WWF DETOX CAMPAIGN

Factsheet

Chain of Contamination: The Food Link

Alkylphenols (octylphenol and nonylphenol isomers)

Background

Alkylphenols (APs) are high production volume man–made chemicals, used primarily to manufacture alkylphenol ethoxylates (APEs). APs and APEs have been in use for over 50 years and are important to a number of industrial processes, including pulp and paper, textiles, coatings, agricultural pesticides, lube oils and fuels, metals and plastics (APERC, 2004).

The most commercially important alkylphenols are nonylphenol (NP) and octylphenol (OP). They exist in different forms, or "isomers", and are used to make nonylphenol ethoxylates (NPEs) and octylphenol ethoxylates (OPEs). However, restrictions are now in place in the EU (Directive 2003/53/EC) governing the marketing and use of NP and NPEs (EU, 2003) (see "Major Uses"). NPEs were used primarily as surfactants in detergents. NPs are also used to produce resins and plastics and as antioxidants and stabilisers in plastics (APERC, 2004, ECB 2002). In 1997, prior to the restrictions on the use of NPEs, production and total usage of NP in the EU was 73,500 tonnes and 78,500 tonnes respectively (ECB, 2002).

OPs are used mainly to make phenolic resins, although following the restrictions on NP/NPEs it has been suggested that OPEs might be used in place of NPEs in some of their applications (EA, 2005). Approximately 23,000 tonnes of OP (4- tert octylphenol) were consumed in the EU in 2001 (EA, 2005).

Due to their widespread use as surfactants (mostly NPEs), APEs are commonly found in wastewater discharges and effluents from sewage treatment plants. Breakdown (degradation) of APEs in wastewater treatment plants or by environmental processes generates the more persistent parent APs such as NP and OP (through the loss of the ethoxylate chain), as well as other APE metabolites (Ying et al., 2002). The discharge of wastewaters, sewage effluents and waste from industries using APs or APEs, results in the widespread presence of APs and APEs in surface waters and the aquatic environment (rivers, estuaries, coastal marine environments) (Cespedes et al., 2006, Chen et al., 2006, EA, 2005, ECB, 2002, Fenet et al., 2003, Ferguson et al., 2001, Heemken et al., 2001, Kannan et al., 2001, Petrovic et al., 2002, Ying et al., 2002).

Following input into receiving waters, the more persistent APs tend to accumulate in sediments, particularly under anaerobic conditions (Ying, 2006, EA 2005, Kannan et al., 2001, Warhurst, 1995). APs can also bind strongly to soil following application of sewage sludge to agricultural land (ECB, 2002, EA, 2005), although aerobic degradation is thought to occur, leading to a decrease in the levels in soil over time (ECB, 2002, Staples et al., 2001, Warhurst, 1995). Another input to the terrestrial environment is through the direct application of pesticide formulations containing APs such as nonylphenol (ECB, 2002). Waste materials disposed of in landfill can also contribute APs to leachates (Asakura, et al., 2004). APs have been detected in indoor and outdoor air (Rudel et al., 2003, Saito et al., 2004, Xie et al., 2006, Ying et al., 2002). In indoor air, a source of APs is building materials, as APs are used as antioxidants for polymer resins in wall or floor coverings (Saito et al., 2004).

Alkylphenolic compounds are moderately persistent[1] (EA, 2005, Warhurst, 1995), "lipophilic" (they preferentially bind to fat) and can bioconcentrate[2] in aquatic biota (Croce, et al, 2005, ECB, 2002, Guenther et al., 2002, Sabik et al., 2003). APs and APEs have been detected in fish and invertebrates (e.g. shrimp, lobster, mussels, oysters, snails) inhabiting polluted waters (Cheng et al., 2006, Ferrera et al., 2001, 2005, Rice et al., 2003, Schmitz-Afonso et al., 2003, Vethaak et al., 2005, Verslycke et al., 2005, Wenzel et al., 2004). APs can also accumulate in animals higher up the food chain (e.g. osprey) due to the consumption of contaminated prey (Schmitz-Afonso et al., 2003).

Despite the potential for human exposure due to their widespread use, information on the occurrence of NPs and OPs in humans is limited (ECB, 2002). NP and OP can be detected in human blood plasma and serum (Inoue et al., 2000), and have been detected in maternal and umbilical cord blood serum (WWF & Greenpeace, 2005). Nonylphenol has also been detected in urine (Calafat et al, 2005, Wilson et al., 2006).

Both nonylphenol and octylphenol are acutely toxic to aquatic organisms (ECB, 2002, EA, 2005). The restrictions (see below) on the uses of NP (and NPEs) are based on the evidence of it's toxicity to aquatic organisms (ENDS Report, 2004b). However, concerns regarding the environmental impacts of APE and APs have focussed on their endocrine disrupting properties.

Endocrine disrupting effects

There is a large body of evidence on the endocrine (hormone) disrupting properties of alkylphenols. The oestrogenic properties of APs were demonstrated as early as 1938 (Dodds and Lawson, 1938), and they have since been shown to be estrogenic (capable of mimicking the action of the female hormone oestrogen, or "estrogen"), in animal cells (Jobling & Sumpter, 1993, Nimrod & Benson, 1996, Soto et al., 1991, 1995, White et al, 1994). Recent attention has focussed on the effects on fish and wild fish populations (including roach, rainbow trout, gudgeon, eel and flounder) of estrogenic chemicals (including alkylphenols) in sewage effluents discharged into UK rivers and estuaries (Allen et al., 1999, Jobling and Sumpter, 1993, Peters et al., 2001, Purdom et al., 1994, Simpson et al., 2000, Sumpter, 1995). In some cases, for industries using APE surfactants (such as the textile industry), APs are suspected of contributing the majority of the estrogenic activity of the effluent (Sheahan et al., 2002). Estrogenic components of sewage effluents (Rodgers-Gray et al., 2001) have been implicated in the widespread "feminisation" of male fish observed in rivers and estuaries in the UK and other parts of Europe (Jobling et al., 1998, Sumpter, 1995, Vethaak et al., 2005). Effects observed in male fish include the expression of the female egg yolk protein vitellogenin, the presence of intersex characterisitics such as "ovotestes" (the development of eggs [oocytes] in the testis), feminisation of the reproductive ducts, reduced sperm production and reduced fertilization success (Allen et al., 1999, Bjerregaard et al., 2006, Jobling et al., 1998, 2002a,b, Kleinkauf et al., 2004, Peters et al., 2001, Rodgers-Gray et al., 2001, Simpson et al., 2000).

A recent study on the Pacific oyster (*Crassostrea gigas)* has shown that NP can induce long-term and transgenerational effects. The study showed that a single 48h exposure of larvae at a key stage in their development to environmentally relevant concentrations of NP induced long-term, sexual developmental effects (altered sex ratio towards females and an increase in the incidence of hermaphroditism). Gamete viability was also affected, resulting in poor embryonic and larval development (up to 100% mortality) of the subsequent generation.

Research in rodents has also highlighted the potential for estrogenic endocrine disruption in mammals. Exposure to OP has been shown to reduce the size of testes and accessory sex organs, disrupt sperm production, increase the incidence of sperm deformities and alter circulating hormone levels in rats (Boockfor et al., 1995, Herath et al., 2004, Kim et al., 2004, Sharpe et al., 1995).

[1] Octylphenol fulfils the UK Government's Chemicals Stakeholder Forum's criteria for persistent, bioaccumulative and toxic (PBT) chemicals, although it is not considered particularly bioaccumulative (EA, 2005)

[2] Bioconcentration refers primarily to aquatic species and environments and is the result of uptake and accumulation of chemical contaminants (at a rate that exceeds metabolism and excretion) by organisms to higher concentrations than that of the surrounding medium i.e. water.

Experiments with human breast cancer cell lines have shown that OP and NP bind to oestrogen receptors and can increase cell proliferation (Blom et al., 1998, Soto et al., 1991, White et al., 1994).

Major uses

Prior to their restrictions on their use (see below), NPEs were used in industrial detergents, in industrial processes (e.g. emulsion polymerisation), leather processing, in paints, spermicidal lubricants, pesticide formulations, hair dyes, cosmetics and personal care products (APERC, 2004, ECB, 2002, Warhurst, 1995).

Recent legislation (EU Directive 2003/53/EC), effective from January 2005, has now banned the most dispersive uses of NP and it's ethoxylates (EU 2003, ENDS Report 2004b, DEFRA, 2004, UK CSF, 2005). Use of NP and it's ethoxylates are prohibited (with specific exceptions) in industrial and institutional cleaning systems, domestic cleaning, textiles and leather processing, as an emulsifier in agricultural teat dips, in metal working, manufacturing of pulp and paper, cosmetics and personal care products and in pesticides and biocides formulations (EU, 2003). The importance of official legisaltion is highlighted by the results of a study carried out by the UK Chemicals Stakeholder Forum (UK CSF, 2005) on the the voluntary agreement in place prior to the EU's Directive on NP/NPEs. In advance of the Directive coming into force, various manufacturers and users of APs agreed to stop the manufacture or import of products containing NP/OP/NPE/OPEs. The data supplied by these companies suggested that this voluntary agreement was successful in reducing the risks from NP/NPE/OP/OPE in advance of the Directive, as significant reductions in alkylphenol ethoxylate sales were reported. However, on closer inspection, the figures revealed an increase in sales of NP (by 25%). The use of NPEs in domestic detergents has been banned in the UK since 1976 (Warhurst, 1995).

OP (4- tert octylphenol) is used mainly to make phenolic resins (98%), with the remainder converted into ethoxylates to produce surfactants (EA, 2005). It can also be present as an impurity in NP along with other OP isomers. The phenolic resins are used in rubber processing to make tyres (82%) and in printing inks, electrical insulation varnishes and in the production of ethoxylated resin for offshore oil recovery (EA, 2005). OPEs are mainly used in emulsion polymerisation, textile processing, water-based paints, pesticide and veterinary medicine formulations (EA, 2005).

How do alkylphenols get into the environment and food chain?

Release of sewage effluent containing APs and APEs is the primary input of these compounds into the aquatic environment and application of sewage sludge to agricultural land contributes a significant amount of APs/APEs to the terrestrial environment (see above).

How are people exposed to alkylphenols?

Exposure to APs can occur in the workplace if a person uses APs or APEs directly (occupational exposure), through the use of consumer products containing APs or indirectly through contaminated food or drinking water.

Information on potential human exposure for OPs is, unfortunately, limited (EA, 2005) and many exposure routes for NPs may not be applicable now, given the recent restrictions on the use of NPs and NPEs (ENDS Report, 2004b). The main source of occupational exposure to NPs is reported to be through the use of specialty paints (ECB, 2002) either through dermal (skin) absorption or inhalation. Exposure to NPs can also occur through the use of pesticides (which can contain NPs as part of their formulation), via food packaging materials or through the repeated use of hair dyes containing NPs (ECB, 2002). Other potential sources of past exposure to APs may have included absorption through the skin (from shampoos, cosmetics and spermicidal lubricants) (Warhurst, 1999). Inhalation of indoor air has also been suggested as an exposure route, as APs have been detected in indoor air and dust (Rudel et al., 2003, Saito et al., 2004, Wilson et al., 2006).

Alkylphenols in food

Due to the contamination of the environment and food chain, exposure can occur via food and, to a lesser extent, contaminated drinking water (ECB, 2002). Alkylphenols have been found in edible fish and shellfish species, as well supermarket foods (see table 1).

Inputs of APs ands APEs into the aquatic environment can account for their presence in fish and shellfish, and application of sewage sludge to agricultural land introduces APs and APEs to soils used for growing crops and grazing livestock. Nonylphenols may also migrate from food contact materials, as they can be used as additives (stabilisers, antioxidants) in plastic packaging (Greenpeace, 2003, Guenther et al., 2002, ENDS Report, 2004a). A comprehensive study of German supermarket foods has shown that nonylphenols are ubiquitous in food (Guenther et al., 2002). The authors suggest numerous different pathways that could be responsible for NPs finding their way into foods. They suggest the past use of NPEs in surfactants, disinfectants, cleaning agents or as emulsifiers in pesticide formulations (in food industries and agriculture) can result in the formation (via degradation) of NPs, which could then accumulate in food. For example, the high concentrations of NPs found in apples and tomatoes could be attributed to pesticide application, as the lipophilic NPs can accumulate in their waxy skins.

Food item(s)	Reference(s)	Comments
Lobster, mantis shrimp, Anchovy, European hake, red mullet, common sole, Atlantic mackerel, angler.	Ferrara et al., (2005). Chemosphere, 59(8), pp1145-50.	8 edible marine species (2 crustaceans, 6 fish) from the Adriatic Sea (Italy) analysed for NP, OP and OPEs, which were found in all samples, at ng/g (ppb) levels. NP detected at highest concentrations.
Turkey/chicken breast fillets, cheese (brie).	Greenpeace (2003).The determination of additives in food products.	Investigation of migration of NP from food packaging. NP (in the ppm range) found in outer layer of food (in contact with packaging). NPEs also found.
Market basket of foods from German supermarket incl: peanut butter, pasta, sugar, lard, mayonnaise, milk, tuna, pineapple, marmalade, liver sausage, butter, cheese, chocolate, orange juice, beer, apples, spinach, quark, chicken, Potatoes, creme fraiche infant formula, tomatoes, bread, coffee	Guenther et al., (2002). Environ Sci Technol., 36(8), pp1676-80.	All food samples contained NPs (concentration range of 0.1-19.4 µg/kg). Despite the lipophilic properties of NPs, high levels were found not only in fatty foods such as butter, lard or liver sausage, but also in non-fatty food like marmalade, apples and tomatoes.
Shellfish (edible molluscs): clams, mussels, cuttlefish squid.	Ferrara et al., (2001). Environ Sci Technol., 35(15), pp3109-12.	Analysis of seafood from the Adriatic Sea (Italy) for NP, OP, NPE and OPE - detected in all samples, in the ng/g (ppb) range. NP found in highest concentrations, OP found at levels 30 times lower than NP. OPE always found at lowest concentrations. NPE not detected.

Table 1: Alkylphenols in food items – examples from the literature

What health effects are associated with exposure to alkylphenols?

Information on the human health effects of long term, low level exposure to APs is scarce. A recent risk assessment suggests the mutagenicity and carcinogenicity of NP is low and acute toxic effects of exposure seem unlikely (ECB, 2002).

However, there is concern over the potential for APs, along with other chemicals, to interfere with hormonally controlled processes in the body, based on the ubiquity of exposure to APs and their endocrine disrupting (estrogenic) properties (Harrison et al., 1997, Sharpe & Irvine, 2004). Exposure to endocrine disrupting chemicals (EDCs), which include alkylphenols, but also phthalates, bisphenol-A, organochlorines and brominated flame retardants amongst others, is suspected to be playing a role in various human health problems, many of which are increasing in incidence. These include certain types of cancer (breast, testicular, prostate), obesity, diabetes, precocious puberty, fertility problems and impacts on neurological development (Fenton, 2006, Heindel, 2003, Singleton & Khan 2003, Skakkebaek, 2002).

Recent studies have linked exposure to EDCs (including APs) with precocious puberty and ambiguous genitalia. Precocious puberty in children has been associated with higher serum levels of endocrine disrupting

chemicals compared to normal children, with 4-NP exerting the greatest influence (Lu et al., 2006). Estrogenic activity of the serum of newborn boys was found to be higher in those with ambiguous genitalia (characterised by cryptorchidism and hypospadias) suggesting fetal exposure to endocrine disruptors (i.e. maternal exposure to environmental pollutants during pregnancy) (Paris et al., 2006). The human placenta has also been shown to be responsive to NP – estrogen receptors capable of binding NP have been identified in placental tissues – raising concerns regarding maternal exposure to NP during the early stages of pregnancy (Bechi et al., 2006).

How can exposure to alkylphenols be reduced?

Reducing exposure to alkylphenols is best achieved by regulation of their use (see above) as many inputs of OP and NP into the environment will arise from diffuse sources.

As there are currently no restrictions on the use of APs/APEs in pesticide formulations, choosing organic food is a way to avoid the consumption of these compounds.

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