Drugs in the environment: emission of drugs, diagnostic aids and disinfectants into wastewater by hospitals in relation to other sources – a review

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Abstract

After administration, pharmaceuticals are excreted by the patients into wastewater. Unused medications are sometimes disposed of in drains. The drugs enter the aquatic environment and eventually reach drinking water if they are not biodegraded or eliminated during sewage treatment. Additionally, antibiotics and disinfectants are supposed to disturb the wastewater treatment process and the microbial ecology in surface waters. Furthermore, resistant bacteria may be selected in the aeration tanks of STPs by the antibiotic substances present. Recently, pharmaceuticals have been detected in surface water, ground water and drinking water. However, only little is known about the significance of emissions from households and hospitals. A brief summary of input by different sources, occurrence, and elimination of different pharmaceutical groups such as antibiotics, anti-tumour drugs, anaesthetics and contrast media as well as AOX resulting from hospital effluent input into sewage water and surface water will be presented. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Pharmaceutical; Drug; Hospital effluent; Antibiotic; Cytotoxic; Antineoplastic; Diagnostic agent; Disinfectant; Anaesthetic; AOX; Gadolinium; Platinum

1. Introduction

1.1. Use

Several thousands of active ingredients are used for drugs in even more products. For example, about 50,000 drugs were registered in Germany for human use, 2700 of which accounted for 90% of the total consumption and which, in turn, contained about 900 different active substances (Glaeske, 1998; Kümmerer, 2001). In the UK, approximately 3000 active substances are licensed (Ayscough et al., 2000). In hospitals as well as in surgeries a variety of substances besides pharmaceuticals are in use for medical purposes as diagnostics and disinfectants. Besides the active substances, formulation adjuvants and, in some instances, pigments and dyes are also drug components. Disinfectants, in particular, are often highly complex products or mixtures of active substances. After application, many drugs are excreted non-metabolised by the patients and enter into wastewater. After their use and sometimes as residual quantities, diagnostic agents and disinfectants also reach the wastewater. Animal husbandry, i.e., veterinary use or use as growth promoters as well as use in aquaculture also discharges drugs and their metabolites as well as disinfectants into the environment through liquid manure and (waste) water or with storm water run-off from...
fields after application of manure. The substances may finally enter groundwater via soil after application of liquid manure or sewage sludge as fertilisers.

1.2. Occurrence in the environment and risk

It is often anticipated that pharmaceuticals are easily (bio)degradable in the environment, since they are transformed to some extent in humans. First findings of drugs in the aquatic environment were reported in the 1970s (Tabak and Brunch, 1970; Norpoth et al., 1973; Garrison et al., 1976). Some investigations showed the existence of drugs in public-owned treatment works’ (POTWs) effluents. They have been mainly carried out in the UK in the eighties (e.g., Fielding et al., 1981; Richardson and Bowron, 1985; Aherne et al., 1990). The concentrations measured in surface waters and STP effluents were in the ng/l to μg/l range (Table 1). Substances have been detected in effluents from sewage treatment plants as well as in the aquatic system, e.g., in small creeks and big rivers such as the rivers Rhine, Elbe, Neckar, Danube, Po, and others (Ternes, 1998; Klinger and Brauch, 2000; Zuccato et al., 2001) as well as lakes (e.g., Lake Constance, Swiss lakes) (Poiger et al., 2001), in ground water (Heberer et al., 1995; Scheytt et al., 2000) as well as the North Sea and the Adriatic Sea (Buser and Müller, 1998; Zuccato et al., 2001). Emissions from a landfill containing reminders from pharmaceutical production were also reported (Holm et al., 1995).

The detected compounds include a wide variety such as hormones, lipid regulators, pain killers, antibiotics, anti-cancer drugs and other cytotoxic compounds, anti-epileptics as well as those regulating blood pressure (Ayscough et al., 2000).

Tetracycline is one of the most important antibiotics used in agriculture. It was detected in topsoil (Hamscher et al., 2000) in high concentrations (20 mg/kg soil). This concentration is twice as high as the PEC set as a trigger value by the EU for the need of further investigations. Evidence of a wide variety of different active substances in the aquatic environment as well as in liquid manure (Böhm, 1996; Winckler and Grafe, 2000) and in the soil also shows that the active substances are at least not

Table 1
Detection of pharmaceuticals in the aquatic environment

<table>
<thead>
<tr>
<th>Active substance group</th>
<th>Wastewater</th>
<th>Surface water</th>
<th>Groundwater (GW), Drinking water (DW)</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics/ antiinflammatory agents</td>
<td>2.4</td>
<td>Up to 0.5</td>
<td></td>
<td>UBA (1997)</td>
</tr>
<tr>
<td>20</td>
<td></td>
<td>Up to 0.5</td>
<td>0.006 (DW)</td>
<td>Ternes (1998)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td></td>
<td></td>
<td></td>
<td>Heberer and Stan (1997)</td>
</tr>
<tr>
<td>Approx. 1</td>
<td></td>
<td></td>
<td></td>
<td>Hirsch et al. (1998)</td>
</tr>
<tr>
<td>0.1–1.7</td>
<td></td>
<td></td>
<td></td>
<td>UBA (1997)</td>
</tr>
<tr>
<td>Up to 1</td>
<td></td>
<td></td>
<td></td>
<td>Ternes (1998)</td>
</tr>
<tr>
<td>Lipid lowering agents</td>
<td>1.7</td>
<td>0.55</td>
<td>0.17 (DW)</td>
<td>Stan and Linkerhagner</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1992)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Ternes (1998)</td>
</tr>
<tr>
<td></td>
<td>Up to 1</td>
<td></td>
<td>7.5 (GW)</td>
<td>Heberer and Stan (1996)</td>
</tr>
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<td></td>
<td></td>
<td>Heberer and Stan (1997)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.07 (DW)</td>
<td>Stumpf et al. (1996)</td>
</tr>
<tr>
<td>Psychopharmacological agents</td>
<td>&lt;1</td>
<td></td>
<td></td>
<td>UBA (1997)</td>
</tr>
<tr>
<td></td>
<td>Up to 6.1</td>
<td></td>
<td></td>
<td>Ternes (1998)</td>
</tr>
<tr>
<td>Cytostatic agents</td>
<td>Upto 5</td>
<td>Up to 0.02</td>
<td></td>
<td>Aherne et al. (1990)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Up to 4*</td>
<td></td>
<td>Kümmerer et al. (1997a),</td>
</tr>
<tr>
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<td></td>
<td>Kümmerer (1998),</td>
</tr>
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<td></td>
<td></td>
<td>Steger-Hartmann et al.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1996)</td>
</tr>
<tr>
<td>X-ray contrast media</td>
<td>9*</td>
<td></td>
<td></td>
<td>Steger-Hartmann et al.</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td>(1998)</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>Hirsch et al. (2000)</td>
</tr>
</tbody>
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* Effluent from sewage treatment plants.
completely eliminated in sewage treatment or in the environment.

Drugs and disinfectants are applied, in contrast to many other chemical substances, because of their specific biological effect. Drugs used in veterinary medicine and husbandry for therapy as well as for prophylactic use and as growth promoters have been assessed (Montforts, 2001). Up to now there is not sufficient data available on the occurrence, fate and effects of drugs in the environment and the risks for humans and the environment possibly connected with (Römcke et al., 1996; Halling-Sørensen et al., 1998; Stuer-Lauridsen et al., 2000; Kümmener, 2001). According to present knowledge, for risk assessment most pharmaceuticals can be handled like pesticides. The mode of action should be taken into consideration when assessing effects of pharmaceuticals against organisms with standard tests. Some groups need special attention (Kümmener, 2001):

- Cytostatic agents and immunsuppressive drugs, because of their frequently evident carcinogenic, mutagenic or embryotoxic properties as well as other genotoxic compounds (e.g., some antibiotics).
- Antibiotics and disinfectants, because of their pronounced bacterial toxicity and their potential of fostering resistance.
- Hormones, because of their high efficiency/low effect threshold.
- Chlorophenols, chlorine-releasing reagents such as sodium hypochlorite, dichloroisocyanuric acid and others used as disinfectants and as bleaching agents or diagnostics such as organic iodine-containing X-ray contrast media because they contribute to the adsorbable organic halogen compounds (AOX). These are very often not biodegradable and spread widely in the aquatic environment and/or enter the food web.
- Heavy metals, e.g., as part of disinfectants and preservatives containing mercury, cytostatic agents containing platinum or MRI contrast media containing gadolinium, as they are not degradable and highly toxic in some oxidation states.

Other groups of drugs, for instance analgesics or sedatives, are also of interest. Barbiturates were reported to influence DDT-metabolism in fish. They also may modulate behaviour and predator–prey relations by lowering swimming velocity and influencing reaction times.

1.3. Sources of pharmaceuticals in the aquatic environment

For risk assessment as well as for risk management it is necessary to know the different sources of emissions of pharmaceuticals into the environment. For most compounds, data are still lacking related to their emission into the environment by different sources such as households or hospitals. Especially for hospitals, data on a nation-wide scale are scarce. The amounts of substances emitted by hospitals are often neglected when predicted environmental concentration (PEC) is calculated. Furthermore, the use patterns of pharmaceuticals are often quite different from the ones in households, i.e., the prescriptions by practitioners. Some antibiotics are used only in hospitals, others only prescribed by practitioners. Furthermore, use patterns of several compounds may vary within different countries. Vancocin, for example, is widely used as a first-line antibiotic in the USA. In Europe, it’s use is very restricted.

In this paper the emission and environmental impacts of antibiotics and cytotoxics, diagnostics and disinfectants by hospitals are described as important sources of the introduction of these substances into the aquatic environment. According to available data, biodegradation is more the exception than the rule. The release from hospitals is compared with other sources as far as data are available. This knowledge is important for risk assessment as well as for risk management. Data, mainly from German and European hospitals of different size and medical service spectrum, are used for this purpose.

2. Emissions by hospitals

2.1. Antibiotics

2.1.1. Medicine

In Europe, about 10,000 t of antibiotics are consumed per year (FEDESA, 1997). According to these data, 5000 t are due to veterinary purposes (prophylactic use, therapy approx. 3500 t, growth promoting approx. 1500 t). 5000 t are used in medicine. About 2000 t of antibiotics have been manufactured for different purposes in Germany in the early 1990s.

In 1999, approx. 411 t of antibiotics have been used for human applications, 105 t in hospitals. This accounts for 26% of the total consumption. Between 1994 and 1998, the total consumption increased by about 50 t. Considering the excretion rates, this would mean that the entire discharge volume of antibiotic agents into the wastewater is about 86 t from hospitals. The predicted concentrations of antibiotics in hospital effluents are in the range of the semi-maximum inhibitory concentration (MIC$_{50}$) of sensitive pathogenic bacteria for some active substances and especially for groups of active substances (0.1–2.9 mg/l). The development of resistance in biological films (i.e., in areas of high bacterial density), e.g., of sewage pipes or in activated sludge can therefore not be excluded. Concentrations measured for β-lactams in hospital effluents were 20–80 μg/l in hospital effluent during a day course (Cerovec, 2000). Hartmann and co-workers measured 2–83 μg/l of ciprofloxacin in the effluent of a large Swiss hospital (Hartmann et al., 1998).
The amounts of antibiotics emitted in total correspond to a mean antibiotics concentration in municipal wastewater approaching 50 μg/l. The part of active substance emitted unchanged is different in relation to its chemical structure. Tetracyclines, for example, are hardly discharged into the wastewater because of their high metabolic rate; moreover, they form relatively stable complexes with calcium ions.

Active substances represent a large proportion of antibiotics such as quinolones, nitroimidazoles or sulphonamides are of low biodegradability (Al-Ahmad et al., 1999; Kümmener et al., 2000a). Ingolfsen and Halling-Sørensen (2000) found that sulphonamides are even worse degraded than the recalcitrant pentachlorophenole. The results agree with the low biodegradability determined for other antibiotic agents in soil (Hübener et al., 1992; Marengo et al., 1997; Weersinghe and Towner, 1997). In tests with laboratory-scale sewage treatment plants, about 65% of ciprofloxacin was eliminated. 78% of this amount could be re-extracted from the sludge (Kümmerer et al., 2000c) indicating only bad biodegradation. Ciprofloxacin was eliminated by adsorption onto sediment in a test vessel (Bayer, 1991). For other compounds, adsorption to sewage sludge was reported (Möehle et al., 1999). Due to adsorption in activated sludge, it cannot be excluded that resistance and disturbance of the biological treatment processes can occur as well as of the sludge reconditioning, in soil or in sediments. In higher concentrations in test systems, effects against environmental bacteria have been observed (Wiethan et al., 2000). Fluoroquinolon carboxic acids are photolysed in aqueous solutions under environmental conditions (Burhenne et al., 1997a,b). This path of elimination is of no significance for ingredients of effluents from hospitals on the way to and in the wastewater treatment facility. Turbidity, water shading, and water depth, as well as the seasonal changes in sunlight exposure have a substantial impact on compounds in surface waters. Also, these substances may be sorbed by sediments and hence be no longer amenable to photochemical degradation (Kümmerer et al., 2001). Some β-lactams may hydrolyse until they reach the STP and surface water. Half-lives up to 200 days have been reported for some β-lactams (Christensen, 1998); for other β-lactams, half-lives of some days were found in test systems. Other antibiotics such as tetracyclines or quinolones have half-lives up to several hundred days in aquatic environments (Holten-Lützhof, 2000). After emission into the aquatic environment, compounds excreted as glucuronides can be cleaved by bacteria, gaining the unmetabolised compound (Möehle et al., 1999).

Reduction of used amounts by 50% seems to be possible for use in medicine by proper use as well as for farming-related applications (Harrison and Lederberg, 1998).

2.1.2. Veterinary medicine and husbandry

Antibiotics are also used in farming and in aquaculture for prevention, for therapy and as antimicrobially active substances to improve nutrient uptake in the gastrointestinal tract (growth promoters). Consumption in prevention and therapy is largely determined by modern animal breeding and fattening methods and conditions. In veterinary use, in total, 5000 t are used in Europe (FEDESA, 1997). Tetracyclines are by far the most important group for therapy and prophylaxis (FEDESA, 1997). Among the four growth promoters licensed in the EU, monensin and tylosin are the most important. Most of the compounds were used for pig and poultry fattening. Only a few percent of the total quantity is used for other species (cattle, calves, geese, etc.) (Winckler and Grafe, 2000). Tylosin is not authorised any more in the EU. Based on the data presented by Winckler and Grafe using total number of animals from the federal statistical agency (Statistisches Bundesamt), a total consumption of approx. 900 t can be estimated for Germany per year. Approximately 50% of the used amount is due to consumption as growth promoters. These figures are only rough estimations due to the lack of nationwide data. It was reported only recently by the Union of Concerned Scientists (2001) that more than 70% of veterinary antibiotics consumption in the USA is as growth promoters. Up to now it is unknown which part of the used amount will end up in surface water by run-off from farmland after application of manure as fertiliser or in ground water after passage of the soil. Antibiotic agents are also used in aquaculture (fish farming) and for pets. They end up in sediments after application in aquaculture. Tetracyclines were not eliminated during the storage of the manure over a period of 120 days (Winckler and Grafe, 2000). Strong reduction of the use of growth promoters was already demonstrated in Sweden and Denmark. Developing and using vaccines is a successful way to use the need for antibiotics in aquaculture as has been demonstrated in Norway.

2.2. Cytostatic agents

Cytostatic agents are far below the quantitative relevance of other drugs. Seen from the aspect of potential impact on the environment, cytotoxics are an important group of drugs in terms of their risk potential for humans and the environment. These compounds are only used in medicine. Carcinogenicity, mutagenicity and fetotoxic properties are often well demonstrated (Skov et al., 1990). They are mostly used in hospitals. An increasing amount is prescribed by practitioners for out-patient treatment. For some important cytotoxics (ifosfamide and cyclophosphamide, Fig. 1) the amounts used were estimated to be 200–400 kg/yr in Germany (Kümmerer and Al-Ahmad, 2001). In different hospitals,
up to 5 kg/yr of a single substance were used. Some of the amount administered in hospitals is excreted at home into municipal sewage by out-patients. The amounts used in practical surgeries are not documented (Schwabe and Paffrath, 2000). The anticipated annual average concentrations nation-wide are a few ng/l in the wastewater and presumably below 1 ng/l in surface waters (Kümmerer and Al-Ahmad, 2001). Expected concentrations in hospital effluents are 5–50 µg/l in hospital effluents for single compounds. Concentrations measured during a 24-h course differed between a few ng/l and the µg/l range within a week indicating a high variability of the emissions.

It was shown that biodegradability of cytostatics is largely independent from the mode of action and the chemical structure. Most of the active substances investigated proved to have a low biodegradability. Out of 20 compounds only two met the criteria for inherent biodegradability (e.g., Kümmerer et al., 1996; Al-Ahmad et al., 1997; Kümmerer and Al-Ahmad, 1997; Steger-Hartmann et al., 1997; Al-Ahmad and Kümmerer, 2001; Kümmerer et al., 2000b,c). Therefore, the active substances are expected to pass unchanged through municipal sewage treatment plants and thus reach surface waters (Kümmerer et al., 1997b; Steger-Hartmann et al., 1997; Kümmerer and Al-Ahmad, 2001) as far as they are not eliminated by adsorption onto sewage sludge. To judge from the results, an elimination of the substances by adsorption (e.g., in activated sludge) may be expected only in a small number of compounds such as mitoxantrone and epirubicin (Kümmerer and Al-Ahmad, 1999). The elimination of ifosfamide in a sanitary landfill was investigated with a laboratory lysimeter. Up to 50% of the ifosfamide dissolved in the percolation water was eliminated under methanogenic conditions after 120 days (Schecker et al., 1998).

Due to their effective threshold in relation to bacteria, an impairment of the self-cleaning capacity of water or of the biological wastewater purification by cytostatic agents is not to be expected. Synergistic toxic effects of 5-fluorouracil with β-lactam antibiotics, cephalosporines, norfloxacin and other antibiotic agents against bacteria as described in the medical literature also occurred in the presence of wastewater from hospitals. This is due to antibiotic agents present in hospital effluents and, in lower concentrations, also in municipal wastewater. In tests with hospital effluents, the IC₅₀ was much lower than 1 mg/l as it was for 5-FU in tap water (>128 mg/l) (Kümmerer and Al-Ahmad, 1997). Effects against higher aquatic organisms such as fish or algae have not been studied intensively for these compounds up to now.

As the cytostatic substances occur in much higher concentrations in patients’ urine, a potential health hazard must be assumed for personnel entrusted with collecting the excretions of patients treated with cytostatics (Eitel et al., 2000). At the present state of knowledge, this risk is much higher than for the general population possibly ingesting these substances with drinking water. For this reason, collecting patients’ excretions is not recommended (Kümmerer and Al-Ahmad, 2001).

2.3. Anaesthetics

For inhalative anaesthesia, organic flouro(chloro) compounds are used. They are emitted into the atmosphere. They possess different ozone depletion potentials and global warming potentials (Langbein et al., 1999). For total invasive anaesthesia, amongst others, alkylphenol compounds are used. They are excreted into wastewater. The most important compound is propofol. Up to 10% is metabolised within a few hours to 2,6-diisopropyl-1,4-quinol (Fig. 2); (Guitton et al., 1997). The rate of the excretion of the unchanged drug is about 90%. Data for the total amounts used are not available. Both the metabolite and the mother compound are supposed to be biodegradable in sewage treatment plants. Data are not available, but it is known that simple phenols are well biodegraded in the environment.

![Fig. 1. Formula of some widely used cytotoxics: 5-fluorouracil, cyclophosphamid, ifosfamide, cis-platinum and carboplatinum (from left to right).](image1)

![Fig. 2. Metabolisation of propofol.](image2)
However, the role of the two isopropyl groups in the ortho position of the hydroxy group is open to question.

2.4. Disinfectants

Large quantities of disinfectants are used in hospitals for surface, instrument and skin disinfecting, in glue and size production and use, in food processing and others. If used for surface disinfecting, product ingredients almost inevitably reach the wastewaters. Alcohols and aldehydes as well as chlorine-containing compounds such as recalcitrant chlorophenols are used as active ingredients. Others release chlorine (see Section 2.6) e.g., chloramine T which exhibits a lower AOX-forming potential (Hahn et al., 1994). Quaternary ammonium compounds (QACs) are cationic microbicidal compounds which are important ingredients of widely used disinfectants for disinfection of surfaces (Russell et al., 1992). They are one of the most important active ingredients besides alcohol and aldehydes. The technical compound consists of homologues of different alkyl chain lengths. 12,349 t of QACs were sold in Germany in 1997, 777 t in Belgium, 21,450 t in France and 28,892 t in the UK (Statistisches Bundesamt, 2000). Detailed data of the use of QACs in the different sectors are not available. Concentrations of BzCl up to 6 mg/l have been measured in hospital effluents. 0.05–0.1 mg/l are expected for QACs in municipal sewage (Kümmerer et al., 1997a). From the concentrations measured in hospital effluents and the size of the hospital (in terms of beds in use), one can calculate that about 10–20 t/yr of BzCl are used by German hospitals (Kümmerer et al., 1997a). In a large Austrian hospital, about 900 kg/yr had been used before measures had been taken to reduce QAC use (Kümmerer et al., 1997a,b,c). Data are not available for the loads of other QACs emitted by the different sources.

For QACs, contradictory results were reported for elimination, biodegradability and toxic effects against micro-organisms in STPs as well as in biodegradability testing (Gerike et al., 1978; ECETOC, 1993; Sánchez-Leal et al., 1994).

QACs such as BzCl or didecyldimethylammonium chloride (DDMAC) (Fig. 3) form hydrophobic ion pairs in the presence of anionic surfactants such as LAS and SDS. The ion pairing changes the physical and chemical properties and the surfactant character is masked. The elimination rates of ion pairs are different from those of the individual components QAC and anionic surfactant. Sorption to sludge flocs also depends on other compounds present (Table 2) (Kümmerer et al., 2001). The improved elimination of QACs in the presence of LAS (Gerike, 1982) is probably not due to a better biodegradability of QACs in the presence of LAS, but to the higher lipophilicity of the ion pair and hence higher degree of sorption onto the sludge.

The nature of the inorganic counter ion influences the biodegradability (Janosz-Rajczyk, 1992). The same results were obtained for organic ions such as the surfactants linear alkylbenzenesulfonate (LAS) and sodium dodecylsulfate (SDS). The biodegradability of the organic anions was even worse in the presence of the QACs than the pure compounds (Kümmerer et al., 1998).

QACs are known to be effective against aquatic micro-organisms, even in low concentrations (Tubbing and Admiraa, 1991). An efficiency gap exists in relation to gram-negative bacteria (Russell et al., 1992). The dose–effect curve of benzalkonium chloride is very steep. An inhibitory concentration of $IC_{50} = 10$ mg/l and $IC_{100} = 30$ mg/l has been found for non-adapted activated sludge, whereas the figure was $IC_{77} = 100$ mg/l for adapted activated sludge (Bayer, 1995). Inhibitory effects against denitrifying bacteria have been measured with concentrations as low as 1–2 mg/l (Wagner and Kayser, 1991). Sánchez-Leal et al. (1994) found an EC50

![Fig. 3. Formula of two important quaternary ammonium compounds (QAC) used as disinfectants.](image-url)
of 0.2–18 mg/l in the Microtox™ test for QACs. They are likely to disturb the wastewater purification process (Augustin et al., 1982; Guhl and Gode, 1989). Hingst and co-workers found elevated prevalence of bacteria with less sensitivity against BzCl in STP effluents (Hingst et al., 1995). As a consequence of their low biodegradability, the Freiburg University hospital has largely eliminated products containing benzalkonium chloride or other QACs for a number of years. Therefore, the QAC concentration in the effluent from this hospital was much lower than in the ones from hospitals of comparable size and medical service spectrum and even smaller hospitals (Kümmerer et al., 1997b).

Alcohols and aldehydes are easily biodegraded in STPs. Aldehydes were reported to be present in a concentration of 4 mg/l which is supposed to affect bacteria present in the wastewater (Jolibois et al., 2001). Many others of the active substances such as chlorinated phenols are of low biodegradability.

2.5. Heavy metals

Concentrations of heavy metals in hospital effluents are comparable to the ones found in municipal sewage (Gartiser et al., 1994; Leppold, 1997). Concentrations of platinum, mercury and gadolinium are higher.

2.5.1. Platinum

Platinum can be discharged into various environmental compartments from a variety of sources (Lustig et al., 1997). Hospital effluents contain platinum from excretions by patients treated with the cytostatic agents cis-platinum and carboplatinum and others (Kümmerer et al., 1999). Platinum emission from dental surgeries are only of little importance as platinum is emitted as easily collectible particles. Because of its high price, most platinum-containing waters are collected in surgeries and dental laboratories. The platinum of cytostatic agents is excreted by the patients and reaches the municipal sewer system. The concentrations in 2-h mixed wastewater samples were between 20 and 3580 ng/l, with a daily average between <10 and 660 ng/l. Absolute emissions are lower in hospitals with fewer care services and of smaller size. The specific emissions per bed and year differ less than the concentrations, with values between 14 mg (low medical service spectrum) and 150 mg per bed and year (maximum medical service spectrum). Total platinum emissions into the public sewage systems via hospitals were approx. 14.3 kg/yr in Germany in 1996, which corresponds to 12% of total Pt emissions from cars and hospitals. 6% and 3.3% were estimated for the Netherlands and Austria, respectively (Kümmerer et al., 1999). Emissions from other sources such as electronic devices production, jewellery or glass manufacture, cannot be quantified at present (Helmers and Kümm erer, 1999). High concentrations have been found in sewage sludge of cities with a high degree of jewellery industries (Lottermoser, 1994).

2.5.2. Mercury

In spite of successfully reduced emissions into the aquatic environment in the past, mercury continues to be one of the heavy metals whose discharged volume is still too high. The discharge of mercury from public health institutions is attributable to preservatives containing mercury usually found in diagnostic agents (e.g., Thiomersal®) and active ingredients of disinfectants (Merbromin ( = Mercurochrome®), Nitromersol) as well as in diuretic agents such as mercurophyllin (Craig, 1986).

The mercury concentrations measured in the central wastewater channel of European hospitals of different sizes were between 0.04 and 2.6 µg/l (Gartiser et al., 1994; Leppold, 1997), corresponding to an annual load of approx. 220–250 g for big hospitals. As far as the skin disinfectant Mercurochrome® was concerned, it was shown that the administration of this agent at the Freiburg University Clinical Centre alone accounted for about 1–1.5% of the sludge contamination at the sewage treatment facility in 1996. Based on the volume of prescriptions collected by the national health insurance institutions in 1994, approximately 100 kg of mercury were used through Mercurochrome® in Germany, most of which is likely to have reached the wastewater during or after its application. Mercurochrome® was eventually replaced by mercury-free alternatives at the Freiburg University Clinical Centre (Kümmerer, 1998). Other sources can be broken thermometers. Using electronic thermometers instead will help to improve the safety for the personnel as well as to reduce mercury emissions.

Oxidising components of cleaning or disinfecting agents help to remobilise mercury in amalgam separators of dental treatment units (Kümmerer et al., 1997c). The remobilisation of mercury in amalgam separators with oxidising disinfecting components is expected to cause an additional mercury load of about 32.5 kg/yr in Germany. This appears to be little when compared with other sources and the quantities actually retained by mercury separators. The International Commission for the Protection of the River Rhine (IKSR) states in its interim report that the mercury concentration in surface water is still two to four times the value of the target specification. About 44% (of a total of 1.100 kg/a) of the point-to-point emissions originate from municipal wastewater (approx. 440 kg/a) (IKSR, 1994). The report expressly notes that further measures for reducing discharges from the municipal/public sector must be taken at the source, i.e., at the inlet site. The mercury load remobilised from dental amalgam through oxidising disinfecting components in amalgam separators accounts for an average of 7.3% of the public wastewater,
which could be lowered to 0.3% if disinfectants without oxidising properties were used (Kümmerer et al., 1997c). Part of the mercury emitted into the wastewater is also discharged together with the sludge; the proportion is unknown. From the medical point of view, the regular disinfecting of suction units of dental treatment units is unnecessary, although this is still done in many hospitals and private dental surgeries. Replacing disinfectants containing oxidising agents with disinfectants or cleaning agents without oxidising components could help to reduce the mercury emission into the aquatic environment to a substantial degree. In view of the significance of mercury in terms of environmental hygiene and the high toxicity of methyl mercury, biotically formed mainly in sediments or through different bacteria (Craig, 1986), this measure is reasonable and highly efficient in terms of the efforts involved.

2.5.3. The rare earth elements (REE) gadolinium, indium and osmium

Besides its application in medicine, gadolinium is also used in nuclear engineering and, together with other REE, in the production of colour screens. Due to its high magnetic moment, gadolinium is used in magnetic resonance imaging (MRI) in the form of organic complexes (Hammond, 1995). Gadolinium complexes typically used in MRI are gadodiamid and gadopentat (Fig. 4). The Gd-pentate complexes have also been used for tracer experiments in hydrology (Gutiérrez et al., 1997). Since only recently, the analogue complexes of indium are in use for MRI. Following administration, the organic complexes are very quickly excreted unchanged (>95% within 24 h; Nycomed, 1994). The gadolinium complexes are emitted into public sewage systems and into surface waters via the hospital wastewater. The concentrations measured in hospital effluents are in the range of a few µg/l to 100 µg/l (Kümmerer and Helmers, 2000). The natural background concentration of gadolinium in rivers is about 0.001 µg/l, peak concentrations of as much as 1.1 µg/l in the effluent from STPs have been measured (Bau and Dulski, 1996). Increased concentrations have been found in rivers in regions with high population density for Gd and also for In (Nozaki et al., 2000). Concentrations of Gd of 0.2 µg/l have been measured in rivers influenced by STPs discharge (Bau and Dulski, 1996). With 0.12–0.3 µg/l, the estimated average gadolinium concentration due to the emission of contrast media into surface waters in Germany is within this range, which suggests that the concentrations well above the natural background are in part due to the emission of contrast media containing gadolinium (Kümmerer and Helmers, 2000).

Falter and Wilken (1998) have measured between 0.3 and 1.9 mg/kg in waterworks sludges. Vivian (1986) found 0.6–2 mg/kg in sewage sludges; in own measurements 1.3 ± 0.05 mg/kg (n = 4) of dry substance were found. From the good correspondence of these data it may be assumed that there is no substantial enrichment in sewage sludge.

The Gd-containing contrast media were shown to be not biodegradable (Nycomed, 1994). Bau and Dulski (1996) suspect that the gadolinium complexes are stable enough to pass through municipal sewage treatment facilities. With a stability constant of K = 10^{23} the stability of Fe(III)–EDTA complexes is much greater than those of the appropriate gadolinium complexes (K = 10^{23}) (Falter and Wilken, 1998). However, since iron(III) salts are used as flocculation agents, gadolinium could be supplanted by Fe(III) from these complexes, with the effect that toxic Gd(III) is released. Gd^{3+} is very toxic to humans when not complexed. GdCl₃ may alter the susceptibility of hepatocytes to toxicity caused by certain chemicals (Badger et al., 1997) and induce macrophage apoptosis (Mizgerd et al., 1996). The short-term toxicity of the Gd-containing MRI compounds against aquatic organisms is low (e.g., EC_{10} in Ps. putida-growth inhibition test 870 mg/l; Nycomed, 1994). Bioaccumulation of Gd in carp was investigated by Tu et al. (1994). Reaction of Gd(DTPA)²⁻ with Zn²⁺ and Cu²⁺ (25% and 21% in equilibrium, respectively) is reported (Tweddle and Kumar, 1999). Both ions are present in wastewater.

2.6. AOX and iodised X-ray contrast media

The major mass carriers for the AOX in hospital effluents are most likely iodised X-ray contrast media, solvents, disinfectants, cleaners and drugs containing chlorine. Studies conducted at a number of German
hospitals have shown the AOX concentration in mixed daily samples taken at the discharge points into the public sewage system is in the range 0.13–0.94 mg/l (Ø 0.43 mg/l), but that the AOX contamination in wastewater part flows from individual sectors of hospitals can be substantially higher (Gartiser et al., 1994). In 24-h mixing samples from European hospitals, AOX concentrations varied from 1.1–7.76 mg/l (Haib et al., 1998). In general, the maximum contribution of drugs to the AOX is not above 11% (Kümmerer et al., 1998). Beyond that it is also known that the AOX concentration in the urine of persons not treated with drugs is very low. It is normally between 0.001 mg/l (Koppe and Stozek, 1993) and 0.2 mg/l (Schulz and Hahn, 1997). Due to the dilution effect, no substantial contribution from this source is consequently expected.

Chloramine T and other agents such as sodium hypochlorite or 1,3-dichloroisocyanuric acid form elementary chlorine which is responsible for the disinfecting effect of these substances. Organic halogen compounds are formed by reaction of chloride with organic wastewater compounds. An additional AOX in the wastewater will result. According to the literature, the AOX formation through chloramine T is, however, substantially lower than through other elementary chlorine formers such as sodium hypochlorite (Hahn et al., 1994). 4–6% of the latter generate AOX (Schulz and Hahn, 1997). This additional AOX pollution can be avoided by dispensing with chlorine-forming ingredients such as hypochlorite or 1,3-dichloroisocyanuric acid in cleaners and disinfectants, or in direct chlorine bleach. The disinfecting with active substances and electro-chemical procedures not splitting off elementary chlorine can also help to reduce AOX (Schulz and Hahn, 1997). PVP-iodine-based disinfectants do not contribute to AOX. Brominated organic compounds are negligible for the AOX in the effluents from hospitals. However, hospitals cannot be neglected as contributors to AOX in urban wastewater.

A surprisingly high proportion of AOI in the AOX was found in municipal wastewater. The organic iodine compounds may account for about 50% of the AOX as AOI input into municipal wastewater. Also, unlike the AOC1, it showed a pronounced weekly progression with minimal values at weekends. With reference to chloride, the proportion of AOI fluctuated between 23% and 53% of the total AOX. The proportion of AOI was particularly high when effluents from hospitals were discharged (Jekel and Wischnak, 2000). During the examination of the distribution of the molecular weight of the water ingredients detected with organic sum parameters, it was found that 80% of the organic substances in the AOI belong to the low molecular fraction (mol. mass below 1000; Jekel and Wischnak, 2000). The molecular weights of most organic iodine X-ray contrast media are in the range 700–900. Surveys and comparisons with measurements have demonstrated that a large proportion of the AOX from hospital effluents is present as AOI (Ziegler et al., 1997; Erbe et al., 1998; Haib et al., 1998). This may be seen as an indicator that the AOI is mainly caused by X-ray contrast media. Especially in hospitals with major radiological departments, iodised X-ray contrast media make a substantial contribution towards AOX. They are not easily and completely biodegradable (Kalsch, 1992) and have been detected even in the Lake Constance in concentrations up to 10 ng/l (Roßknecht and Hetzenauer, 2000) as well as in drinking water (Hirsch et al., 2000). About 360 t of iodised X-ray contrast media have been used in Germany per year (Jekel and Wischnak, 2000).

The AOI is not necessarily the greatest contributor to the AOX in the effluents from hospitals, instead, organic iodine compounds can account for about 50% of the AOX pollution (Haib et al., 1998). Since iodised X-ray contrast media are not only used in hospitals but also in practical surgeries, a substantial proportion of iodine in the public sewage system could be diffusely discharged through X-ray contrast media. Particularly when inexplicably high AOX values are measured, this could be an indication of a hospital with a radiological department, major radiological surgeries or may be a manufacturer of X-ray contrast media being the discharger.

Compared with other drugs, a particularly low general and local toxicity is specified for contrast media which are always given in high dosage. Contrast media are not allowed to have any intrinsic pharmacodynamic effects. This may be seen as an indicator that their discharge into the aquatic environment is less problematic under the aspect of human toxicity. Therefore, German authorities have agreed not to count AOI for the total AOX. This is seen under aspects of drinking water hygiene and possible long-term effects (e.g., products of photodegradation) not a sustainable approach. Due to their persistence and high solubility in water, contrast media will spread widely in the aquatic environment. Therefore, they ought to be discharged in the smallest quantities possible. The issue of how to assess contrast media with their high persistence and mobility in water in terms of ecotoxicology and environmental hygiene, as well as measures to reduce their environmental burden need to be investigated further.

References


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