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BIODISPONIBILITETI DHE BIOEFIKASITETI I VITAMINËS C DHE E NË LËKURË

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Përmbledhje

Përdorimi i lëndëve ushqyese funksionale për të lehtësuar ndryshimet në lëkurë, si ndjeshmëria ndaj dritës, plakja dhe thatësia, po rritet në tregun e barnave pa recetë. Lëndët ushqyese më të përdorura në këtë kontekst janë vitaminat, karotenoidet, polifenolet dhe mineralet. Për lëkurën, rruga klasike e administrimit së përbërësve aktivë është aplikimi topikal, dhe industria farmaceutike ka përvojë të konsiderueshme në këtë fushë. Megjithatë, një tjetër mundësi për të ushqyer me përbërës bioaktivë lëkurën është administrimi oral, dhe përdorimi i suplementeve orale për përmirësimin e gjendjes së lëkurës po rritet. Në këtë rast, përbërësit bioaktivë të ushqimit duhet të kalojnë disa pengesa përpara se të arrijnë në lëkurë; ata duhet të kalojnë nëpër traktin gastrointestinal, të kalojnë barrierën e zorrëve, të arrijnë në qarkullimin e gjakut, dhe më pas të shpërndahen në indet e ndryshme të trupit, përfshirë lëkurën. Avantazhi i kësaj rruge të administrimit është se përbërësit bioaktivë të ushqimit metabolizohen dhe më pas shpërndahen në të gjithë indet, potencialisht në formë aktive. Po ashtu, gjaku vazhdimisht furnizon lëkurën me këta përbërës bioaktivë, të cilët mund të shpërndahen në të gjitha shtresat e lëkurës, pra, epidermën, dermën, yndyrën nëndermë, si dhe sebumin. Ky artikull prezanton mekanizmat e përfshirë në bioaktivitetin e lëndëve ushqyese si vitaminat C dhe E në nivelin intestinal, si dhe në nivelin e lëkurës, por gjithashtu efikasitetin e tyre në lëkurë. Vitamina E ka treguar se ka një aftësi antioksiduese dhe luan një rol në mbrojtjen nga drita dhe në parandalimin e plakjes, vetëm ose në bashkëpunim me vitaminën C. Literatura për vitaminën C dhe përfitimet e saj për lëkurën është më e bollshme, duke treguar prova për efektin e dobishëm të këtij përbërësi kundër dëmtimit të lëkurës nga UV dhe stresit oksidativ, duke sugjeruar se marrja e suplementeve me vitaminë C mund të jetë i dobishëm për parandalimin e plakjes së lëkurës, mbrojtjes nga drita dhe për tharjen e lëkurës.

Fjalë çelës: *lëkurë*, *lëndë ushqyese funksionale, vitaminën C, vitamina E*

BIOAVAILABILITY AND SKIN BIOEFFICACY OF VITAMIN C AND E

Abstract

The use of functional nutrients to alleviate skin changes, such as aging photo sensitivity, and dryness,

is increasing in the over-the-counter market. The most popular nutrients in this context are vitamins, carotenoids, polyphenols, and minerals. For skin, the classical route of administration of active compounds is by topical application, and manufacturers have substantial experience in this field. However, another means to deliver bioactives to the skin is by using oral administration, and the use of oral supplements for improving the condition of skin is increasing. In this case, food bio actives have to cross several barriers before reaching the skin; they have to pass down the gastrointestinal tract, cross the intestinal barrier, reach the blood circulation, and then be distributed to the different tissues of the body including the skin. The advantages of this route of administration are that the food bio actives are metabolized and then presented to the entire tissue, potentially in an active form. Also, the blood continuously replenishes the skin with these bio actives, which can then be distributed to all skin compartments, that is, epidermis, dermis, subcutaneous fat, and also sebum. This chapter presents the mechanisms involved in the bioavailability of nutrients such as vitamins C and E at the intestinal as well as at the skin level but also their bio efficacies in skin. Vitamin E has been shown to present an antioxidant property, and to play a role in photoprotection and in the prevention of aging, alone or in association with vitamin C. Literature on vitamin C for skin benefits is more abundant, showing evidence for the beneficial effect of this ingredient on dermal matrix formation, or epidermal differentiation, against UV-induced skin damage, and oxidative stress, indicating that vitamin C supplementation may be of interest to target skin aging, photoprotection, and skin xerosis.

Keywords: *Skin, Functional nutrients, Vitamin C, Vitamin E*

Introduction

Skin is constantly exposed to pro-oxidant environmental stresses from an array of sources, such as air pollutants, solar UV light, chemical oxidants, micro-organisms, cigarette smoke, and ozone (Cross et al., 1998; Thiele et al., 1997). Reactive oxygen species have been implicated in the etiology of several skin disorders including skin cancer and photoaging (Dalle & Pathak, 1992; Emeri, 1992; Guyton & Kensler, 1993; Perchellet &PercheIlet,1989). These reactive oxygen species are capable of oxidizing lipids, proteins, or DNA, leading to the formation of oxidized products such as lipid hydroperoxides, protein carbonyls, or 8-hydroxyguanosine, respectively (Beehler et al., 1992; Hu & Tappel,1992; Podda et aI, 1998). Reactive oxygen species constantly generated in skin are rapidly neutralized by nonenzymatic and enzymatic antioxidant substances, which prevent their harmful effects and maintain a pro-oxidant/antioxidant balance, resulting in cell and tissue stabilization. If the antioxidant defence is exhausted, cell damage can occur. Known nonenzymatic scavengers of free radicals in human skin are /3-carotene, vitamin C, and vitamin E, and enzymatic scavengers are seleno-dependent glutathione peroxidases, copperzinc superoxide dismutase, manganese superoxide dismutase, and catalase (Steenvoorden & van Henegouwen,1997; Thiele et aI., 2000). In recent years, particular antioxidants have gained considerable attention as a means to neutralize reactive oxygen species (Mukhtar & Ahmad, 1999) Green tea polyphenols (Katiyar & Mukhtar, 1997), resveratrol (lang et al.,1997), curcumin (Stoner & Mukhtar, 1995), silymarin, ginger (Katiyar et aI.,1996), and diallyl sulfide (Perchellet et aI., 1990; Sadhana et al., 1988) afford protection against the development of skin cancer, both in vitro (in culture system) as well as in vivo (in animal models). Additionally, diets rich in bioactives such as vitamins C and E, /3-carotene, Iycopene, zinc, and selenium have also demonstrated a photoprotective effect against solar irradiation in humans (Cesarini et aI., 2003; Fuchs, 1998; Fuchs & Kern,1998; Greul et al., 2002; McKenzie, 2000; Rostan et al., 2002; Stahl et al.,2000, 2001; Stahl & Sies, 2002). An increase in cellular antioxidants in skin can be obtained by the exogenous administration of antioxidant compounds. In the case of the skin, the classical route of antioxidant administration to skin is topical application. This approach allows delivery of antioxidants to the skin and at the same time avoids possible side effects of excess antioxidants to other organs. However, this topical route of administration can be efficiently achieved only if the particular antioxidant is stable in the preparation as well as on skin, is able to penetrate the skin, and is present in its active form, that is a possible metabolite. Interestingly, a recent publication showed that keratinocytes also have potential to metabolize bio actives as demonstrated for phenolic acids (Poquet et al., 2008).

In addition, penetration of antioxidants into the skin is influenced by environmental factors, such as temperature, hydration, and the presence of other chemicals. Another means to deliver antioxidants to the skin is using oral administration. In this case, antioxidants cross the intestinal barrier to reach the blood, from which they are distributed to different tissues, and specifically for skin to subcutaneous adipose tissue, dermis, epidermis, and sebum. The advantages of this oral administration are that antioxidants are metabolized and then presented to the entire skin potentially in their active forms. In addition, the blood continuously replenishes skin with these antioxidants, which are distributed to all skin compartments in which they could exert a biological activity. In order to be active in skin, dietary bio actives must be able to cross the intestinal barrier and reach the blood circulation. This step could be a limiting factor of the efficacy of these dietary bio actives in skin. This chapter reviews current knowledge on the journey of dietary bio actives, that is vitamin C and vitamin E from the mouth to skin, as well as their biological activities in skin.

Definition of Bioavailability

Bioavailability is defined by the relative amount of a dietary bioactive consumed that crosses the intestinal barrier, reaches the blood circulation, and is available for metabolic processes or storage in the body. Bioavailability comprises various steps summarized in the acronym LADME.L means liberation of the molecule from the dietary matrix (food or supplement); A is absorption, that is, transfer of the molecule from the gut lumen into the blood circulation; D represents distribution of molecules from the blood circulation in all body tissues; M is metabolism, consisting of the further processing of the molecule in the body either in the gastrointestinal tract or in various tissues; and E is elimination out of the body in urine, stools, sweat, tears, or expired air. In the nutritional context, the commonly used definition of bioavailability refers to the proportion of dietary bioactive that crosses the intestinal barrier and reaches the blood circulation. Competition or synergy between dietary bio actives: Dietary bio actives are rarely consumed alone and therefore synergy or competition processes with other food bio actives present in the meal or in the supplement could readily occur. Vitamin C increases the absorption of iron (Levine et al.,1999). Plant sterols also reduce ~-carotene bioavailability by 50% and affecting by 20% that of vitamin E (Richelle et al., 2004). Phosphatidylcholine decreases absorption of carotenoids and vitamin E, whereas lysophosphatidylcholine enhances it (Koo & Noh, 2001; Sugawara et al., 2001).

Distribution and Delivery to the Skin

When dietary bio actives arrive in the blood circulation, they are ready to be distributed to all body tissues, where they can exhibit a biological activity. Although certain dietary bio actives have been reported to exert a biological activity in skin such as photoprotection, collagen synthesis, and cancer prevention, information on their delivery mechanisms to skin is quite scarce. Vitamin E consists of a mixture of different molecules, that is, «-, ~-, y-, and D-tocopherols and a-, ~-, y-, and D-tocotrienols. Due to the presence of three chiral atoms, these molecules exhibit different stereoisomers ranging from RRR, RSR, etc., to SSS. In response to supplementation, the concentration of vitamin E increases immediately in plasma, whereas a rise in concentration is observed only after several days (7 d) in sebum (Vaule et al., 2004; Ekanayake-Mudiyanselage et al., 2004) Vitamin C is an effective antioxidant and an essential cofactor in numerous enzymatic reactions. It comprises two major forms: L-ascorbic acid, the reduced form, and L-dehydroascorbic acid, the oxidized form. Man and other primates have lost the ability to synthesize vitamin C as a result of a mutation in the gene encoding for L-gulono-y-lactone oxidase, an enzyme equired for vitamin C biosynthesis. In man, plasma ascorbic acid concentrations are maintained between 10 mM and 160 mM (1-15 mg/ml) and any excess of the vitamin is excreted by the kidney (Fuchs & Podda, 1997).

Bioefficacy in Skin

Vitamin E and vitamin C play a role in skin, and various biological effects are presented in the fol-

lowing paragraphs.

1.*Vitamin E and Skin Photoprotection*

In vitro, Jones et al. (1999) demonstrated that exposure of skin fibroblasts to ultraviolet radiation (UVR) leads to generation of reactive oxygen species as well as the oxidation of biomolecules and induction of adaptive responses. Interestingly, supplementation with Trolox, a vitamin E analog, suppressed UVR-induced oxidative stress, suggesting a photoprotective effect of vitamin E on skin fibroblasts. Similarly, Jin et al. (2007) reported that vitamin E was able to limit the generation of reactive oxygen species, reduce cell death, and increase endogenous antioxidant enzyme activity.

2 *Vitamin E and Skin Aging*

Aging is associated with an increased protein kinase C activity, in vitro as a function of cell passage number and in vivo as a function of the donor's age. This increase of protein kinase C activity is associated with collagenase overexpression and activity, resulting in collagen degradation and skin aging. Ricciarelli et al. (1999) reported that vitamin E decreases collagen degradation in vitro. Although in vitro and animal studies have suggested that vitamin E supplementation alone could participate in skin photoprotection and in consequence may slow skin aging, only one human study showed a convincing effect (for reviews, see Boelsma et al., 2001 and Swindells & Rhodes, 2004). A major reason for this may be that the presence of other antioxidants, for example, vitamin C, are necessary for recycling UVR-induced a-tocopherol radicals (Kagan et al., 1992; Wefers & Sies, 1988).

3.Vitamin C and Antioxidant Properties

Vitamin C exhibited in vitro antioxidant activity. However, this activity was only reported in a few in vivo studies. InMcArdle et al. (2002), a daily oral vitamin C supplementation (500 mg/day) for 8 weeks resulted in a reduction of skin malonaldehyde content, a biomarker of lipid oxidation, but also in a reduction of the skin content of total glutathione and protein thiols, which also are important antioxidant molecules. McCall and Frei (1999) reported that oral vitamin C supplementation induced a reduction of lipid oxidative damages, thought to be an important etiologic factor in skin aging, in nonsmokers as well as in smokers.

4.Vitamin C and Aging

In vitro, vitamin C enhances synthesis of collagens I and III in the dermis and collagens IV and VII, tenascin C, fibrillin, and versican at the basement membrane level, improving both skin dermal matrix quality and dermal-epidermal junction morphogenesis (Murad et al., 1981; Chan et al.,1990; Nusgens et al., 2001; Heber et al., 2006; Marionnet et al., 2006; Kim et al., 2006; Amano et al., 2007).The role of vitamin C on collagen synthesis has been confirmed in vivo using preclinical models. Vitamin C deficiency induced a decrease of hydroxyproline, which is responsible for assembling triple-helical collagen molecules in the dermis (Bates & Tsuchiya, 2003). Vitamin C treatment caused a dose-dependent elevation in the wound contraction, indicating a protection of mice against radiation-induced damage as well as an improved healing of wounds after exposure to whole-body gamma radiation (Jagetia et al., 2004). A recent study reveals indeed that higher vitamin C intakes were associated with lower wrinkled appearance and senile dryness (Cosgrove et al., 2007).

5. Vitamin C and Photoprotection

In vitro using a melanocyte-keratinocyte coculture model, vitamin C treatment induces modification of melanocyte dendricity (Regnier et al., 2005), which is known to participate in the beneficial effect of vitamin C for photoaging by preventing UV-induced hyperpigmentation and spots. In a human dermal fibroblast culture, vitamin C treatment counteracted matrix metalloproteinase 1 mRNA increase, which was induced 10- to IS-fold following UVA radiation exposure (Offord et al., 2002).

Skin ascorbic acid significantly decreases with age and that ascorbic acid concentrations were lower in sun-exposed sites (face) versus sun-protected sites (abdomen). These results suggested that vitamin C supplementation can prevent deficiencies in skin, and thus skin photoaging, but more studies are needed to evaluate if the decrease of vitamin C is a consequence of impaired vitamin C bioavailability or simply a result of reduced food intake. With age the sensory capacity is often decreased, oral status is poor, and gastrointestinal changes are observed (e.g., Helicobacter pylori infection). Food intake-related lower vitamin C level with increasing age can be compensated for by oral supplementation. This might support the idea that oral vitamin C can counteract skin deficiencies and so prevent skin damage appearing with age.

Conclusions

Dietary bio actives such as vitamins E and C have demonstrated beneficial effects to maintain and improve skin integrity and physiology as well as to reduce deleterious effects induced by aging and environmental stresses, and more specifically UV-induced skin damages. Beneficial effects have been demonstrated with the use of topical application of these ingredients. More recently, oral supplements containing these ingredients have also been reported to be beneficial for skin. However, consumption of dietary bio actives does not guarantee obtaining a beneficial effect on human skin; indeed this ingredient must cross the intestinal barrier, and if necessary must be metabolized and distributed to the skin. Absorption of dietary bio actives in the gut and in the skin could be modulated based on understanding the key parameters involved in the absorption process, that is, role of transfer proteins, physical and chemical properties of the dietary bio actives, and competition and/or interaction with other dietary bio actives. In conclusion, when dietary bio actives have been selected for their incorporation into an oral supplement, bioavailability of individual dietary bioactives present in the oral supplement as well their interaction with the different constituents of the supplement have to be carefully evaluated and, if necessary, improved. The importance of active versus inactive forms, appropriate concentrations, and product stability remain hurdles-and information that is missing in most of the published literature. The administration of these bio actives by the oral route offers several advantages over their topical application: the intestines absorb bio actives, which are sometimes compromised in topical application due to their low stability or low skin penetration; and bio actives reach the entire skin of the body; bio actives are distributed to all the skin compartments, for example, epidermis, dermis, hypodermis, blood vessels, and sebum, allowing bio efficacy in all these compartments.

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