Report by UWI doctoral researcher Fatima El-Athman (T6)

Project number: T6
First and last name of doctoral researcher: **Fatima El-Athman**
(Working) title of doctoral project: **Deiodination of iodinated contrast media in bank filtration of urban waters**
Name of supervisors: Prof. Dr.-Ing. Martin Jekel (TUB), Prof. Dr. rer. nat. Anke Putschew (TUB), Prof. Dr. rer. nat. Lorenz Adrian (UFZ Leipzig)

2. Description of doctoral project and research results achieved to date:

Motivation

Iodinated contrast media (ICM) are applied in high doses for medical examinations and are known for their stability concerning degradation in the aquatic environment [1]. ICM are found at much higher concentrations than any other pharmaceuticals in waste water, surface water and bank filtrate. They are persistent to deiodination in aerobic environments but side-chain transformations lead to various metabolites [2]. Field data from bank filtration transects demonstrate at least a partial deiodination in reducing soil/water environments [3] but the mechanism responsible for this deiodination is unknown. This project aims to examine the biotic and abiotic factors involved in the deiodination reaction of ICM.
Cultivation of the dehalogenating bacterial strain *Dehalococcoides mccartyi* CBDB1 with the ICM iopromide and diatrizoate has been tested and did not show any cell growth. However, the cultures and abiotic controls without inoculum showed a concentration decrease of the iodinated compounds with simultaneous iodide release [4]. Since the growth medium contained the corrinoid vitamin B_{12}, the abiotic deiodination in the presence of corrinoids was further investigated. Corrinoids are cobalt-organic complexes which are able to function as electron shuttles between a reducing agent and a halogenated electron acceptor [4]. Vitamin B_{12} and its precursor were found to be very strong catalysts for the reductive deiodination of ICM and other iodinated benzoic acid derivatives under oxygen free, reducing conditions [4]. Our experiments demonstrated a linear correlation between the corrinoid concentration and the deiodination rates of the ICM [4]. Further, we could show that the release of the three iodine atoms can be described by a consecutive first-order reaction with two partial iodinated intermediate products and three different rate constants (Figure 1) [5].

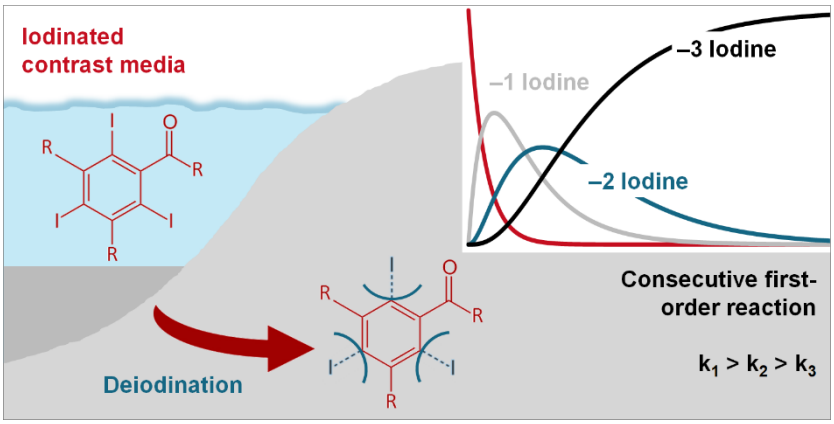

Figure 1: Scheme of the deiodination of iodinated contrast media

Experimental Methods

The ICM iopromide, iopamidol and diatrizoate as well as two different triiodobenzoic acids, 5-amino-2,4,6-triiodoisophthalic acid and three iodobenzoic acids are used as model compounds. All experiments are performed under oxygen free conditions within a glove-box (100% N_2).
Deiodination by microorganisms is tested with the dehalogenating bacterial strain *Dehalococcoides mccartyi* CBDB1 which has been cultivated before with hexachlorobenzene and titanium(III) citrate or cysteine as reducing agent. Over a period of several months, the deiodination of the iodinated compounds and the cell growth of the microorganisms are analyzed. The cell densities are quantified by staining the suspension with SYBR Green and subsequent direct epifluorescence microscopy.
Abiotic deiodination was tested with different electron shuttles, corrinoids and quinones, and with different reducing agents (e.g. titanium(III) citrate). Besides the influence of different reactants, influencing factors like concentration, temperature and pH value are investigated.
Iodinated compounds are quantified by LC-UV and iodide by IC-UV. Transformation products are identified by LC-MS.

Current State of Work

The experiments of this project are divided into biotic and abiotic tests. Biotic tests did not give evidence of a deiodination of ICM caused by microorganisms. Toxicity of ICM on bacteria strain CBDB1 could be excluded by tests with chlorinated compounds in the presence of ICM. Current experiments compare the dehalogenation and bacteria growth of CBDB1 using chlorinated and analogous brominated and iodinated compounds as substrate.
The project concentrated mainly on the abiotic deiodination catalyzed by free corrinoids. The influence of different types of corrinoids and of reducing agents as well as the concentrations of the compounds involved was investigated. Parameters like the redox potential, the temperature and the pH value were varied as well. Current tests are investigating the reaction kinetics over a period of several months. Single-iodinated benzoic acids show a significantly slower deiodination than the tested triiodinated compounds.

Future Work planned

Currently, the manuscript of journal paper 2 is in progress which focuses on the reaction kinetics of the corrinoid-mediated deiodination of ICM and other iodinated organic compounds. The results illustrate the three-stage deiodination reaction of the iodinated compounds. The values of the three rate constants of each partial reaction will be determined by modeling the reaction kinetics using the simulation tool AQUASIM.
Current cultivation tests compare the dehalogenation of chlorinated and brominated compounds with the not occurring deiodination of analogous iodinated compounds. The results of these tests and of previous biological experiments will be published in journal paper 3.

Collaboration

The biological experiments were conducted at the UFZ Leipzig with close collaboration and laboratory support by Prof. Lorenz Adrian and his group.
Some of the experiments were conducted within the anaerobic tent of the Chair of Environmental Microbiology of Prof. Ulrich Szewzyk (TU Berlin) with the help of Marcella Nega (N1). The Chair of Environmental Microbiology also lent us a microplate reader which was used for deiodination activity tests.
Within the internship at the German Federal Institute of Hydrology (BfG) in October 2017, LC/MS-Q-TOF analyses of selected samples were done with the help of Maria Redeker (Referat G2).

References

1. Speck,U. & Hübner-Steiner,H. (1999): Pharmakologie und Toxikologie, 2. Edition ed., E. Oberdisse, E. Hackenthal and K. Kuschinsky (Eds.), Berlin, Heidelberg, New York: Springer
2. Schulz,M., Löffler,D., Wagner,M. & Ternes,T.A. (2008): Transformation of the X-ray contrast medium iopromide in soil and biological wastewater treatment. *Environmental Science & Technology*, *42*, 7207–7217
3. Schittko,S., Putschew,A. & Jekel,M. (2004): Bank filtration: a suitable process for the removal of iodinated X-ray contrast media? *Water Science and Technology*, *50*, 261–268
4. El-Athman,F., Adrian,L., Jekel,M. & Putschew,A. (2018a): Abiotic reductive deiodination of iodinated organic compounds and X-ray contrast media catalyzed by corrinoids. *Environmental Science & Technology*, submitted
5. El-Athman,F., Putschew,A., Adrian,L. & Jekel,M. (2018b): Reaktionskinetik der Corrinoid-katalysierten Deiodierung von Röntgenkontrastmitteln. *Proceedings of the Annual Conference of the Water Chemistry Society*, Papenburg, Germany

3. Comments on the qualification programme and supervision strategy:

The core courses were helpful to gain a basic understanding of the topics of all UWI students. It was also interesting to get an insight into the methods and techniques used in other research fields. The summer schools and the interim meeting were very well organized and gave me the opportunity to follow the research results of the other UWI members regularly.
The gender courses about self positioning and successful negotiation provided a good framework for discussing problems and possible solution approaches. The information and strategies given to us might be also useful for future employments and our career in general.
The supervision strategy which includes a board of supervisors and regular meetings brought my research forward and provided an easy opportunity for close cooperation with another research institution.

Participation in the following Research Training Group events:

1. Core courses
   - I – Urban interface processes – fluxes, transport, interactions (3 ECTS)
   - II – Modelling and measuring concepts of interface processes (3 ECTS)
   - III – Urban freshwater ecology (3 ECTS)
2. Elective courses
   - Effektive Gesprächsführung
   - Zukunftsorientiertes Zeit- und Selbstmanagement
   - Lösungsorientiertes Konfliktmanagement
3. Gender courses
   - Time is honey – the new approach to time, self and workload organization
   - Self positioning
   - Successful negotiation
   - Project management
4. UWI lectures and Colloquium Water Quality Control: Participated in several UWI lectures as well as in the Colloquium of the Chair of Water Quality Control
5. Other UWI events
   - Orientation Seminar and UWI Opening Ceremony (08. – 09.09.2015)
   - Exposé Talks (08.12.2015)
   - Summer School (13. – 14.09.2016)
   - Kollegiate Seminar (22.09.2016)
   - Interim Meeting (19.05.2017)
   - Summer School (05. – 06.09.2017)
   - Student Research Council (17. – 18.03.2017) and course on Collaborative Writing (17.03.2017)
   - Summer School (18.-20.09.2018)

Research stays or internships at other research institutions both at home and abroad.
Internship at the German Federal Institute of Hydrology (BfG), Prof. Dr. Thomas Ternes, Referat G2 (02.10. – 03.11.2017, Koblenz, Germany)

Participation in conferences, congresses, etc., at home and abroad:

2015:

- 16th International Conference on Chemistry and the Environment (20. – 24.09.2015, Leipzig, Germany)

2016:

- 5th Research Unit FOR1530 Conference (14. – 15.04.2016, Weimar, Germany)
- Annual Conference of the Water Chemistry Society (02. – 04.05.2017, Bamberg, Germany)

2017:

- Wasser Berlin International (28. – 31.03.2017 Berlin, Germany)
- Annual Conference of the Water Chemistry Society (22. – 24.05.2017, Donaueschingen, Germany)
- 16th International Conference on Chemistry and the Environment (18. – 22.06.2017, Oslo, Norway)
- 10th IWA Micropol & Ecohazard Conference (17. – 20.09.2017, Vienna, Austria)

2018:

- Annual Conference of the Water Chemistry Society (07. – 09.05.2018, Papenburg, Germany)

4. Individual publications:

II. Conference, poster presentations etc.:

- El-Athman,F., Schröder,C., Putschew,A., Adrian,L. & Jekel,M. (2017a): Abiotische reduktive Deiodierung von iodierten Röntgenkontrastmitteln in Anwesenheit von Corrinoiden (Vitamin B_{12}-Derivate). *Proceedings of the Annual Conference of the Water Chemistry Society* (22. – 24.05.2017, Donaueschingen, Germany), abstract, oral poster presentation and poster (poster award)
- El-Athman,F., Putschew,A., Adrian,L. & Jekel,M. (2017b): Abiotic reductive deiodination of contrast media and the influence of corrinoids. *Proceedings of 16th International Conference on Chemistry and the Environment* (18. – 22.06.2017, Oslo, Norway), abstract and oral presentation
- Broecker,T., Scharper,J., El-Athman,F., Gillefalk,M., Hilt,S. & Hinkelmann,R. (2017c): Surface Water – Grounwater Interactions. *Proceedings of the 37th IAHR World Congress* (13. – 18.08.2017, Kuala Lumpur, Malaysia), reviewed paper and oral presentation
- El-Athman,F., Putschew,A., Adrian,L. & Jekel,M. (2017d): Abiotic reductive deiodination of iodinated contrast media mediated by corrinoids. *Proceedings of the 10th IWA Micropol & Ecohazard Conference* (17. – 20.09.2017, Vienna, Austria), abstract and oral presentation
- El-Athman,F., Putschew,A., Adrian,L. & Jekel,M. (2018): Reaktionskinetik der Corrinoid-katalysierten Deiodierung von Röntgenkontrastmitteln. *Proceedings of the Annual Conference of the Water Chemistry Society* (07. – 09.05.2018, Papenburg, Germany), abstract and oral presentation