Chemical and toxicological assessment of transformation product and by-product formation

Picture (optional)

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Title: Chemical and toxicological assessment of transformation product and by-product formation

Summary: The chemical and toxicological assessment of oxidation by-products and transformation products for various source water compositions is presented here within two case studies: A) Formation of by-products during UV and UV/H_2O_2 processes: effect of process conditions and water quality on the response of Ames fluctuation assays; and B) Ozonation kinetics of cetirizine, fexofenadine and hydrochlorothiazide and identification of their transformation products.

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Deliverable author(s):	Christa S. McArdell, Ewa Borowska, Marc Bourgin, Juliane Hollender, Urs von Gunten (Eawag) Cornelia Kienle (Ecotox Centre Eawag-EPFL) Roberta Hofman-Caris, Kirsten Baken (KWR)
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Summary

The formation of oxidation by-products and transformation products in oxidative treatment technologies needs to be evaluated in detail due to their potential toxicity. Within the deliverables D31.1 (Demonstration of design, application, controlling and long-term stability in wastewater oxidation technology) and D31.2 (Demonstration of design, application, controlling and long-term stability of drinking water oxidation technology), the application of ozonation for wastewater treatment and the application of ozone, O_3/H_2O_2 and UV/H_2O_2 in drinking water treatment have been demonstrated and discussed. The formation of oxidation by-products (bromate and *N*-nitrosodimethylamine (NDMA)) and transformation products has been investigated in detail at different treatment steps. The ecotoxicity of wastewater after ozonation and after a subsequent treatment step with biological activity such as sand filtration was assessed with a range of bioassays and is presented in D31.1. In the decision bases presented in deliverable D32.3 (Decision basis for implementation of oxidation technologies) different parameters of the various source water compositions that influence the efficiency of oxidation and the formation of by-products are discussed.

Therefore, in this report, we focus on two issues within the topic of "Chemical and toxicological assessment of transformation product and by-product formation" which have not been presented elsewhere:

1) Formation of by-products during UV and UV/H_2O_2 processes; effect of process conditions and water quality on the response of Ames fluctuation assays

2) Ozonation kinetics of cetirizine, fexofenadine and hydrochlorothiazide and identification of their transformation products: a study of specific transformation products and their toxicological effect

1 Formation of by-products during UV and UV/H_2O_2 processes; effect of process conditions and water quality on the response of Ames fluctuation assays

Previous research had shown that application of UV processes in water may result in the formation of byproducts which cause a positive response in Ames Fluctuation Assays. It was suggested that this response was caused by the formation of nitrogen containing aromatic compounds from the natural organic matter (NOM), as a result of the photolysis of nitrate. Therefore it was studied which factors affect the formation of such byproducts, using well defined laboratory conditions.

For this research Ames Fluctuation Assays were carried out, in which the concentrated sample is tested with two bacterial strains (TA98 and TA100), with and without liver extract S9. If these bacteria are affected they will show a color change. The number of positive wells obtained indicates the degree of mutagenicity of the sample.

For UV disinfection in general a UV dose ≤ 70 mJ/cm^2 is applied. In full scale disinfection processes no mutagenicity was observed. However, for advanced oxidation processes, based on UV in combination with H_2O_2, much higher doses are applied, which may result in the formation of mutagenic byproducts. For this research water was used of which it was known that it could give a positive response in an Ames Fluctuation Assay after irradiation with a higher UV dose than commonly used in disinfection processes, i.e. > 100 mJ/cm^2). By means of membrane filtration the NOM content of this water was increased, at the same time decreasing the nitrate and hydrogen carbonate concentrations. Later, these NOM, nitrate and hydrogen carbonate concentrations were adjusted for the experiments. The following parameters were tested:

- Type of UV lamp
- UV dose
- Nitrate concentration
- TOC concentration (NOM originally present in the water was concentrated and used)
- Presence of H_2O_2

It was found that low pressure (LP) UV-lamps did not cause a positive Ames response, regardless of the presence of H_2O_2. Medium pressure (MP) UV-lamps, however, caused an increasing number of positive wells with increasing UV dose. The Ames response increased with increasing nitrate concentration and/or increasing TOC concentration. The addition of H_2O_2 resulted in a lower number of positive wells. These results were statistically evaluated, showing the importance of the various parameters. The experimental results indicate that the formation of mutagenic byproducts depends on both nitrate and NOM concentrations. Former results already showed that probably aromatic nitrogen containing compounds are involved. Therefore, it is assumed that the mutagenic activity is caused by the photolysis of nitrate, which results in a rather complicated reaction scheme, involving all kinds of reactive compounds. Probably such reactive nitrogen reacts with NOM or photolysis products of NOM, resulting in the formation of compounds that cause this positive Ames response.

Although it still is not known which mutagenic compounds exactly are formed during UV irradiation of water, companies applying UV-processes can estimate whether or not the formation of such compounds is to be expected. If so, measures can be taken to prevent this formation, e.g. by lowering the concentrations of nitrate and/or NOM, or by excluding wavelengths of 200-240 nm (which cause the photolysis of nitrate). Furthermore, it has already been shown that GAC-filtration can effectively remove these mutagenic compounds. Such a filtration step in general is applied during treatment in order to remove the required excess of H_2O_2.

The detailed results are presented in a report that is available on the DEMEAU website:

Formation of byproducts during UV and UV/H_2O_2 processes; effect of process conditions and water quality on the response of Ames fluctuation assays

By Roberta Hofman-Caris and Kirsten Baken

KWR Watercycle Research Institute, The Netherlands

2 Ozonation kinetics of cetirizine, fexofenadine and hydrochlorothiazide and identification of their transformation products

In this study the efficiency of the ozonation was investigated for the abatement of three nitrogen-containing pharmaceuticals, two antihistamine drugs, cetirizine (CTR) and fexofenadine (FXF), and the diuretic drug, hydrochlorothiazide (HCTZ), in wastewater. Species-specific second-order rate constants for the reaction of these compounds with ozone were determined for the molecular and dissociated forms of the compounds. All three compounds are very reactive with ozone in the direct reaction (apparent second order rate constants at pH 7: $k_{O3,pH7}$ of $1.7 \cdot 10^5$ M^{-1} s^{-1}, $9.0 \cdot 10^3$ M^{-1} s^{-1} and 8.5 10^4 M^{-1} s^{-1}, for CTR, FXF and HCTZ, respectively). Transformation product (TP) structures were elucidated using liquid chromatography coupled with high resolution tandem mass spectrometry, also using isotope-labelled standards. For cetirizine 8 TPs, for fexofenadine 7 TPs and for hydrochlorothiazide 8 TPs were identified and their occurrence quantified. The main TPs of cetirizine and fexofenadine are cetirizine N-oxide and fexofenadine N-oxide, respectively, whereas for hydrochlorothiazide, chlorothiazide, formed by an electron transfer mechanisms, were found to be the main TPs. In the bacteria bioluminescence assay only during the ozonation of cetirizine the toxicity was slightly increased at very high cetirizine concentrations. The main TPs detected in bench-scale experiments were also detected in full-scale ozonation of municipal wastewater, while the parent compounds were eliminated > 90 % with 2 g ozone m^{-3}.

The detailed results are presented in a scientific paper that is currently (October 2015) ready for submission to an ISI-Journal:

Ozonation kinetics of cetirizine, fexofenadine and hydrochlorothiazide and identification of their transformation products

By Ewa Borowska[1,2], Marc Bourgin[1], Juliane Hollender[1,3], Cornelia Kienle[4], Christa S. McArdell[1*], Urs von Gunten[1,3,5*]

[1]*Eawag, Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf, Switzerland*

[2]*Silesian University of Technology, Faculty of Power and Environmental Engineering, Environmental Biotechnology Department, PL-44100 Gliwice, Poland*

[3]*Institute of Biogeochemistry and Pollutant Dynamics (IBP), ETH Zurich, CH-8092 Zurich, Switzerland*

[4]*Swiss Centre for Applied Ecotoxicology Eawag-EPFL, Überlandstrasse 133, CH-8600 Dübendorf, Switzerland*

[5]*School of Architecture, Civil and Environmental Engineering (ENAC), Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland*