Efficiency, costs and benefits of AOPs for removal of pharmaceuticals from the water cycle

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ABSTRACT

Different advanced oxidation processes (AOP) were developed for the treatment of highly loaded wastewater streams. Optimisation of removal and improvement of efficiency were carried out on a laboratory, semiworks and pilot plant scale. The persistent cytostatic drug cyclophosphamide was selected as a reference substance regarding elimination and evaluation of the various oxidation processes because of its low degradability rate. The investigated processes are cost-efficient and suitable regarding the treatment of wastewater streams since they lead to efficient elimination of antibiotics and antineoplastics. A total reduction of toxicity was proven by means of the umuC-test. However, in order to reduce pharmaceuticals from the water cycle, it must be considered that the input of more than 80% of the pharmaceuticals entering wastewater treatment systems results from private households. Therefore, advanced technologies should also be installed at wastewater treatment plants.

Key words | AOP, LC-MS/MS, ozone, pharmaceuticals, wastewater treatment

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INTRODUCTION

The detection of pharmaceuticals in the aquatic environment has led to many investigations on entry, residue, stability, and degradation of pharmaceuticals in different environmental compartments (Halling-Sorensen *et al.* 1998; Jorgensen & Halling-Sorensen 2000; Heberer 2002; Kümmerer 2004; Reemtsma & Jekel 2006). Elimination of organic micro-pollutants from wastewater is a major challenge in environmental technology (Huber *et al.* 2005; Joss *et al.* 2008). Numerous studies have shown that a multitude of pharmaceuticals, some of them with toxic, carcinogenic, endocrine or resistance promoting effects, are present in different aquatic systems (Kümmerer 2004; Joss & Ternes 2006).

It is known that the composition of hospital wastewater is comparable to municipal sewage. However, hospital effluents should rather be regarded as problematic wastewater streams because of their contamination with medicine, diagnostics, disinfectants and laboratory chemicals (DWA 2009; Heberer & Feldmann 2005; Ort *et al.* 2009). It is known from different studies that hospital effluents often show mutagenic and bacterial toxic characteristics (Hartmann *et al.* 1998; Jolibois & Guerbet 2005; Ferk *et al.* 2009). The reason for these properties is the presence of pharmaceuticals with mutagenic side effects such as antineoplastics used during chemotherapy and of certain antibiotics like fluorochinolones (Hartmann *et al.* 1998).

The active agents and their metabolites enter the sewer with the patients' excreta. According to estimative calculations and first measurements, the concentration of antibiotics in toilet effluents amounts to approx. 1 mg/L and the concentration of antineoplastics is in the range of 0.01–0.1 mg/L. It was found that the majority of pharmaceuticals are not sufficiently biodegradable in laboratory tests (Kiffmeyer *et al.* 1998; Kümmerer *et al.* 2000*a*,*b*). This is the reason why they are present in the same concentration range in inflows and effluents of wastewater treatment plants (WWTPs). Aside from WWTP effluents

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some of these persistent substances, or their metabolites, have also been identified in surface, ground and raw water of water works (Golet *et al.* 2001; Heberer 2002; Kümmerer 2004).

In order to minimise the release of micropollutants into the environment, a pilot plant for the investigation of different advanced oxidation processes (AOPs) was developed. AOPs offer a comparatively simple, efficient and cost-effective alternative for applications at direct and indirect dischargers. Especially economic criteria such as treatment costs per m^3 and per compound load accruing from hospitals and WWTPs will be compared for the different technologies.

MATERIALS AND METHODS

Chemicals

Acetonitrile (HPLC-grade) was purchased from LGC Standards (Wesel, Germany). Cyclophosphamide (CP), carbamazepine (CBZ), chloramphenicol (CAP), ciprofloxacin (CFX), sulfamethoxazole (SMX) and hydrogen peroxide were purchased from Sigma-Aldrich (Taufkirchen, Germany). High-purity deionised water was produced in house by an Elix 10–Milli-Q Plus water purification system (Millipore, Eschborn, Germany). 10 mg of the reference compound was dissolved in 20 mL water:acetonitrile (50:50, v/v) to prepare a stock solution with a concentration of 0.5 g/L. The calibration standards were dissolved in deionised water. Matrix calibration was done using a blank wastewater for diluting the stock solutions. The stock solutions were stored up to 3 months at 4°C, whereas the calibration solutions were freshly prepared every day.

Analytical methods

The samples were analysed directly by LC-MS/MS after filtration through a 0.45 μm cellulose acetate filter (Schleicher & Schuell, Dassel, Germany). The separation was performed on a 125 × 2 mm Nucleodur® 100-3 C18 EC column (Machery-Nagel, Düren, Germany) with an acetonitrile-water gradient of 0.1% formic acid in water (v/v) (phase A) and 0.1% formic acid (v/v) in pure acetonitrile (phase B) with a flow rate of 0.3 mL/min at 30°C. The pharmaceuticals were measured by an API 3000 triple quadrupole mass spectrometer (Applied Biosystems MDS Sciex, Darmstadt, Germany) equipped with a TurboIonSpray™ interface operating at 400°C in multiple reaction mode (MRM) in three periods in positive and negative mode with dwell times of 100 ms and a settling time of 700 ms. MS parameters are shown in Table 1 together with the limits of detection (LOD). Quantification was done by matrix calibration. Additional luminescent bacteria test and genotoxicity (umuC) were carried out in accordance with German DIN methods.

Equipment

Advanced oxidation processes using UV/H_2O_2 and ozonisation were evaluated and optimised from laboratory scale to pilot plant operation. A laboratory plant manufactured by Heraeus Noblelight (Hanau, Germany) was used to investigate the oxidative degradation of cytostatic drugs and antibiotics. The experiments included the assessment of different types and levels of UV-radiation (low pressure mercury lamp – Hg-LP–and medium pressure mercury lamp – Hg-MP), quality and quantity of oxidising agents (hydrogen peroxide and/or ozone) and treatment time.

Table 1 | MS/MS parameters and limits of detection of the investigated pharmaceuticals

	Orifice voltage (V)	Ring voltage (V)	Collision energy (eV)	Precursor ion (amu)	Product ion I (amu)	Product ion II (amu)	LOD* (μg/L)
Cyclophosphamide	31	60	31	261	139	233	0.2
Carbamazepine	91	120	25	237	194	192	0.2
Chloramphenicol	−76	−330	−24	322	152	257	0.5
Ciprofloxazin	56	340	27	332	288	245	2
Sulfamethoxazole	71	350	23	254	156	92.1	0.5

*LOD: limit of detection at a signal to noise ratio of 3:1.

Table 2 | Specifications of the used UV systems

Installation	Lamp character	Manufacturer	Identification	Reactor volume (mL)	Power (W)	Emission power (W)
Laboratory scale	Hg-LP	Heraeus	TNN 15/32	950	15	3 W (254 nm)
	Hg-MP	Heraeus	TQ 150	800	150	6.3 W (UV-A), 3.6 W (UV-B), 4.5 W (UV-C)
Semiworks	Hg-LP	UMEX	ABOX® 60–600 lg	200	25	8 W (254 nm)
	Hg-MP	UMEX	ABOX® MS 2	375	800	160 W (UV-C), 48 W (UV-C, $<$190 nm)
Pilot plant	Hg-LP	Wedeco	XLR 10/IQ	1,600	80	8 W (185 nm), 32 W (254 nm)
	Hg-LP	IBL	IBL-UV-2 KW	800	2,000	140 W (UV-A), 160 W (UV-B), 300 W (UV-C)

In addition, experiments on a semiworks scale were carried out (IBL Umwelt- und Biotechnik GmbH, Heidelberg, Germany). The volume of the plants ranged from 800 to 950 mL (laboratory plant) and from 4 to 6 L (semiworks plant), respectively. In order to thoroughly mix the wastewater and to improve sampling and temperature control, the wastewater was circulated by means of a peristaltic pump. The circulation of wastewater was also carried out inside the semiworks plant. Table 2 summarises the reactor specifications of the different UV systems.

A COM-CD-HF 2 ozone generator (115 g ozone per m^3 and 0.04 Nm^3/h volume flow rate) manufactured by Anseros (Tübingen, Germany) was used to achieve ozonisation at laboratory scale. Ozone experiments on the semiworks scale were carried out on site at Wedeco AG (Herford, Germany). Instead of porous glass diffusers at the laboratory reactor and the semiworks (1 and 4 cm diameter, respectively) the pilot plant was equipped with a pump-injector system for the efficient usage of the total ozone.

Figure 1 shows photographs of the installation of the Hg lamps in the different plants.

Sample collection and experimental

All experiments were carried out with wastewater of 14 toilets (urine, faeces, rinsing water and hand basin effluent). For the laboratory scale and semiworks collection and sedimentation were done in a 100 L barrel. Wastewater for the pilot plant was collected in a closed 1 m^3 settling tank, wherein the solids had been allowed to sediment for more than 24 h. After pumping the supernatant to the reaction tank (standard experiment: 230 L) it was spiked with 100 μg/L of each compound. To avoid interactions with acetonitrile of the stock solution, spiking of the experiments was performed with diluted water solutions (for example 23 mg of the investigated compounds were dissolved in 2 L deionised water and flushed to the filled reactor of the pilot plant).

The different tests were carried out in batch-treatment mode. Samples were withdrawn from the pilot plant at different times and the degradation of the compounds was measured by LC-MS/MS. Recovery rates from spiking were between 95% and 104%. Evaluation of the degradation efficiency was done relatively (c/c_0). Finally the sediments and the clean water (after control analysis) were released to the sewer.

RESULTS

First degradation experiments were carried out at laboratory scale (approx. 1 L) with a mixture of seven cytostatic drugs and six antibiotics in spiked toilet wastewater. These preliminary experiments show almost complete degradation of active pharmaceutical ingredients ($>$99%) as well as significant reductions of eco-toxicological characteristics (67% luminescent bacteria and 99% umuC) can be achieved (Türk 2007). Furthermore, experiments with different AOP variants and different experimental sizes were carried out and the previous described pilot plant was constructed. The selection of the investigated pharmaceuticals was done according to consumption data, environmental relevance and the worse oxidation efficiency for cyclophosphamide and chloramphenicol at the previous

Figure 1 | Photographs of the four different reactors for UV treatment in combination with H_2O_2. (a) laboratory reactor equipped with a Hg-LP-lamp, (b) semiworks equipped with a Hg-LP-lamp, (c) Hg-LP-lamp and (d) Hg-MP-lamp of the (e) pilot plant.

studies (Sayder *et al.* 2008). The measured removal efficiencies of the three investigated oxidation processes of the pilot plant are shown in Figure 2.

Regarding degradation time, ozone and the medium pressure mercury lamp (which requires the highest input of energy) are seven or six times faster than the application of the low pressure mercury lamp (which requires the smallest input of energy), respectively. Treatment times for 95% removal of these pharmaceuticals are shown in Table 3. The genotoxicity value (G_{EU} [−]) of the spiked wastewater before treatment was 48. Irrespective of the kind of treatment process used, the G_{EU} value dropped to 1.5 for each oxidation process. This indicates that the total genotoxicity of the samples was reduced

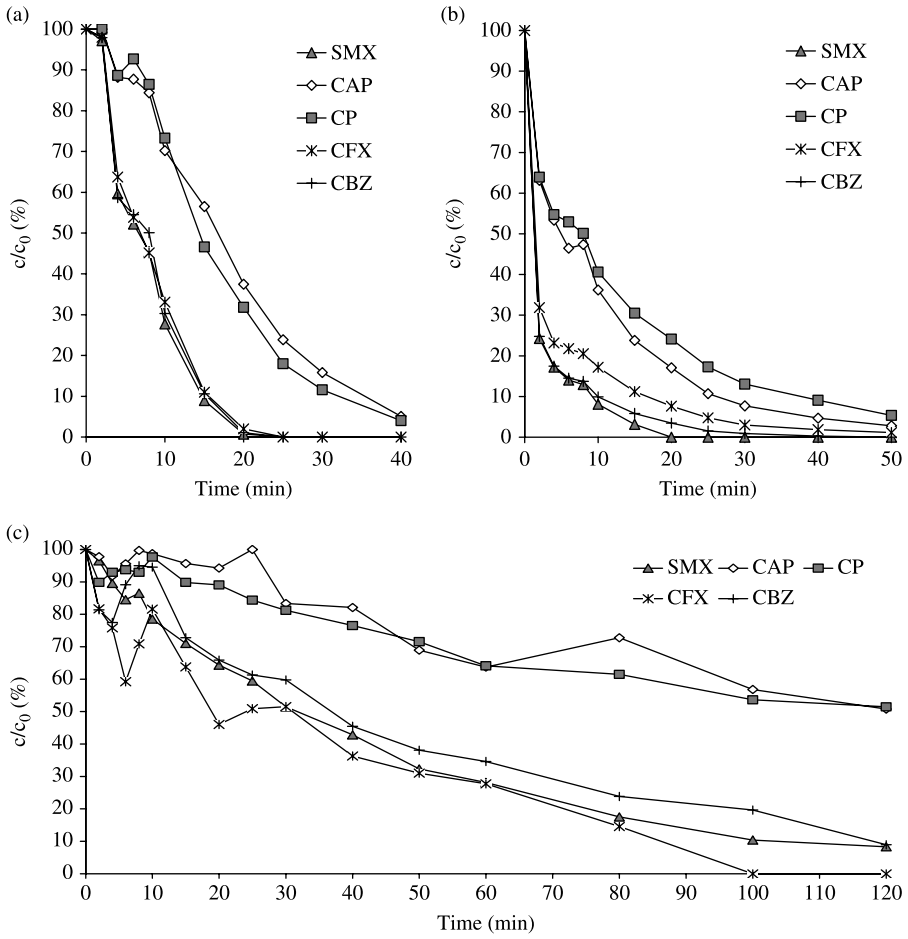

Figure 2 | Comparison of three different oxidation processes for the degradation of cyclophosphamide (CP), carbamazepine (CBZ), chloramphenicol (CAP), ciprofloxacin (CFX) and sulfamethoxazole (SMX) ($c_0 = 100\,\mu g/L$) in 230 L toilet wastewater at pilot plant scale. (a) Ozonisation, (b) Hg-MP, (c) Hg-LP.

by the advanced oxidation processes. Measurements of the spectral absorption coefficient (SAK) showed no correlation between TOC, COD and the degradation efficiency. TOC was between 8 and 40 mg/L and SAK between 20 and 80 m^{-1}.

The persistent cytostatic drug cyclophosphamide was selected as a reference substance regarding the evaluation of the various oxidation processes because of its low degradability rate. Standardised treatment times (minutes per litre wastewater) for the removal of 95% cyclophosphamide are compared for all processes in the following diagram (Figure 3).

Table 3 | Treatment times for 95% compound removal of the three investigated oxidation processes

	Treatment time for degradation of 95% (min)*				
Process	**CP**	**CBZ**	**CAP**	**CFX**	**SMX**
Hg-LP + H_2O_2	285	185	275	95	140
Hg-MP + H_2O_2	52	17	39	25	13
Ozone	40	18	40	19	18

*Based on 230 L wastewater.

The improved removal efficiency in the pilot plant is based on its optimised reactor geometry of the UV reactor. Thickness of the water film was reduced from 50 mm in the laboratory reactor to 5 mm in the pilot plant. Ozone was injected through a glass frit in laboratory and semiworks (1 and 4 cm diameter, respectively). In the pilot plant a pump-injector system was used for an effective ozone usage. During the degradation no ozone could be detected at the off gas of the pilot plant. Increased off gas ozone concentrations indicate the end of the process. Therefore

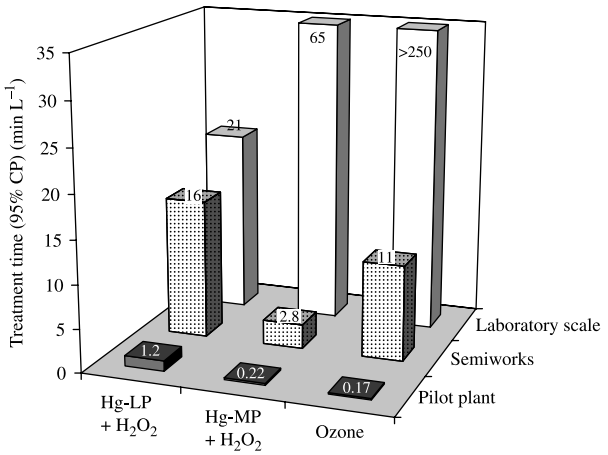

Figure 3 | Comparison of treatment times for 95% degradation of cyclophosphamide from toilet wastewater using three different oxidation processes from laboratory to pilot plant scale.

this parameter could be used for control of this batch process. In addition to the treatment time, economic parameters like consumption of chemicals, maintenance time and total costs are important for an investment decision. In order to improve comparability of the three oxidation processes the calculation of the treatment costs was based on four low pressure mercury lamps (4 × Hg-LP). This resulted in an improved maximum treatment volume of 2.6 m^3/d. On this basis Table 4 shows the detailed cost calculations for the three investigated oxidation processes and the dependence of specific costs and wastewater volume is shown in Figure 4.

Based on the calculations above, Figure 4 shows the dependence of specific costs per year and wastewater volumes for the three processes.

All investigated processes are suitable for the treatment of hospital wastewater. The specific and total costs of these treatment processes are comparable. Therefore, our results do not favour a specific process. The decision for one of the alternative processes has to be based on the detail requirements of a specific project. For example, removal of pharmaceuticals from wastewater at the hospital of Waldbröl, Germany, is done by biological pre-treatment using a membrane bioreactor (MBR) followed by an ozonisation unit (Beier *et al.* 2008).

Calculating the costs of removal per amount of toxic substance demonstrates the advantage of the direct treatment of highly loaded hospital wastewater. Because of available data for ozonisation of wastewater treatment plant effluents (Huber *et al.* 2005; Joss & Ternes 2006; Siegrist *et al.* 2009), the following comparison was carried out with the antibiotic sulfamethoxazole instead of the least degradable cytostatic drug cyclophosphamide. Based on the treatment times for SMX in Table 3 the costs for the removal of 1 g sulfamethoxazole from hospital wastewater using the developed pilot plant are in the range of 4.6 to 5.8 € (c_0 = 1,000 µg/L; 95% removal).

Additional elimination of sulfamethoxazole from the effluent of an activated sludge wastewater treatment plant can be calculated as follows. Median concentrations of SMX in the effluent of WWTPs range between 600 and 800 ng/L. Comparable removal efficiencies of approx. 95% for sulfamethoxazole were achieved for WWTP effluents using additional ozonisation with 600 to 900 mg O_3/g DOC at treatment costs between 0.04 and 0.14 €/m^3 (Joss & Ternes 2006; Siegrist *et al.* 2009). This results in estimated

Table 4 | Cost calculations for the three oxidation processes (based on 95% degradation of cyclophosphamide)

	4 × Hg-LP	Hg-MP	Ozone
Invest (€)	**34,100**	**28,100**	**41,000**
Annuity (12 years operation, 6% interest) (€/year)	4,067	3,352	4,902
Electric energy costs (0.10 €/kWh) (€/year)	876	2,398	648
Operation facilities (0.45 €/kg H_2O_2) (€/year)	431	515	–
Maintenance costs (3% of invest) (€/year)	1,023	843	1,233
Personnel (0.5 or 0.2 h/week, 40 €/h) (€/year)	1,040	1,040	416
Yearly costs for treatment of max. volume (€/year)	7,437	8,148	7,199
Treatment duration for 230 L toilet wastewater (min)	71	52	40
Max. treatment volume per day (m^3/d)	2.6	3.1	3.5

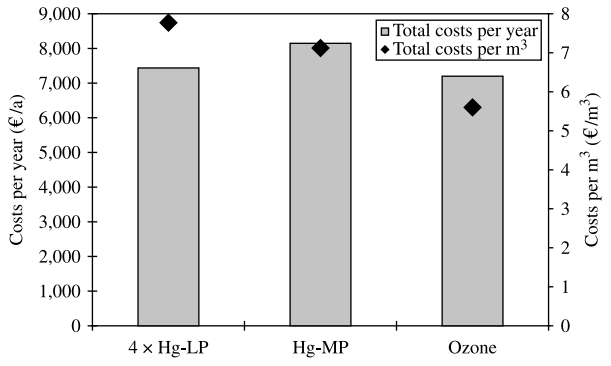

Figure 4 | Dependence of specific costs and wastewater volumes for the three processes.

total costs between 50 € and 200 € for the removal of 1 g active ingredient ($c_0 \approx 0.7$ mg SMX/m^3 → 1,429 m^3 × 0.14 €/m^3 = 200 €/g SMX removal).

A comparison of the specific costs for a single compound reveals that direct treatment is significantly cheaper than treatment of WWTP effluents. More detailed cost calculations for the application of ozone to hospital wastewaters and to WWTP effluents will be investigated within the next 2 years.

In contrast to the positive results for the removal of active pharmaceutical ingredients, it has to be mentioned that oxidative treatment technologies are not suitable for all relevant substances in hospital wastewater. Especially diagnostic compounds like iodated contrast media cannot be removed sufficiently. Figure 5 shows the treatment of amidotrizoic acid (diatrizoate), iopromide, iomeprol and iopamidol with a mercury medium pressure lamp in combination with continuous hydrogen peroxide addition.

Exclusive consideration of the specific LC-MS/MS results might lead to the conclusion that an effective degradation has occurred. However, if the sum parameter AOX (adsorbable organic halogens) is also taken into consideration it is obvious that only a transformation has taken place and that the triiodinated benzoic acid structure was not affected by the oxidative process.

Therefore, the developments of additional concepts or new removal processes for these diagnostic compounds are a task for prospective works.

However, in order to reduce pharmaceuticals from the water cycle, it has to be considered that the input of more than 80% of the pharmaceuticals entering wastewater treatment systems results from private households. Therefore, the adding of advanced technologies has to be considered to treat the discharge of biological WWTPs. Especially in cases where high concentrations are found and where the water body receiving the discharge is used for drinking water production, the installation of a micropollutant removal stage is highly recommended. Ozonisation as well as adsorption on activated carbon, which is more suitable for the removal of diagnostics, can be technically and economically feasible alternatives (Metzger *et al.* 2005; Joss *et al.* 2008).

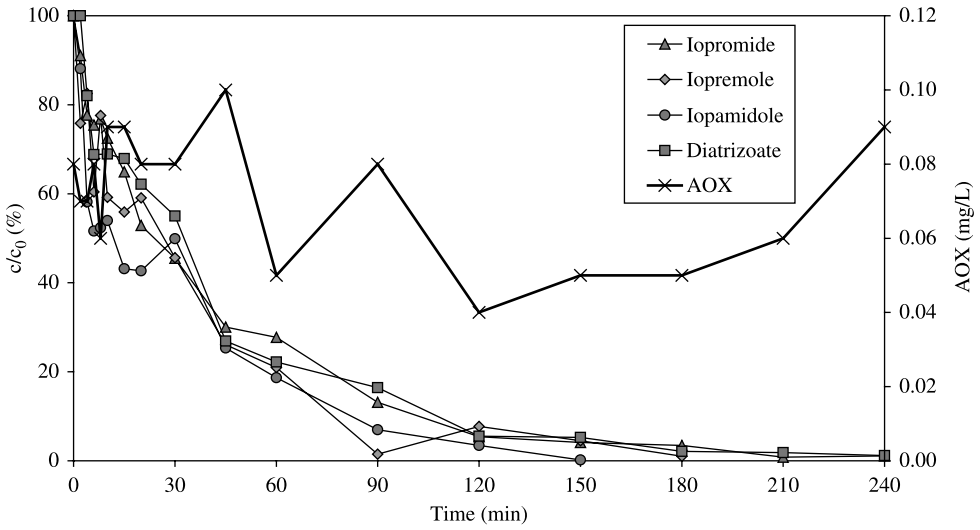

Figure 5 | Degradation curves of four different X-ray contrast media (100 μg/L) with Hg-MP and 32 g H_2O_2/h.

CONCLUSIONS

From laboratory to pilot plant scale, different advanced oxidation processes for the removal of pharmaceuticals from hospital wastewater have been applied and optimised. Low and medium pressure mercury lamps in combination with hydrogen peroxide and ozone were found to be suitable processes. These oxidation processes can be applied to complex matrices like (solids-free) toilet wastewater from hospitals. They offer a comparatively simple, efficient and cost-effective solution for the removal of micro pollutants at these important points of source (Lenz *et al.* 2007; Sayder *et al.* 2008).

A load comparison showed that it is significantly cheaper to eliminate the compounds directly in the hospital instead of treating effluents from WWTPs. However, in order to reduce pharmaceuticals from the water cycle, it has to be considered that more than 80% of the pharmaceutical input is caused by private households. Therefore, for an effective reduction of environmental loads, advanced technologies should be installed at the effluent of wastewater treatment plants especially if the water body receiving the discharge is used for drinking water production.

For the protection of the environment and due to economic reasons, high effluent loads of very effective and/or toxic drugs should additionally be treated before discharging them into the sewer. Therefore, we especially suggest the on-site treatment of toilet effluents from oncological and psychiatric hospitals.

Regarding the elimination of iodine containing contrast media, AOPs are not sufficiently effective. Alternative concepts or new removal processes for these compounds still have to be developed.

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