

# Endocrine disruptors – harmful for the endocrine system

published in *Kosmetik International* 2018 (1), 52-55

Various substances have an effect on the hormonal balance. They occur in food, pharmaceutical drugs or cosmetics. Some of them have impeding effects.

**B**ody functions and body growth are controlled by hormones. Accordingly, hormones are essential components of our body. Sexual hormones, for instance, are responsible for growth in childhood, for puberty, reproduction, menopause and aging. Depending on the phase of life, hormone concentration varies and hormone levels fluctuate – as for instance during the female menstrual cycle. There are numerous artificial interventions into the natural hormonal balance, as for instance with the intake of hormone preparations or synthetic hormone-analogues such as

- oral contraceptives,
- hormone replacement therapy (HRT) during menopause and post-menopause,
- hair growth preparations and
- hormone therapy in the case of cancer (e.g. breast, prostate gland).

Besides the sexual hormones of testicles and ovaries, the body produces other glandular hormones as for instance in the hypothalamus (brain), hypophysis, thymus (part of the immune system), thyroid gland, kidneys and pancreas. Also the various locally produced tissue hormones should be mentioned in this context.

## Positive and negative effects

Everyday substances can influence the hormonal balance. Among them also are food components such as phytohormones that can attenuate the effects of the aging process. The body also absorbs substances that have harmful effects. They are called endocrine disruptors.

"Disruption" is a synonym for "damage", and "endocrine", in this context, means that it is related to the hormonal system. Accordingly, the World Health Organization (WHO) defines the characteristics of endocrine disruptors, also called endocrine disrupting chemicals (EDC), as follows: Endocrine disruptors (EDC) are exogenous substances or compounds that may interfere with the hormonal balance –

either in the particular organism, its progeny or in a population – thus influencing or damaging the health. This rather general formulation shows that the EDC definition is not limited to humans but also includes the animal world. According to a WHO report issued in 2012, it is a statistical fact that hormonally controlled diseases and abnormal development are on the increase. Among them are

- decreasing semen quality in men – with high significance in particular countries
- genital malformation
- premature delivery and decrease in weight in newborns
- behavioural disorders in children due to thyroid damages
- global increase of cancers of the breast, uterus, ovaries, prostate gland, testicles and thyroid gland
- premature breast development in girls associated with an increased risk for cancer later on
- adiposity and diabetes type 2

Also changes in the lifestyle and culture have a bearing on the above-mentioned developments. However, a good deal of influence comes from substances absorbed via air, water, food, pharmaceutical drugs, chemicals at the working place or in the leisure sector, and last but not least via cosmetic products. There is not only talk of industrially produced chemicals. Also natural substances are involved.

## Proven – and banned

Some substances are assumed to have endocrine effects whereas this assumption is based on individual observations. The following substances, however, are proven to have endocrine effects, e.g. diethylstilbestrol (medical drug), polybrominated diphenyl ethers (flame retardants), polychlorinated diphenyls (hydraulic and transformer fluids), DDT (insecticide), polychlorinated dioxins (released by combustion processes) and numerous pesticides; in the meantime, the mentioned substances ei-

ther are completely banned or the threshold values have been considerably reduced.

The effects of EDCs are multifarious and unpredictable as they mostly are absorbed in rather small quantities over a longer period of time. Storage and the resulting accumulative effects in the fatty tissue play a significant part. This applies above all if it is a matter of fat-soluble substances that metabolize very slowly or not at all, a fact which complicates or even impedes the identification of dose-effect-relationships and the stipulation of relevant threshold values.

The results of short-term studies with cell cultures (in vitro) or with animal tests (in vivo) only can partly be transferred to humans. The reason is, that the relatively high doses usually used in these studies differ greatly from the "low-dose" and long-term effects humans indeed are exposed to.

Thus, results and consequences often are based on statistical data. It has to be mentioned though that these are not always reliable, often have procedural deficiencies or are insignificant. In other words, this procedure only can result in a "supposed" effect. In the meantime, WHO maintains a list of several hundred substances that have proven endocrine effects or are so-called "questionable" substances. Noteworthy is the high number of chemical structures with ring-shaped aromatic systems and increased lipid solubility. Their degradation and elimination from the body is extremely slow, all the more, if it is a matter of halogenated substances containing chlorine or brome.

Endocrine disruptors mainly are geared towards

- influencing the natural hormone syntheses of the body
- systemic and/or local interacting with hormone receptors
- changing the hormone degradation and affecting the metabolites

### Controversial substances

In the cosmetic field, the following substances are discussed:

- **Parabens:** The esters of 4-hydroxybenzoic acid are preservatives and listed in the annex of the Cosmetic Directive; they are frequently used in skin care preparations in combination with phenoxyethanol. There are controversial studies concerning their endocrine potency, though. Even if there were a health risk related to parabens,

it should be rather low since parabens are split relatively fast and then eliminated via kidneys. In 2011, the EU (Scientific Committee on Consumer Safety) declared the dosage of propyl- and butyl paraben up to 0.19% as safe for the human health.

- **Triclosan:** Triclosan, with its chemical term 5-chloro-2-(2,4-dichlorophenoxy)-phenol, is used for the preservation of aqueous cosmetic products. There are discussions on its impacts on fertility, myasthenia, as well as its carcinogenic potential. The substance has already been found in breast milk. The EU Regulation 2014/358 limits the use of triclosan to products that are rinsed off after application. It is no longer licensed for the use in body lotions and skin care creams. Until today, the No-Observed-Adverse-Effect-Level (NOAEL) for humans could not be identified yet. Hence a threshold value has not yet been stated.

With exposure to heat and UV radiation (sun), triclosan tends to form halogenated dibenzodioxins. Where this decomposition process takes place actually is unpredictable due to the widespread use of the substance in everyday objects. Triclosan is degraded in sewage plants only to a minor degree.

- **Phthalic acid ester (plasticizer):** Diethyl phthalate is used to denature alcohol which then as alcohol denat. (INCI) is non-taxable and used in the preparation of cosmetics. In 2007, the German Federal Environmental Agency (UBA) issued a warning concerning the use of phthalates since they are, among others, toxic for reproduction. The UBA recommends replacing dimethyl phthalate and diethyl phthalate (DEP) in cosmetics by less critical alternatives.

In years past, the Bavarian State Office for Health and Food Safety reported on DEP concentrations of about 1% in cosmetics. A study on the urine of 163 toddlers born from 2000-2005 found phthalate metabolites which correlated with the number of skin care products used. Phthalic acid esters also find their way into the body either orally or topically via food packaging as well as via plastic objects. Phthalic acid esters cause an enlargement of fat cells and excess weight gain in mice.

### Originally used as protection

- **Sun screens:** UV filters such as ethylhexyl methoxycinnamate, butyl methoxy dibenzoylmethane, octocrylene, 4-methylbenzylidene camphor and benzophenone could be detected in human breast milk even if the women did not use sun protection products. It is assumed that the substances were absorbed via day creams and lip sticks which often are equipped with UV filters. Among experts, the endocrine effects are discussed controversially. Current data are based on in-vitro tests as well as artificial animal model systems.

### The role of phytohormones

- **Isoflavones:** The European Food Safety Authority (EFSA) has issued an all-clear signal for the endocrine isoflavones, also called phytohormones. The natural substances occur in soya, leguminous plants and red clover and are used in antiaging products and skin care preparations for bad skin. According to EFSA there are no indications for harmful effects on breast, uterus and thyroid gland of postmenopausal women. The assumption is based on a daily intake of 35 up to 150 mg with food or food supplements. On the contrary: the low estrogen effect may even prevent breast cancer.
- **Hair growth products:** The medical treatment of hair loss in women includes estrogens or testosterone antagonists, and steroid-5 $\alpha$ -reductase inhibitors are used in the treatment of men.  
An increased growth of the eyelashes is reported as a side effect in the prostaglandin F<sub>2 $\alpha$</sub>  based treatment of glaucoma. In the meantime, derivatives of the related prostanoid acid or of cloprostenol are used for this purpose. Since harmful effects on unborn children cannot be excluded, the labels of products with PGF<sub>2 $\alpha$</sub>  analogues show warnings for women of child-bearing age. In 2011, FDA (Food and Drug Administration, USA) already issued a warning concerning the use of isopropyl cloprostenate.

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