An endocrine disrupter is, as defined by WHO/IPCS in 2002 (1), “an exogenous substance or a mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations”. Although the main focus has been on sexual hormonal systems, other endocrine system related to the pituitary-, thyroid-, pancreatic- and adrenal gland may also be affected. Different classes of chemical contaminants with the potential to affect the endocrine system have been found in food (1,2). One major group is persistent organohalogen compounds such as the old pesticides (DDT and metabolites, hexachlorocyclohexane (HCH), aldrine/dieldine/endrine, camphechlor, hexachlorobenzene (HCB), polychlorinated dioxins and -furans (PCDD/F), polychlorinated biphenyls (PCB) and polybrominated diphenylethers (PBDE). Other chemical contaminants of various sources such as food packaging material (bisphenol A, phtalates) and others (parabens, nonyl-phenol, cadmium and tributyl tin may also have the potential to cause endocrine disruption. In addition a series of natural compounds either present in food plants or produced by contaminating fungi, also causes endocrine disruption.

So-called phytoestrogens found in food plants and the mycoestrogen zearalenone, produced by Fusarium species, bind to the oestrogen receptors α and β with affinity 1 to 4 orders of magnitude lower than that of 17β-estradiol (E2). Major groups of phytoestrogens are isoflavones e.g. in soy, coumestanes in clover or beans, and lignans in rye and flax seed (2-4). These compounds, which are found as precursors such as glycosides in the plants and food, are hydrolysed by the gut microflora. Their hormonal activity shows both similarities and dissimilarities with that of E2, which is probably caused by differences in their relative affinity to the two oestrogen receptors, and also their ability to recruit co-activators and co-repressors in various tissues expressing oestrogen receptors. In that respect, they may share properties with the synthetic oestrogen receptor modulators (SERM) pharmaceuticals, which show oestrogenic activity different from that of the natural hormone E2 (4,5). It should be noted that phytoestrogens have biological effects in addition to those mediated through endocrine systems.
The disruptive effects of persistent chlorinated organic compounds on sexual endocrine systems are complex, both direct and indirect mechanisms. For example differences in chlorine substitution of PCB and hydroxyl substitution in para position determine whether oestrogenic, anti-oestrogenic or thyronine activity can be observed (6-8). Chlorine substitution in meta position, combined with hydroxyl in para position, is characteristic for triiodothyronine activity and no oestrogenic activity, while absence of chlorine substitution in meta position to the hydroxyl substitution is required for oestrogen activity. PCDD/F and dioxin like PCB show mainly anti-androgenic activity (e.g. reduced prostate weight, reduced testosterone, reduced sperm production) particularly following exposure during foetal life. o,p-DDT and p,p-DDT and their DDE metabolites show variable oestrogenic and/or androgenic or anti-androgenic activity (1,2,9). Whereas the level of exposure to persistent chlorinated pesticides and dioxins and PCBs via food and also compounds from packaging material, generally is too low to cause oestrogenic effects, such effects may occur from foods rich in phytoestrogens (2,5). The notion that man-made contaminants with low level oestrogenic activity should cause adverse sexual endocrine disruption whereas phytoestrogens should only have positive health effects, as is often claimed by the promoters of “Health-food products”, is not scientifically sound (10).

Other natural compounds in food may affect non-sexual endocrine glands. Examples of this are glucosinolates and their hydrolysis products: thiocyanates, isothio-cyanates and cyclic sulphuric compounds inhibit iodine uptake in the thyroid gland and thereby can cause so-called cabbage- or legume goitre (10). Both low and high intake of iodine, which is an essential trace element, may severely affect the function of the thyroid gland (11,12). Iodine deficiency combined with goitre and hypofunction is probably the most important factor in food affecting endocrine systems worldwide. Circumstantial evidence has linked a high dietary intake of iodine to autoimmune thyroid disease as an increased prevalence is seen in populations with a high iodine intake in comparison with populations on more moderate intake levels. Except for iodine deficiency, thyroiditis is the most common thyroid disease in iodine replete populations with a disease prevalence of about 10% in women (11,12).

Glycyrrhetic acid, the aglucone of glycyrrhizin found in liquorice is another example of a natural agent in food causing endocrine disruption at doses at or only slightly above those commonly consumed (2,13,14). Liquorice is well known for its ability to induce a syndrome of apparent mineralocorticoid excess, which is characterised by oedema and hypertension. In early years it was believed that glycyrrhetic acid bound to the aldosterone- or mineralocorticoid receptor in tissues, e.g., kidney and large bowel, which are involved in regulation of potassium and sodium homeostasis. However, it became clear that glycyrrhetic acid has a very low affinity to the receptor, 0.0001 to 0.0003 to that of aldosterone, but caused an inhibition of the enzyme 11-hydroxysteroid dehydrogenase 2 that inactivates cortisol to cortisone in mineralocorticoid sensitive tissues
(13,15). This would cause cortisol, which occurs in concentrations 1000 fold higher than aldosterone, to work as an aldosterone analogue since cortisol also binds to and activate the mineralocorticoid receptor. Patients suffering from essential hypertension, and in particular women, appear to be more sensitive to liquorice (16). Later it has been revealed that glycyrrhetic acid also has the ability to inhibit enzymes in steroid metabolism, i.a. in the synthetic pathway of testosterone lowering the serum level of testosterone and other derivatives (17-19).

In summary, many contaminants and natural compounds found in food have the ability to cause disruption of endocrine systems, being related to sex hormones or to hormones of the adrenal- and thyroid gland. The mechanisms of actions are several, binding to the hormone receptor, modulation of intracellular hormone concentrations or interfering with synthesis or degradation of hormones. Although screening for possible endocrine disruptive effects can be done in vitro receptor binding assays or in cellular systems, it is important to check the relevance of possible findings in vivo. With regard to anthropogenic chemical contaminants with endocrine disruptive potential in food, the exposure to such compounds is believed to be below that causing an effect (2,20) whereas natural compounds, particularly in special food plants, may occur in concentrations that, combined with a high intake, might well cause in vivo endocrine effects.

References


