosplenomegaly
Hipogonadism (testicles size reduction, abnormal testicles function); testosterone concentration decrease, infertility, oligospermia

Table II

Consequences of zinc deficiency in the skin

Skin immune system weakness
Delayed wound healing; delayed keratinization;
Infection return; skin lesions, ulcers
Nail plate dystrophy
Alopecia; also eyebrows depletion
Acne and dandruff intensification;

SOURCES OF ZINC

Zinc deficiency is frequent subject of medical literature discussion. Some studies performed in different countries demonstrated that zinc deficiency is a world nutritional problem concerning developed and developing countries. It was estimated that independently of age, race or sex, median intake range between 50-80% of recommended dietary allowance [6]. It is likely that our body, hair, nails and the skin will take consequences of low zinc dietary level. Thus, we try to protect from zinc deficiency manifestations, usually by oral supplementation. Zinc sulfate, gluconate, glicynate and asparaginate are used in pharmaceutics the most frequently.

It should be mentioned that it is not only proper zinc concentration, which is a primary importance. The homeostatic balance of zinc and other divalent metals is very important as well. There are evidence that zinc interferences with such metals as calcium, copper or iron. High concentration of zinc significantly limits the amount of those metals absorption and leads to their deficiency. Moreover, when in excess, zinc may inhibit some metabolic processes, which these divalent metals are involved in. Similar chemical and biochemical properties result the possibility of one cation replacing by another. It is especially dangerous when the change concerns the active site of metalloenzyme. Studies with zinc-rich diet rats showed a significant decrease of lysyl oxidase, a copper enzyme responsible for collagen crosslinking [13]. Thus, taking of copper is often recommended during zinc supplementation. However, it should be obvious that excess of copper or iron may affect zinc absorption in the same way [5].

Zinc is found in significant quantities in meat (especially liver), fish and shellfish, leguminous plant seeds (pea, bean, brad bean), cocoa. Vegetables and fruits are rather poor in zinc. Unrefined cereals (wheat, rye, corn) are considered as zinc rich food. However, bioavailability of the metal from these sources is strongly limited due to the presence of large amounts of phytates. Zinc assimilation may be also affected by divalent cations like iron, copper, calcium and toxic heavy metals (cadmium, lead). In the group of absorption inhibitors there are also zinc chelating agents: some drugs, tannins, fiber, oxalic acid, phosphates. On the contrary, vitamin B6 and several amino acids: glycine, histydine, cysteine and metionine belong to absorption activators. [5].

ZINC IN COSMETIC PRODUCTS

Beneficial effects of zinc on the skin processes resulted in introduction its compounds into pharmaceutical formulations for topical application, and then, into cosmetic products. There are over 30 zinc compounds used in cosmetic preparation. All of them are presented in the *International Cosmetic Ingredient Dictionary*.

Zinc compounds belong to the main cosmetic astringents. They act as antiseptic and deodorising agents. Organic salts like zinc acetate, lactate, salicylate, citrate or *p*-phenolsulfonate are used more frequently due to their less skin irritating potential. However, some inorganic compounds also can be found in cosmetic formulations. These are zinc chloride ($ZnCl_2$) and sulphate ($ZnSO_4 \cdot 7H_2O$). All these salts are common antimicrobial and antiseptic constituent of oral care preparations (mouthwashes, toothpaste). The amount of zinc salt present in a mouthwash is typically 0,02-0,5% by weight in terms of zinc ion based on the total amount of the composition. Zinc salts in oral care products may also retard the formation of calculus on to surface. Among the most effective inhibitors are pyrophosphate, pyrophosphate plus polymer (for example PVM/MA) and zinc salts. These agents absorb to the growing crystals of calcium phosphate and they reduce the formation of crystalline phases allowing calcium phosphate to remain in amorphous phase. Some studies demonstrated however, that zinc salts require higher concentration for efficacy (above 2%). With a lower concentration (0,5%), the efficacy against calculus formation is very poor [14].

Zinc salts are also used in after-shaving products, deodorants, face powder and others. *P*-phenolsulfonate is introduced in shaving products. Thanks to its strong astringency power it facilitates shaving process, especially by electric safety razor.

Zinc salts such as propionate, caprylate, stearate and especially undecylenate are introduced into foot care preparations. They act as deodorising and antiseptic agents as well as they inhibit the bacterial growth.

Zinc salt of ricinoleic acid (Fig. 1) has no bactericidal properties.

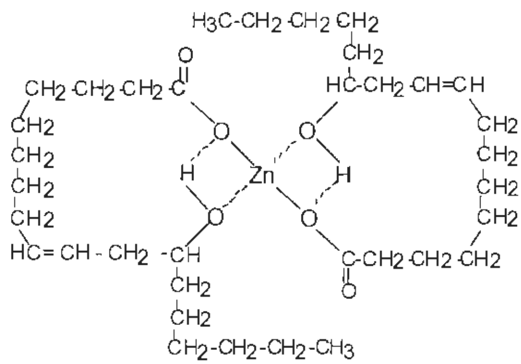

Fig. 1 *Zinc ricinoleate (15)*

However it is used in deodorants due to its high reactivity with free fatty acids as well as low molecular weight organic compounds which have –SH and –NH groups. These compounds (mercaptans and amines) are released from sweat as a result of microorganisms' activity. The efficacy tests of zinc ricinoleate provided by different independent units demonstrated that the deodorising effect maintains up to 24 hours since application. It is interesting that this effect can not be obtained by the combination of zinc with other fatty acids such as stearic and oleic acid. Other metal salts (such as copper, cobalt or nickel) exhibit similar odour-eliminating properties, but they cannot be used in cosmetic products because of toxicological reasons [15].

Among others zinc compounds that are used in deodorants, zinc glycinate is the very interesting one. Like zinc ricinoleate, zinc glycinate shows no inhibitory effect against various bacteria. The mechanism of its activity is based on the inhibition of hydrolytic exoenzymes from underarm bacteria that are present on skin surface [14].

Zinc oxide also exhibits deodorising effect. There is evidence that zinc oxide forms in the presence of fatty acids the corresponding water insoluble and non-volatile compounds. It is especially important in case of short chain fatty acids (C_5-C_{10}) responsible for unpleasant sweat odour. Odourless zinc salt is formed in the reaction between ZnO and a malodour short chain fatty acid:

$$\underset{\text{malodour substance}}{2RCOOH + ZnO} \longrightarrow \underset{\text{odourless substance}}{(RCOO)_2Zn + H_2O}$$

Zinc oxide particles can aggregate to form a massive lump. This leads to clogging of aerosol products. In order to avoid such effect hybrid powders were developed in which zinc oxide covers the surface of spherical nylon or polyethylene powder. The advantage of this technology is the increased surface area of ZnO and thus enhanced deodorising effect [16].

Zinc oxide is one of the basic ingredients of decorative cosmetics. It is thoroughly used as a pigment in face powders due to its good covering capacity. It also acts as sunscreen providing protection from UV radiation. It is usually introduced into cosmetic products in micronised form in order to increase its efficacy. Moreover, micronisation of ZnO makes possible to obtain a product, which applied, will not appear whitish. It is not likely when traditional ZnO form is used. Zinc stearate and myristate can be found in face powders for their good adhesion. Zinc stearate is also good w/o emulsion stabilising agent.

Thoroughly used in cosmetics products zinc oxide is considered to be safe and very effective sunscreen. However, it should be mentioned that there are some doubts concerning its usage in personal care products. ZnO particle is capable of absorbing a photon (from ultraviolet radiation). An electron is released as a result of this reaction and it may interact with oxygen, forming superoxide radical anion. The positive ion ZnO^{+} can interact with water, converting into ZnO and producing a proton and hydroxyl radical

$$ZnO + h\nu \longrightarrow ZnO^{\cdot}$$
$$ZnO^{\cdot} \longrightarrow ZnO^{+} + e^{-}$$
$$e^{-} + O_2 \longrightarrow O_2^{\cdot-}$$
$$ZnO^{+} + H_2O \longrightarrow ZnO + H^{+} + OH^{\cdot}$$

Thus, the very dangerous radicals can be formed as a result of interaction of UV radiation with zinc oxide. ZnO coated with other materials such as alumina or alumina/ silica (some grades) decreases the risk of photooxidation [17].

Protective creams containing zinc oxide are often used to cover the skin of the babies with diaper dermatitis. Theses are usually water-in-oil (w/o) emulsions which contain ZnO with its astringency and deodorising effects, and a large number of lipophilic substances (petrolatum, lanolin, paraffin, waxes and others). When applicated, the preparation forms highly viscous film, which inhibits penetration of different xenobiotics through fully occluding baby's skin [14].

It is thoroughly known that zinc oxide may regulate sebum secretion and it has mild astringency power. Therefore, it is usually introduced in cosmetic products for oily skin. However, the latest studies demonstrated that ZnO can also provide some benefits for dry skin, strengthen skin barrier and reduce of TEWL [18].

Zinc pyrithione (Fig.2) exerts a high antibacterial (Gram (+) and Gram (-) bacteria) and antifungal action against many pathogenic microorganisms, including *Pityrosporum ovale* [19]. It reduces itching and flaking scalp, which is usually associated with seborrheic dermatitis as well as dandruff. Therefore, it is a common main ingredient of market antidandruff shampoo. Zinc pyrithione is water insoluble. Its solubility is about 10-20 ppm (pH~7, 20°C), so that the shampoos are always in suspension form.

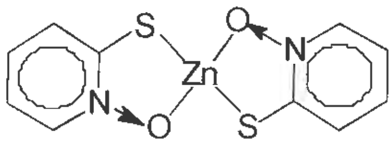

Fig. 2 Zinc Pyrithione

Zinc 2-pirrolidone 5-carboxylate is the zinc compound of the most frequent use in cosmetic products. (Fig.3). It is used in tonics as well as emulsions for oily and acne skin. Like many other zinc compounds, ZnPCA exhibits astringent and antimicrobial action (active against *Propionibacterium acnes and Staphylococcus epidermidis).*

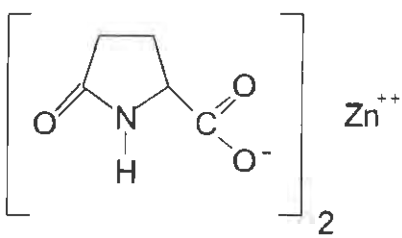

Fig. 3 Zinc 2-pirrolidone 5-carboxylate

Zinc Lauryl Ether Sulfate (ZnLES) is a quite new zinc compound that can be used in skin cleansing products [20]. It combines typical activity of zinc ion (reduction of sebum secretion, antiperspiration,

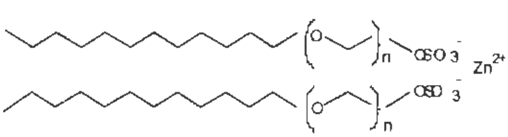

Fig. 4 Zinc Lauryl Ether Sulfate.

deodorising and antibacterial properties) with detergency and foaming of alkyl ether sulfate derivatives. There is evidence that ZnLES shows much less skin irritation both alone and in combination with other surfactants. Critical micelle concentration value (CMC) is the parameter, which provides comparison of potential cutaneous aggression of tensides towards skin. It was demonstrated that:

$$CMC_{MgLES} \sim CMC_{ZnLES} < CMC_{SLES}$$

Maximum concentration allowed for Zinc Lauryl Ether Sulfate corresponds to 12,5% active matters. Solubility of zinc ion strictly depends on acidity. At pH higher than 5, product appearance turns from transparent into opalescent then to milky, according to ZnLES concentration. This is the result of zinc hydroxide precipitation. Therefore, product pH should be adjusted around 4,5-6,0 before adding ZnLES [20].

POSSIBILITY OF ZINC COMPOUNDS PENETRATION THROUGH THE STRATUM CORNEUM

Although zinc compounds are thoroughly used in cosmetics, there are not many data regarding the quantitative skin absorption of zinc. The measurements of the rate of skin penetration of zinc compounds are sometimes contradictory and sometimes difficult to interpret. It is due in part to the homeostatic dynamics of zinc, a rapid exchange between exogenous applied zinc and the large pool of endogenous zinc [1]. Correlation with other metals is also important in this area. Moreover, some studies with zinc oxide demonstrated that in case of zinc deficient organisms, its skin „becomes more permeable" for this substance. Topical application of a concentrated ZnO ointment to healthy subjects with proper zinc level in the body did not result a significant increase in their serum zinc concentration. However, when similar test was made with zinc deficient patients, serum zinc concentration raised to normal and constant level. Additionally, in vivo studies with rats demonstrated that the zinc deficiency in rats can be treated by dermal application of zinc compounds [1,21].

The next problem during skin penetration studies is the fact, that applied zinc compound is not totally soluble in a vehiculum. It is more often zinc compound suspension in water or another medium rather than zinc compound solution. This leads to difficulties in measurements (overestimation of real value), because some quantity of the compound remains on the skin surface or in hair follicles.

Studies regarding the impact of topically applied zinc compound include several aspects. Firstly, the evaluation of irritant potential of a compound. Secondly, checking the possibility of skin penetration. Here, the results are often based on indirect proofs, ex: increase in metallothionein synthesis or decrease in skin copper concentration. Finally, the third aspect concerns the trials of quantitative evaluation of zinc ion penetration through the epidermis and deeper layers of dermis. The results from different studies are often incomparable because obtained under different conditions, ex. under occlusion or not. However, a large number of conclusions can be drawn.

Zinc oxide (ZnO) is one of the best-known zinc compounds. It is widely used in cosmetics (as a sunscreen or pigment in decorative cosmetics) as well as medicine (as a wound-healing agent). Zinc oxide is non-toxic and does not result in skin irritation or allergy. It can be applied at high concentration without risk of adverse effects. The concentration of zinc oxide in so-called zinc ointment is up to 20%. Agren studied *in vivo* the penetration of zinc oxide through the skin of healthy human volunteers under occlusion conditions [22]. Zinc concentration in the dressing was 25% and the application time was 48 hours. The penetration of zinc (~23mg/cm^2/48h) was determined as difference between mean zinc content of new and used zinc dressing. Such calculations take into consideration total amount of zinc that was supplied to the skin as a function of time. It was found however, that a large quantity of zinc was retained in the horny layer (the concentration in epidermis increased 10 times). Therefore, Agren et al. admitted that the evaluated mean permeability rate was (**J~5μg/cm^2/h**) overestimated. Changes in skin pH were also observed after ZnO application. Zinc-treated skin had a significantly higher pH after treatment (5,6±0,3) than before (5,1±0,5). Additionally, the studies demonstrated that ZnO in an occlusive dressing dissolves gradually enabling transport of zinc through the skin. Thanks to it, local ZnO supply can influence biochemical reaction in the epidermis and dermis. The rate of releasing (dissolving) of zinc from occlusive dressing and its absorption through the skin is pH dependent and increases with pH decreasing. It was confirmed in *in vitro* studies with diffusion cells as well as the studies by Hallmans et al. [23].

The first trials of quantitative absorption measurements were carried out in the sixties. Rats and guinea pigs were the subjects of the studies then. These early studies brought the proofs of possibility of zinc penetration through the skin. Topical application (3,1 cm^2 area) of aqueous solution of $^{65}ZnCl_2$ for 5 hours followed by the discovery of ^{65}Zn in different tissues of guinea pigs: liver, kidneys and intestine. Wahlberg et al. also studied $ZnCl_2$ penetration through the skin of 95 guinea pig subjects. Aqueous solutions of $^{65}ZnCl_2$ at various concentrations (0,005-4,87M) and various pH were used. The results of absorption rates through the skin were diversified. The permeability coefficient Kp ranged from $6,4*10^{-4}$ do $25*10^{-4}$ cm/h what was equal about 1-3,9% of applied zinc. However, in the later work regarding toxicological effects of zinc on the skin Wahlberg presented the average absorption rate of 0,239m. $ZnCl_2$ as below 157nmol/h/cm^2; this is equivalent of **Kp<$6,6*10^{-4}$ cm/h** [1,24].

Pirot et al. studied *in vitro* (Franz diffusive cell) the permeability of zinc compound through the human skin [25]. Octanol-water partition coefficients were determined for two substances: $ZnCl_2$ and $ZnSO_4$. It is widely known that octanol-water partition coefficient is used for compound lipophilicity estimation as well as the prediction of its stratum corneum penetration capability. As expected for highly hydrophilic compounds (well water-soluble), the octanol-water partition coefficients for zinc chloride and sulphate were very low. The determined LogP values were -2,827 for $ZnCl_2$ and –6,137 for $ZnSO_4$. Quite a big difference in partition coefficient of these two compounds shows the influence of counter-ion on their character and confirms much greater capability of $ZnCl_2$ penetrating through the skin. The studies were performed in the presence of copper salts and from different systems (petrolatum and hydrogel). The results are shown in Table 3.

Tab III

Permeability coefficient of $ZnCl_2$ and $ZnSO_4$ from different formulations [25]

Formula	Permeability coefficient Kp [cm h^{-1}] x10^6
$ZnSO_4$-$CuSO_4$-Petrolatum	4,82±2,91
$ZnSO_4$-$CuSO_4$-Carbopol 940™ (hydrogel)	5,95±0,71
$ZnCl_2$-$CuCl_2$-Petrolatum	8,21±2,5
$ZnCl_2$-$CuCl_2$-Metolose 60 SH™ (hydrogel)	29,17±11,61

Prolonged skin contact with various substances, for example repeated application of cosmetic product, may lead to skin changes, cause the skin irritation or even much serious effects. Therefore, some studies deal with irritant potential of the studied compounds and omit the absorption kinetics. It was demonstrated that zinc compounds do not produce any allergy or irritants at low concentrations. It was also proved that organic salts of zinc are much less irritant for skin than inorganic compounds.

CONCLUSIONS

Zinc is one of the most important microelements in human body. It is a constituent of a great number of enzymes. It influences on many metabolic processes and provides proper fnnctioning of all body tissues and organs. Zinc protects from free radicals and UV radiation, regulates keratinization and fibroblast proliferation. Topically applied zinc fastens wound healing, regulates sebum secretion, and exhibits antiseptic and antibacterial activity.

Zinc compounds are cosmetic ingredients of frequent use. Although we know the wide range of skin biochemical processes in which zinc takes part, it seems we are still far from the possibility of its full use in cosmetic products.

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