Review

Alkylphenol ethoxylates and alkylphenols – update information on occurrence, fate and toxicity in aquatic environment

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Abstract

Alkylphenols and their precursors, alkylphenol etoxylates, are a group of manmade chemicals used mainly as surfactants in domestic and industrial applications worldwide. It has been well established that they have endocrine disruption activity, hepatotoxic, genotoxic and other negative effects on animal and human health. In spite of the effort to reduce their use, they persist in the environment not only in industrial but also in remote regions, and were detected in the variety of natural matrices including air, water, soil as well as food products, and human blood and urine worldwide. This article summarizes their occurrence, fate in natural conditions, and toxicity including mode of action. A subject of our concern was the aquatic environment as the most important reservoir and target of their deleterious impact.

Key words: Nonylphenol, octylphenol, wastewater, xenoestrogen, fish, vitellogenin

Abbreviationsand units

AhR – aryl hydrocarbon receptor
AP – alkylphenol
APE – alkylphenol ethoxylates
EDC – endocrine disrupting chemicals
EO – ethoxylate portmon
ER – oestrogen receptor
NP – nonylphenol
OP – octylphenol
STP – sewage treatment plants
WWTP – wastewater treatment plant

Introduction

Alkylphenol ethoxylates (APE) are one of the most widely used classes of surfactants. Recently, approximately 500,000 tons have been produced worldwide annually (Renner 1997) and it makes APEs the world's third largest group of surfactants in terms of production and use (Ying et al. 2002). They can be used as detergents, wetting agents, dispersants, emulsifiers, solubilizers and foaming agents. APEs are important to a number of industrial applications, including pulp and paper, textiles, coatings, agricultural pes-

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R = C_9H_{19}, nonyl
C_8H_{17}, octyl
R is usually branched

Alkylphenol polyethoxylate
(APnEO, n = m + 1)

Alkylphenoxycarboxylic acid
(ApnEC)

Alkyphenol polyethoxylate
AP(n - 1)EO

Progressive shortening
of ethoxylate chain

Alkylphenoxyacetic acid
(AP 1 EC)

Alkylphenol monoethoxylate
(AP 1 EO)

Alkylphenol (AP)
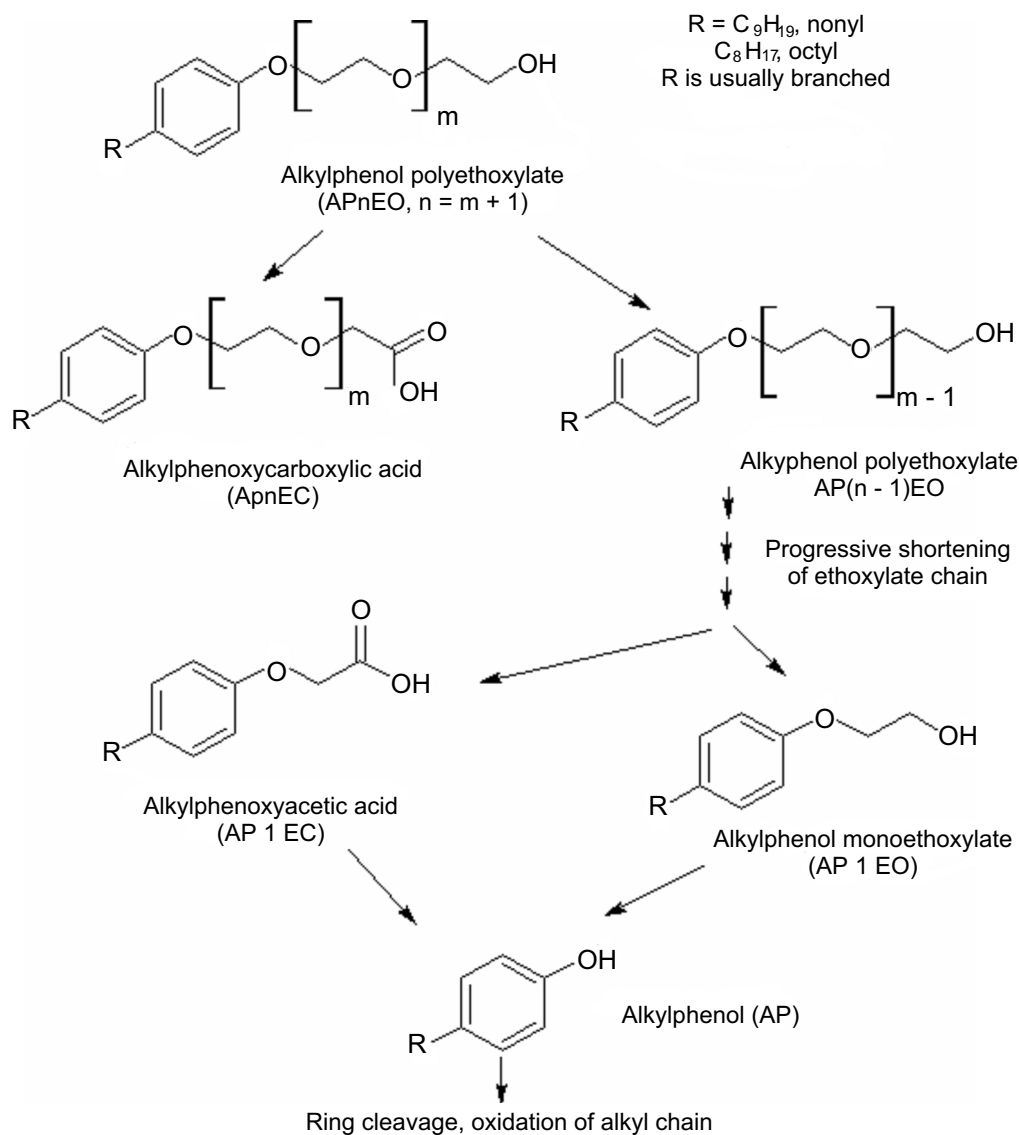
Ring cleavage, oxidation of alkyl chain

Fig. 1 Degradation pathway of alkylphenolethoxylate (Renner 1997).

ticides, lube oils and fuels, metals and plastics. Industrial applications comprise 55% of the APE market. The remaining uses include industrial and institutional cleaning products (30%), household cleaning products (15%) and other miscellaneous uses (< 1%). APEs are surfactants manufactured by reaction of alkylphenols (AP) with ethylene oxide. APE molecule consists of two parts – AP is fairly non-polar portion which allows to dissolve grease and other materials that have small water solubility, and the ethoxylate portion (EO) of the surfactant is water-soluble and aids in the transfer of material to the aqueous phase. This structure makes most of polar APEs soluble in water and helps disperse dirt and grease from soiled surfaces into water (Snyder et al. 2001).

APs, in addition to their role as a raw material for APEs, are used in the preparation of phenolic resins, polymers, heat stabilizers, antioxidants and curing agents. From this group of chemicals, nonylphenol (NP) is by far the most commercially important AP in Europe, with an annual production of about 75,000 tons, 60% of which is used to make NPEs (RPA 1999). Moreover, NP as well as octylphenol (OP) and AP mono- to triethoxylates (APE1, APE2 and APE3) are more persistent and more toxic metabolites generated by degradation of APEs. These metabolites are ubiquitous in the environment because of widespread use of APEs surfactants and widespread lack of adequate wastewater treatment, and these compounds have been detected in air, water, sediment, soil and biota at different levels in different parts of the world (Giger et al. 1984).

Occurrence in environment

APEs and their degradation products are not produced naturally. Their presence in the environment is solely a consequence of anthropogenic activity. Due to their exceptional nature they can be considered as amphophilic compounds. Lower APE oligomers (EO < 5) are usually described as water-insoluble or lipophilic, whereas higher oligomers are described as water-soluble and hydrophilic (Ahel and Giger 1993, Jonsson et al. 2008). Another very important feature of these chemicals is their ability to bind with organic matter because of their very low partition coefficient (log Kow for APEs metabolites between 3.90 and 4.48) (Ying et al. 2002). Therefore, APEs and/or their metabolites were determined in whole range of abiotic and biotic matrices all over the world. As mentioned above, APEs are readily biodegraded under both aerobic and anaerobic conditions in the environment (Paasivirta and Rantio 1991) including microbial degradation, losing most of EO units; the final breakdown products are APEs with one or two EO (APE1, APE2), alkylphenoxy carboxylic acid, and APs (Fig. 1). Many studies assessing levels of APEs and their emerging metabolites have been published in recent years and have shown the ubiquitous distribution of these chemicals in sewage treatment plant discharges, sediments and live organisms.

Occurence in wastewater discharges

This partial biodegradation was observed in a majority of sewage treatment plants (STP) during sewage treatment processes that makes from sewage treatment plant effluents and wastewater discharges an important source of this type of compounds (David et al. 2009). The efficiency of wastewater treatment plants (WWTPs) in removal of NP was found to be highly variable ranging from 11% to 99% depending on type of treatment process unit employed (Berryman et al. 2004). A treatment process composed of ozonation and subsequent activated carbon filtration with chlorination was the most effective (removal of 95% of NP) (Petrovic et al. 2003). If contaminants are adsorbed on activated sludge particles, they accumulate in the WWTPs sludge. In this case, the application of digested sludge, as fertilizer, on agricultural fields may cause a potential contamination of soil and ground water (Olea et al. 1996). Concentrations of ΣAPE metabolites in treated wastewater effluents, for example in the US, ranged from < 0.1 to 369 µg/L (Rudel et al. 1998), in Spain they were between 6 and 343 µg/L (Sole et al. 2000) and concentrations up to 330 µg/L were found in the UK (Blackburn and Waldock 1995).

Occurrence in water

Many communities worldwide, such as Europe, use surface or groundwater resources for drinking water production, which contain a significant portion of wastewater effluent (Sonnenschein and Soto 1998). In some drinking wells these chemicals were detected at concentrations ranging from < limit of detection to 32.9 µg/L (Rudel et al. 1998). To date, the amount of APs pollution detected in aquatic environments mostly ranges from nanograms to milligrams per litre (Uguz et al. 2003). Same data were presented also by Naylor et al. (1992), who reported that water concentration of NP seldom overwhelms 10 µg/L, though at some "hot spots" concentrations reach 1000 µg/L (Warhurst 1995).

In groundwater samples APs concentrations were usually higher than those found in surface water. The removal of contaminants is in fact very slow in groundwater since chemical and biological characteristics in the aquifers are not favourable for degradation process. Groundwater temperatures are in the psychrophilic range and both carbon sources and oxygen are limited. Microbiological resources of such ecosystems are restricted and contaminants undergo extremely slow degradation process allowing contaminants to disperse up to several kilometers from the contamination source and to exist for decades (Soares et al. 2008).

In surface water the amount of this type of pollutants is lower (Arditsoglou and Voutsa 2008). In Asia, NP concentrations were found within the range of 0.3 to 2.8 µg/L (Basheer et al. 2004). Nevertheless, even these numbers exceed environmental quality standards established by EU authorities to achieve the good surface water quality status. The environmental quality standards, as annual average concentration, for NP and OP in surface water were proposed to 0.3 µg/L and 0.1 µg/L, respectively, however, environmental quality standards are still not harmonised throughout the EU (European Commission 2006). Furthermore, these environmentally realistic concentrations of NP may have toxic effect on aquatic fauna (Ying et al. 2002). Interestingly, APs contamination in surface water shows seasonal variations. NP and OP concentrations were observed higher in the warmer season than in the colder part of year (Tsuda et al. 2000, Isobe et al. 2001). It was suggested that a microbial activity at warmer temperatures leads to an enhanced degradation of NPE and OPE (Li et al. 2004) as well as photolysis induced by sunlight can influence the concentration of APs in the surface layer of natural waters during summer (Ahel et al. 1994). Just as temperature and light availability also salinity was determined as a factor influencing the presence of APs

in the water (Li et al. 2005). Sampling locality choice influenced measured concentrations in a very important manner. A shallow part of continental shelf, along the coast, is the most sensitive due to smaller volume of water and proximity of point and diffuse sources of wastewater discharge or other specific source of APs pollution such as produced water. The produced water is a by-product of current oil-production technology and consists of seawater containing an extremely complex mixture of dispersed oil, polycyclic aromatic hydrocarbons, APs, organic acids, metals and traces of production chemicals (Meier et al. 2011). In contrast, in deep sea areas concentrations decrease rapidly as the distance from the coast increases (Xie et al. 2006). Measurements of APs content in water column have obvious shortcomings caused by the unfavourable physicochemical characteristics. The environmental distribution is estimated to 25% in water, more than 60% in sediments, more than 10% in soil (Nordic Council of Ministers 1996).

Occurrence in water sediments

In the aquatic environment AP was found at higher concentrations in associations with sediments rather than dissolved in the aqueous phase. Although, organic content of the sediments was one of the important determinants of adsorption process. In sediments free of organic matter, adsorption was also observed indicating that not only organic content is relevant for NP. It was chased up that NP adsorption is controlled by two major interactions: hydrophilic interaction with mineral components and hydrophobic interaction with organic matter (John et al. 2000). NP concentrations of up to 20,700 ng/g were found in sediments sampled near a sewage outlet in Tokyo Bay (Kurihara et al. 2007). NP was also found at high levels (13700 ng/g) in sediment in Jamaica Bay (USA) impacted by sewage inputs (Fergusson et al. 2001). Remarkably, in a study of Kelly et al. (2010) chemical analysis of representative site samples of the Shannon International River Basin District in Ireland also identified APs in water and sediments in mg/L and mg/kg concentrations, respectively. In sediments there was determined another interesting phenomenon like the vertical distribution of APEs and APs. It could be influenced by many factors as vertical transport by pore water diffusion or physical and/or bio mixing. Peng et al. (2007) found a decline in NP concentrations in the layer dated to the end of 1980s, corresponding to the onset of wastewater treatment, whereas the recorded increase in the NP concentration in the layer dated to 1990s could be explained by the increased economic growth and the lack of effi-

cient wastewater facilities. Sediments are the main medium, where persistent organic pollutants with some lipophilic nature can be stored. For the NP a risk of release from sediment has been evaluated and it was concluded that, due to an unfavourable ratio of sizes of the hydrophilic and hydrophobic parts of the molecule, NP is not subject to micelle formation. Thus, NP is not expected to be able to mobilize, e.g., hydrophobic pollutants as PAHs (Brix et al. 2001). In accordance with this findings the estimation of APs half-lives was provided. Ekelund et al. (1993) reported the half-lives of NP based on ultimate biodegradation of about 58 days in seawater and 35 days in aerobic seawater plus sediment at 11ºC while Shang et al. (1999) reported NP's half-life in sediments more than 60 years.

Occurrence in biological matrices

The accumulation tendency of these group of substances is evident not only in inorganics but also in the biological matrices, particularly aquatic biota (Ahel et al. 1994). However, in a study presented by Arukwe et al. (2000) it was suggested that NP does not accumulate in tissues and that a half-life of NP in the tissues of the rainbow trout (*Oncorhynchus mykiss*) is about 24-48 hours. Based on many other studies it was concluded that APs are able to accumulate in several aquatic species, including aquatic plants, algae, fish and mussels (Liber et al. 1999, Lintelman et al. 2003). In fish, the highest concentration of APs was found in the fat of exposed organisms (Shiraishi et al. 1989) and it was reported that NP bioaccumulates up to 410-fold in fish (Tsuda et al. 2000, Snyder et al. 2001). High accumulation potential was also determined for oysters and snails that both serve as transport media and potential sources of APs in marine environment (Cheng et al. 2006). It was also noted that an ability of marine organisms to accumulate APs depends on their feeding strategy. A higher proportion of APs was found in organisms with the highest exposure to sediments (e.g. filter feeding organisms) and so APs concentrations in marine organisms were higher in benthic and pelagic organisms that live close to the sediment than in fish (David et al. 2009). These findings revealed that the main source of APs for marine organisms is not water column and intake through gills but sediments and dietary uptake, both depending on the AP distribution in the aquatic environment. On the other hand, uptake through skin and gills was also demonstrated (Ferreira-Leach and Hill 2001). A distribution of APs in live organisms was also investigated and, due to partly lipophilic nature of APs, their target tissues in fish (such as the adipose tissue,

brain, liver, kidney, muscle, skin and eye) are rich in grease (Ferreira-Leach and Hill 2001). The study, using radio-labelled compounds demonstrating their distribution, indicates that the liver and bile are a main excretion route for absorbed APs, and the concentration of AP metabolites excreted in bile increased with increasing degree of alkylation. It should be emphasized that uptake, metabolism and elimination of xenobiotics, including APs, vary with compound, exposure route and fish species (Tollefsen and Nilsen 2008). The muscle tissue of the chub (*Leuciscus cephalus*) in the Czech Republic contains 1.92-6.11 ng/g w.w. of ΣNP + OP (Zlabek et al. 2006). Some fish species from Adriatic Sea, Italy, have NP levels from 12 to 1,431 ng/g w.w. and OP levels of 0.3-4.7 ng/g w.w. (Ferrera et al. 2005). Basheer et al. (2004) presented concentrations of NP about 60.5 ng/g w.w. and OP about 31.4 ng/g w.w. in fish in Singapore. Fish in the UK were found to contain up to 0.8 ng/g w.w. of NP in the muscle tissue (Ying et al. 2002), whereas geometrical mean of NP in snails and oysters was calculated in range of 380-1,560 ng/g and 92-1,080 ng/g d.w., respectively. Bioconcentration factors for oysters and snails exceed those in fish (Cheng et al. 2006). Reported bioconcentration factor of NP in whole fish ranged from 280 to 1,300 (Ferreira-Leach and Hill 2001). As mentioned above the highest values of APs were determined in fish bile, because glucuronic acid conjugates are the main excretion form of APs. In the study of Jonsson et al. (2008) the levels of OP reached 579 ng/g and NP 19 ng/g of fish bile in the North Sea. The levels of NP detected in fish bile in the UK reached 195-2,453 ng/mL and, in fish exposed to wastewater discharge, values were even up to 12,678 ng/mL (Fenlon et al. 2010). It could be concluded that variability in APs accumulation in water organisms is affected by feeding habits, metabolism, levels of contamination in the individual habitats, biotransformation and excreting capacity.

Toxicity and risk factors

An increasing concern for APs occurrence in the environment was initiated by investigations of feminized male fish found near sewage outlets in several rivers all over the world; a mixture of chemicals containing APs that results from degradation of detergents during sewage treatment seemed to be a causal agent of this endocrine disruption (Purdom et al. 1994, Auriol et al. 2006). Even though suspicion of toxicity of APs was declared in 1938 by Dodds and Lawson (1938) and confirmed by Soto et al. (1991), the aim to restrict the use of this group of chemicals

was accomplished in Europe in 2001 by their inclusion in the list of priority hazardous substances for surface waters (European Commission 2000) and in the USA by developing "chronic criteria recommendations" for NP by US EPA (2005). This procedure is in accordance with the fact that the majority of chemicals that have been in production before 1981 has not been subjected to the present requirements for the environmental evaluation of new chemicals (Wallstrom 2004). Therefore, only 3% of 2,500 high-volume chemicals currently in use are well-tested, including their long-term effects (Soares et al. 2008). Intensive research focused on mode of action as well as other toxicologic potential of these compounds was started since the ability of NP, OP and APE1, APE2 and APE3, present in the environment at sufficient levels, to mimic natural hormones and disrupt endocrine function was demonstrated (Tabata et al. 2001). Besides the main detrimental xenoestrogenic effect, these compounds were confirmed as potential carcinogens (Pedersen et al. 1999, Uguz et al. 2003), hepatotoxins (Meier et al. 2007), genotoxins (Hwang et al. 2010) and behavioural modulators affecting basic survival reflexes such as locomotors activity or aggression (Xia et al. 2010). On the molecular basis, APs have been reported to bind to oestrogen receptors (ER) of both fish and mammals (Gutendorf and Westendorf 2001, Tollefsen 2002) and activate estrogen-responsive element regulating reporter genes (Kuiper et al. 1998, Legler et al. 1999). They are capable to interfere with steroid hormone receptor activity (Kudo and Yamaguchi 2005), steroid metabolism (Arukwe et al. 1997) and plasma endogenous steroids in aquatic animals (Tollefsen 2007), too. It indicates that this group of pollutants acts through multiple mechanisms to cause potentially endocrine disruption.

In general, the endocrine and reproductive effects of chemicals are believed to exist due to their ability to: (1) mimic the effect of endogenous hormones, (2) antagonize the effect of endogenous hormones, (3) disrupt the synthesis and metabolism of endogenous hormones, and (4) disrupt the synthesis and metabolism of hormone receptors (Sonnenschein and Soto 1998). APs have been shown to cover more than two of these effects. Very interesting outcomes that some of the APs displayed apparent antagonistic activity at low micromolar concentration whereas acting as weak estrogens at high concentrations were presented by Silva et al. (2002). Thus APs and alkylated non-phenolics act as both agonist and antagonistic estrogens depending on concentration. Antiandrogenic activity through affecting aromatase activity and a function of the aryl hydrocarbon receptor (AhR) was also confirmed by Bonefeld-Jogensen et al. (2007). It follows

that, except to "classical" oestrogen receptors, APs are able to bind to the AhR, which regulates some ER-responsive genes (Safe and Gaido 1998); the pregnant X receptor, which may regulate endogenous steroid metabolism (Masuyama et al. 2000), the nicotinic receptor, where NP directly modulates ion current (Nakazawa and Ohno 2001) and even cAMP responsive element as a key signalling route of many hormones and substances (Cheshenko et al. 2008). Some APs also induced significantly a p53 gene expression, as demonstrated in copepod, indicating the involvement of p53 in such stress-responses (Hwang et al. 2010). Recently, Yang et al. (2006) also assumed that p53 gene would be closely related to the impacts of endocrine disrupting chemicals (EDCs) on ecosystem biota and human health. They were also determined as potent inhibitors of Ca^{2+}-ATPase disrupting Ca^{2+} homeostasis in fish, perhaps contributing to cell and tissue damage during key stages in the development and thereby influencing normal endocrine function later in life (Kirk et al. 2003). A recently discovered neuropeptide, kisspeptin, crucially important substance for the triggering of puberty and for future fertility in mammals (Oakley et al. 2009), and similar function in teleost of fish (Katashi et al. 2009) is suspected to be affected by APs, too.

It has been reported that NP exerts its biochemical effects by down regulating an activity of microsomal cytochrome P4501A while stimulating an increase in the cytochrome P4503A protein in the liver of mammals and fish (Uguz et al. 2003). It was shown that 220 μg/L of NP induce neoplastic proliferation of reticuloendothelial cells in fish hepatopancreas after 2 weeks and an increase in glutathione S-transferase activity after 1 week and replacement of the normal liver parenchyma by the fibrous tissue after 4 weeks (Arukwe et al. 2000). Thus, it could be assumed that NP has also the ability to cause variations in isoforms of hepatic cytochrome P450-dependent steroid and xenobiotic metabolizing enzymes (Servos 1999). Finally, not all APs are able to disrupt the reproductive function in a live body. Interesting observations pertaining to structure-function relationships were made: (i) the alkyl chain must have at least 3 carbons, (ii) only the p-isomers are estrogenic, (iii) polyalkylated, hindered phenols like butylated hydroxytoluene and Irganox 1640 (Ciba-Geigy) are not estrogenic while they are effective antioxidants, and (iv) fused rings like naphthols are not estrogenic in spite of being an integral part of the A and B ring of natural steroids (Sonnenschein and Soto 1998). The estrogenicity is dependent on ligand-binding affinity, transcriptional and post-transcriptional regulation of ER-dependent genes, and the toxicokinetics of the compound (Beresford et al. 2000, Katzenellenbogen et al. 2000).

Since the toxicity potential of APs was determined, monitoring strategies to assess these compounds and their biological impact in the environment have been developed. As endocrine disrupting chemicals they can affect a number of reproductive parameters in fish, including gonadal development (Meier et al. 2007), induction of plasma vitellogenin in male and juvenile fish (Jobling and Sumpter 1993), inhibition of spermatogenesis (Jobling and Sumpter 1993) and oogenesis (Weber et al. 2003), all of them could be used as markers of endocrine disruption. The hepatic induction of vitellogenin production in male and juvenile oviparous fish, which occurs normally only in maturing females under stimulation of 17β-estradiol, has been proposed as a sensitive biomarker of the exposure to estrogenic chemicals of endogenous and exogenous origin (Sumpter and Jobling 1995, Randak et al. 2009). Interestingly, the calculated contribution of the anticipated NP and OP to the potential estrogenicity of discharge from healthcare facilities was found greater than 65% of the total potential estrogenicity (Nagarnaik et al. 2010). Healthcare facilities like hospitals, nursing facilities, assisted living facilities, and independent living facilities, were suspected of releasing immense amount of natural or synthetic hormone metabolites and of responsibility for endocrine disruption. According to the study of Nagarnaik et al. (2010) their share of endocrine disruption is based more on releasing of APs that have weaker estrogenic effectsthan hormones but the APs are released in higher amounts. APs were present in part per billion concentrations in water samples taken near healthcare facilities compared to the part-per-trillion concentrations of hormones. An intensive use of detergents in healthcare facilities and industry could be more important source of NPs in the environment because NPE based detergents enter the municipal system and enhance their participation in endocrine disruption in the aquatic ecosystem. Finally, levels in the environment that are capable to induce reproduction impairment were determined. The acute toxicity with 96hLC50 calculated for NP has been determined for at least 22 different species of fish with reported 96hLC50s ranging from 17 to 3,000 μg/L, although most of the values ranges from 100 to 300 μg/L (Gray and Metcalfe 1997, Dwyer et al. 1999). Chronic toxicity values (NOEC) are as low as 6 μg/L in fish and 3.7 μg/L in invertebrates (Servos 1999) and LOEC was at nominal dose of 4 μg/kg body weight of AP for the effects of timing of puberty, and 20 μg/kg body weight of AP for the delay effect in mature fish (Meier et al. 2011. Likewise, Bellingham et al. (2010) demonstrated that developing foetus is sensitive to environmentally relevant concentrations of EDCs that may have serious impact on the future

development of the reproductive system. The body burden corresponds to water exposure in the ng/L concentration range and this is 100times lower than the APs concentrations (µg/L) that have previously been reported to induce vitellogenin in male or juvenile fish and have been documented in surface water all over the world (Meier et al. 2011). Further indicators of EDCs toxicity could be sex steroid-binding protein determination (Tollefsen and Nilsen 2007) or behavioural changes assessment (Xia et al. 2010). It was demonstrated that APs and alkylated non-phenolics are able to bind successfully to the rainbow trout sex steroid-binding protein. Unfortunately, the most ubiquitous AP like NP was not proved to bind to rainbow trout sex steroid-binding protein (Tollefsen and Nielsen 2007). On the other hand, measurements of several behavioural endpoints, especially locomotors activity, aggression displays and group preference, may provide an effective assessment of NP in the aquatic ecosystem but this measurement has some limitations like biotic and abiotic factors in field conditions (Spence et al. 2008, Xia et al. 2010). Other studies are needed to establish more sensitive and specific markers of APs detrimental activity but, as well documented, chemicals exist as complex mixtures in the environment and groups of compounds may cause mixed toxicity even though each compound is present below its threshold for effect (Silva et al. 2002).

Conclusions

Recently provided information demonstrated serious damaging impact of EDCs on aquatic organisms, in particular. Besides natural/synthetic hormones, PCBs, dioxins, some insecticides and bisphenol-A, APs and APEs constitute very potent EDCs as well as persistent substances with multiple toxicity, deleterious effect and bioaccumulative features. In spite of the fact that their use was reduced in Europe, USA and Japan in last few years, they are still very popular in some other countries and contamination of the environment with these chemicals is of substantial concern in the whole world. Not only sex in reversal fish (Sumpter 1998), but also altered social and reproductive behaviour in birds (Fox 2001), impaired penile development in alligators (Guillette et al. 1999), cryptorchidism and infertility in the Florida panther (Facemire et al. 1995) are virtual consequences of an increase in EDCs in the environment. These findings have implications for the study of human conditions that are suspected to be caused by environmental estrogens, such as undescended testis, breast cancer and a decrease in sperm counts and quality during last 50 years (Wolf et al. 1993). Furthermore, APs have ap-

peared to be able to interfere with the regulatory systems of different types of cells by several mechanisms and thus are not compounds of single harmful effect. It is an alarming finding that NP is ubiquitous in foodstuffs at concentrations ranging from 0.1 to 19.4 µg/kg with an estimated daily intake of 7.5 µg/day for an adult (Guenther et al. 2002). The ubiquity of this type of pollutants in the environment supports a need for greater knowledge of APs bioaccumulation process and their human or animal health alteration potential. Options of waste water treatment process improvement and/or also APs/APEs possible substitution in the industrial use with another type of substances are still animated issues for further investigation.

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