Removal of pharmaceutical residues using ozonation as intermediate process step at Linköping WWTP, Sweden

Christian Baresel, Jonas Malmborg, Mats Ek and Robert Sehlén

ABSTRACT

Pilot tests as basis for the design, implementation and operation of a future full-scale oxidation plant completing the existing sewage treatment in Linköping, Sweden, were performed. Using an ozonation step between bio-sedimentation and post-denitrification processes, the primary goal was the removal of the highest priority substances to effluent water levels that will not cause adverse effects in the recipient considering the natural dilution. The study included initial emission screenings, dose control trials, treatment performance studies and eco-toxicity studies. At an ozone dose of 5 mg O_3/L, most substances could be removed. Ecotoxicological tests showed no negative effect for the tested ozone doses. High levels of oxygen into the denitrification could be rapidly reduced in the biology. The number of bacteria in the treated water could be significantly reduced even at relatively low ozone doses. Based on these results, the planning for the full-scale implementation of the treatment system was initiated in 2015.

Key words | ecotoxicity, ozonation, pharmaceutical residues, waste water

Christian Baresel (corresponding author)
Mats Ek
IVL Swedish Environmental Research Institute,
Valhallavägen 81,
10031 Stockholm,
Sweden
E-mail: *christian.baresel@ivl.se*

Jonas Malmborg
Robert Sehlén
Tekniska verken i Linköping AB,
Box 1500,
58115 Linköping,
Sweden

INTRODUCTION

Pharmaceutical residues and other priority and emerging substances pass through most wastewater treatment plants (WWTPs) and end up in the receiving waters through the effluent and sludge spreading (Loos *et al.* 2013; Hörsing *et al.* 2014). For pharmaceutical residues and other emerging substances, emissions from WWTPs are the most significant source of loads on the receiving waters. Several studies have indicated concentrations in receiving waters above expected effect concentrations on aquatic organisms (Wert *et al.* 2007; Hollender *et al.* 2009; Wahlberg *et al.* 2010; Gerrity & Snyder 2011; Falås *et al.* 2012; Vasquez *et al.* 2014). These increased concentrations may also affect the aquatic food web and cause effects in higher organisms, including humans. Antibiotics in the WWTPs' effluent may contribute to the increase of antibiotic resistant bacteria. Furthermore, steroid hormones have a potent effect on the endocrine system of aquatic wildlife.

The EU Water Framework Directive (WFD) requires already today actions for a number of prioritised substances that are emitted to the aquatic environment. In July 2013, the European Parliament decided to include three pharmaceuticals in the 'watch list' of emerging pollutants that may be placed on the WFD priority list (Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy, European Parliament 2013). Switzerland has already introduced requirements for additional treatment for the reduction of pharmaceutical residues in larger WWTPs. Future defined environmental quality standards might lead to additional requirements for discharges from WWTPs.

Pharmaceuticals are designed for potent pharmacological effect and any chemical transformation is likely to reduce target potency. However, these substances are also designed against rapid degradation, making them persistent. Hence, traditional treatment processes of current WWTPs will have to be completed in order to remove pharmaceutical residues. Various removal technologies for this purpose have been evaluated in several large projects, such as REMPHARMAWATER (2003), POSEIDON (2004) and RiSKWa (2013). In Germany and Switzerland, advanced treatment technologies have been tested on a large scale (Abegglen & Siegrist 2012; ARGE 2013). Also in Sweden, the most promising technologies have been tested in pilot scale at WWTPs (Wahlberg *et al.* 2010; Ek *et al.* 2013a, 2013b, 2013c, 2014; Baresel *et al.* 2014). One of the processes that are recommended by these studies is the treatment with ozone. Generally, ozone treatment implies both a direct chemical reaction of the ozone molecule as well as

doi: 10.2166/wst.2016.045

indirect reactions with hydroxyl radicals, breaking specific chemical bonds within the targeted substances.

There exist several studies investigating complementary treatment by ozone (Wert *et al.* 2007; Abegglen *et al.* 2010; Stalter *et al.* 2010a, 2010b, 2011; Wahlberg *et al.* 2010; Gerrity & Snyder 2011; Reungoat *et al.* 2011; Altmann *et al.* 2012; Magdeburg *et al.* 2012, 2014; Arge 2013; Ek & Baresel 2013; Baresel *et al.* 2014, 2015a, 2015b, 2015c; Maus *et al.* 2014). Applied ozone doses range between these studies (0.3–1.2 g O_3/g dissolved organic carbon (DOC) or about 3–12 g O_3/m^3 water) and a sufficient removal of some substances could not be reported even at very high doses. One main disadvantage of ozone treatment, however, is the fact that the process does not completely degrade most substances. These may be transformed into other substances, normally without aromatic structures. Some of these metabolites might be more or less toxic. The formation of bromate and NDMA (*N*-nitrosodimethylamine) and their negative effects have, for example been indicated by several studies (Wert *et al.* 2007; Abegglen *et al.* 2010; Stalter *et al.* 2010a, 2010b; Gerrity & Snyder 2011; Magdeburg *et al.* 2012, 2014). An extra treatment step introduced after the ozone treatment in order to reduce the possible toxic oxidation products may or may not reduce such concentrations to acceptable levels, as shown by several of these studies. At the same time, some studies did not indicate any increase in toxicity (Altmann *et al.* 2012). A proper handling of this potential risk of creating toxicity and at the same time achieving an efficient removal of targeted substances is therefore an open research topic.

A pilot study was conducted by the Linköping Nykvarn WWTP owner Tekniska verken (Sweden) and IVL Swedish Environmental Research Institute. These tests with ozonation were planned as basis for the design, implementation and operation of a future full-scale plant at WWTP. The special requirements and prerequisites at this WWTP implied a solution that consists of an ozonation step between biosedimentation and post-denitrification processes. This setup may have the advantage that potential toxic oxidation products from the ozonation process could be reduced by the following biological treatment and so not reach the effluent. At the same time, possible interference of the ozone treatment with subsequent biological treatment processes had to be examined. The main goal was the removal of the highest priority substances to effluent concentrations that would not cause adverse effects in the recipient.

METHODS

In order to investigate ozonation as an intermediate treatment step to remove pharmaceuticals and other substances, tests with a pilot plant were conducted at Nykvarn WWTP during several months in 2014. The intended process configuration, as shown in Figure 1, was chosen to avoid the risk of increased effluent toxicity through

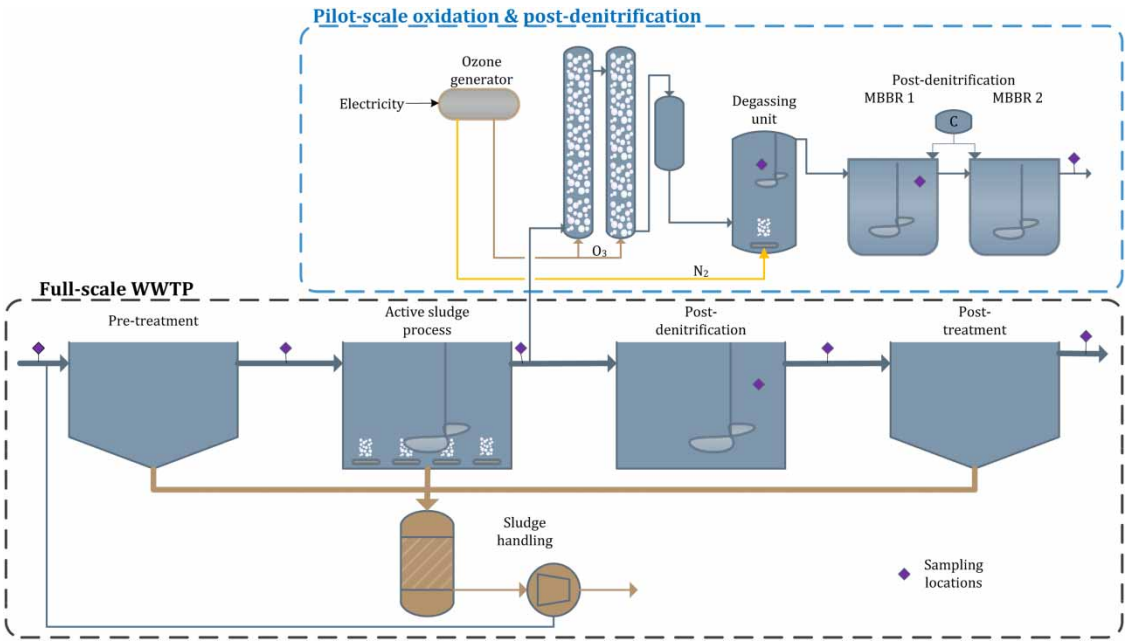

Figure 1 | Schematic layout of the investigated system including sample locations.

oxidation by-products. The Nykvarn WWTP is designed for 235,000 pe and the treatment process includes mechanical, chemical and biological treatment.

Experimental setup

The pilot ozonation plant was operated with effluent from the bio-sedimentation at a flow of 1.5 m^3/h. Ozone treatment equipment was provided by Wedeco (Xylem, EFFIZON GSO 10) consisting of oxygen production from air (pressure swing method), ozone generator, radiator, ozone destructor, ozone gauges, reaction vessels and degassing chamber. The ozone generator capacity was about 35 g O_3/h at a gas flow of 320 L/h (25 mg O_3/L or 2.5 g O_3/g DOC at an average DOC content of 10 mg/L). The tested ozone dosages were between 1.8 and 23.1 mg O_3/L (corresponding to 0.18–2.31 mg O_3/mg DOC). The reaction vessels consisted of two series-connected columns with downstream (column 1) and upstream (column 2) flow and ozone addition through the diffuser at the bottom of both columns. Each column had a volume of 115 L and a height of 4.2 m. The residence time in the reaction columns was kept constant at 11 min (at a rate of 1.5 m^3/h). A degassing column removed residual ozone. The ozone-treated water was passed into an equalisation tank to reduce dissolved ozone and oxygen. In a subsequent sampling tank, dissolved oxygen could further be reduced by stripping with nitrogen from the oxygen generator. From the sampling tank, water was going to the biological stage, which consisted of a functioning moving bed biofilm reactor (MBBR)-pilot for denitrification (Pilot-EDN). The full-scale denitrification (Ref-EDN) was used as reference. Here, carbon source and phosphoric acid were dosed corresponding to the full-scale operation (Ref-EDN).

Targeted substances

Investigated substances included 42 pharmaceuticals, which were selected based on earlier reported concentrations in Swedish wastewaters and their ecotoxicological effects (Table 1).

Pharmaceuticals were analysed using aliquots of 100 to 200 mL thawed composite samples that were spiked with

Table 1 | Investigated pharmaceutical substances and effects

No.	Substance	Mode of action	Nr	Substance	Mode of action
1	Amlodipine	*Antihypertensive*	22	Ketoconazole	*Antifungal*
2	Artemisinin	*Malaria medicine*	23	Ketoprofen	*Anti-inflammatory*
3	Atenolol	*Antihypertensive*	24	Levonorgestrel	*Hormone*
4	Bisoprolol	*Antihypertensive*	25	Metoprolol	*Antihypertensive*
5	Caffeine	*Stimuli*	26	Naproxen	*Anti-inflammatory*
6	Carbamazepine	*Sedative*	27	Norethindrone	*Hormone*
7	Cetirizine	*Antihistamine*	28	Norfloxacin	*Antibiotic*
8	Ciprofloxacin	*Antibiotic*	29	Oxazepam	*Sedative*
9	Citalopram	*Antidepressant*	30	Paracetamol	*Anti-inflammatory*
10	Diclofenac	*Anti-inflammatory*	31	Progesterone	*Hormone*
11	Doxycycline	*Antibiotic*	32	Propranolol	*Antihypertensive*
12	Enalapril	*Diuretic*	33	Ramipril	*Antihypertensive*
13	Estradiol	*Hormone*	34	Ranitidine	*Histamine-2 blocker*
14	Estriol	*Hormone*	35	Risperidone	*Antipsychotic*
15	Estrone	*Hormone*	36	Sertraline	*Antidepressant*
16	Ethinylestradiol	*Hormone*	37	Simvastatin	*Cholesterol-lowering*
17	Finasteride	*Prostate*	38	Sulfamethoxazole	*Antibiotic*
18	Fluoxetine	*Antidepressant*	39	Terbutaline	*Asthma medicine*
19	Furosemide	*Diuretic*	40	Tetracycline	*Antibiotic*
20	Hydrochlorothiazide	*Antihypertensive*	41	Trimethoprim	*Antibiotic*
21	Ibuprofen	*Anti-inflammatory*	42	Warfarin	*Anticoagulant*

50 μL internal standard carbamazepine-13C15N (2,000 ng/mL) and ibuprofen-D3 (2,000 ng/mL). One millilitre of 0.1 wt % ethylenediaminetetraacetate (EDTA-Na_2) dissolved in methanol:water (1:1) was added. Prior to extraction using solid phase extraction (SPE) cartridges (Oasis HLB, 6 mL, Waters), the sample was shaken. Cartridges were conditioned with methanol followed by Milli-Q (MQ) water. Thereafter, the samples were applied to the columns at a flow rate of two drops per second. The substances were eluted from the SPE cartridges using 5 mL methanol followed by 5 mL acetone. The supernatants were transferred to vials for final analysis on a high performance liquid chromatography triple quadrupole mass spectrometer (HPLC-MS/MS). The final determination of the amount of pharmaceuticals in the samples was performed on a binary liquid chromatography (UFLC) system with auto injection (Shimadzu, Japan). The chromatographic separation was carried out using gradient elution on a C18 reversed phase column (dimensions 50 × 3 mm, 2.5-μm particle size, XBridge, Waters, UK) at a temperature of 35 °C and a flow rate of 0.3 mL/ min. The mobile phase consists of 10 mM acetic acid in water.

From initial emission screenings, a priority list (Table 2) was established. It was based on the risk ratio of average effluent concentrations (environmental concentration (EC)) from the Nykvarn WWTP and the highest substance concentration at which toxic effects on the aquatic environment are not reported in literature (predicted no effect concentration (PNEC)). The sensitivity of the analytical method did not allow detection of steroid hormones at relevant concentrations. Previously reported data from Swedish wastewater formed a basis for concentration estimations of these compounds instead (see Table 2). PNEC was calculated considering various safety factors and an average dilution in the receiving water (the river of Stångån):

$$PNEC = \frac{NOEC \times Average\ dilution}{Safety\ factor}$$

where NOEC describes the reported no effect concentration. Safety factors, considering how many ecotoxicological studies that exist in literature for specific substances, were derived from the Swedish pharmaceutical database www.fass.se updated against the Wikipharma database and are according to EC (2003). Two acute and one chronic test using three different trophic levels give a factor of ×100. Two chronic and one acute test using three different trophic levels give ×50; three chronic tests using three different trophic levels

Table 2 | Priority list of pharmaceuticals with a risk EC/PNEC ≥ 0.01

	Substance	EC (μg/L)	NOEC (μg/L)	Safety factor	Dilution in recipient	EC/PNEC
High risk	Oxazepam	0.30	1.8	1,000	27	6.3
	Metoprolol	3.09	1	50	27	5.7
	Estrone*	<0.023	0.008	100	27	2.3
	Trimethoprim	0.14	0.29	100	27	1.9
	Ethinyl estradiol*	<0.158	0.00003	10	27	1.2
Moderate	Estradiol	<0.146	0.0004	10	27	0.9
	Propanolol	0.13	0.5	50	27	0.5
	Levonorgestrel*	<0.432	0.0008	10	27	0.5
	Diclofenac	0.48	0.5	10	27	0.4
	Amlodipine	0.09	10	1,000	27	0.3
	Carbamazepine	0.57	1	10	27	0.2
	Fluoxetine	0.01	0.029	10	27	0.1
Low risk	Paracetamol	0.26	30	100	27	0.03
	Estriol*	<0.08	0.075	10	27	0.02
	Caffeine	11.63	1,000	50	27	0.02
	Furosemide	0.78	142	100	27	0.02
	Naproxen	0.33	32	50	27	0.02
	Ciprofloxacin	0.06	1.2	10	27	0.02
	Citalopram	0.30	105	100	27	0.01
	Ibuprofen	0.28	10	10	27	0.01
	Atenolol	2.39	1,000	100	27	0.01
	Tetracycline	0.05	310	1,000	27	0.01
	Sertraline	0.03	9	50	27	0.01

*For ethinyl estradiol and levonorgestrel EC 0.1 ng/L was used; For estradiol EC 1 ng/L; For Estrone and Estriol EC 5 ng/L.

give ×10. In the absence of chronic tests, a factor of 1,000 was used. The dilution factor of 27 was calculated based on annual averages of WWTP effluent and stream flow measurements. If dilutions below this average factor occur, durations are short, which implies lower risk for possible acute and chronic toxic effects caused by effluent emissions.

The calculated risks were then defined as high for a risk ratio 1 or higher; in the range of 0.1–1, risk was considered moderate. Five substances (oxazepam, metoprolol, estrone, trimethoprim and ethinylestradiol) were classified as high-risk compounds and seven subjects were classified as moderate risk after the initial inventory (Table 2).

Selection of other substances to be evaluated in the study was based on previous surveys (Lilja *et al.* 2010), and European Parliament and Council Directive on priority substances (European Parliament 2013). This included organotin compounds (dibutyltin (DBT), tributyltin (TBT) and triphenyltin (TPhT)), phenolic compounds (4-nonylphenol, bisphenol A, triclosan), phthalate ester diethylhexyl phthalate (DEHP), the perfluorinated substance perfluorooctane sulfonate (PFOS), and polyaromatic hydrocarbons.

Further, coliform bacteria, *Escherichia coli* and antibacterial resistance were analysed. The IDEXX Collert-18 and standard SS-EN ISO 7899–2:2000 were used at an accredited Eurofins laboratory. Multi resistant bacteria tests included the determination of the presence of extended spectrum beta-lactamase (ESBL) forming *E. coli* and vancomycin-resistant *Enterococcus faecium* (VRE). For the quantitative determination, samples were filtered through 0.45-micron filters then placed on agar plates containing antibiotics. For the qualitative determination, enriched antibiotic resistant bacteria were spread on agar plates and colonies were then selected for resistance testing. Resistance testing was done using the standard methods of microdilution developed by the Clinical and Laboratory Standards Institute (CLSI 2013). Antimicrobial used (VetMic) is the same used for national monitoring of resistance state in healthy herds (SVA 2013). From water samples positive for ESBL and VRE, resistance patterns were determined for five colonies using VetMicTM GN-mo (version 4) and VetMicTM E-cocci (version 3) (SVA 2013). ESBL suspect colonies resistant to ampicillin (MIC> 16 μg/mL) and cefotaxime (MIC> 0.25 g/mL) were further confirmed by Sensititre custom EUVSEC2 plate (Oxoid AB, Sweden).

Toxicity tests included micro (green algae) and macro algae (red seaweeds), crustaceans (Nitocra), estrogen activity (YES test) and AMES genotoxicity tests (TA98, TA100 and YG7108). Activity test in the MBBR-system involved nitrification and denitrification rate tests of substrates from both pilot and full-scale denitrification processes. Nitrogen, phosphorus and organic carbon analyses using standard methods completed the study. For a more detailed description of sampling procedures and analysis methods, see Sehlén *et al.* (2014).

RESULTS AND DISCUSSION

At an ozone dose of 5 mg O_3/L there remained only one substance with a high risk (oxazepam, ratio 2) and two compounds with moderate risk (metoprolol, ratio 0.5 and estrone, ratio 0.13). To achieve an EC/PNEC ratio = 1 for oxazepam an ozone dose of about 6 mg O_3/L is required, as indicated in the complete dosage–response curve (Figure 2).

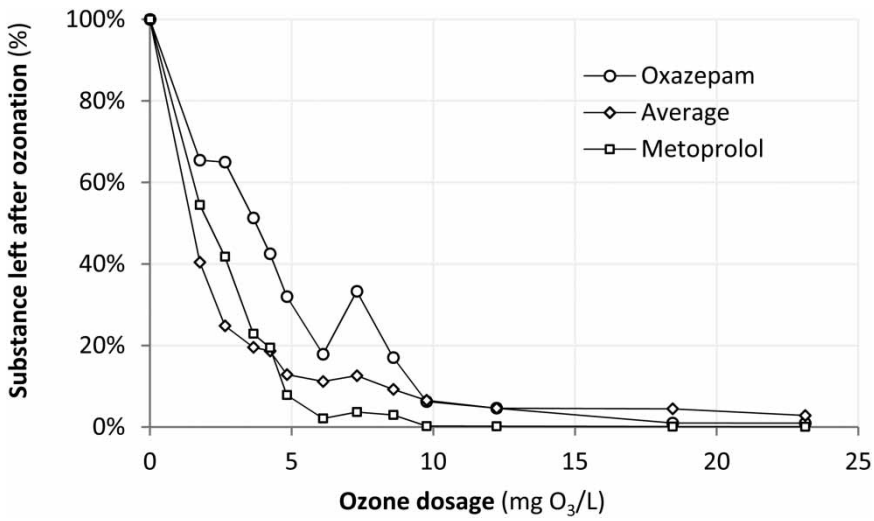

Figure 2 | Average reduction of pharmaceuticals at different ozone dosage compared with reduction of oxazepam and metoprolol.

The observed peak of oxazepam at the dose of 7.3 mg O_3/L is probably due to a load change during the experiment resulting in decreased reduction. At higher doses, the concentration of these substances can be reduced even more; however, also the risk of increased ecotoxicity caused by oxidation by-products increases. As these results are based on studies with real sewage, natural variations in loads to and performance of preceding process steps were naturally affecting the results. This was also observed in repeating tests. The presented results, however, provide a good base and agree with other recent studies with similar conditions (Baresel *et al.* 2015a).

Ecotoxicological tests at ozone doses of 9.8 and 18.4 mg O_3/L consisting of green and red algae, nitocra- and Ames-tests showed no negative effect for the tested ozone doses. Estrogenic activity tests showed concentration of 1.4 ng estradiol equivalents (EEQ)/L after the common biological treatment, which is in line with reported values in a well-functioning biological treatment system. An ozone dose of 9.8 mg O_3/L implied estrogenic activity below limit of quantification, in this case below 0.5 ng EEQ/L. After the final denitrification, estrogenic activity was below 0.1 ng EEQ/L. High levels of the carcinogenic compound bromate could not be detected at reasonable ozone doses. High levels of oxygen into the denitrification could be rapidly reduced in the subsequent biological treatment.

The number of bacteria in the treated water could be significantly reduced even at relatively low ozone doses. Levels of total coliforms measured before ozonation were for most samples above the method's limit of 2.4×10^6 cfu/100 mL. Also, levels of intestinal enterococci exceeded in many samples the determination limits of 1×10^3 or 2×10^3 cfu/100 mL (depending on sample). For *E. coli*, levels varied from 0.2×10^5 to 9.2×10^5 cfu/100 mL. The reduction of *E. coli* was dose-dependent down to about 3.5 log, but seemed to level off so that doses over 12 mg O_3/L provided no further reduction. Levels after ozonation were about 50 cfu/100 mL. The reduction of total coliforms and enterococci was lower, with a reduction of about 2 log for samples with measurable initial levels. Levels after ozonation were in the order of 1×10^4 down to a few cfu/100 mL. Multi resistant bacteria test indicated that antibiotic-resistant bacteria remained qualitatively after ozonation. However, VRE was reduced completely.

Performed activity measurements in the post-denitrification following the ozonation showed no negative effect. Denitrification rates measured were around 3.6 g N/(m^2·d) in both the reference line and the pilot MBBR at a load of 2.4 g N/(m^2·d). However, an increased availability of organic material, phosphorus and hitherto organically bound nitrogen could be detected at high ozone doses (18.4 mg O_3/L).

Figure 3 shows that the nitrogen removal during the test period was very good except during malfunctions of equipment (omitted values). The continuous monitoring in the pilot MBBR indicated no disturbances in the denitrification during the test period. Between days 63 and 95, online nitrate probes were moved to the inflow of the pilot MBBR. Although oxygen concentrations at the inflow to the pilot MBBR were about 10 mg/L, a nitrate reduction of about 70–80% was achieved (Figure 3).

The process configuration could further reduce bacteria in the order of one to two orders of magnitude at the proposed dose, and estrogenic effects were reduced more than

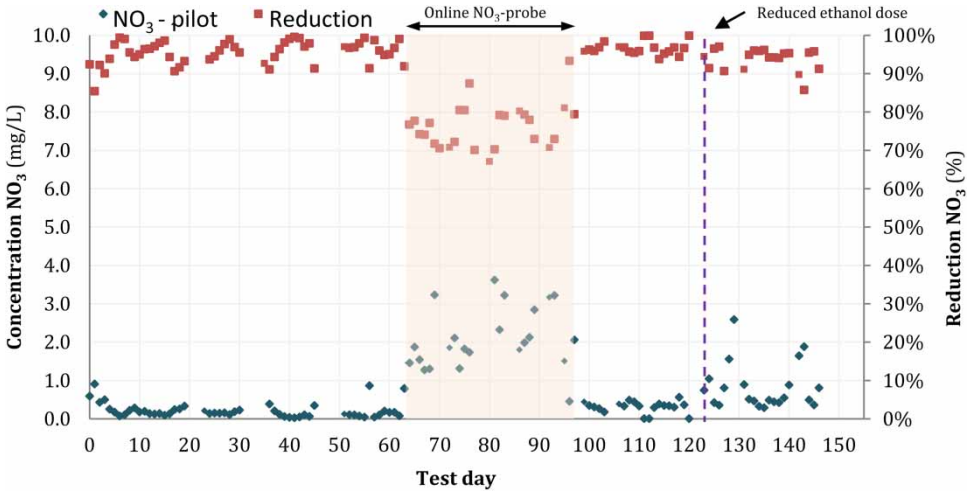

Figure 3 | Nitrate concentrations and nitrate reduction in the pilot MBBR during the project.

18-fold. In addition, other organic pollutants either can be reduced or are not adversely affected by ozonation in the proposed dosage range. The test further indicated that implementation of an ozonation step in the proposed process solution would not lead to increased toxicity to aquatic organisms.

CONCLUSIONS

The pilot studies show that ozonation, as intermediate treatment step, is a feasible option for the efficient removal of pharmaceutical substances that at the same time minimises the risk for harmful effects in the recipient by a biological post-treatment before discharge. A dose of ozone of 0.5–0.8 mg O_3/mg DOC was required to remove identified priority substances below the level of risk of adverse effects, except for a substance that is barely above risk ratio. No adverse effects have been found in red algae, green algae or Nitocra in the relevant dose range. The subsequent post-denitrification was also not adversely affected by ozonation. Nitrate purification worked well despite high oxygen concentrations in the incoming water after ozonation.

Results further indicate that the process design does not imply any other adverse effects in operation or general handling in the treatment. Moreover, the project showed that ozonation does not affect the subsequent biological process in any respect. Thus, there would be no need for a bacterial inoculation to maintain the biological activity.

REFERENCES

Abegglen, C. & Siegrist, H. 2012 Micropollutants from municipal wastewater. A method for further elimination in sewage treatment plants, Bundesamt für Umwelt; Bern, Umwelt-Wissen Nr. 1214, 210 S (in German).

Abegglen, C., Escher, B., Hollender, J., Siegrist, H., von Gunten, U., Zimmermann, S., Häner, A., Ort, C. & Schärer, M. 2010 Ozonation of treated wastewater for the elimination of organic trace substances. Large-scale pilot project Regensdorf (Switzerland). KA Korrespondenz Abwasser. *Abfall* **57** (2), 155–160 (in German).

Altmann, D., Schaar, H., Bartel, C., Schorkopf, D. L. P., Miller, I., Kreuzinger, N., Möstl, E. & Grillitsch, B. 2012 Impact of ozonation on ecotoxicity and endocrine activity of tertiary treated wastewater effluent. *Water Res.* **46**, 3693–3702.

Arge Spurenstoffe NRW, Teilprojekt 6 2013 Elimination of pharmaceuticals and organic trace elements: development of concepts and innovative, cost-effective cleaning method – Final Report for Phase 2 (in German).

Baresel, C., Ek, M., Harding, M. & Bergström, R. 2014 Treatment of biologically treated wastewater with ozone or activated carbon. IVL Swedish Environmental Research Institute Report B2203, Stockholm (in Swedish).

Baresel, C., Cousins, A. P., Hörsing, M., Ek, M., Ejhed, H., Allard, A. S., Magnér, J., Westling, K., Wahlberg, C., Fortkamp, U. & Söhr, S. 2015a Pharmaceutical residues and other emerging substances in the effluent of sewage treatment plants – Review on concentrations, quantification, behaviour, and removal options. IVL Swedish Environmental Research Institute, Report B2226, Stockholm.

Baresel, C., Dahlgren, L., Almemark, M. & Lazic, A. 2015b Municipal wastewater reclamation for non-potable reuse – environmental assessments based on pilot-plant studies and system modelling. *Water Sci. Technol.* **72** (9), 1635–1643.

Baresel, C., Dahlgren, L., Nikolic, A., de Kerchove, A., Almemark, M., Ek, M., Harding, M., Ottosson, E., Karlsson, J. & Yang, J. 2015c Reuse of treated wastewater for non-potable use (ReUse) – Final Report. IVL Swedish Environmental Research Institute, report B2219.

CLSI – Clinical, Laboratory Standards Institute 2013 *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals.* Approved Standard – Fourth Edition VET01-A4. Wayne, PA, USA.

EC European Commission 2003 Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk assessment for new notified substances, Commission Regulation (EC) 1488/94 on Risk assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part 2. Publication No. EUR 20418/EN/2.

Ek, M. & Baresel, C. 2013 *Ozonation for removal of pharmaceutical residues at Himmerfjärden WWTP.* IVL Swedish Environmental Research Institute, Report U4201, Stockholm (in Swedish).

Ek, M., Bergström, R., Magnér, J., Harding, H. & Baresel, C. 2013a *Activated carbon for the removal of pharmaceutical residues from the treated wastewater.* IVL Swedish Environmental Research Institute, Report B2089, Stockholm (in Swedish).

Ek, M., Bergström, R. & Baresel, C. 2013b *Separation of pharmaceutical residues with granulated activated carbon – Pilot tests at Himmerfjärden WWTP.* IVL Swedish Environmental Research Institute, Report U4492, Stockholm (in Swedish).

Ek, M., Baresel, C., Magnér, J., Bergström, R. & Harding, M. 2014 Activated carbon for the removal of pharmaceutical residues from treated wastewater. *Water Sci. Technol.* **69** (11), 2372–2380.

European Parliament 2013 European Parliament and Council Directive 2013/39/EU of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. *OJ L 226* **12/08/2013**, 1–17.

Falås, P., Andersen, H. R., Ledin, A. & la Cour Jansen, J. 2012 Occurrence and reduction of pharmaceuticals in the water phase at Swedish wastewater treatment plants. *Water Sci. Technol.* **66** (4), 783–791.

Gerrity, D. & Snyder, S. 2011 Review of ozone for water reuse applications: toxicity, regulations, and trace organic contaminant oxidation. *Ozone: Sci. Eng.* **33**, 253–266.

Hollender, J., Zimmermann, S. G., Koepke, S., Krauss, M., McArdell, C. S., Ort, C., Singer, H., von Gunten, U. & Siegrist, H. 2009 Elimination of organic micropollutants in a municipal wastewater treatment plant upgraded with a full-scale post-ozonation followed by sand filtration. *Environ. Sci. Technol.* **43**, 7862–7869.

Hörsing, M., Wahlberg, C., Falås, P., Hey, G., Ledin, A., Jansen, J. & la Cour Jansen, J. 2014 Reduction of pharmaceuticals in Swedish sewage treatment plants – Knowledge Compilation (in Swedish) (SVU-rapport No. 2014-16).

Lilja, K., Remberger, M., Kaj, L., Allard, A.-S., Andersson, H. & Brorström-Lundén, E. 2010 *Chemical and biological monitoring of sewage effluent water*. IVL Swedish Environmental Research Institute, Report B1897, Stockholm.

Loos, R., Carvalho, R., António, D. C., Comero, S., Locoro, G., Tavazzi, S., Paracchini, B., Ghiani, M., Lettieri, T., Blaha, L., Jarosova, B., Voorspoels, S., Servaes, K., Haglund, P., Fick, J., Lindberg, R. H., Schwesig, D. & Gawlik, B. M. 2013 EU-wide monitoring survey on emerging polar organic contaminants in wastewater treatment plant effluents. *Water Res.* **47** (17), 6475–6487.

Magdeburg, A., Stalter, D. & Oehlmann, J. 2012 Whole effluent toxicity assessment at a wastewater treatment plant upgraded with a full-scale post-ozonation using aquatic key species. *Chemosphere* **88**, 1008–1014.

Magdeburg, A., Stalter, D., Schlüsener, M., Ternes, T. & Oehlmann, J. 2014 Evaluating the efficiency of advanced wastewater treatment: target analysis of organic contaminants and (geno-)toxicity assessment tell a different story. *Water Res.* **50**, 35–47.

Maus, C., Herbst, H., Ante, S., Becker, H.-P., Glathe, W., Bärgers, A. & Türk, J. 2014 Guidance on the interpretation and design of ozonation plants for micropollutants elimination. Korrespondenz Abwasser. *Abfall* **61**, 998–1006 (in German).

POSEIDON 2004 Assessment of technologies for the removal of pharmaceuticals and personal care products in sewage and drinking water facilities to improve the indirect potable water reuse. Project reference: EVK1-CT-2000-00047. http://www.eu-poseidon.com.

REMPHARMAWATER 2003 Ecotoxicological assessments and removal technologies for pharmaceuticals in wastewaters. Project reference: EVK1-CT-2000-00048. http://www.unina.it.

Reungoat, J., Escher, B. I., Macova, M. & Keller, J. 2011 Biofiltration of wastewater treatment plant effluent: effective removal of pharmaceuticals and personal care products and reduction of toxicity. *Water Res.* **45**, 2751–2762.

RiSKWa 2013 Risk Management of Emerging Compounds and Pathogens in the Water Cycle. Bundesministerium für Bildung und Forschung (BMBF). http://www.bmbf.riskwa.de.

Sehlén, R., Malmborg, J., Baresel, C., Ek, M., Magnér, J., Allard, A.-S. & Yang, J. 2014 *Pilotanläggning för ozonoxidation av läkemedelsrester i avloppsvatten vid tekniska verken i Linköping AB*. IVL Swedish Environmental Research Institute, Report B2218 (in Swedish).

Stalter, D., Magdeburg, A., Weil, M., Knacker, T. & Oehlmann, J. 2010a Toxication or detoxication? In vivo toxicity assessment of ozonation as advanced wastewater treatment with the rainbow trout. *Water Res.* **44**, 439–448.

Stalter, D., Magdeburg, A. & Oehlmann, J. 2010b Comparative toxicity assessment of ozone and activated carbon treated sewage effluents using an in vivo test battery. *Water Res.* **44**, 2610–2620.

Stalter, D., Magdeburg, A., Wagner, M. & Oehlmann, J. 2011 Ozonation and activated carbon treatment of sewage effluents: removal of endocrine activity and cytotoxicity. *Water Res.* **45**, 1015–1024.

SVA – Statens Veterinärmedicinska Anstalt 2013 The National Veterinary Institute of Sweden. SVA. http://www.sva.se/en/Antibiotika/SVARM-reports/.

Vasquez, M. I., Lambrianides, A., Schneider, M., Kümmerer, K. & Fatta-Kassinos, D. 2014 Environmental side effects of pharmaceutical cocktails: what we know and what we should know. *J. Hazard. Mater.* **279**, 169–189.

Wahlberg, C., Björlenius, B. & Paxéus, N. 2010 Pharmaceutical residues in aquatic Stockholm – Presence, prevention, and treatment of sewage. Stockholm Vatten AB (in Swedish).

Wert, E. C., Rosario-Ortiz, F. L., Drury, D. D. & Snyder, S. A. 2007 Formation of oxidation byproducts from ozonation of wastewater. *Water Res.* **41**, 1481–1490.

First received 20 October 2015; accepted in revised form 12 January 2016. Available online 27 January 2016