Endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) in the aquatic environment: implications for the drinking water industry and global environmental health

M. F. Rahman, E. K. Yanful and S. Y. Jasim

ABSTRACT

Endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) are a group of chemical compounds with diverse physical and chemical properties. Recent studies have indicated undesired effects of EDCs and PPCPs at their reported trace concentrations (ng l\(^{-1}\) to \(\mu\)g l\(^{-1}\)). This paper reviews the current knowledge on the sources, properties, occurrence and health impacts of EDCs and PPCPs, and their removal from drinking water using ozonation and ozone/hydrogen peroxide-based advanced oxidation. The paper also examines the potential threats posed by these chemicals to drinking water and public health. While these compounds are known to have adverse effects on ecosystem health, notably in the fish population, a similar link is yet to be established between ingestion of these compounds through drinking water and human health. In addition, data on the effectiveness of existing methods for the removal of these compounds are not conclusive. Further studies are required to characterize risks, and also to evaluate and optimize existing removal processes. Also concerted international effort is urgent to cut down the risk of exposure and restrain the production and marketing of toxic chemicals.

Key words | advanced ozonation, drinking water, EDCs, environmental health, PPCPs

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>OH</td>
<td>hydroxyl radical</td>
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<td>AOP</td>
<td>advanced oxidation process</td>
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<tr>
<td>BPA</td>
<td>bisphenol-A</td>
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<td>DOC</td>
<td>dissolved organic carbon</td>
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<td>EDCs</td>
<td>endocrine disrupting compounds</td>
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<tr>
<td>EE2</td>
<td>17(\alpha)-ethinylestradiol</td>
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<tr>
<td>GAC</td>
<td>granular activated carbon</td>
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<tr>
<td>H(_2)O(_2)</td>
<td>hydrogen peroxide</td>
</tr>
<tr>
<td>NOM</td>
<td>natural organic matter</td>
</tr>
<tr>
<td>O(_3)</td>
<td>ozone</td>
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<tr>
<td>PAC</td>
<td>powdered activated carbon</td>
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<tr>
<td>PAHs</td>
<td>poly aromatic hydrocarbons</td>
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<tr>
<td>PCBs</td>
<td>polychlorinated biphenyls</td>
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<tr>
<td>POPs</td>
<td>persistent organic pollutants</td>
</tr>
<tr>
<td>PPCPs</td>
<td>pharmaceuticals and personal care products</td>
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<tr>
<td>RO</td>
<td>reverse osmosis</td>
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<tr>
<td>STP</td>
<td>sewage treatment plant</td>
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<tr>
<td>USEPA</td>
<td>United States Environmental Protection Agency</td>
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<td>USGS</td>
<td>United States Geological Survey</td>
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<td>UV</td>
<td>ultraviolet</td>
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INTRODUCTION

It was reported as early as 1930 that certain chemical compounds and plant tissues can have an impact on the hormone system (Walker & Janey 1930; Cook et al. 1934).
With the advances in analytical capability, the presence of a long list of chemically diverse compounds at trace concentrations has been identified in the environment. Endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) are almost ubiquitous in municipal sewage treatment plant (STP) effluents and source waters for drinking water treatment plants (Snyder et al. 2005). Many studies have indicted trace level occurrence of EDCs and PPCPs causing adverse impacts in humans and in ecosystems. There is a perceived risk of indirect contamination via drinking water as studies have shown that conventional treatment systems perform poorly in removing these chemicals from drinking water (Snyder et al. 2005; Westerhoff 2003; Stackelberg et al. 2004). Thus the drinking water industry faces a challenge as regulatory bodies and the public become aware of the presence of these compounds in water, which were previously not detectable (Westerhoff 2003). This paper attempts to provide a summary of the properties of EDCs and PPCPs, their occurrences in the aquatic environment, health impacts, and discusses their removal from water using ozonation and ozone-based advanced oxidation. The paper lists some of the challenges these micro-pollutants present to the drinking water industry. It also discusses the threats EDCs and PPCPs pose to public health, and addresses the current gaps in knowledge and future research needs. It is hoped that this work would encourage readers from various disciplines to get involved and contribute to the ongoing discussion on the presence of EDCs and PPCPs in the aquatic environment.

**EDCS AND PPCPS: SOURCES AND PROPERTIES**

EDCs are either naturally occurring or synthetic substances that interfere with the functioning of hormone systems resulting in unnatural responses (Birklett 2005). The United States Environmental Protection Agency (USEPA) defines EDCs as agents that ‘interfere with the synthesis, secretion, transport, binding, or elimination of natural hormones in the body that are responsible for maintenance of homeostasis, reproduction, development and/or behaviour’ (Birklett 2005). A number of steroid hormones, both natural and synthetic, alkylphenols, pesticides, organic oxygen compounds, poly aromatic hydrocarbons (PAHs) and dioxins have so far been confirmed as EDCs. Drugs are designed for specific biological action in target receptors (Halling-Sorensen et al. 1998; Jones et al. 2005). However, they can cause adverse impacts to non-target receptors (Jones et al. 2005; Jasim et al. 2006) and some of them (certain oral contraceptive medications, thyroid hormones administered as medications, and estrogen replacement pharmaceuticals) can act as EDCs. To date no exhaustive list of EDCs exists, because, for many chemicals, there is limited and incomplete evidence of endocrine disrupting activity or evidence of endocrine activity which is controversial and also because most chemicals in the market have not been tested for their endocrine toxicity (Snyder et al. 2006a; Kim et al. 2007).

The endocrine system controls various basic functions such as reproduction, synchronization of physical development and maintenance in animals and plants with the help of hormones (Lintelmann et al. 2003; Birklett 2005). Of the various mechanisms by which EDCs affect the hormone system, the principal three (Pocar et al. 2003) are as follows. They may act as a hormone mimic by binding to the receptor sites of the target cells and activating a response. This is defined as an agonistic effect. In the case of an antagonistic effect, the chemical will act as a hormone blocker and no response is produced as the chemical binds to the receptor and prevents natural hormones from interacting. Figure 1 illustrates these endocrine disruption processes (agonistic and antagonistic effects). Sometimes agonists and antagonists bind to the same receptors resulting in subtle changes in receptor conformation (Birklett 2005).

EDCs and PPCPs found in the aquatic environment are structurally diverse. Water solubility, adsorption coefficient (log KOC), bioconcentration (log KOW) and Henry’s law constant (Birklett 2003; Lintelmann et al. 2003) are some of the important properties that determine the fate and behaviour of EDCs. A low water solubility and high octanol/water partition coefficient (log KOW) or high carbon/water coefficient (log KOC) will promote sedimentation or association with biota (Birklett 2003). PPCPs are biologically active, not readily biodegradable and often have high water solubility relative to their molecular weight (Jorgensen 2001). Despite having short half-lives, many
PPCPs can still become persistent in the aquatic environment owing to their continual disposal and release in the aquatic environment (Jasim et al. 2006).

EDCs and PPCPs find their way into watercourses by many routes including direct discharges into water; excretion and inappropriate disposal after use of drugs and chemicals by householders; agricultural and cattle feedlot runoff; industrial and STP effluents; accidental releases (through spills, run off, atmospheric deposition); and release of compounds indirectly through diffuse sources such as storm water runoff (Jones et al. 2004; Sumpter 2005; Falconer et al. 2006). Moreover pollutants can be transported via watercourses to new areas far from their sources, for example persistent organic pollutants (POPs) can accumulate in areas such as the Arctic where they have never been used or produced (Lintelmann et al. 2003). Due to strict regulations, point sources such as manufacturing industries of both human and veterinary medicines do not contribute to pharmaceuticals pollution as much as non-point sources such as households and agricultural runoff (Jones et al. 2003). About 33% of the total volume of drugs and 25% of the total sold is disposed of with household waste or in drains in Germany and Austria, respectively (Kummerer 2004). A survey in the United Kingdom found that 63.2% of unwanted medicines are disposed of with household waste or in drains in Germany and Austria, respectively (Kummerer 2004). A survey in the United Kingdom found that 63.2% of unwanted medicines are disposed of with household waste or in drains in Germany and Austria, respectively (Kummerer 2004). A survey in the United Kingdom found that 63.2% of unwanted medicines are disposed of with household waste or in drains in Germany and Austria, respectively (Kummerer 2004). A survey in the United Kingdom found that 63.2% of unwanted medicines are disposed of with household waste or in drains in Germany and Austria, respectively (Kummerer 2004).

Table 1 lists some EDCs and PPCPs, and their main sources or pathways and important physicochemical properties.

**OCCURRENCES IN THE AQUATIC ENVIRONMENT**

Herbicides constitute more than half of all pesticides used in the developed world (Hua et al. 2006a). A number of studies have reported the occurrence of pesticides and herbicides and their metabolites in surface water, groundwater and near-surface aquifers in the United States (Thurman et al. 1992; Kolpin et al. 1996, 1998a,b, 2000, 2002; Boxall et al. 2004). Kolpin et al. (1998a) detected pesticides including atrazine, metachlor and prometon, in 54.4% of groundwater samples in 1,034 sites across the United States. However, concentrations of the detected contaminants were generally less than 1 µg l⁻¹. Atrazine, of which about 3 × 10⁶ kg per year is used in the great lakes basin, has also been frequently detected in river waters in Ontario, Canada (Frank & Logan 1988; Hua et al. 2006a,b; Jasim et al. 2006). A detailed survey conducted by the United States Geological Survey (USGS) in 139 streams across 30 states in the United States detected 82 of 95 target compounds that included steroids, plasticizers, detergent metabolites, veterinary medicines and other organic water contaminants. Steroids and nonprescription drugs were the most frequently detected contaminants with over 80% occurrence (Kolpin et al. 2002).

Metabolites of chemicals are also important; Boxall et al. (2004) reported occurrences of metabolites more frequently than their parent compounds. Acetachlor ESA and acetachlor OXA were detected 30% more frequently than their parent compound acetachlor (Boxall et al. 2004). Similar conclusions were also drawn by Kolpin et al. (1998b). Degradates often have a much lower KOC value than their parent compounds. Thus those degradates are more likely to be released by STP effluents or be...
<table>
<thead>
<tr>
<th>Name</th>
<th>Main source or pathways</th>
<th>CAS registry no.</th>
<th>Molecular weight</th>
<th>Water solubility@ 25°C (mg l⁻¹)</th>
<th>Log Kow</th>
</tr>
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<tbody>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
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<tr>
<td>Estriol</td>
<td></td>
<td>50–27–1</td>
<td>288.4 (Westerhoff et al. 2005)</td>
<td>13.25 (Lintelmann et al. 2003)</td>
<td>2.43</td>
</tr>
<tr>
<td>17β-estradiol (E2)</td>
<td></td>
<td>50–28–2</td>
<td>272.2 (Westerhoff et al. 2005)</td>
<td>12.96 (Lintelmann et al. 2003)</td>
<td>4.01</td>
</tr>
<tr>
<td>17α-ethinylestradiol</td>
<td></td>
<td>57–63–6</td>
<td>296.2 (Westerhoff et al. 2005)</td>
<td>4.83 (Lintelmann et al. 2003)</td>
<td>3.67</td>
</tr>
<tr>
<td>Diethylstilbestrol (DES)</td>
<td></td>
<td>56–53–1</td>
<td></td>
<td></td>
<td>5.07</td>
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<tr>
<td>Alkylphenols</td>
<td></td>
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<tr>
<td>Nonylphenol-ethoxylate</td>
<td></td>
<td>27986–36–3</td>
<td>264(Ying et al. 2002)</td>
<td>3.02 (Lintelmann et al. 2003)</td>
<td>4.17</td>
</tr>
<tr>
<td>4-tert-octylphenol</td>
<td></td>
<td>104–66–9</td>
<td>206 (Ying et al. 2002)</td>
<td>12.6 (Lintelmann et al. 2003)</td>
<td>4.12</td>
</tr>
<tr>
<td>Triazine herbicides</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Atrazine</td>
<td>Plant &amp; Davis (2005) Widely used worldwide, mainly on maize. Enters by agricultural runoff as diffuse pollution into groundwater. Non-agricultural uses have been banned in developed countries</td>
<td>1912–24–9</td>
<td>215.1 (Westerhoff et al. 2005)</td>
<td>30 @ 20°C (WHO 1996)</td>
<td>2.61</td>
</tr>
<tr>
<td>Simazine</td>
<td></td>
<td>122–34–9</td>
<td>201.7 (Schwarzenbach et al. 2003)</td>
<td>5 @ 20°C (WHO 1996)</td>
<td>2.18</td>
</tr>
<tr>
<td>Organochlorines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-p’ DDT</td>
<td>Plant &amp; Davis (2005) May enter environment through groundwater, atmospheric transport and agricultural runoff. DDT is still being used in some developing countries and may be concentrated in imported goods. But main sources in developed countries are likely to be historically contaminated sites</td>
<td>50–29–3</td>
<td>354.5 (Westerhoff et al. 2005)</td>
<td>0.0034 (Lintelmann et al. 2003)</td>
<td>6.20</td>
</tr>
<tr>
<td>p-p’ DDE</td>
<td></td>
<td>72–55–9</td>
<td>315.9 (Westerhoff et al. 2005)</td>
<td>0.024 (Lintelmann et al. 2003)</td>
<td>5.76</td>
</tr>
<tr>
<td>Name</td>
<td>Main source or pathways</td>
<td>CAS registry no.</td>
<td>Molecular weight</td>
<td>Water solubility(^{25,^\circ}\C) (mg l(^{-1}))</td>
<td>Log K(_{ow})</td>
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<td>Dieldrin</td>
<td></td>
<td>60–57–1</td>
<td>380.9 (Westerhoff \textit{et al.} 2005)</td>
<td>0.186 @ 20°C (Health Canada 1995)</td>
<td>6.2 (Health Canada 1995)</td>
</tr>
<tr>
<td>Polyaromatic hydrocarbons (PAHs)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Pyrene</td>
<td>Lintelmann \textit{et al.} (2005) Generated during incomplete combustion of organic matter. Emission from anthropogenic sources such as traffic, heating and industrial processes like steel and aluminium production. May also enter from natural events such as volcanic eruption and forest fire</td>
<td>129–00–0</td>
<td>202.3 (Westerhoff \textit{et al.} 2005)</td>
<td></td>
<td>4.88 (Westerhoff \textit{et al.} 2005)</td>
</tr>
<tr>
<td>Other substances</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Bisphenol A</td>
<td>Plasticizer, fungicide and disinfectant. May enter via industrial effluents and also from products in use and waste products</td>
<td>80–05–7</td>
<td>228.29</td>
<td>120 (Lintelmann \textit{et al.} 2003)</td>
<td>3.4 (Lintelmann \textit{et al.} 2003)</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Carbamazepine</td>
<td>STP effluents: domestic use, excretion and inappropriate disposal. Failure of the STPs to efficiently remove these trace organic compounds leads to their aquatic occurrences</td>
<td>298–46–4</td>
<td>236.28 (Nentwig \textit{et al.} 2004)</td>
<td>17.7 (Nentwig \textit{et al.} 2004)</td>
<td>2.45 (Nentwig \textit{et al.} 2004)</td>
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<td>Name</td>
<td>Main source or pathways</td>
<td>CAS registry no.</td>
<td>Molecular weight</td>
<td>Water solubility at 25°C (mg L⁻¹)</td>
<td>Log Kow</td>
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<tr>
<td>Caffeine</td>
<td></td>
<td>58–8–2</td>
<td>194.2</td>
<td>Slightly soluble</td>
<td>&lt;0 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td></td>
<td>103–90–2</td>
<td>151.2</td>
<td>0.46 (Westerhoff et al. 2005)</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen</td>
<td></td>
<td>15687–27–1</td>
<td>206.1</td>
<td>21 (Scheytt et al. 2005)</td>
<td>3.97 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Naproxen</td>
<td></td>
<td>22204–53–1</td>
<td>230.1</td>
<td>27 (Mura et al. 2002)</td>
<td>3.18 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td></td>
<td>25812–30–0</td>
<td>250.2</td>
<td></td>
<td>4.77 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Erythromycin-H₂O</td>
<td></td>
<td>114–7–8</td>
<td>733.9</td>
<td>Slightly soluble</td>
<td>3.06 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td></td>
<td>738–70–5</td>
<td>290.1</td>
<td></td>
<td>0.91 (Westerhoff et al. 2005)</td>
</tr>
<tr>
<td>Clofibric acid</td>
<td></td>
<td>882–09–7</td>
<td>214.65</td>
<td>583 (Nentwig et al. 2004)</td>
<td>2.57 (Nentwig et al. 2004)</td>
</tr>
<tr>
<td>Iopromide</td>
<td></td>
<td>73334–7–3</td>
<td>790.9</td>
<td></td>
<td>&lt;0 (Westerhoff et al. 2005)</td>
</tr>
</tbody>
</table>
transported to surface and ground waters from the soils. Persistent and mobile degradates are often difficult to identify and the costs associated with their analysis can be high (Boxall et al. 2004).

About 100 pharmaceuticals have now been detected in rivers, lakes and coastal waters throughout Europe and the United States in trace concentrations (Hemminger 2005). Analgesics (ibuprofen, naproxen), lipid regulators (gemfibrozil, clofibric acid), antidepressants, steroid hormones, anti-epileptics (carbamazepine), X-ray media contrasts (iopromide), stimulant caffeine and detergent metabolites have been reported in the concentration range of a few ng l\(^{-1}\) to \(\mu\)g l\(^{-1}\) in various water matrices including surface waters and STP effluents (Halling-Sorensen et al. 1998; Ternes 1998, 2001; Stumpf et al. 1999; Kolpin et al. 2002; Metcalfe et al. 2003; Solaiman et al. 2004; Servos et al. 2005). Bioaccumulation of 17α-ethinylestradiol (EE2) and nonylphenol in biota samples (Mediterranean mussels) in Venice lagoon, Italy, in the concentration range of 7.2–240 ng l\(^{-1}\) have been found (Pojana et al. 2007).

Available occurrence data for EDCs and PPCPs in drinking water are sparse (Snyder et al. 2005). Stackelberg et al. (2004) studied the occurrence of organic wastewater contaminants in a United States drinking water treatment plant. Of the 106 target contaminants, 34 contaminants were detected in 10% of the raw water samples and more than 11 contaminants (such as bisphenol A, carbamazepine, caffeine, cotinine, tetrachloroethylene) in finished drinking water (Stackelberg et al. 2004). DEET (an insect repellent) was found as the most common contaminant in both raw and finished drinking water in recent research by the American Wastewater Research Foundation (Khiari 2007). The foundation also reported frequent occurrences (>65% of samples) of ibuprofen, meprobamate, dilantin and iopromide in finished drinking water. Atrazine occurred at the highest concentrations of any contaminant tested in both raw and finished water but far below the maximum contaminant level of 3 \(\mu\)g l\(^{-1}\) (Khiari 2007). In Ontario, Canada, ibuprofen was detected in finished drinking water with a median concentration of 0.5 ng l\(^{-1}\) and 13 ng l\(^{-1}\) when the sources of water were lakes and rivers, respectively, which were contaminated with upstream STP effluents (Metcalfe et al. 2004). Zuccato et al. (2000) reported the occurrence of the antibiotic tylosin, a veterinary growth promoter, in drinking water at a concentration of 0.6–1.7 ng l\(^{-1}\).

EDCs such as bisphenol A (BPA), alkylphenols, phthalates and PAHs can leach into drinking water when plastics pipes are used in supply lines. BPA is used for relining drinking water supply lines and as coatings for many fittings. Concentrations of BPA up to 1 mg l\(^{-1}\) have been reported in water supplies. BPA may also leach from lacquer in food cans into water supplies (Gomes & Lester 2003). PAHs can be remobilized into the drinking water when water mains are coated with coal-tar pitch. Maier et al. (2000) as cited by Gomes & Lester (2003) noted that disinfection with chlorine might lead to the leaching of PAHs from coal-tar pitch.

### HEALTH EFFECTS OF EDCS AND PPCPS

Exposure to EDCs and PPCPs can result from chronic dose rather than bioaccumulation, thus making them toxic to receptor organisms. Fish probably bear the brunt of occurrence of the chemicals in the aquatic environment. Impaired reproduction and sexual anomalies have been observed in some fish species. Some of the reported adverse health impacts of EDCs and PPCPs on wildlife are presented in Table 2.

In recent years, incidences of breast, prostate and testicular cancers have increased a great deal. This increase has been linked to the EDCs (Plant & Davis 2003). The consequences of prenatal exposure to diethylstilbestrol, such as reproductive disorders, cognitive impairment and miscarriage have been reported (Birmbaum 1994; Damgaard et al. 2002; Falconer et al. 2006; Inadera 2006). Exposures to industrial chemicals and organochlorine pesticides have often been blamed for causing early onset of puberty in girls, delayed puberty in boys and impaired fertility in men (Sharpe & Irvine 2004; Snyder et al. 2005). Colon et al. (2000) detected high levels of phthalate esters in Puerto Rican girls with premature breast development (premature thelarche). Prolonged or permanent neurological injuries including cognitive impairment and behaviour abnormalities may occur in children, particularly to the foetus if exposed to dioxins and PCBs (Falconer et al. 2006).
<table>
<thead>
<tr>
<th>Species</th>
<th>Health effects</th>
<th>Environmental exposure/indicted contaminant</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rainbow trout</td>
<td>Feminization (male fish producing eggs and female hormones such as vitellogenin) and sterility</td>
<td>Ethinyl-estradiol (EE2) and alkylphenol ethoxylates present in sewage treatment plant (STP) effluents</td>
<td>PURDOM ET AL. (1994)</td>
</tr>
<tr>
<td>Alligators</td>
<td>Reproductive tracts disorder including reduced penis size in males and population decrease</td>
<td>Organochlorines such as DDTs, DDEs</td>
<td>GUILLÉTTE ET AL. (1994) AND SAFE (2000)</td>
</tr>
<tr>
<td>Gulls, terns, herons and other predatory birds</td>
<td>Feminization and other sexual abnormalities, thin walled eggshells</td>
<td>Polychlorinated biphenyls (PCBs), DDTs, DDEs</td>
<td>SAFE (2000) AND FRY (1995)</td>
</tr>
<tr>
<td>White-backed (Gyps bengalensis) and long-billed (Gyps indicus) vultures</td>
<td>Kidney failure leading to death. These species are on the verge of extinction in South Asia</td>
<td>Veterinary use of diclofenac</td>
<td>PROFFITT &amp; BAGLA (2004)</td>
</tr>
<tr>
<td>Daphnia pulex</td>
<td>Impaired reproduction</td>
<td>Simazine</td>
<td>FALCONER ET AL. (2006)</td>
</tr>
<tr>
<td>Ewes/sheep</td>
<td>Infertility</td>
<td>Observed in sheep that were grazed in clover pastures rich in phytoestrogen. Formononetin in clovers is primarily held responsible</td>
<td>ADAMS (1990)</td>
</tr>
</tbody>
</table>
In the Great Lakes area close to the Aamjiwnaang First Nations reserve near Sarnia, Ontario, Canada, fish with intersex gonads (both male and female) have been reported in Lake St Clair (Kavanagh et al. 2004). The Polluted Children, Toxic Nation study released by Environmental Defense (2006) reported that the abnormality in reproductive systems in this area may occur in humans as well, as indicated by declining boy to girl sex ratios. The study observed the accumulation of chemicals, such as PCBs and organochlorine pesticides (e.g. DDT) in residents. Of the reported chemicals, 23 are already listed as EDCs (Environmental Defense 2006). Declined sperm counts, sperm quality and sex ratios in Canada and the United States have also been reported (Allan et al. 1997; Safe 2000; Mackenzie et al. 2005). In Canada the sex ratio is generally reported to be 105 liveborn male births to 100 liveborn female \( (m = 0.512) \) (Allan et al. 1997). In Aamjiwnaang the sex ratio was reported to be \( m = 0.348 \) during 1999–2003 (Mackenzie et al. 2005). During 1970–1990 the proportion of Canadian males declined by 2.2 live births per 1,000 live births (Allan et al. 1997).

However, a number of studies have ruled out substantial changes in sperm counts and male reproductive capacity. Also many have suggested that association of organochlorines and xenoestrogens in female breast cancer is not likely (Safe 2000). Possible human health impacts from EDCs via drinking water have been refuted by several scientists as reported concentrations of those chemicals in water are much lower compared with phytoestrogens and other estrogenic compounds present in food sources (Safe 2000; Snyder et al. 2003). Thus there still remains a debate concerning the impacts of EDCs and xenoestrogens on humans and this glaring gap in knowledge clearly demonstrates the need for further research.

**REMOVAL OF EDCS AND PPCPS FROM DRINKING WATER: OZONE-BASED OXIDATIVE TREATMENT**

The removal or degradation of organic contaminants present in drinking water depends on several factors including source water quality, treatment processes and goals, and intrinsic chemical properties of contaminants such as molecular weight, relative hydrophobicity, aromatic carbon content and functional group composition (Westerhoff 2003; Jasim et al. 2006; Stackelberg et al. 2007). Conventional treatments such as coagulation, sedimentation and filtration have been found to remove less than 25% of most EDCs and PPCPs and are largely ineffective for removing dissolved organic contaminants (Westerhoff 2003; Vieno et al. 2006; Kim et al. 2007). Stackelberg et al. (2007) found that clarification process with ferric chloride (FeCl3) as coagulant accounted for the removal of only 15% of the average concentration of organic contaminants during drinking water production at a US drinking water treatment facility. The removal of diclofenac, ibuprofen, benzaflurbate, carbamazepine and sulfamethoxazole by ferric sulphate-assisted coagulation in both milliQ water and natural water was studied by Vieno et al. (2006). All the PPCPs studied showed poor removal (< 10%), except diclofenac (66%). Free chlorine and chloramines can treat a range of EDCs and PPCPs, mainly hydrophilic compounds (Stackelberg et al. 2007; Snyder 2008). However, free chlorine is much more efficient than chloramines at removing EDCs and PPCPs (Khiari 2007; Snyder 2008).

Advanced water treatment technologies such as ozonation, granular activated carbon (GAC) adsorption, and ultraviolet (UV) irradiation have shown promise in removing EDCs and PPCPs. For UV treatment, a typical disinfection dose of (5 – 50 mJ cm\(^{-2}\)) was found to be several orders of magnitude lower than doses required for the removal of most chemicals (Snyder et al. 2003; Westerhoff 2003; Khiari 2007; Snyder 2008). USEPA recommends GAC as the best available treatment for removal of many endocrine disrupting compounds including methoxychlor, endosulfan, DDT and polychlorinated biphenyls (USEPA 2001). However, there are several drug compounds with high water solubility and/or poor degradability that can be resistant to GAC (Jones et al. 2005). Iopromide, ibuprofen, naproxen and diclofenac, sulfamethoxazole and meprobamate are some compounds that were found to be recalcitrant for activated carbon removal (Khiari 2007). Powdered activated carbon (PAC) is less expensive than GAC but is labour intensive and is less efficient (USEPA 2001). However, PAC can be very useful in short-term applications such as for removal of pesticides after the first storm following their applications (USEPA 2001). Reverse osmosis (RO) and nanofiltration have been found to be highly
effective in removing EDCs and PPCPs (Snyder et al. 2006a; Snyder 2008). But they are very costly and a portion of the water is lost as brine. Disposal of brine is a significant problem (Snyder et al. 2005) and the finished water has a corrosive nature (Westerhoff 2003). Thus most drinking water treatment facilities are not likely to install RO (Westerhoff 2003).

A number of studies have shown that ozone treatment or ozone-based advanced oxidation treatment of water or wastewater can successfully reduce or eliminate EDCs and PPCPs. This paper discusses several aspects of ozone-based treatment and summarizes the results of selected previous studies. Ozone primarily is used for disinfection purposes in drinking water treatment. It can also bring secondary benefits including the removal of organic contaminants, colour, taste, odour, iron and manganese. Ozone (O₃) attacks organic contaminants either by direct reaction (as molecular O₃), or through the formation of free radicals, such as the hydroxyl radicals (·OH). O₃ is a selective oxidant; some organic contaminants are oxidized readily and others are not oxidized at all (Von Gunten 2003). On the other hand, the ·OH radical, the most powerful oxidant after fluorine, is non-selective and can oxidize a broad range of organic and inorganic compounds (Von Gunten 2003; Gultekin & Ince 2007). Oxidation of organic compounds by ozone or ·OH radicals results in the formation of simpler organic molecules that are readily biodegradable and may be withdrawn by biological filters (Von Gunten 2003; Rakness 2005).

The advanced oxidation process (AOP) involves the oxidation of target contaminants by ·OH radicals (Rosenfeldt et al. 2006). In ozone/hydrogen peroxide-based AOP, hydrogen peroxide (H₂O₂) initiates and propagates the decomposition of ozone, which in turn, generates ·OH radicals through a series of complex reactions that can increase the concentration of ·OH radicals (Rakness 2005). Thus AOPs may effectively remove organic compounds that are recalcitrant to ozone alone. Also ozone-based AOPs would cut down the reaction time and allow application of higher ozone dosages without leaving excessive ozone to be quenched at the outlet of the reactor (Von Gunten 2003). Increasing the reaction time after ozone addition or raising the pH can also enhance AOPs. However addition of H₂O₂ is cheaper than the other two options and is, therefore, most commonly used in drinking water treatment (Von Gunten 2003). AOPs are environmentally friendly as they neither generate substantial amounts of hazardous sludge nor transform pollutants from one phase to another (Gultekin & Ince 2007).

Ozone concentration, ·OH radical concentration and second order rate constants for the reaction of the target compounds with molecular O₃ (Kₒₒₒ) and ·OH radicals (Kₒₒ) are the three factors which govern the oxidation of target compounds during ozonation (Ternes et al. 2002; Von Gunten 2003; Huber et al. 2005). Chemicals containing phenolic groups, deprotonated amines and double bonds tend to show high oxidation rate constants with molecular O₃. Fortunately these functional groups are common constituents of many PPCPs (Mcdowell et al. 2005; Westerhoff et al. 2005; Rakness 2005). Generally compounds with Kₒₒₒ > 10⁴ M⁻¹ s⁻¹ can be considered as fast reacting with ozone and thus are expected to show rapid degradation during ozonation (Von Gunten et al. 2006). Second order reaction rate constants of some organic compounds and pharmaceuticals are listed in Table 3. High Kₒₒₒ values of carbamazepine, diclofenac, EE2, sulfamethoxazole and roxithromycin indicate that these pharmaceuticals will react with ozone quickly and undergo rapid transformation (Huber et al. 2003). On the other hand, compounds such as atrazine, geosmin, iproprimide, diazepam and ibuprofen have higher Kₒₒ values and lower Kₒₒₒ values, suggesting that AOPs would perform better in removing them.

Water matrices can also have a significant effect on oxidation of organic compounds. Dissolved organic carbon (DOC) and alkalinity of natural water control O₃ stability, and formation and scavenging of ·OH radicals (Von Gunten 2005). Also ozone stability depends on pH (Von Gunten 2005). It has been observed that ozone half-life is significantly higher in natural water with high alkalinity and low DOC compared with water with low alkalinity and high DOC (Acero & Von Gunten 2001; Huber et al. 2003). Typically ·OH exposure is lower at higher alkalinity due to the increased OH scavenging rate of carbonate, and higher at lower natural organic matters (NOM) concentration (Rakness 2005). Thus AOPs in natural waters with high ozone stability (that is low DOC and high alkalinity) can considerably increase the oxidation of O₃ recalcitrant...
<table>
<thead>
<tr>
<th>Compound/Class</th>
<th>Use</th>
<th>pKa</th>
<th>Reactive group</th>
<th>$K_{O3}(\text{M}^{-1}\text{s}^{-1})^*$</th>
<th>$K_{OH} \times 10^5 (\text{M}^{-1}\text{s}^{-1})$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>17α- Ethinylestradiol (EE2)</td>
<td>Steroid hormone</td>
<td>10.4</td>
<td>Phenol</td>
<td>$-7 \times 10^9$</td>
<td>9.8 ± 1.2</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Benzaafibrate</td>
<td>Lipid regulator</td>
<td>3.6</td>
<td>R-oxy group</td>
<td>590 ± 50</td>
<td>7.4 ± 1.2</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Anti-epileptic</td>
<td></td>
<td>Double bond</td>
<td>$-3 \times 10^5$</td>
<td>8.8 ± 1.2</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Anti-epileptic</td>
<td></td>
<td></td>
<td>0.75 ± 0.15</td>
<td>7.2 ± 1.0</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Dichlofenac</td>
<td>Analgesic</td>
<td>4.2</td>
<td>Aromatic amine</td>
<td>$-1 \times 10^6$</td>
<td>7.5 ± 1.5</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Analgesic</td>
<td>4.9</td>
<td></td>
<td>9.6 ± 0.1</td>
<td>7.4 ± 1.2</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Iopomide</td>
<td>X-ray contrast media</td>
<td></td>
<td></td>
<td>&lt;0.8</td>
<td>3.3 ± 0.6</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>Antibiotic</td>
<td>5.7</td>
<td>Aromatic amine</td>
<td>$-2.5 \times 10^6$</td>
<td>5.5 ± 0.7</td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Roxithromycin</td>
<td>Antibiotic</td>
<td>8.8</td>
<td>Tertiary amine</td>
<td>(4.5 ± 0.5) × 10^6</td>
<td></td>
<td>Huber et al. (2003)</td>
</tr>
<tr>
<td>Atrazine (ATRA)</td>
<td>Pesticides</td>
<td></td>
<td></td>
<td>6.0</td>
<td>3.0</td>
<td>Acero et al. (2000)</td>
</tr>
<tr>
<td>ATRA-imine</td>
<td>Degradation products of ATRA</td>
<td></td>
<td></td>
<td>&lt;1</td>
<td>1.7</td>
<td>Acero et al. (2000)</td>
</tr>
<tr>
<td>DEA</td>
<td></td>
<td>0.18</td>
<td></td>
<td></td>
<td>1.2</td>
<td>Acero et al. (2000)</td>
</tr>
<tr>
<td>DIA</td>
<td></td>
<td>3.1</td>
<td></td>
<td></td>
<td>1.9</td>
<td>Acero et al. (2000)</td>
</tr>
<tr>
<td>MTBE</td>
<td>Fuel additive</td>
<td>0.14</td>
<td></td>
<td></td>
<td>1.9</td>
<td>Von Gunten (2003) (at ambient temperature)</td>
</tr>
<tr>
<td>Geosmin</td>
<td>Algal product</td>
<td></td>
<td></td>
<td>&lt;10</td>
<td>8.2</td>
<td>Von Gunten (2003) (at ambient temperature)</td>
</tr>
<tr>
<td>2 Methylisoborneol (MIB)</td>
<td>Algal product</td>
<td></td>
<td></td>
<td>&lt;10</td>
<td>3</td>
<td>Von Gunten (2003) (at ambient temperature)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Antibiotic</td>
<td></td>
<td></td>
<td>0.4 × 10^3</td>
<td>4.1 ± 0.3</td>
<td>Vieno et al. (2007)</td>
</tr>
</tbody>
</table>

Estimated rate constants of PPCPs and EDCs that are expected to show high reactivity with molecular ozone

**Beta blockers**  
Beta blocker  
Amine  
$(1 - 10) \times 10^3$  
Huber et al. (2003)

**Fluoroquinolones**  
Antibiotic  
Amine  
$(1 - 10) \times 10^3$  
Huber et al. (2003)

**Macrolides**  
Antibiotic  
Amine  
$> 10^5$  
Huber et al. (2003)

**Sulfonamides**  
Antibiotic  
Amine  
$> 10^5$  
Huber et al. (2003)

**Tetracyclines**  
Antibiotic  
Phenol  
$(1 - 10) \times 10^6$  
Huber et al. (2003)

**Triclosan**  
Antimicrobial  
Phenol  
$> 10^6$  
Huber et al. (2003)

**Oxybenzone**  
Sunscreen agent  
Phenol  
$(1 - 10) \times 10^6$  
Huber et al. (2003)

**Estradiol**  
Hormone  
Phenol  
$10^6$  
Huber et al. (2003)

**Testosterone**  
Hormone  
Double bond  
$10^5$  
Huber et al. (2003)

**4-nonyl phenol**  
Detergent metabolite  
Phenol  
$(1 - 10) \times 10^6$  
Huber et al. (2003)

**Biphenol-A**  
Plasticizer  
Phenol  
$(1 - 10) \times 10^6$  
Huber et al. (2003)

$^* T = 20^\circ C.$
pharmaceuticals \citep{Huber2003}. Ozone stability in natural water is difficult to assess, as the effect of NOM is variable and unknown. It can act as both an initiator and an inhibitor of ozone decomposition and scientists are yet to be able to estimate the fractions of NOM responsible for promotion or inhibition of ozone decay \citep{VonGunten2003}. \textit{Huber et al.} \citeyear{Huber2003}, however, observed that, regardless of the water matrix, relatively low ozone doses \((0.5–2 \text{mg l}^{-1})\) are sufficient for complete transformation of pharmaceuticals with \(K_{\text{O}_3} > 10^7 \text{M}^{-1} \text{S}^{-1}\). In the case of AOPs, an initial \(\text{O}_3\) concentration similar to the DOC value of the water matrix might ensure availability of sufficient ozone for reaction with \(\text{H}_2\text{O}_2\) \citep{Zweiner2000}. In summary it can be observed that the overall efficiency of AOPs and ozonation would largely depend on the \(\cdot\text{OH}\) radical scavenging capacity of natural water, NOM content and type, and oxidation reaction kinetics of the targeted chemicals \citep{Zweiner2000, Huber2003, VonGunten2003}.

The removal of clofibric acid, benzaafibrate, carbamazepine, primidone and dichlofenac during drinking water treatment was investigated by \textit{Ternes et al.} \citeyear{Ternes2002}. While dichlofenac and carbamazepine were almost completely eliminated at an ozone dose of \(0.5 \text{mg l}^{-1}\), removal of clofibric acid was \(\leq 40\%\) even at elevated ozone doses of \(2.5–3.0 \text{mg l}^{-1}\). Moderate removal for benzaafibrate and primidone were observed with \(50\%\) removal at ozone doses of \(1.5 \text{mg l}^{-1}\) and \(1.0 \text{mg l}^{-1}\), respectively, and removals of \(>80\%\) at an ozone dose of \(5.0 \text{mg l}^{-1}\). Another study by \textit{Ternes et al.} \citeyear{Ternes2003} found X-ray contrast media such as iopromide, iopamidol, diatrizoate, and iomeprol were extremely recalcitrant at an ozone dose of \(5 \text{mg l}^{-1}\). Diatrizoate was the most recalcitrant compound showing only \(36\%\) removal even at \(15 \text{mg l}^{-1}\). 

\textit{Nakada et al.} \citeyear{Nakada2007} studied the removal of 24 PPCPs during sand filtration and ozonation at a STP. They observed that sand filtration was generally inefficient in removing the target pollutants. Ozonation on the other hand attenuated the concentration of the phenolic antiseptics, sulfonamide antibiotics and 17\(\beta\)-estradiol (E2) by \(80\%\) or above. \textit{Jasim et al.} \citeyear{Jasim2006} observed a \(67–96\%\) removal of atrazine following ozonation compared with only \(0–13\%\) removal in conventional treatment. Almost \(95\%\) elimination of all target antibiotics was achieved by \textit{Adams et al.} \citeyear{Adams2002} within 1.5 minutes with an \(\text{O}_3\) residual of less than \(0.05 \text{mg l}^{-1}\). \textit{Acero et al.} \citeyear{Acero2000} found that \(\text{O}_3/\text{H}_2\text{O}_2\) can significantly accelerate the rate of degradation of atrazine compared with \(\text{O}_3\) alone. While conventional ozonation with an ozone dose of \(2 \text{mg l}^{-1}\) took 30 minutes to reach \(60\%\) degradation, it took only 2 minutes to reach the same level of degradation when \(0.8 \text{mg l}^{-1}\) \(\text{H}_2\text{O}_2\) was combined with an ozone dose of \(2 \text{mg l}^{-1}\) \citep{Acero2000}. \textit{Zweiner & Frimmel} \citeyear{Zweiner2000} reported \(90\%\) removal of clofibric acid, ibuprofen and dichlofenac using a \(3.7 \text{mg l}^{-1}\) \(\text{O}_3\) dose coupled with \(1.4 \text{mg l}^{-1}\) \(\text{H}_2\text{O}_2\) and more than \(98\%\) removal at a concentration of \(5 \text{mg l}^{-1}\) \(\text{O}_3\) and \(1.8 \text{mg l}^{-1}\) \(\text{H}_2\text{O}_2\). \textit{Vieno et al.} \citeyear{Vieno2007} were able to reduce the concentration of most of their target compounds, which included beta blockers, anti-epileptic drugs and anti-inflammatory drugs, below the detection limit following an ozone dose of \(1 \text{mg l}^{-1}\). Ciprofloxin was found to be the most obstinate compound in their study \citep{Vieno2007}.

A PPCPs and atrazine removal study at the A.H. Week drinking water treatment plant in Windsor, Canada, found that, while conventional coagulation/flocculation/sedimentation and dual media filtration treatment were largely ineffective, ozonation followed by conventional treatment substantially enhanced the removal of carbamazepine, continine, caffeine and atrazine \citep{Hua2006a}. The mean elimination ranges for carbamazepine, continine, caffeine and atrazine were \(78–99\%, 83–93\%, 67–81\%\) and \(66–96\%,\) respectively \citep{Hua2006a}. \textit{Snyder et al.} \citeyear{Snyder2006b} studied the removal of 36 different EDCs and PPCPs in both surface water and wastewater using \(\text{O}_3\) and \(\text{O}_3/\text{H}_2\text{O}_2\). Ozone doses of \(1.25 \text{mg l}^{-1}\) or greater were found to be sufficient to achieve more than \(80\%\) removal of 22 compounds in surface water. Results of the study indicate that use of \(\text{O}_3/\text{H}_2\text{O}_2\) could reduce the contact time required by \(\text{O}_3\) alone. However, given sufficient contact time the overall removal using \(\text{O}_3/\text{H}_2\text{O}_2\) will probably not increase significantly and might even lead to a net decrease in contaminant removal \citep{Snyder2006b}. Addition of \(\text{H}_2\text{O}_2\) to \(\text{O}_3\) showed slightly higher removal for most compounds but for certain compounds, such as androstenedione, progesterone, testosterone, caffeine, metolachlor and pentoxifylline, overall removal was \(15\%\) lower compared with \(\text{O}_3\) alone \citep{Snyder2006b}. Also disinfection by \(\cdot\text{OH}\) radicals is poor compared with \(\text{O}_3\) and there is a
possibility of forming additional disinfection by-products (Snyder et al. 2006b; Wert et al. 2007).

To date little is known about the formation, fate, detection and toxicity of oxidation by-products of EDCs and PPCPs (Westerhoff 2003). Bromate, which does not undergo degradation in biological filters, is the only by-product of ozonation regulated in drinking water treatment (Von Gunten 2003). Huber et al. (2003) noted that typical ozone doses for removing fast reacting pharmaceuticals would not produce significant amounts of bromate. Although the target of the ozonation is to degrade the parent compounds to effectively reduce their biological activity, Vieno et al. (2007) noted that recent studies have observed that this goal might not always be achieved. Quinolone, which is primarily responsible for the pharmacological effect of ciprofloxacin, is not attacked by ozone (Vieno et al. 2007). Thus by-products of oxidation of EDCs and PPCPs are of concern since they might as well be toxic (Huber et al. 2003; Snyder et al. 2006b; Vieno et al. 2007).

**CHALLENGES POSED BY EDCS AND PPCPS TO THE DRINKING WATER INDUSTRY**

Currently there exist no regulatory guidelines to control the occurrence of EDCs and PPCPs in the environment. Moreover, a significant portion of the contamination is occurring from non-point sources. With growing public concern at the presence of EDCs and PPCPs in water, the drinking water industry faces a challenge as to which compounds should be treated and to what level they should be treated as maximum contaminant levels are not known (Jasim et al. 2006).

Extremely low concentrations of these compounds in the environment pose an analytical challenge (Snyder et al. 2005). Although there have been some recent advances in analytical methods (Westerhoff 2003), differing polarities and functionalities of various compounds still make it hard to identify them at a concentration range of μg l⁻¹ to ng l⁻¹. Moreover, very few laboratories have the necessary facilities to analyse them and costs can be substantial (Snyder et al. 2005). As these compounds have varying composition and physicochemical properties, their removal requires advanced treatment processes which would need significant capital investment and skilled labour, and the public may not be willing to pay for the extra cost for risks that have not been well established (Snyder et al. 2005). Furthermore, contamination will vary from region to region and will probably change with time as well, depending upon the use of specific chemicals or medicines. For example clofibric acid, a lipid regulator, is no longer widely used in North America and thus its occurrence in North American waters compared with Europe is sparse (Betts 2002; Boyd et al. 2003).

Ozonation and ozone-based AOPs have significant potential for removing EDCs and PPCPs from drinking water. Unfortunately, data on the efficiency of ozonation and advanced oxidation processes in removing these contaminants are not conclusive (Betts 2002). Moreover economically feasible ozone doses will probably form by-products that could also be toxic (Snyder et al. 2006b). However, as NOM concentration in natural waters is several magnitudes higher than trace contaminant concentrations, it is probably more prudent to prioritize research on by-product toxicity from NOM rather than those from trace contaminants (Snyder et al. 2006b). The cost of the operation of advanced treatment technologies might seem expensive even in some communities in the developed world. Thus advanced water treatment technologies for the removal of EDCs and PPCPs might seem a luxury for most developing countries as their water quality programmes are already combating a wide range of problems and are doing so in an economic environment that is severely restricted. Removal of EDCs and PPCPs can occur through natural phototransformation or biotransformation, which is increased considerably during summer (Vieno et al. 2007). For many hot climate countries where adequate sun is available for longer periods of the year, this could be a viable option for removal of EDCs and PPCPs in lagoons and research should be directed towards how to maximize the photo-transformation of micro-pollutants using natural light.

Comparison of daily or life intake of pharmaceuticals via drinking water (2 litres per day over 70 years) with therapeutic doses indicates that the exposure levels are low and well below the dosages that can cause pharmacological effect (Webb et al. 2003). However, one potential concern is the presence of cytotoxic drugs such as anti-neoplastics (e.g. cyclophosphamide), which are carcinogenic, teratogenic
and risks may exist at any level of exposure (Webb et al. 2003). The use of therapeutic doses to estimate the risk thus may not be applicable to genotoxins such as cyclophosphamide (Webb et al. 2003). Moreover, at present, individual toxicity of a compound is considered while setting up drinking water guidelines, but the synergistic, long-term, low concentration effect of multiple organic compounds present in water is not known (Stackelberg et al. 2004).

Due to the soaring demand for water and depleting fresh water resources, artificial ground water recharge with STP reclaimed water is being considered in many parts of the world, in arid regions in particular. However, there is increasing concern that groundwater recharge would contaminate groundwater with EDCs and PPCPs (Betts 2002). Factors such as location of the treatment plant, treatment technologies used at the drinking water treatment facility and the relative degree of contamination of the source water greatly influence the contamination profile and concentration in finished drinking water (Metcalfe et al. 2004). Given the current paucity of data and the fact that the contamination from EDCs and PPCPs differs geographically and temporally, it is necessary that further research be directed to detect the level of occurrence of EDCs and PPCPs in raw water, to determine temporal and spatial factors influencing the contamination of raw water and effects of the treatment technologies used in the production of drinking water (Metcalfe et al. 2004).

EDCS AND PPCPS: IMPLICATIONS FOR GLOBAL ENVIRONMENTAL HEALTH

Contamination of the aquatic environment by EDCs and PPCPs has raised concerns over threats to public health and ecosystems. Such contamination can easily defy geographical boundaries and contaminate newer areas, as is the case with persistent organic pollutants. Some of the organochlorine pesticides, which are already banned in industrialized countries, are still being used to fight diseases such as malaria in developing countries. High levels of organochlorine pesticides have been identified in the environment and, also, in human breast milk in many developing countries (Kunisue et al. 2004; Minh et al. 2006). Concentrations (ng g⁻¹) of DDTs found in breast milk in Iran, China, Turkey and Mexico were 3–27 times higher than those found in countries such as Japan, Canada, Sweden and Germany (Kunisue et al. 2004). Often chemicals or drugs that are expired or have been banned from the market or fail to register in the industrialized countries find their way to markets in developing countries (Jamall & Davis 1991; Okeke et al. 1999). For example, between 1987 and 1989, manufacturers in the United States produced and exported nearly 5,000,000 pounds (2,290,000 kg) of the insecticides chlordane and heptachlor, which had already been banned in the United States (Jamall & Davis 1991). As most developing countries are still fighting more immediate problems such as water supply, sanitation, waste disposal, war and famine, in many of these countries the long-term risk of EDCs may not be seen as a pressing issue at the present time. Smith (2000) questioned ‘If malaria were killing a million people a year in North America and Europe, would the case for globally banning DDT be argued so forcefully?’ Thus to strike an optimum balance in meeting the goals of protecting human health and conserving the environment, it is necessary for the scientific community to look for low cost sustainable alternatives to these chemicals (Seagren 2005).

The reported incidences of hormone-related cancers are significantly higher in industrialized countries. For example, death from breast cancer is almost ten times higher in North America and Northern Europe compared with Asia and Africa (Sasco 2003). Incidences of hormone-related cancers are also increasing in the developing world but are probably under-reported. For example in Punjab, Pakistan, there has been a sharp rise in cancer patients in the area. Elevated serum levels of endocrine-disrupting pesticides were detected in farmers in the same area (Ejaj et al. 2004). Estimates show that there are about 20,000 deaths each year in the world due to acute pesticide intoxication, 99% of which probably take place in developing countries where only 20% of agro-chemicals are used (Jamall & Davis 1991; Vineis 2000). Pesticides have often been reported to induce immune dysfunction. Environmental estrogens have the potential to bioaccumulate in body fat and may subsequently amount to a considerable dose (Ahmed 2000). They may be released from body fat during starvation and can also enter infants during pregnancy or through breast milk. This could lead to a bi-directional interaction between
the immune system and the endocrine system. EDCs may alter the reproductive system, which in turn may affect the immune system and vice versa (Ahmed 2000). A significant portion of the population in developing countries is under the stress of malnutrition and infectious diseases. Environmental toxins would interact with malnutrition and infectious disease to magnify their individual impact and, also, the impact on the immune system (Jamal & Davis 1991).

Moreover, lack of a regulatory framework to minimize the exposure to chemicals exacerbates the pollution scenario in those regions of the world (Jamal & Davis 1991). Thus people in developing countries are often at higher risk of exposure to toxicants leading to adverse health effects (Craft et al. 2006).

One particular concern with PPCPs in water is the global rise of antibiotic resistance. Antibiotics may escape the STPs, find their way to the watercourses and increase resistance in natural bacterial populations (Jones et al. 2005). Tamiflu, the effective antiviral for avian influenza, can escape STPs and even UV radiation cannot substantially degrade it (Fick et al. 2007). Thus there is a concern that tamiflu and its metabolites (especially oseltamivir carboxylate) may be released into the aquatic environment and lead to increased resistance in the bird-flu virus. Poor quality antibiotics including degraded and expired antibiotics, misuse and overuse of antibiotics by physicians in clinical practice, misuse by the public, improper sales together with crowding and improper sewage disposal contribute to the development of antibacterial resistant strains in developing countries (Okeke et al. 1999). Also political unrest, abject poverty, mass migration and unhygienic environments with a lack of health care facilities nurture antibiotic resistance in those countries (Kapil 2005). This has increased the overall medical costs of communities due to frequent hospitalizations, longer hospital stays and elevated treatment costs. This increase in cost due to bacterial resistance is of greater consequence, notably in the developing countries where the economy is already overburdened. Resistant genes could very well be transported to other areas via watercourses and even through migration of people and tourists.

Industrialized nations, along the pathway of their development, have observed a shift in the epidemiological transition to the suite of chronic illness such as asthma, learning disabilities, congenital malformations and cancers as the leading causes of death (Suk et al. 2003). It is probably the exposure to synthetic chemicals in the air, water, soil and food chain that are contributing to the changing patterns of paediatric diseases, especially the increasing incidences of chronic diseases in children. The availability of cheap child labour, the lack of occupational and environmental protection in conjunction with constant export of hazardous chemicals and toxic wastes from industrialized countries to developing countries have placed children in those regions at a twofold risk of infectious diseases and chemical hazards (Suk et al. 2003). The health implications of the exposure to toxic chemicals for children is considerably higher compared with adults as their developing systems are more delicate and they might not be able to repair the damage that is triggered by early exposure to toxicants (Suk et al. 2003).

**CONCLUDING REMARKS**

The risk of water borne diseases still prevails in many parts of the world. Emerging technologies such as ozonation will probably not be able to totally replace chlorine as a water purifier and disinfectant (Shiru 2000). Although data on adverse impact of EDCs and PPCPs on humans via drinking water is not conclusive, as a precautionary principle we can say that our drinking water should be free of chemicals that have the potential to cause hormone disruption. Thus further research is warranted to study the occurrence and elimination of EDCs and PPCPs from drinking water. No single treatment process will be able to remove all contaminants from water and, therefore, multiple treatment systems would probably be required to achieve water treatment goals (Snyder et al. 2006b). Advanced water treatment technologies will also act as secondary barriers for drinking water contaminants, such as microorganisms, and might as well remove many other unknown chemicals that are yet to be reported (Botts 2002; Reynolds 2003). However, the cost of advanced treatment technologies must be justified before they are implemented.

Due to various socio-economic factors, the risk of exposure to chemicals causing endocrine disruption is significantly higher in developing countries. However, little
has been done towards addressing this issue, partly because they are still fighting with other immediate socio-economic and health-related problems. There is also a significant gap in scientific knowledge and awareness regarding the potential adverse impact of EDCs and their handling technologies. Thus in developing countries often the long-term risks posed by EDCs do not receive appropriate attention from the government and other concerned agencies. But it would not be pragmatic to ignore the long-term risks. Each society perceives and manages risks according to its own values and priorities (Craft et al. 2006). Therefore, the technologies to handle emerging contaminants such as EDCs and PPCPs will fail if passed to the developing countries without building the capacity to identify and perceive the ill-effects of EDCs. Research on EDCs should, therefore, be promoted in developing regions as well, and timely and appropriate assistance from developed countries is necessary.

The global nature of many environmental problems is becoming more and more evident. Thus a holistic international approach is necessary to fight the challenges of the emerging pollutants in water. It is indeed necessary to establish concerted international as well as local policies to ensure minimal exposure to EDCs, and also their limited and appropriate usage. Collaborative research should be undertaken to monitor high-risk groups to identify the pathways of exposure and potential adverse impacts. Appropriate drug disposal practices, manufacturing environmentally friendly chemicals, minimizing the overuse and inappropriate use of pesticides and drugs, and appropriate treatment of STP effluents are some options that could be considered to minimize pollution from EDCs and PPCPs. Effective communication and translation of the risks of EDCs and PPCPs in terms of individual regions or cultures, preparing experts in the relevant fields, education and formulation of policies that are compatible with local conditions would probably minimize the global risk.

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