# Vitamins in cosmetics

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**While many other cosmetic active agents experience their ups and downs, vitamins continue to be in vogue. They are essential components of natural and of physiological cosmetics.**

Vitamins (the term is derived from the Latin word vita = life) are differently structured organic compounds. Already minimal amounts are of vital importance since the human body is not able to synthesize vitamins at all or only in insufficient amounts. Essential fatty acids, formerly also called vitamin F, and essential amino acids do not pertain to the vitamins. Originally it was assumed that vitamins consist of amines – that is the reason for the second word component "amin". However, this is no longer applicable for the vitamins known to the present day.
The vitamin needs of humans and animals vary considerably, even the different species have different needs and some of them also can synthesize vitamin C. The lower the evolutionary stage of an organism the more developed is the ability to synthesize vitamins. That is the reason why vegetable food can fully cover the human vitamin needs.
Many of the substances contained in nutritional supplements and described as vitamin-related only are of importance for the marketing of the respective product.

## Availability

Vitamins control metabolic processes; they have protective and other vital functions and are important for the immune system. Vitamins are ingested with the daily nutrition and partly absorbed via the activity of the intestinal flora. Besides free vitamins also their derivatives or provitamins are assimilated:

- Derivatives are compounds of vitamins with other substances. Frequently they are esters of acids such as acetic acid and palmitic acid as e.g. Tocopheryl Acetate and Tocopheryl Palmitate (INCI terms). In the cases mentioned, the vitamin already has assumed its final structure and only needs to be released in the tissue by ester hydrolyzing enzymes. Frequently the derivatives are less sensitive in atmospheric conditions. In the form of lipophilic esters they are easier to absorb and their dosage in skin care products, among others, can be reduced.
- Provitamins are the pre-stages of vitamins whose structures are biochemically transformed in the body. A typical example here is beta-Carotin that needs several steps in order to form vitamin A and vitamin A acid.

There are water-soluble (hydrophilic) and fat-soluble (lipophilic) vitamins. The higher the solubility in fat, the better the vitamins can be reabsorbed and retained. Water-soluble vitamins occasionally will not be absorbed and will be discharged, if ingested in high dosages. This specifically applies for vitamin C.
It is the "packaging" that counts in skin care applications. Free vitamin C only has superficial effects on the skin similar to a fruit acid, or may possibly be used as an antioxidant in skin care products. Substantial effects in the skin can only be achieved by derivatives in combination with penetration enhancing substances such as liposomes (hydrophilic) or nanodispersions (lipophilic).

## Natural sources

In cosmetic products quite often raw materials can be used that already contain vitamins as natural accompanying substances. In this context, particularly fatty oils such as wheat germ oil, avocado oil or extracts should be mentioned. The skin does not really care whether the vitamins are derived from natural or synthetic sources if the molecules are chemically identical.
This is not the rule, though. While their basic structure remains the same, the number and position of the methyl groups differ in the natural forms of tocopherol (vitamin E), α-, β-, γ- and δ-tocopherol. On the other hand, every single one of the tocopherols can occur in their mirror-imaged d- and l-forms. d-α-tocopherol shows the highest biological efficacy and is denominated as vitamin E in the narrower sense. The synthetic vitamin E frequently is a 1:1 mixture of d-α-tocopherol und l-α-tocopherol.

## Dosages

As vitamins use up when they fulfill their respective functions in the body, they need to be replenished constantly. This applies for the organism as a whole as well as for the skin in particular. Topical applications are in so far advantageous to the oral systemic application as the dosages basically are low however with regard to the area where they are applied they are relatively high. The topical application of vitamin A for instance allows monitoring the effects of vitamin A acid generated by the epidermal oxidation of the vitamin.
Considering the systemic effects, local overdosages usually have no impact. As far as vitamin K is concerned, its application was banned in November 2009 as it is supposed to cause sensitizations which definitely rule out its use as pharmaceutical drug in emergencies. This ban however is controversially discussed in expert groups due to the fact that the root cause for said sensitizations has not yet been clearly isolated.
Considerable amounts of anti-oxidative vitamins such as C and E are used as antioxidants in food and cosmetic products.

## Vitamin A

Vitamin A (retinol) is a diterpene alcohol which abundantly occurs in fish liver and egg yolk. There is a whole series of derivatives and provitamins:

- Retinyl Acetate, Retinyl Palmitate and Retinyl Propionate are esters of vitamin A. They are enzymatically hydrolyzed in the skin.
- Retinal is vitamin A oxidized into an aldehyde. It occurs in the eyes and is significant for the vision. Like Retinol, Retinal is oxidized in the skin into vitamin A acid (retinoic acid).
- Beta-Carotin (provitamin A), the coloring agent of carrots, is enzymatically hydrolyzed into two vitamin A molecules. The carotenoid family consists of numerous liposoluble tetraterpenes with a colouring ranging from red via orange to yellow (tomatoes, peppers, rose hips, oranges etc.).
- 3-Dehydroretinol also occurs in the liver of cold water fish and is referred to as vitamin $A_2$.

Retinoids are sensitive to atmospheric oxygen – hence cosmetic preparations should not be applied at daytime in blazing sun. The specific effect on the skin primarily results from the conversion of retinoids into vitamin A acid. For many years, vitamin A acid has been banned in skin care products however denominated as tretinoin it is licensed in dermatological applications. Isotretinoin differs from tretinoin by another position of the acid group (cis- instead of trans-position). Retinoids are used to treat:

- hyperkeratoses and scars
- compromised skin and acne caused by cornification disorders on the exits of the sebaceous glands
- stimulation of cell growth and collagen synthesis in the epithelial tissue
- aging skin: frequently in combination with the antioxidative vitamins E and C

Retinoids can cause irritations (irritation threshold), which means that typical vitamin A acid effects such as erythema can be observed with higher concentrations and penetration supporting nanodispersions. The number of vitamin A receptors however increases with the duration of the treatment. Hence it is recommended to start the treatment with low doses and then slowly increase the concentrations.
An oral overdose can have teratogenic effects in pregnant women. This should also be kept in mind in terms of nutrition (liver, innards). A cosmetic treatment does not involve systemically relevant concentrations.

## B vitamins

Vitamin $B_1$ (thiamin) is water-soluble and a natural ingredient of cereal and yeast extracts (faex extract). In aqueous solutions it is deactivated by heat. The decomposition products partly generate the meaty flavour which is characteristic for cooked food. As a coenzyme component the vitamin plays an important part in the carbohydrate metabolism. In cosmetic applications it is used as a salt (hydrochloride) and frequently combined with other B-vitamins (vitamin B complex) for the treatment of compromised skin.

Vitamin $B_2$ (riboflavin): Sources of riboflavin are yeast, milk, liver and other innards. The vitamin is involved in the formation of numerous oxidoreductases. It is used as a yellow colouring agent (E 101) in food and cosmetic products.

Vitamin $B_3$ (niacin) occurs either as nicotinic acid or nicotinamide (INCI: Niacinamide). As a component of the coenzymes NAD and NADP, hence dehydrogenases, it is found in non-processed food (meats, cereals) and involved in the biochemical redox reactions. The vitamin is reabsorbed as nicotinic acid in the intestinal tract. In cosmetic products, the amide is used

for skin recovering purposes due to its better water-solubility.

**Vitamin $B_5$ (pantothenic acid):** As a component of coenzyme A it is contained in milk, liver and vegetables. In the cosmetic field sometimes the calcium salt (Calcium Pantothenate) is used, however frequently the easily penetrating provitamin (D-Panthenol) is preferred which is oxidized in the skin into pantothenic acid. Fields of application are:

- enhanced skin hydration
- treatment of inflammatory processes
- cell formation and epithelisation after skin lesions
- suppression of itching
- hair cures

**Vitamin $B_6$ (pyridoxine)** in its original form is an alcoholic compound. Also pyridoxal with its aldehyde function and pyridoxamine with an aminomethyl group belong to the vitamin $B_6$. The three compounds show the same vitamin activity as they can be transformed into each other. Yeast extract, milk, seeds and nuts are typical sources of this vitamin. Pyridoxal phosphate is a coenzyme of numerous enzymes of the amino acid metabolism. Vitamin $B_6$ deficiencies lead to various forms of dermatitis. Predominantly the hydrochloride of pyridoxine is used in skin care products.

**Vitamin $B_7$ (biotin)** has an interesting double ring structure that contains a urea group, among others. The former term "vitamin H" indicates its significance for the skin. In low concentrations it is ubiquitous in food. The highest concentration occurs in yeast. The vitamin is a key component in the enzymes of the amino acid and fatty acid metabolism. Deficiencies lead to growth disturbances of the hair, nails and the skin. Consequences are loss of hair and dermatitis.

**Vitamin $B_9$ (folic acid):** The yellow compound is rich in nitrogen and occurs in vegetables, liver and cereals. It plays a significant role in the C1 metabolism, i.e. in the transfer of methyl-, methylene or formyl groups, where it is effective in the form of tetrahydrofolic acid. Folic acid participates in the DNA synthesis.

**Vitamin $B_{12}$ (cobalamin)** is a macro molecule that contains cobalt and can only be synthesized by micro-organisms living in the intestinal tract of animals or on the surface of soiled food. Hence, it can only be assimilated with animal food where it occurs in concentrated form in liver and kidneys; an exception though is the algae spirulina maxima. Deficiencies can occur in vegetarians or vegans however also pathological conditions of the intestinal micro flora inhibit the resorption of the vitamin. The vitamin as such is inactive and can only be activated by its conversion into coenzyme $B_{12}$. Coenzyme $B_{12}$ catalyzes specific rearrangement reactions in the body. Its use in skin care products is controversially discussed as it is assumed that the molecule is able to bind nitrogen oxide. However, this function can also be assumed by the amino acids of the NMF.

**Vitamin C**

The water-soluble vitamin C (ascorbic acid) is sufficiently supplied with fruit and vegetables. It participates in the biosynthesis and the cross-linking of collagen but also is involved in many other metabolic activities in the field of steroids, amino acids and catecholamines. Main functions in cosmetics are:

- product protection (antioxidant)
- deactivation of free radicals
- keratolytic effects of free, concentrated ascorbic acid at a low pH level analogous to the AHA acids.
- prevention of hyper pigmentation
- stimulation of the collagen formation

While the first three features are reliably accomplished by free ascorbic acid, the remaining two functions can only be successfully achieved by its derivatives due to the fact that free ascorbic acid tends to be instable on the one hand and on the other hand will practically not penetrate into the skin in the form of a polar molecule. Hence it is essential to use derivatives and carrier substances:

- Ascorbyl Phosphate is applied in the form of sodium or magnesium salts. It is the water-soluble ester of vitamin C with phosphoric acid and enzymatically hydrolyzed after having passed the skin barrier. The carrier substance is phosphatidylcholine in the form of liposomes.
- Ascorbyl Palmitate und ascorbyl stearate as well as their respective multiple esters are the fat-soluble variants that are appropriately encapsulated in nanodispersions where the phosphatidylcholine also has penetration enhancing effects. Analogously, the esters are enzymatically hydrolyzed into ascorbic acid, palmitic acid respectively stearic acid. Phosphatidylcholine is produced naturally in the body and hence compatible with all barrier and cell structures of the body.

The ester hydrolysis exclusively generates substances that occur naturally in the skin. Esters basically are more resistant to the atmospheric oxygen and therefore less suited to be used as antioxidants for the preservation of the products. In practice, the difference between esters and free ascorbic acid can easily be observed in the context of laser depilation: Free ascorbic acid applied before the depilation treatment turns into a brownish colour and practically has no influence on the melanin formation while liposomal sodium ascorbyl phosphate completely suppresses the melanin formation. Already concentrations of about 0.1 % are sufficient to achieve this effect.

### Vitamin D

The most significant sources of vitamin D (calcitriol) are the provitamin $D_2$ (ergosterol) that occurs in mushrooms and wheat germ oil among others, and provitamin $D_3$ (7-dehydrocholesterol) that is found in egg yolk, liver and fish oils. Vitamin $D_2$ (ergocalciferol) and vitamin $D_3$ (cholecalciferol) are formed from provitamin $D_2$ resp. provitamin $D_3$ under the influence of sunlight. They are transported into the liver and there transformed into 25-hydroxycholecalciferol (calcidiol). After the transport into the kidneys via blood stream, it is transformed into the active form of vitamin D (1,25-Dihydroxycholecalciferol = calcitriol). From there the blood stream again transports it into the target organs where it is bound to proteins. Calcitriol controls the calcium and phosphate metabolism in the small intestine, the bones and the kidney.
The European Cosmetics Directive explicitly bans the use of vitamin $D_2$ (ergocalciferol) and vitamin $D_3$ (cholecalciferol). However this does not apply to the provitamins that also in the US are licensed for the use in skin care products. A whole series of interesting effects in the skin are described in the context of vitamin D:

- Calcitriol influences the differentiation and the growth process of keratinocytes. This function plays an important role in the psoriasis treatment.
- Calcitriol participates in the proper maintenance of the calcium gradients in the skin.
- Calcitriol stimulates the formation of antimicrobially effective peptides such as defensins and cathelicidins. The effect of these peptides is particularly interesting in the context of inflammatory processes in neurodermatitis cases.
- Calcitriol prolongs the self-protection of the skin during the exposure to UVB radiation. It stimulates the heat shock proteins.
- Several studies even describe a repigmentation in vitiligo cases after the application of calcitriol or vitamin D analogous products.

### Vitamin E

Vitamin E (d-$\alpha$-tocopherol) is equipped with a terpene side chain that is bound to a chromane ring and belongs to the group of fat-soluble vitamins just as the vitamins A, D and K. As a natural antioxidant, vitamin E occurs in all unsaturated vegetable oils. Wheat germ oil is on top position in this regard. Outstanding physiological function of this vitamin is the protection of oxygen sensitive cellular components such as omega-3 and omega-6 fatty acids. In the cosmetic field, the free vitamin and its derivatives are used. The derivatives are the esters of organic acids. As the esterification occurs on the phenolic hydroxyl group, they lack the antioxidative effects. Hence they do not have antioxidative functions in the products but are stable active agents that are hydrolyzed by esterases after having passed the skin barrier. The ester hydrolysis activates the antioxidative features. The following vitamin E derivatives are of significance:

- Tocopheryl Acetate is the ester of acetic acid.
- Tocopheryl Palmitate is the ester of palmitic acid.
- Tocopheryl Linoleate (ester of linoleic acid) shows a combination of antioxidative effects with the effects of an essential omega-6 acid.
- Tocopheryl Nicotinate (ester with nicotinic acid) is a combination of vitamin E with vitamin $B_3$. The ester supports the microcirculation in the skin without the features that are typical for short-chained nicotinic acid esters such as generating heat or erythema.

A whole series of vitamin E features are used in the cosmetic field:

- Antioxidative effects and radical scavenger features – in this context it is important to select the appropriate concentration as high concentrations will trigger the pro-oxidative features of vitamin E.
- Protection of vitamin A and derivatives in combination with vitamin C.

- The radical scavenger features also naturally involve a reduction of the stress caused by UV radiation. The same applies to inflammatory processes.
- Stimulation of cell formation (epithelisation)
- The moisture retention capacity of the skin is improved.

## Vitamin K

Vitamin K belongs to the fat-soluble vitamins and occurs in two natural forms, vitamin $K_1$ (phyllochinone; 2-methyl-3-phytyl-naphthochinone) and vitamin $K_2$ (menachinone, 2-methyl-3-difarnesyl-1.4-vitamin. The phytyl side chain of vitamin $K_1$ is equivalent to a monoterpene with 20 C-atoms. In contrast to vitamin $K_1$, vitamin $K_2$ can have differently sized terpene side chains. Vitamin $K_1$ is mainly assimilated with vegetable food, while vitamin $K_2$ is formed by intestinal bacteria such as escherichia coli. Hence, vitamin K deficiencies will appear, if an antibiotics treatment has affected the intestinal flora or it has not yet been formed as e.g. in newborns.
Vitamin K is a blood coagulation factor and, among others, supports the steady flow characteristics of the blood. Vitamin K deficiencies slow down the blood coagulation and can be responsible for increased bleedings after injuries. Also the disposition to form hematomas, purpura (efflorescence-like skin bleedings), nose bleeding as well as gastrointestinal or mucous tissue bleedings can be caused by vitamin K deficiency.
Topically applied, the vitamin stabilizes the superficial capillary system and firms the skin. That is why vitamin K can also be used to treat rosacea and couperosis. Despite of the 2009 imposed ban of vitamin K, the epoxide of the vitamin, a pre-stage, still is licensed although its sensitization potential is incomparably higher due to its reaction with protein components on the skin surface. The vitamin K content in vegetable sources such as wheat germ, Brussels sprouts, spinach and tomatoes is too insignificant to use it for skin care purposes.

## Conclusion

From a present-day perspective, skin conditions caused by hypovitaminoses such as pellagra e.g. can practically be excluded as today's nutrition is multi-faceted and rich in vitamins. The vitamins $B_{12}$ and D constitute an exception though and should be kept in mind when following a vegetarian or vegan diet. Vitamin D deficiencies then become all the more serious, if the daily skin care routine involves creams with UV filters.
Apart from the daily minimum requirement, some of the vitamins also show effects that make them valuable components of products for the daily skin care, for the treatment of skin disorders and the prevention of premature skin aging. Aside from that, they meet the criteria for natural and physiological cosmetics.

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