

Antioxidants – an overview

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During the past years, no other active agent class has attracted more attention as a cosmetic ingredient than the group of antioxidants with their radical scavenging properties. Now it is time to draw the balance and compile an orientation guide as to the large variety of active agents.

If we refer to antioxidants in connection with the skin, we generally speak of substances that are able to scavenge free radicals. In chemical terms, a radical is defined as a molecule that contains an unpaired (single) electron. The electrons in molecules usually occur as pairs and are in a low energy state. By contrast, radicals are highly reactive. They attack other molecules and to some extent start "chain reactions". In this context, undesired reaction products will form as well as new radicals that can cause damages in the skin or in the body.

Oxidative stress

The good news: whenever two radicals meet, they destroy each other. This is the case with antioxidants; after reacting with a radical they transform into a low energy radical which will scavenge another high-energy radical, neutralize it and hence put an end to this disastrous chain. That is why antioxidants also are called "radical scavengers" in this context. High-energy radicals are very short-lived. Their half-life period is somewhere in the range of 10^{-5} and 10^{-9} seconds. They form in the course of various processes – frequently in combination with external radiation and/or with the participation of heavy metal traces such as for instance iron. The human organism itself also produces radicals and utilizes them in order to

- generate energy in the mitochondria
- kill bacteria, viruses and foreign bodies through "oxidative burst" during phagocytosis
- transfer signals

This radical formation occurs in a controlled way comparable to a nuclear reactor and is limited to physiological processes. Environmentally generated free radicals however form in an uncontrolled way through

- UV-radiation (sun)
- thermal bond cleavage
- gamma-radiation

- heavy metal traces (iron, cobalt, nickel)
- nitrogen oxidation (nitrogen monoxide and nitrogen dioxide)
- reactive oxygen compounds

The reactive oxygen compounds belong to the group of Reactive Oxygen Species (ROS) which comprises oxygen-rich radicals but also their high-energy pre-stages:

- Hydroxyl radical: $\text{HO}\cdot$
- Superoxide anion: O_2^-
- Hydrogen peroxide: H_2O_2
- Singlet oxygen: $^1\text{O}_2$
- Ozone: O_3
- Organic hydroperoxides (R-OOH), peroxy radicals (R-OO \cdot) and alkoxy radicals (R-O \cdot); they develop through oxidation of lipids. [R = hydrocarbyl]

Analogous to the ROS, there exists a Reactive Nitrogen Species (RNS) class which comprises nitrogen monoxide (NO \cdot) that belongs to the nitrogen oxides, and peroxyxynitrite anion ONO_2^- . In the human body, the "oxidants" ROS and RNS, both also are utilized in physiological processes, are paired by antagonists in the form of "antioxidants" which means that in normal healthy conditions there is a balance of oxidants and antioxidants. The physiological antioxidants control the endogenous ROS and RNS systems and react immediately when exogenous ROS and RNS compounds from the environment infiltrate the body. However in cases where the biological antioxidants are overcharged, lipid damages ("lipid peroxidation") or protein damages ("protein oxidation") will occur. Damaged cell structures trigger inflammatory processes and skin modifications up to carcinoma; DNA damages have been proved to be responsible for aging processes. In the context of ROS, such situations are called "oxidative stress" while we deal with "nitrosative stress" in combination with RNS.

Radical scavengers

The human body keeps a whole arsenal of antioxidants on hand which react in different ways depending on where and how the radicals form and also depending on the relative energy state. It is differentiated between selective antioxidants i.e. focused on particular radicals and unspecific antioxidants respectively radical scavengers that are less finicky about their prey.

Selectively acting are the following enzymes:

- Superoxide dismutase (SOD) transfers superoxide anions into hydrogen peroxide.
- Glutathione peroxidase (GPX) contains selenium (selenocysteine) and generates water from hydrogen peroxide.
- Catalase (CAT) reacts with hydrogen peroxide into water and oxygen.
- Thioredoxin (TXN) belongs to the oxidoreductases that can have reducing and radical scavenging but also oxidizing effects depending on the particular metabolic processes.

Unspecific antioxidant activities show among others:

- Vitamin C (ascorbic acid), vitamin E (tocopherol), vitamin K in its reduced (hydroquinone-) form, provitamin A (beta-carotene) and carotenoids in general
- Coenzyme Q₁₀ in its reduced (hydroquinone-) form
- NMF of the skin (amino acids)
- Fatty acid amides, ureic acid, urea
- Various peptides and proteins
- Saccharides, hyaluronic acid and glucans

The vitamins C (water soluble) and E (liposoluble) complement each other in the protection of the cell membrane against lipid peroxidation. They have the same function in cosmetic preparations: they also protect the lipids. Derivatives of vitamin E such as tocopheryl acetate, palmitate, stearate, linoleate however only are effective in the skin after being enzymatically hydrolyzed into free vitamins and acids.

Due to the above mentioned sensitive balance between antioxidants and oxidants required for the complex metabolism of the human body, it is not the best solution to blindly maximize and boost the efficacy of antioxidants. It should be emphasized that too much of antioxidants at

the wrong place can be harmful for the body since it will disturb the natural ROS system. Studies have shown that antioxidants in food supplements are not beneficial unless severe deficiency symptoms have been observed. An increased dosage of vitamin E in cosmetic formulations will change the mode of action from antioxidant to pro-oxidant effects based on the fact that higher concentrations of vitamin E maintain their own chain reaction. Similar effects have been observed in technical alkanolamine containing liquids after adding vitamins in order to protect the substances against the formation of nitrosamines through nitrogen oxides. In contrast to all expectations, the nitrosamine formation intensified. Just like so often, "a lot helps a lot" is not applicable for antioxidants either. "

Compounds used in cosmetics

Besides some of the above mentioned antioxidants, the following compounds are used in cosmetic preparations:

Phenols:

- Vitamin E (E 306-309): After reacting with a radical, vitamin E itself forms a low reactivity radical that can be regenerated into vitamin E through vitamin C.
- 3,5-Di-tert-butyl-4-methylphenol (BHT; E 321) and BHA (E 319), which is a mixture of 2- and 3-tert-butyl-4-hydroxyanisole, are synthetically produced. Similar to vitamin E they form low reactivity radicals.

Polyphenols and hydroquinones

- Carnosic acid occurs in rosemary (E 392) and sage extracts.
- 4-Hexylresorcinol (E 586) and 2-tert-butylhydroquinone (E 319) are synthetic antioxidants and serve as food additives.
- Resveratrol (trans-3,5,4'-trihydroxystilben) occurs in red wine and many fruits.
- Flavonoids (flavones) such as quercetin and taxifolin belong to the secondary plant compounds and form a multifaceted and widely spread substance class. Their glycosides (compounds with saccharides) are water soluble. Flavones are present in coffee, green and black tea as well as pomegranate extract among others.
- Isoflavones alias phytoestrogens mostly are gained from soybeans and red

- clover.
- Gallates (E 310-312) are the synthetic ethyl-, propyl- and dodecyl esters of 3,4,5-trihydroxybenzoic acid (gallic acid). Complex natural esters of the gallic acid for instance are the tannins in hamamelis extracts (witch hazel extract) or the epigallocatechin gallate of green tea. Free gallic acid also has antioxidant effects.
- Anthocyanins (E 163) are used as food colorants. Related natural pre-stages are the oligomeric proanthocyanidines (OPC); which are highly efficient antioxidants and abound in grape seed extracts.

Carotenoids

- Typical representatives are beta-carotene (provitamin A, E 160a), lutein (E 161b), lycopene (E 160c) capsanthin (E160c) and astaxanthin (E 161j). Their colouring ranges from yellow through to red.
- Vitamin A

Reductones

- Vitamin C (L-ascorbic acid) and its salts and esters (E 300-302, 304) belong to the group of strongly reducing reductones (endiols).
- Erythorbic acid (E 315-316) is a synthetic isomer of vitamin C and also a strong antioxidant however biologically inactive.

Sulphur compounds

- Under the influence of oxidants or radicals, the natural amino acid L-cysteine will form cysteine which contains a disulfide bridge.
- α -lipoic acid is a coenzyme which in its reduced form (dihydrolipoic acid) is an effective radical scavenger will cyclise with forming a disulfide group.
- Glutathione (GSH), a tripeptide with L-cysteine unity, reacts with radicals or oxidants similar to L-cysteine.
- Under the influence of ROS, sulphur dioxide resp. sulphurous acid and its salts (E 220-228) are oxidized into sul-

phuric acid and sulphates. Its use in cosmetic preparations is restricted.

Reaction products

Through reaction of phenols, polyphenols, hydroquinones and carotinoids with free radicals new and persistent radicals or reaction products may form that however are no longer harmful. Particularly phenolic compounds will darken in colour which can easily be observed when a cup of black tea is exposed for some time to atmospheric oxygen.

The peroxy radicals resulting from the lipid peroxidation (autoxidation) of polyunsaturated ω -3 and ω -6-acids cause resin formation in lipids. In cosmetic preparations, linseed oil and kiwi seed oil with their soothing and anti-inflammatory effects often are protected with antioxidants such as vitamin C, E and urea but also through nanoparticulate encapsulation.

This also enhances the protection of oxidation sensitive natural substances:

- Complexing agents (including their salts) such as EDTA (E385) citric acid (E 330-333), tartaric acid (E334-337), phosphoric acid (E338-343), etidronic acid (1-hydroxyethan-1,1-diphosphonic acid) but also saccharides as well as polyphenols scavenge the traces of heavy metal ions of the elements iron, cobalt and nickel that form radicals when exposed to UV light. The resulting heavy metal complexes (chelates) are completely inactive.
- UV light filters transform the radical forming UV light into heat. For this purpose they are put into an excited state but only as transient as possible since otherwise there will be an increased risk of radical formation instead of heat.

By the way: In terms of the daily consumption, coffee with its polyphenol content ranges on number one on the list of ingested antioxidants. The percentage shares of tea, fruits and vegetables are statistically lower since smaller amounts are consumed.

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