The ABC of fatty acids

published in Beauty Forum 2009 (12), 40-47

We come into contact with fatty acids day in, day out as they are elements of our daily nutrition and skin care. Already the syllable „fat“ reminds us of calories and even more disagreeable is the idea of something like “acids”. Fatty acids have more influence on our health than we generally assume, though. Their metabolic products control a multitude of functions in our body and in the skin.

The issue is highly complicated and keeps myriads of scientists busy all over the world. In the past three decades a genuine knowledge explosion on the physiological significance of fatty acids has occurred.

General remarks

Fatty acids are hydrocarbons with a carboxyl group (-COOH). This carboxyl group is responsible for the acidic character. The most basic fatty acid is **acetic acid** with the formula CH_3-COOH. While we still notice an intense acidic smell of the water soluble acetic acid as well as a weak caustic effect to be observed when used as de-scaling agent, the fatty acids with long hydrocarbon residues are almost scentless and no longer mixable with water. They behave like lipids and oils. **Stearic acid** ($C_{17}H_{35}$-COOH) feels like a wax and is the base substance for candle production. **Oleic acid,** by contrast, has a hydrocarbon chain of equal length but is an oil. It only differs from stearic acid by its lower content of hydrogen atoms ($C_{17}H_{33}$-COOH). As it no longer contains the highest possible number of hydrogen atoms it is called “unsaturated”. Instead, it has a double bond and belongs to the **omega-9 family**.

Stearic acid:

CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-COOH

Oleic acid (red: double bonds):

CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-**CH=CH**-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-COOH

The position of the first double bond in a chain determines the type of fatty acid family it belongs to. Counting starts at the end (omega) i.e. at the CH_3-group. Oleic acid has its double bond at the ninth C-atom. Also the double unsaturated **linoleic acid** ($C_{17}H_{31}$-COOH) has a liquid consistency like most of the unsaturated acids.

Linoleic acid (red: 2 double bonds):

CH_3-CH_2-CH_2-CH_2-CH_2-**CH=CH**-CH_2-**CH=CH**-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-COOH

The first double bond begins at the sixth C-atom. That is why linoleic acid is a member of the **omega-6 family** while the triple unsaturated **alpha-linolenic acid** belongs to the **omega-3 family** (first double bond at the third C-atom).

Alpha-linolenic acid (red: 3 double bonds):
CH_3-CH_2-**CH=CH**-CH_2-**CH=CH**-CH_2-**CH=CH**-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-COOH

Fatty acids of the omega-6 and omega-3 families are **essential** for the human body. Or in other words: the human organism cannot live without them as it is not able to produce them

itself. The body has to assimilate them with the nutrition.

Essential fatty acids

Linoleic acid and alpha-linolenic acid are omnipresent in the vegetable kingdom. In the animal organism they are transferred into other acids with the help of enzymes. Among others, **gamma linolenic acid** and **arachidonic acid** e.g. form from linoleic acid**,** and **eicosapentaenoic acid** develops from alpha-linolenic acid. Gamma-linolenic acid can be assimilated by consuming borage oil and evening primrose oil, arachidonic acid is assimilated with meat and eicosapentaenoic acid with fish.

Fatty acids are frequently abbreviated: C18:2 n-6 is interchangeable with linoleic acid and means: 18 C-atoms, 2 double bonds, omega-6. The abbreviation for alpha-linolenic acid is C18:3 n-3: 18 C-atoms, 3 double bonds, omega-3.

The following enzymes participate consecutively in the fatty acid metabolism which is subject to certain sequences:

(1) **Delta-6-desaturase**: This enzyme introduces a double bond at position 6 of the fatty acid chain (counted from the carboxyl group!).
(2) **Elongase**: The enzyme integrates 2 C-atoms into the carbon chain thus elongating the chain. This process occurs at the carboxyl group.
(3) **Delta-5-desaturase**: introduction of a double bond at position 5
(4) **Elongase** (see above)
(5) **Delta-4-desaturase**: introduction of a double bond at position 4

Omega-6 sequence:
Linoleic acid (C18:2 n-6) → (1) → gamma-linolenic acid (C18:3 n-6) → (2) → dihomo-gamma-linolenic acid (C20:3 n-6) → (3) → arachidonic acid (C20:4 n-6) → (4) → C22:4 n-6 → (5) → docosapentaenoic acid (22:5 n-6)

Omega-3 sequence:
Alpha-linolenic acid (C18:3 n-3) → (1) → C18:4 n-3 → (2) → C20:4 n-3 → (3) → eicosapentaenoic acid (C20:5 n-3) → (4) → docosapentaenoic acid (C22:5 n-3) → (5) → docosahexaenoic acid (C22:6 n-3)

Omega-9 sequence (non-essential):
Oleic acid (C18:1 n-9) → (1) → (C18:2 n-9) → (2) → (C20:2 n-9) → (3) → eicosatrienoic acid (C20:3 n-9) → (4) → C22:3 n-9 → (5) → C22:4 n-9. Oleic acid is assimilated with vegetable oils or formed in the human body from stearic acid.

Metabolism

The different acids are bound in **phospholipids** (membrane lipids) and may achieve substantial concentrations. Just to mention an example: epidermal phosphatidylcholine may contain about 9 percent arachidonic acid. From phospholipids – above all from phosphatidylcholine – the acids then are selectively released through phospholipase A_2, if the enzyme is activated by hormones, neurotransmitters or exogenic stimulants. Immediately after this process, cascades of highly active substances are formed: **eicosanoids** develop from C20 acids and **docosanoids** from the C22 acids. Like hormones, already minor concentrations of these substances control coagulation factors, blood pressure, blood fats (triglycerides), inflammations, fever, pain, blood vessel muscles, the course of pregnancy and immune responses (allergies, asthma etc.).

Body cells produce eicosanoids with the help of oxygen transmitting enzymes (oxygenases), partly even non-enzymatically:

- **Cycloxygenases** form
  - Prostaglandins, who have pro or anti-inflammatory effects
  - Thromboxanes, which trigger blood coagulation
  - Prostacyclins with anticoagulant and vaso-dilating activity.
- **Lipoxygenases** form
  - Hydroxyeicosanoids
  - Leukotriens: they are formed by 5-lipoxygenase and cause inflammations, asthma and allergy symptoms.
  - Lipoxins: are generated by double reaction of 5- and 12- or 5- and 15-lipoxygenase. They control leucocyte functions and have anti-inflammatory effects.
  - Hepoxilins: they are products of the 12-lipoxygenase and control secretions and contractions of the smooth muscles.
  - Trioxilins
- **Monooxygenases** form
  - Hydroxyeicosanoids and
  - Epoxyeicosanoids
- **Non-enzymatically formed are**
  - Isoprostanes: they influence the smooth muscles.

Good or bad?

Many functions of the reaction products still are unknown today: every now and then new substances are discovered. They partly compete with each other showing antagonistic effects. That is why it is vital to adequately balance the fatty acids in our daily nutrition. Deficiencies in omega-3 acid for instance result in cardiovascular diseases, rheumatic conditions and skin diseases like psoriasis and neurodermatitis. We roughly differentiate between several series of eicosanoids.

- **Series 1 from dihomo-gamma-linolenic acid**
  Example: prostaglandin E_1 has anti-inflammatory effects
- **Series 2 from arachidonic acid**
  Example: prostaglandin E_2 supports inflammations and induces vaso and bronchodilatations; prostaglandin F_2 causes vaso and broncho constrictions.
- **Series 3 from eicosapentaenoic acid**
  The metabolites compete with series 2 and reduce e.g. the risk of heart attacks and arteriosclerosis.

In this context there are reports on good or bad eicosanoids. This is, however, a very simple approach and ignores the significance of these substances. Besides the competition between the different series there are also dependencies between the acid sequences. A high intake of linoleic acid of vegetable oils for instance inhibits the formation of arachidonic acid. Many individuals suffering from neurodermatitis show a high linoleic acid level. Concluding now that linoleic acid has negative effects on this group of persons is not really supportive in this context as many neurodermitics are not able to transform linoleic acid into gamma-linolenic acid due to a defective delta-6 desaturase. That is the reason why it accumulates. On the other hand this group of individuals can be supported with gamma linolenic acid, whereas the topical application is most effective. This also applies for topically applied linoleic acid which helps to repair the disordered skin barrier. An insufficient supply of linoleic acid in the diet leads to a dry and scaly skin.
The symptoms of people suffering from psoriasis as well as from very low alpha-linolenic acid and high arachidonic acid levels can be reduced with fish oil. The few examples mentioned above show the complicated interaction between these essential acids.
Docosahexaenoic acid with its resulting **docosanoids** to which neuroprotectins, resolvines and docosatriens belong to, have significant functions in nerve and brain cells as well as the retina. Unlike cow's milk, breast milk contains docosahexaenoic acid which is produced in the mammary glands. It is assumed that it significantly influences the brain development of infants. Just like **eicosapentaenoic acid**, this substance occurs in coldwater sea fish like herring, salmon and mackerel and is stored in their fat tissue in form of triglycerides and phospholipids.

Things are different on and in the skin

The situation is rather different, though, if essential fatty acids aren't assimilated via daily nutrition but via skin surface. In case of topically applied oils, the fatty acids are released by epidermal ester-cleaving lipases or through hydrolysis (reaction with water) which is further intensified by humidity and heat. Unlike other body cells and above all the universally acting liver cells, only very few of the major metabolites will form. Linoleic acid, alpha and gamma-linolenic acid are used without modification of their fatty acid chain or alternatively oxidized by epidermal 15-lipoxygenase (15-LOX) into unsaturated hydroxy fatty acids with anti-inflammatory characteristics. In particular, the following processes are significant:

- Linoleic acid is a substrate for ceramide I into which it is integrated without modifying the fatty acid chain. This process is beneficial for the recovery of the skin barrier.
- 15-LOX at first peroxides linoleic acid into 13-hydroperoxy-9,11-octadecadienoic acid (13-HPODE) which then is immediately reduced into the anti-inflammatory 13-hydroxy-9,11-octadecadienoic acid (13-HODE).
- Analogous to this process is the reaction of 15-LOX with gamma-linolenic acid from which the anti-inflammatory 13-hydroxy-6,9,11-octadecatrienoic acid (13-HOTrEg) is formed via hydroperoxy-6,9,11-octadecatrienoic acid (13-HOTrEg).
- Alpha-linolenic acid is transformed by 15-LOX via 13-hydroperoxy-9,11,15-octadecatrienoic acid (13-HPOTrE) into 13-hydroxy-9,11,15-octadecatrienoic acid (13-HOTrE). This explains the strong anti-inflammatory effect of linseed oil which formerly used to be a component of bandages. Today it is used as watery nanoparticle dispersion.

Essential fatty acids and appropriate vegetable oils can be successfully used for the skin care of inflammatory skin conditions like neurodermatitis and psoriasis.
It is assumed that the excellent efficacy of linoleic acid for acne conditions can be ascribed to the anti-inflammatory 13-HODE, the formation of linoleic acid containing ceramide I (heals cornification disorders) as well as the liquefied sebum.

Side effects of drugs

Together with the fats in our food the individual endogenic and exogenic factors decide whether human body and skin are in a healthy balance. With a detailed analysis of the symptoms and a well-balanced nutrition and skin care, a great number of skin problems can be significantly improved or even completely eliminated without any drugs.
By inhibiting the enzymes involved, many pharmaceutical drugs purposefully prevent the formation of specific fatty acid metabolites and thus sooth pains and inflammations or influence the coagulation. Inevitably, however, all the additional functions of the now missing fatty acids are not carried out either which leads to typical side effects of drugs. Only recently, the KOSMETISCHE PRAXIS 2009 (2), 11-14, reported on drug side effects that affect the skin. Appropriate orally taken drugs systemically impede identical reactions in the whole body. As eicosanoids frequently trigger organ specific reactions right in the neighboring areas where they are formed, rather different side effects may locally develop. The local application of topical drugs against skin diseases in form of creams and tinctures is more selective and hence, even more effective. This also applies for cosmetic raw materials which inhibit the inflammation-triggering 5-lipoxygenase (see also BEAUTY FORUM 2008 (9), 114-116).

Dr. Hans Lautenschläger