Fire and fire brigade – functioning of free radicals and antioxidants

published in Kosmetik International 2019 (4), 30-33

Free radicals and antioxidants can be explained with the example of fire and fire brigade. Although fire actually is dangerous, it is beneficial when under control. Antioxidants can limit the damage when they are used in the right context. Superfluity of them is useless and even counterproductive. Dr Lautenschläger reports on the positive and negative aspects of radicals and antioxidants.

Free radicals are aggressive chemical individuals that destroy the organic substances in their environment by means of oxidation. If antioxidants are in the vicinity, they are the first to be attacked. The radicals lose their damaging potential in this process and harmless reaction products are formed. In chemical-physical terms it means that an electron is transferred from the antioxidant to the radical.

Where are radicals formed?

Thus antioxidants can protect the organic structures from radicals. So far, so good. The body has a variety of substances in store that fulfil this task and decides – to stick to the example with the fire brigade – whatever out of the tools is needed: water, powder extinguisher or fire extinguishing foam. In other words, radicals differ greatly in terms of their formation, structure and destructive energy.
Quite a number of radical reactions take place in the body particularly during energy generation in the mitochondria, the power plants in our cells. Fatty acids or glucose are oxidized in this process and finally degraded into carbon dioxide and water. This process is enzymatically controlled, much in the same way as in a stove designed for different combustibles. By its very nature, radical formation and burner capacity increase with hard manual work and during sports activities.
The situation is different with phagocytosis, i.e. the radical-induced destruction of microorganisms and unwanted foreign bodies that penetrate into the body. This process also is called "**oxidative burst**". With the process in full swing, the body temperature rises. We catch a **fever**. Fever is the symptom for a perfectly functioning defence system. Accordingly, studies show that the body's fight against infections takes longer when antifebrile drugs are administered. These drugs are only useful in emergencies. It also could be observed that high fever or artificially induced overheating of the body (hyperthermia) can destroy internal, degenerated cells. This, to a certain degree, natural **chemotherapy** of the body can even lead to spontaneous healings in cases of cancer. Conventional chemotherapies induced by pharmaceutical drugs basically work in the same way, they produce radicals that preferably attack the more sensitive cancer cells. In this particular situation, high doses of antioxidants in the form of food supplements are counterproductive and can make chemotherapy ineffective.
Radicals also form during

- external treatment of inflammations by infrared radiation,
- interaction of LED blue light with bacterial metabolites in the case of juvenile acne or,
- destruction of tumour cells by LED red light and photosensitizing 5-aminolevulinic acid in the photodynamic therapy (PDT).

The above-mentioned examples show that low-energy radiation can be quite useful for healing processes. High energy (sun radiation) and thus related oxidative processes, however, can cause premature aging of the skin, among others. Medical drugs, metabolic- and foreign substances etc. are detoxified by means of oxidation and excreted via kidneys.
A further internal source of radicals is signal transduction. Besides oxygen radicals also nitrogen oxide (NO) belongs to the repertoire; the latter-mentioned plays a quite inglorious role in the discussions around diesel engines.

External sources

Outside the body, radicals form through radiation on the skin (sun, cosmic radiation), a process that also induces melanin formation and thus establishes a protective barrier against radiation. Melanin is an excellent UV filter. It completely converts sun radiation into heat

without formation of further radicals. Melanin, however, should not be overcharged with this task. Hence, slowly adapting to the sun and applying sun protection products with UV filters in the case of high radiation exposure are useful remedies to avoid skin damages such as melanoma and actinic keratosis. Completely inhibiting the melanin formation twenty-four-seven with UV filters and antioxidants is not purposeful, though.
Radionuclide radiation also leads to radical formation. In terms of external radiation, mainly the γ-radiation is relevant particularly in cases where the skin is the passageway for radiation.
Besides administering lipid substances, the preservation of the NMF (Natural Moisturizing Factor) by applying amino acids and urea is important since they do not only retain the moisture but also have **radical scavenging** functions, similar to antioxidants. They react, above all, with the atmospheric nitrogen oxide radicals NO and NO_2 to form elementary nitrogen and the natural alpha-hydroxy acids of the body.
Catalysts for the radical formation in radiation- and thermal stress conditions are the traces of heavy metals such as iron that get on the skin with dust or find their way into cosmetics when using jar products and thus accelerate the spoilage. That is why often complexing agents, such as phosphates, citric acid and EDTA, are added to these preparations. They bind and inactivate heavy metals such as iron. The highly effective EDTA, however, is being discussed due to its persistence and the chemical bonding of physiological iron.
Radicals do not only form in the combustion engines of motor vehicles, ships and airplanes but also abundantly occur in natural surroundings through interaction of herbal emissions and sun radiation as well as through electric discharge and smog weather conditions.

Protection measures

The term "**Reactive Oxygen Species**" (ROS) summarizes radicals and other reactive oxygen derivatives and the term "**Reactive Nitrogen Species**" (RNS) refers to nitrogen-derived radicals. The most important ROS are hydroxyl radicals, superoxide anion, hydrogen peroxide, singlet oxygen, ozone as well as organic hydroperoxides, peroxy- and alkoxy-radicals. The latter mentioned form during the oxidation of lipids. Nitrogen monoxide (NO) and peroxynitrite anion belong to the group of RNS.
The list of reactive compounds implies that humans just as all other living organisms have been exposed to a mix of ROS and RNS since the year one and that they obviously have developed effective protection measures to control internal and external radicals in order to keep damages at a minimum. In other words, when things get out of hand there is a mix of perfectly balanced physiological antioxidants available.
Among them are selective antioxidants that are specialized in the internal protection and monitoring of a definite ROS, and non-specifically acting substances that are in charge of the external defence against a variety of different radicals.
Enzymes, above all, have selective functions. Just to mention superoxide dismutase (SOD) that converts superoxide anions into hydrogen peroxide. The seleniferous glutathione peroxidase (GPX) makes water from hydrogen peroxide. Catalase (CAT) reacts with hydrogen peroxide to form water and oxygen. Then there are the oxidoreductases such as thioredoxin (TXN) that can have reducing- and radical-binding-, however also oxidising effects, depending on the particular metabolic processes.
Nonspecific antioxidants are, among others, carotenoids, the vitamins C, E and K and coenzyme Q_{10} each in their reduced hydroquinone forms, the amino acids of the dermal NMF, fatty acid amides, uric acid, urea, saccharides and their derivatives as for instance also hyaluronic acid.

Exceptional circumstances

When the natural antioxidants of the body are overstressed, as happens during local external UV radiation and insufficient melanin protection, the lipids are damaged by "**lipid peroxidation**" and the proteins are damaged by "**protein oxidation**". Potential consequences are inflammatory processes and skin alterations up to carcinomas. Also aging symptoms are traceable to respective DNA damages.
Depending on the origin, we speak of "**oxidative stress**", when ROS are the triggers, or of "**nitrosative stress**" with RNS as triggers. Less known is the term "**reductive stress**" which indicates a deficit of physiological ROS and a surplus of natural antioxidants of the body. It is assumed that reductive stress is present in **hypoxic conditions**, or in other words an oxygen undersupply of the heart, the liver (e.g. in the case of alcohol poisoning), and in the context of degenerative diseases. In such extreme cases, the strong, natural antioxidant NADH (nicotinamide adenine dinucleotide) of the body is disarmed by withdrawal of electrons resulting from methane production from the methyl groups of certain physiological substances as for instance phosphatidylcholine, without involvement of ROS.

Food supplements (online published by medical Beauty Forum)

According to this, the body has a finely tuned balance of ROS, RNS and physiological antioxidants that automatically adapts to the current requirements. Just to mention an example: people engaged in sports activities have an increased ROS formation. Simultaneously also the protective measures against ROS in the cells are intensified. Endurance sports activities increase life expectancy, significantly delay the aging process and also mobilise the immune system.
The related prevention of diabetes observed in this context is completely or partly suppressed by intake of external antioxidants. On top of that, various studies show that antioxidants administered in the form of food supplements are more or less useless in the case of a balanced diet, regardless of whether they are vitamins, polyphenols such as flavonoids and isoflavonoids, or sulphur compounds such as L-cysteine and α-lipoic acid, unless they have additional multifunctional effects.
Not only that, there is also reason to believe that, on a long-term basis, some of the highly dosed antioxidants such as vitamin E and carotenoids support the development of tumours and other diseases. The main cause supposedly is the undifferentiated suppression both of damaging and of useful ROS properties, particularly of signal transduction.

Prevention in the skin care

Under normal conditions, atmospheric radicals are scavenged by the afore-mentioned natural NMF of the skin. In the case that oxidative stress is expected such as sun exposure, UV filters are beneficial, and should be preferred to the administration of antioxidants; that other than UV filters degrade very fast under these conditions (oxygen and radiation). Very high concentrations would be required which again make no sense, since antioxidants such as vitamin E trigger their own **radical chain reactions** under these conditions and then even have pro-oxidative effects.
Essential fatty acids of native oils are popular components of skin care preparations since they have anti-inflammatory effects, and since the abundantly contained linoleic acid is a ceramide-I-substrate. It should however be kept in mind that they are subject to the already mentioned **lipid peroxidation** and hence have to be protected on sunny days by adding antioxidants such as vitamin E and C or preferably be applied in the evenings either without or with a small dosage of antioxidants.

ROS in therapy

While the high-energy UV rays (sun) and γ-radiation cause serious cell damages respectively adverse effects, radiation therapies with relatively low-energy dosage and the thus related radical formation stimulate the organism to implement highly beneficial **repair- and regenerative activities**. Treatments with artificial ROS are a molecular alternative. The use of benzoyl peroxide for acne therapy and ozonised native oils against infections, mycoses and for disinfection purposes can be mentioned as an example in this context. Physical full-body- and local hyperthermia treatments that increase radical formation similar to fever conditions have not gained acceptance, though. Obviously consumers have continued with Granny's remedy to take a hot bath in the case of infections.
Apart from that, the local post-inflammatory hyperpigmentation (PIH) is a visible indicator for the participation of radicals in **healing processes** and the related melanin formation. There is also exactly the opposite: In the case of vitiligo the hydrogen peroxide balance is disturbed – among others induced by low catalase concentrations in the skin. In this case, oxidative and possibly also nitrosative stress is involved which suppress the formation of melanin. Antioxidants are completely useless in this case: they have effects on the ROS on the one hand but simultaneously suppress tyrosinase activities on the other hand.
Still unresolved are the effects of antioxidants of skin care preparations on the vital **microbiome** of the skin and their oxidoreductases that produce acids through oxidation and thus ensure the acidic pH level of the skin. This effect can lead to unwanted selections similar to preservatives.

Dr Hans Lautenschläger