

Fragrances, vitamins and hormones – the ABC of terpenes

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They are a main component of natural essential oils - terpenes. The chemical compounds are primarily used as aromatic or flavoring substances in perfumes and cosmetics. Yet, they are also major intermediate products of the human metabolism.

Terpenes are natural substances par excellence and provide evidence of the fact that vegetable, animal and microbial life all has the same origin. There is a multitude of different forms ranging from ethereal aromatic and seasoning substances, internal scaffolding of cells up to hormones and vitamins.

Nature prefers modular structures. And this is clearly evident in terpenes since they all have a branched hydrocarbon called **isoprene** consisting of **5 carbon atoms**. The combination of two isoprene units results in **monoterpenes** with 10 carbon atoms in all. This array can be continued in analogy: **diterpenes** have 20, **triterpenes** 30 and **tetraterpenes** feature 40 carbon atoms. By stringing together a multiple of these 10 carbon units, natural **polyterpenes** like e.g. caoutchouc and gutta-percha will generate which are used in form of rubber and natural plastic. A further significant group are **sesquiterpenes** (10 C + 5 C = 15 carbon atoms). By means of functionalizing the terpene base bodies, alcohols, aldehydes, ketones, ethers and acids will form as well as their esters and, not forgetting, also a multitude of cyclic compounds such as steroids, among others, which have been covered in detail in Kosmetische Praxis 2010 (1), 10-13.

Well-known & significant

Geraniol (monoterpene alcohol): in the human body it is generated from activated acetic acid and bound to phosphoric acid which is the reason why the fragrance cannot unfold. Free geraniol occurs in geranium and rose oil for instance. It is a frequent component in perfumes with a floral note.

Farnesol (sesquiterpene alcohol): is formed from geraniol in the human body and occurs also in bound form. Lime blossoms and rose oil contain free farnesol which is not only fragrant but also has antibacterial effects.

Squalene (triterpene): as a liquid and unsaturated hydrocarbon it is one of the main components of the human sebum and discarded via

the sebum glands. It works well as a re-fattening component in skin care products. For this purpose squalene is gained from yeast. Due to its sensitivity to atmospheric oxygen it is frequently used in hydrogenated (saturated) form. The technical term then is squalane.

Lanosterol (tetracyclic triterpene alcohol): is biosynthesized from squalene as a key intermediate product in all life forms equipped with nuclei and cell membranes (eukaryotes). Animal organisms process lanosterol into cholesterol, steroid hormones, bile acids and vitamin D₃. Herbal analogies are phytosterols which serve as stabilizing components of the cell membrane structures. The wool fat of sheep contains lanosterol which, besides cholesterol and other higher molecular alcohols, can be used for the manufacturing of W/O emulsions.

Boswellia acids (pentacyclic triterpenes): in form of their acetyl-keto-derivatives they inhibit the collagen-degrading metalloproteinases. They also block the enzyme 5-lipoxygenase which releases the inflammatory mediators. Today, boswellia acids are frequent components in skin care products.

Betulinic acid (pentacyclic tetraterpene hydroxycarboxylic acid): is the natural antigen against protozoa and fungi in the bark of plane and birch trees. Like wool fat, phytosterols and bile acids, betulinic acid can be used to stabilize W/O emulsions. An interesting feature of the acid is its anticarcinogenic effect. It activates the apoptosis of melanoma cells.

Essential oils

Essential oils contain an enormous number of different terpenes. Hence, they are practically found in every perfume oil. Some of them show allergenic potential which led to the fact that in the Cosmetic Decree (KVO) they have been classified as substances that are subject to declaration. That is to say that the allergens contained in cosmetic products have to be

labeled at the end of the INCI list. Subject to declaration are concentrations of more than 0.001 % in products that remain on the skin and concentrations of more than 0.01 % in rinse-off products. Frequently, allergens only form after autoxidation (oxidation with atmospheric oxygen) of the originally non-allergenic terpenes as e.g. ascaridol which generates in tee tree oil with the influence of atmospheric oxygen and light.

Related to the oxidation of terpenes in connection with extended or careless storage also are so called aroma flaws in food and spices. Thus, orange juice takes on a terpeny note after D-limonene has oxidized into carvone; and the oxidation of valencene into nootkatone (both of them are bicyclic sesquiterpenes) results in a grapefruit note.

While showing an identical chemical composition, quite a number of terpenes only differ by their spatial structure, as a matter of fact, sometimes only by their mirror image. Hence, limonene for instance, occurs in a D and its mirror-inverted L-form. Yet, the human nose is sensitive enough to differentiate between the two of them. We perceive D-limonene as an orange-like scent (as e.g. in lemon oil) and L-limonene (as e.g. in peppermint oil) with a turpentine oil-like smell.

A selection of typical monoterpenes and, added in parentheses, their characteristic scent as well as examples of essential oils in which they occur is listed in the following:

Non-cyclic monoterpenes: geraniol (scent: flowery, rose-like; geranium, rose oil), nerol (scent: rose-like; neroli oil, bergamot oil), linalool (scent: lilies of the valley-like, lavender oil) and citronellol (scent: rose-like, rose oil, lemon oil) are terpene alcohols. The terpene aldehydes citral A (geranial), citral B (neral) have a lemon-like scent and occur in both lemon oil and lemon grass oil.

Monocyclic monoterpenes: p-menthane (peppermint-like scent; eucalyptus globulus), limonen (lemon-like scent; lemon oil) and the alcohols menthol (cool mint scent; mint oils), terpineol (lilac-like scent; juniper oil) as well as the ether eucalyptol (1,8-cineol; camphor-like scent; eucalyptus oil) belong to this group. Carvone (caraway oil) is a terpene ketone with a caraway-like scent.

Camphor: is the prototype of a bicyclic monoterpene. It has the typical cooling “camphor scent” which even turned into a technical term used for characterizing other fragrant substances. Camphor occurs in the oil of the camphor tree which belongs to the lauraceae

family. Its irritating and stimulating effect on the microcirculation is used in ointments and creams against muscular pains and neuralgia.

A monocyclic sesquiterpene alcohol as well is **α -bisabolol**, the main active agent of the chamomile with antimicrobial effects which is also found in lower concentrations in further essential oils like e.g. bergamot oil.

Vitamins and provitamins

Some vitamins and provitamins also show a terpene structure:

β -carotene: is an oxygen-sensitive tetraterpene ($C_{40}H_{56}$; E 160a) and occurs in carrots. As provitamin A it is split in the human body into two vitamin A molecules. The carotenoid family consists of numerous fat-soluble tetraterpenes with colors varying from red via orange up to yellow. They are used as coloring additives in food and cosmetic products. E 160c for instance is the code for the crimson-colored **capsanthine** (bell pepper extract) which serves e.g. as a food additive to intensify the color of egg yolks. **Lycopene** (E 160d) is a component of the red color of tomatoes and rose hips. The oxygen-containing xanthophylls as e.g. the orange-yellow colored **lutein** (E161b) are likewise tetraterpenes with colors ranging from yellow to purple.

The colors of carotenoids form through extended conjugated double bond systems which, in their term, also determine the anti-oxidative properties of many of its representatives. This was the reason that anti-carcinogenic and anti-aging effects have been ascribed to these agents which, however, could not be proved in practice. Under certain conditions, though, carcinogenic effects have been observed. Carotenoid consumption (carotene, lycopene) has specific effects on the skin tone and may individually lead to a light sun protection factor of about 2-3.

Vitamin A (Retinol): is a diterpene alcohol ($C_{20}H_{30}O$) which occurs in cod liver oil and egg yolk and has multiple effects on the human metabolism. Vitamin A is frequently used as a recovery-supporting agent in skin care products as it stimulates the cell growth and collagen synthesis. In higher concentrations and in connection with penetration-supporting nano-dispersions vitamin A acid effects like erythema and irritations can be observed. Instead of the free vitamin A, frequently its compound with palmitic acid (retinyl palmitate) is used which is hydrolysed by enzyme in the skin. Vitamin A is sensitive to atmospheric oxygen which is the reason why it should not be ap-

plied in bright day light and sun exposure. Oral overdosage may have teratogenic effects in pregnant women.

Vitamin A acid (retinoic acid, tretinoin): For many years already this diterpenic acid has been banned in skin care products and may only be used in dermatological practices under medical supervision. Indications primarily are acne and hyperkeratoses. Like for vitamin A, the teratogenic effect of an overdosage has to be considered. Isotretinoin (13-cis-retinoic acid) differs from tretinoin (trans-position) by the structurally different cis-position of the acid group. The indications are basically the same.

Related vitamins & Co.

Although the following natural substances have a gross number of hydrocarbons that cannot be divided by 10 or 5 in terms of the terpene rule, they are, in fact, equipped with terpene side chains.

Vitamin K₁ (phyllochinone; 2-methyl-3-phytyl-naphthochinone): the phytyl side chain corresponds with a monoterpene with 20 C-atoms. On the other hand, vitamin K₂ may have terpene side chains of different length. As to their coagulative effects, compounds with long side chains are more active than those with shorter side chains. Unfortunately, the Cosmetic Decree (KVO) has banned the use of vitamin K₁ in cosmetic products since late 2009. It has primarily been used for the care of the rosacea and couperosis skin. The topical application of the vitamin stabilizes the blood vessels near the skin surface and tightens the skin.

Vitamin E (Tocopherol): has a terpene side chain which is integrated into a chromane ring and belongs to the group of fat-soluble vitamins such as the vitamins A, D and K. It is well-known for its anti-oxidative, cell-renewing and moisture-retaining characteristics. The vitamin is used in its non-bound form or as acetic acid ester (tocopheryl acetate).

Ubichinone (coenzyme Q₁₀ among others): the terpene side chain links to a 1,4-benzochinone ring and contains isoprene units in form of differently long strings. The number "10" is a clue for 10 isoprene units which mean that it has to do with a pentaterpene side chain. Coenzyme Q₁₀ is mainly used for the elderly atrophic skin in order to activate the fat metabolism. The molecule's radical scavenger property is only acquired after its reduction into a 1,4-hydrochinone structure in the skin. In the human body coenzyme Q₁₀ occurs above all in

the mitochondria.

Dr. Hans Lautenschläger