KOMPETENZZENTRUM
WasserBerlin

REPORT

Cicerostr. 24
D-10709 Berlin
Germany
Tel +49 (0)30 536 53 800
Fax +49 (0)30 536 53 888
www.kompetenz-wasser.de

Treatment of urine with zero-valent iron to minimize the aquatic pollution with compounds emitted by hospitals PharmaTreat

by

Michael Stieber, Anke Putschew, Martin Jekel
Technische Universität Berlin
Institut für Technischen Umweltschutz,
Wasserreinhaltung, KF 4
Straße des 17. Juni 135
10623 Berlin

for

Kompetenzzentrum Wasser Berlin gGmbH

Preparation of this report was financed through funds provided by

VEOLIA WATER

Berliner Wasserbetriebe

Berlin, Germany

2011

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Title
Treatment of urine with zero-valent iron to minimize the aquatic pollution with compounds emitted by hospitals

Authors
Michael Stieber, Anke Putschew, Martin Jekel, TU Berlin

Quality Assurance
Vincent Georgeaud, Veolia environnement
Regina Gnirss, Berliner Wasserbetriebe

Publication / Dissemination approved by technical committee members:
Yann Moreau-Le Golvan, Kompetenzzentrum Wasser Berlin
Bodo Weigert, Kompetenzzentrum Wasser Berlin

Abstract (English)

Advances in the analysis of organic trace compounds revealed that many of the in high amounts prescribed pharmaceutical active components as well as diagnostic agents are not removed by conventional waste water treatment techniques and that some of them can accumulate in the aquatic environment. Because most of the compounds applied in medicine are excreted via urine the emission into the aquatic environment could be reduced if the urine is separated at the source and treated by a specific process. In the project PharmaTreat it was studied if the reductive treatment with zero-valent iron is a suitable, simple and low cost process for the treatment of urine.

The results show that the selected antibiotics (Ciprofloxacine, Piperacillin, Cefuroxime), cytostatic drugs (Ifosfamide and Methotrexate) and iodinated X-ray contrast media (Iopromide and Diatrizoate) are transformed by the treatment with zero-valent iron. The reaction rate constant depends highly on the pH. Under acidic conditions the mechanism of the transformation is most probably the reaction with adsorbed atomic hydrogen which is produced on the iron surface. The increase of the pH-value from 3 to 7, which might happen if the solution is discharged into the waste water system, leads to the precipitation of the dissolved iron resulting in a strong removal of the transformation products out of the solution by co-precipitation. The toxicity of the remaining transformation products was determined using the growth inhibition test (DIN 38412-37). It could be demonstrated that the biological impact of the pharmaceuticals is reduced by the transformation with zero-valent iron. By using the Zahn-Wellens-Test (DIN EN ISO 9888) it could be shown that the transformation products are better biodegradable in contrast to the original compounds, except for the iodinated X-ray contrast media.

The treatment of one cubic meter urine costs 9.88 Euro. The cost estimation is based on conditions with the lowest material consumption and not on the reaction time. According to the calculated price for on cubic meter the treatment of about 6,525 m^3 urine (the amount of urine produced in all hospitals of Berlin) costs ca. 64,500 Euro/a. By accelerating the reaction the treatment time can be shorten but the specific material consumption is higher whereas the energy costs are lower. In dependence of the actual prices for iron, acid and electricity the costs can be optimized for the treatment.

Abstract (German)

Fortschritte in der Spurenanalytik machten deutlich, dass viele der in großem Umfang verabreichten Arzneimittel aufgrund ihrer persistenten Eigenschaften nicht vollständig in herkömmlichen Kläranlagen zurückgehalten werden können und sich teilweise in der aquatischen Umwelt anreichern. Da die meisten Arzneimittel über den Urin ausgeschieden werden, könnte durch eine Separierung des selbigen mit anschließender Behandlung der Eintrag der Pharmaka in das Abwassersystem verringert werden. Im Projekt PharmaTreat wurde untersucht, ob die reduktive Umsetzung des Urins mit elementarem Eisen ein einfaches und kostengünstiges Behandlungsverfahren darstellt.

Die Ergebnisse zeigen, dass die untersuchten Antibiotika (Ciprofloxacin, Piperacillin und Cefuroxime), Zytostatika (Ifosfamid und Methotrexat) und iodierten Röntgenkontrastmittel (Iopromid und Diatrizoat) durch die Behandlung mit elementarem Eisen transformiert werden können. Die Geschwindigkeitskonstante ist stark pH-Wert abhängig. Unter sauren Bedingungen (pH-Werte von 3 und niedriger) beruht der Transformationsmechanismus wahrscheinlich auf einer Reaktion mit adsorbiertem atomarem Wasserstoff an der Eisenoberfläche. Eine Erhöhung des pH-Wertes, z.B. durch Einleiten der Reaktionslösung in die Kanalisation, führt zur Ausfällung des Eisens, das sich während der Behandlung gelöst hat. Durch diese Ausfällung wird ein großer Teil der Transformationsprodukte aus der Lösung entfernt. Die Untersuchung der Toxizität der verbleibenden Stoffe mittels Wachstumshemmtest (DIN 38412-37) zeigte, dass die biologische Wirkung durch die Transformation deutlich vermindert wird. Die biologische Abbaubarkeit der Transformationsprodukte wurde mit dem Zahn-Wellens-Test (DIN EN ISO 9888) untersucht und konnte im Vergleich zu den Ausgangsstoffen mit Ausnahme der Röntgenkontrastmittel verbessert werden.

Die aus den Versuchsergebnissen (Versuchsbedingungen angepasst an geringen Materialverbrauch) ermittelten Kosten für die Behandlung von einem Kubikmeter Urin belaufen sich auf 9,88 €. Daraus ergeben sich, für die Behandlung von in Berlin jährlich anfallenden 6.525 m^3 Krankenhausurin, Kosten von 64.500 € pro Jahr. Durch Beschleunigung der Umsetzung kann die Behandlungsdauer verkürzt werden, was auf der einen Seite zu einer Erhöhung des spezifischen Materialverbrauches und auf der anderen Seite zu einem niedrigeren Energieverbrauch führt. In Abhängigkeit der Preise für Eisen, Säure und Strom sollte eine Kostenoptimierung durchgeführt werden können.

Abstract (French)

Les progrès réalisés dans le domaine de l'analyse des composés traces ont prouvé que les stations d'épuration classiques ne peuvent pas éliminer totalement un bon nombre des médicaments les plus consommés, lesquels s'accumulent alors dans les milieux aquatiques. La plupart des produits pharmaceutiques étant rejetés dans l'environnement via les urines, il devrait être possible de réduire la teneur en médicaments des eaux usées en prélevant séparément les urines avant de les traiter et de les réinjecter dans les réseaux d'assainissement. Le projet PharmaTreat a permis d'étudier dans quelle mesure la transformation réductive des urines par l'intermédiaire de fer sous son état métallique peut constituer une méthode de traitement simple et à moindre coût.

Les résultats montrent que le traitement avec du fer métallique permet de transformer les antibiotiques (la ciprofloxacine, la pipéracilline et le céfuroxime), les citostatiques (l'ifosfamide et le méthotrexate) et les produits de contraste radiographique iodés (l'iopromide et le diatrizoate) sélectionnés pour l'étude. La constante de vitesse dépend largement des conditions de pH. Dans des milieux acides (pH égal ou inférieur à 3), le mécanisme de transformation semble reposer sur une réaction radicalaire via les molécules d'hydrogène adsorbées à la surface du fer. Une augmentation des valeurs du pH, par injection en ligne dans la canalisation d'une base par exemple, entraîne naturellement la précipitation du fer dissous au cours du traitement. Celle-ci permet l'élimination d'une grande partie des produits de transformation de la solution. L'étude de toxicité des matériaux restants à l'aide d'un essai d'inhibition de croissance (DIN 38412-37) a montré que la transformation contribue à réduire de manière significative l'impact biologique. La biodégradabilité des produits de transformation a été étudiée à l'aide de l'essai Zahn-Wellens (DIN EN ISO 9888) et a pu être améliorée par rapport aux matériaux de base, sauf pour les produits de contraste radiographique.

D'après les résultats des essais (conditions d'essai adaptées à une moindre consommation en matériau), le coût du traitement d'un mètre cube d'urine s'élève à 9,88 €, ce qui correspond à un montant annuel de 64 500 € pour le traitement des 6 525 m^3 d'urines produites chaque année dans les hôpitaux de la ville de Berlin. En accélérant le processus de transformation, il est possible d'obtenir une réduction de la durée du traitement, ce qui entraîne à la fois une augmentation de la consommation de matériau spécifique et une diminution de la consommation d'énergie. Il devrait être possible d'optimiser les coûts en fonction des prix du fer, de l'acide et de l'électricité.

Acknowledgements

We express our thanks to following members of the steering committee for their generous contributions to the realization of the project Pharma Treat. Furthermore we are grateful to all the students (Knut List, Lisa Bethke, Simone Wittig, Marina Sabelfeldt, Mateo Urena, Camille Brison) and the technical assistants (Elke Profft, Ulrike Förster, Gisela Sosna) who have done a tremendous work in the lab.

Steering Committee:

Veolia environment:
Vincent Georgeaud

Berliner Wasserbetriebe:
Regina Gnirss

Kompetenzzentrum Wasser Berlin:
Yann Moreau-Le Golvan,
Bodo Weigert

Special thanks to Bayer-Schering AG for providing us Iopromide and Diatrizoate.

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Chapter 1

1.1 Introduction

In recent years a lot of investigations about the fate and behaviour of pharmaceutical substances and diagnostic agents in the environment demonstrate that these in large quantities prescribed compounds can be found in waste water, surface water, sometimes in ground water and drinking water (Heberer, Schmidt-Baumler et al. 1998; Ternes 1998; Ternes and Hirsch 2000; Putschew and Jekel 2001; Heberer 2002; Carballa, Omil et al. 2004; Loffler, Rombke et al. 2005). Although diagnostics agents exhibit no biological activity in contrast to pharmaceuticals they are named as pharmaceuticals within the report. It is not expected that humans are affected by drinking water uptake, but the long-term effects on environmental organisms can not be estimated. 29 compounds which were detected in high concentrations in the aquatic environment were identified as potentially harmful to the environment caused by their eco-toxic effects and poor environmental degradation (LANUV (NRW 2007)). A further problem is that most probably up to now unknown transformation products exist with unknown impact on the organisms (Ternes 1999).

In Germany the total consumption of antibiotics is estimated to be 250 – 300 tons per year of which about 15 % are prescribed in hospitals (GERMAP 2008). In case of cytostatic drugs and the diagnostic agent, in particular the iodinated X-ray contrast media (ICM), the consumption is more concentrated in hospitals (50 %) and residential physicians (50 %). Cytostatic drugs find a less application than antibiotics but they hold the highest human toxicologically potential. Thus there is an increased risk coming from the hospital waste water. ICM are harmless, but the compounds are classified as persistent which is true at least for the basic structure of the ICM the iodinated aromatic ring (Steger-Hartmann, Lange et al. 1999; Steger-Hartmann, Lange et al. 2002). Due to the high amount of ICM applied (ca. 360 t/a, Germany), the compounds respectively the iodinated aromatic structure will accumulate in the aquatic environment, which is already indicated by ICM detected in ground water (Putschew and Jekel 2001).

Due to the “minimization command” of the German drinking water law the emission of pharmaceuticals into the aquatic environment should be reduced as far as possible. The fact that pharmaceutical compounds can be found in ground and drinking water imply that these partly persistent and hydrophilic substances can not completely be removed by common waste and drinking water treatment (Heberer 1996; Heberer, Dunnbier et al.

1997). Advanced waste water treatment processes could be adsorption on activated carbon, membrane filtration, ozonation, advanced oxidation and source separation.

Activated carbon:

The adsorption of pharmaceutical compounds is strongly influenced by the compound specific adsorption coefficient and the background DOC. Good results are achieved with lipophilic substances while ionic and polar compounds show a poor adsorption. The concentration of non-ionic ICM like Iopromide, Iomeprol and Iohexol can be reduced up to 70 % if 10 mg/L powdered activated carbon is applied. Under the same conditions the concentration of ionic ICM like Diatrizoate can just be reduced by 10 % (Metzger, Kapp et al. 2005). By increasing the dose of activated carbon the elimination of nonionic ICM can be increased.

Membrane filtration:

Membrane filtration involves higher costs and higher requirements in operation compared to conventional systems. Furthermore, the costs as well as the requirements in operation increase with decreasing pore size of the membranes. Nanofiltration or reversed osmosis has to be used for the separation of pharmaceuticals which is inappropriate for the treatment of waste water. In general the most important advantage of membrane filtration, even for membranes with a huge pore size (microfiltration > 0.1 µm) is the good retention of suspended solids and hydrophobic organic substances absorbed onto the suspended material and thus membrane filtration could be a good treatment step to clean up water for a further treatment.

Ozonation:

Several studies show that ozonation is a suitable procedure to remove and/or transform substantial quantities of pharmaceutical residues detected in the effluent of waste water treatment plants. Additionally, a germ reduction can be achieved (Bahr 2007) However, ozonation alone is not very efficient for the removal of the ICM. The combination of H_2O_2 and ozone leads to an elevated concentration decrease of the ICM Iopamidol and Iohexol (Bahr 2007), but the amount of organic bound iodine can just be reduced by 20 % and thus, unknown transformation products are produced (Putschew, Miehe et al. 2007). The formation of these products generates the risk that compounds with a toxic potential are produced. This conclusion is valid for all trace contaminants and not only for the ICM.

Source separation:

Due to the fact that most of the pharmaceuticals are excreted by the kidney, urine separation is an efficient possibility to minimize the input into the aquatic environment. With focus on the high nutrient concentration of urine (45 % of P and 80 % of N in waste water, (Wilsenach, Maurer et al. 2003; Wilsenach, Schuurbiers et al. 2007)) different separation systems are suggested (Udert, Larsen et al. 2003; Udert 2004). Although separation systems like NoMix-toilets are well accepted (80 % of users favour that technology; (Lienert and Larsen 2010)) many problems remain. For a widespread usage the same high standards of conventional bathroom installations are required for NoMix-toilets. But actually no NoMix-toilet available has reached this benchmark (Lienert and Larsen 2010). Common problems are the mixing of urine and faces resulting in a loss of urine or an increased requirement for cleaning. Additionally it is necessary to sit to urinate and there are difficulties if children have to use the NoMix-toilets. A further problem is caused by the matrix urine. The hydrolysis of the urea leads to precipitation and clogging of pipes and the formed ammonia induces bad odour.

The manual collection of urine with a special container was examined by the study “Getrennte Erfassung von iodorganischen Röntgenkontrastmitteln in Krankenhäusern” realized by the KWB. In this study a voluntary participation of ca. 60 % was reached and ca. 50 % of the prescribed ICM were collected. However this method is very expensive and leads to costs of ca. 7 €/L urine (Schuster 2006). With more than 85 % the antibiotics are predominantly used not in hospitals. Considering all pharmaceuticals only ca. 10 % are prescribed in hospitals (ATV-M-775 2001). But due to the fact that ICM and cytostatic drugs are mainly prescribed in hospitals the separation of urine in hospitals could be an effective method to reduce the load of the aquatic environment with these compounds. Several projects like „Eliminierung von Spurenstoffen aus Krankenhausabwässern mit Membrantechnik und weitergehenden Behandlungs-verfahren – Pilotprojekt Kreiskrankenhaus Waldbröl“ and „Oxidative Behandlung von Krankenhausabwasser-Teilströmen zur Beseitigung von persistenten, hochwirksamen Pharmazeutika“ show that a decentralized treatment of hospital waste water respectively toilet waste water is possible and effective for the removal/transformation of cytostatic drugs and antibiotics (Türk 2004; Beier 2009).

The treatment of urine in contrast to waste water has two advantages: the concentration of pharmaceuticals is much higher and the volume of urine produced e.g. within one day in a hospital is much less compared to the waste water produced at the same time. If the contaminated urine is separated, e.g. in hospitals a treatment process is needed to decontaminate the urine, which than ideally can be discharged into the waste water

system. Whereas membrane filtration (Maurer, Pronk et al. 2006; Pronk, Palmquist et al. 2006) and oxidative treatments (Türk 2004; Dodd, Zuleeg et al. 2008) are already examined, in this project the reductive treatment with zero-valent iron is tested. From literature it is known (Bigg and Judd 2000; Farrell, Chuffe-Moscoso et al. 2000; Farrell, Melitas et al. 2000; Melitas, Chuffe-Moscoso et al. 2001; Su and Puls 2001; Alowitz and Scherer 2002; Roy, de Donato et al. 2003; Huang and Zhang 2004) that many organic as well as inorganic water constituents can be transformed by zero-valent-iron. The reductive treatment with zero-valent iron is especially known from the decontamination of groundwater polluted with halogenated organic compounds.

The key reaction of the dehalogenation by zero-valent iron is the iron corrosion. The corrosion of zero-valent iron in water can be described by anodic and cathodic half-reactions. The primary anodic half-reaction is the oxidation of Fe^0 (Matheson and Tratnyek 1994):

$$Fe^0 \rightarrow Fe^{2+} + 2e^- \qquad (1)$$

The relevant cathodic half-reaction depends on the conditions, whereby the mechanism responsible for dehalogenation depends on the target substances (Mccaffer.E and Zettlemo.Ac 1967; Farrell, Melitas et al. 2000; Li 2000)

Under acidic conditions: $2H^+ + 2e^- \rightarrow H_2$ (2)

In the presence of oxygen: $O_2 + 2H_2O + 4e^- \rightarrow 4\ OH^-$ (3)

Under anaerobic conditions: $2H_2O + 2e^- \rightarrow H_2 + 2OH^-$ (4)

The dehalogenation in a Fe^0/water system can be described by three different mechanisms:

(1) A direct electron transfer from iron metal at the metal surface:

$$Fe^0 + RX + H^+ \rightarrow Fe^{2+} + RH + X^- \qquad (5)$$

(2) A reduction by Fe^{2+}, which results from the corrosion of the metal:

$$2Fe^{2+} + RX + H^+ \rightarrow 2Fe^{3+} + RH + X^- \qquad (6)$$

(3) Catalyzed hydrogenation by atomic H that is formed by the reduction of H_2O under anaerobic conditions:

$$H_2 + RX \rightarrow RH + H^+ + X^- \qquad (7)$$

1.2 Aim of the project

The aim of the project PharmaTreat is to develop a simple process for the treatment of contaminated hospital urine with zero-valent iron. Based on model compounds parameters influencing the treatment process shall be identified.

The main work packages of the project are:

- Selection of different pharmaceuticals according to the consumption of the hospitals Charité (Berlin, ca. 3,500 beds) and Caritas Klinik Pankow (Berlin, ca. 240 beds).
- The development of an LC-MS/MS method for analyzing the selected compounds in water and urine.
- Experiments in pure water to evaluate the kinetic and the mechanism, and to study the influence of pH, temperature and stirring speed and the influence of different organic and inorganic main constituents of human urine.
- Bacterial toxicity and biodegradation tests before and after treatment with zero-valent iron.
- Experiments with urine under optimized conditions and tests concerning the multiple use of iron.
- A cost estimation in comparison with other treatment possibilities.

Chapter 2

2.1 Material and methods

2.1.1 Chemicals

The selection of the model compounds is based on the consumption of pharmaceuticals of two different hospitals in Berlin (Charité, ca. 3,500 beds and Caritas Klinik Pankow, ca. 240 beds). For the evaluation of the data see Table 14 – 14, Appendix A1. As model compounds antibiotic and cytostatic drugs as well as iodinated contrast media (ICM) were chosen because of their special impact to the aquatic system and the organisms living there. The following compounds were used as model compounds: Piperacillin, Cefuroxime, Ciprofloxacine, Ifosfamide, Methotrexate, Iopromide and Diatrizoate. Iopromide and Diatrizoate were kindly provided by Bayer-Schering AG, Berlin. The other compounds were purchased by Xiang Ding Chemicals (China).

The iron splints used were purchased from the company Gotthard Mayer Metallpulver GmbH. The density of iron is 7.874 g/cm^3. Other characteristic of the iron are given in

A pre-treatment of the iron has not been done.

Table 1: Characteristics of the iron.

Parameter	**Data**
BET surface area	0.67 m^2/g
particle size	0.125 - 3 mm
shape	needle like
C-content	2.8 - 3.4 %
Si-content	≈ 2 %
Cr-content	< 0.02 %
Ni-content	< 0.02 %

Figure 1: Iron splints.

All other chemicals used (for example HCl, H_2SO_4, formic acid, methanol) were of analytical grade. The ultra pure water (UPW) was produced out of deionized water with an Elga water purification system (Elga, Germany). Before analysis the samples were filtrated with 0.45 µm membrane filters (Sartorius, Göttingen, Germay).

2.1.2 Experimental set-up

The selected compounds dissolved in ultra pure water or urine were treated with granular iron (surface area 0.67 m^2/g, not pre-treated) in 0.5 L plexiglas batch reactors of two different designs (see below). The reactors are impervious to light. The solution was stirred and a chosen pH value was kept constant, in case of kinetic experiments by using a titro-processor 702 SM Titrino from Metrohm (Switzerland) by adding hydrochloric acid. The temperature of the reaction solution was adjusted by wrapping the reactor with a temper water tube (Hacke, Germany). The dependence on the following parameters was determined: pH value, amount of iron added, stirring speed and temperature. The temperature, pH value and the oxygen concentration were monitored on-line using the datalogger ALMEMO (Ahlborn, Germany). The electrodes were also from Ahlborn and calibrated before each experiment. The reactor was sampled regularly (5 ml) and the following parameters were determined: dissolved iron, compound concentrations, dissolved organic carbon (DOC) and adsorbable organic iodine (AOI) in some cases. After sampling the samples were filtrated (0.45 µm), split up and diluted with ultra pure water for the different analytical determinations. The aliquot for the iron determination was acidified with hydrogen chloride to pH 2. Depending on the experiment the selected compounds were treated as a mixture or as single compound. The test solutions were prepared always direct before the experiment started. The initial concentration of the antibiotics and ICM were 100 mg/L and 10 mg/L for the cytostatic drugs. All experiments were done in triplicate.

2.1.2.1 Characterisation of the reactors

Reactor type 1:

The first experiments (preliminary tests with Iopromide) were done in a simple cylindrically Plexiglas® batch reactor without flow disturber. The reactor has a diameter of 9 cm and a height of 10 cm. The volume of 500 ml was stirred by a paddle mixer with a diameter of 6.56 cm. The stirring speed was 200 rpm and due to the high density of the iron it was not possible to generate a homogenous suspension by stirring. It could be observed that the iron accumulate in the middle of the reactor under the stirrer. A further problem of this reactor type 1 is that through the hole for the stirrer a permanent entry of oxygen was possible. For these reasons reactor type 2 was designed.

Reactor type 2:

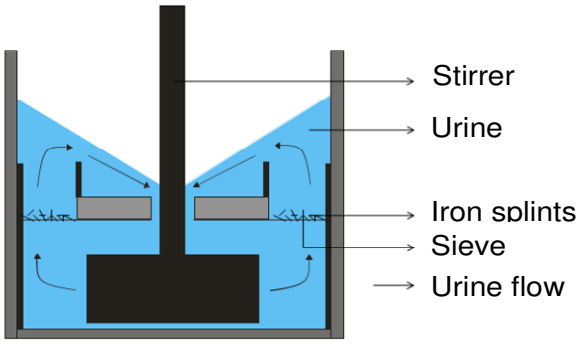

Figure 2: Design of reactor type 2 (volume 500 ml).

The dimensions of reactor type 2 are the same as for reactor type 1. To avoid the problem of the iron accumulation, a sieve insert is placed into the reactor (see Figure 2). The iron is placed onto the sieve and the water passes through the iron. Due to the drag of the sieve the stirring speed could be increased to 560 rpm. Additionally a gas tight bearing for the stirrer was installed. The calculated (equation 8) volume specific power input for reactor type 2 is ca. 1 kW/m^3.

$$\frac{P}{V} = Ne \cdot d^5 \cdot N^3 \cdot \rho \qquad (8)$$

P/V: volume specific power input [KW m^{-3}]
Ne: Newton-number (estimated with 0.5 [(Kraume 2003)])
d: diameter [m]
N: rotary frequency [s^{-1}]
ρ: density [Kg m^{-3}]

Experiments to check the reactor performance of reactor type 2:

a) Experiment with a pigment (qualitative study): A pigment was placed in the bottom part of the reactor and was than slowly filled up with water. After starting to stir it was visible that the colour reached the upper part of the reactor by passing exclusively through the sieve and moved than spiralled through the middle hole of the reactor to the bottom again. After a short time the solution was completely mixed.

A similar experiment was performed by blocking the sieve. Now it was recognized that the upper part of the reactor was colourless for a long period, indicating that the water

must pass through the sieve respectively through the iron and thus, conditions comparable to a homogenous mixed solution are obtained.

b) Iopromide was injected into the bottom part of the reactor (quantitative study): After injection the reactor was gently filled with water. After 5 min a sample was taken out off the lower and the upper part of the reactor. Than the solution was stirred for 10 min and the reactor was sampled again. In all samples the Iopromide concentration was quantified. Before stirring the Iopromide concentration was higher in the solution below the sieve and after stirring equal below and above the sieve.

Reactor type 3:

The design of reactor type 2 is not appropriate to treat higher volumes because the higher amount of iron would inhibit the flow through the sieve. Another problem in case of iron re-use is the dissolution of the iron splints resulting in smaller particles which can not be hold back by the sieve. For these reasons a larger reactor with the goal of complete suspended iron particles was constructed (Figure 3). The reactor type 3 is a cylindrical Plexiglas® reactor and similar to reactor type 2 this reactor has a gas tight bearing for the stirrer. A black plastic cover was used to darken the reactor.

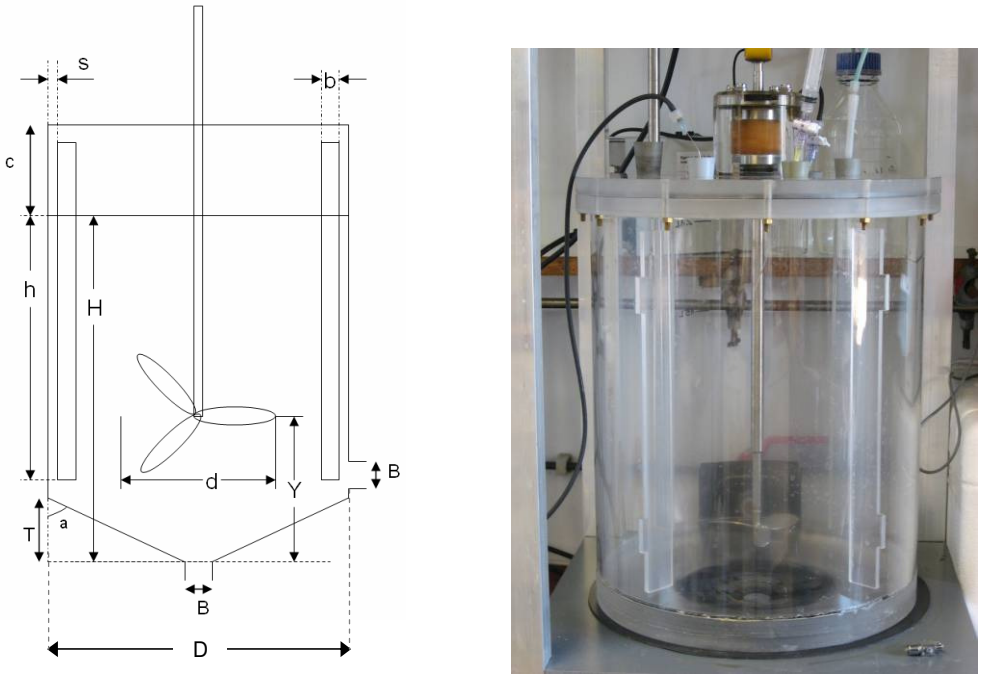

Figure 3: Design of reactor type 3 (volume 21 L).

The design of a reactor to suspend particles in Newtonian fluids can be calculated by the following ratios (Kraume 2003; Paul Edward L. and Atiemo-Obeng 2004):

$$H = D \;;\; d < \frac{D}{2.5} \;;\; Y < \frac{D}{4} \;;\; b = 0.1 \cdot D \;;\; s = 0.02 \cdot D$$

The bottom of the reactor is designed as low cone to avoid badly mixed parts. The used dimensions of the reactor are presented in table 2.

Table 2 Reactor dimensions

Parameter	Data
D	290 mm
H	343 mm
d	100 mm
Y	72 mm
b	29 mm
s	5.8 mm
a	78°

The goal to suspend the iron particles only can be reached by a turbulent flow (Re > 10,000). A propeller stirrer with three blades is used. With these boundary conditions (turbulent flow, propeller stirrer, 4 baffles) there is a constant Newton-number Ne = 0.35 (Kraume 2003). The density of iron is relatively high thus the volume specific power input P / V has to be not less than 2 kW/m^3 (Alexandrova 2010). The resulting required power input for the reactor with 21 L is 42 W. With equation (8) the needed stirring speed can be calculated and amounts N = 1373 rpm.

2.1.3 Examination of the hydrogen gas generation / corrosion rate

The volume of the generated hydrogen gas was quantified during experiments with the gas tight reactors 2 and 3. The hydrogen gas was transferred into a gas tight bottle filled with water which was connected to a second bottle. The produced hydrogen displaces water out of the gas tight bottle into the connected bottle (Figure 4) and by weighing the bottles the volume is calculated. Additionally the amount of dosed acid and the dissolved iron concentration was measured.

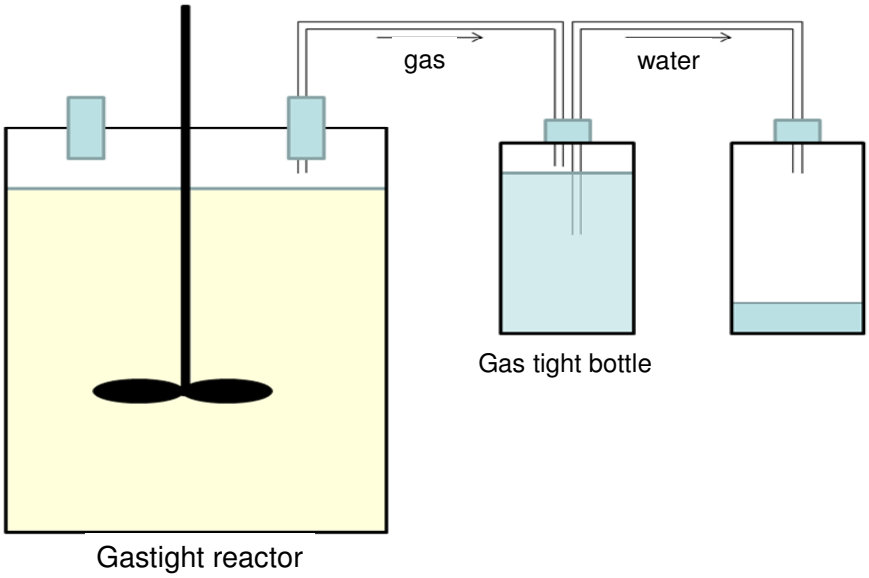

Figure 4: Scheme of the experimental set-up for the determination of the produced hydrogen.

2.1.4 Catalytic hydrogenation

Each of the selected compounds was dissolved in ultra pure water (50 mg/L). After adding 50 mg platinum-(IV)-oxide hydrogen gas was bubbled / introduced into the stirred solutions for 1 h. After that time the reaction flasks were closed and the solutions were stirred over night. Before LC-MS analysis the reaction solutions were filtrated (0.45 µm).

2.1.5 Urine collection and storage

The urine used for the experiments was collected at the department of water quality control and originates exclusively from healthy people, mostly women (Figure 34, Appendix A6). Based on the urine constituents it is recognized that the women at the department have a higher liquid uptake then the men (Table 16 – 17, Appendix A6). Three different experiments were done to evaluated changes of the urine during storage over 3 weeks (Table 3). Experiment III was used to check if the added pharmaceuticals can be found in the urine phase after the storage time.

Table 3: Different storage experiments (open to atmosphere, 18.1 ± 2.4 °C), n=2.

Experiment	I	II	III
batch volume [ml]	1500	1500	250
pre-treatment	-	acidified to pH 2 with HCl (16 %)	-
pharmaceutical addition (each 50 mg/L)	-	-	Iopromide, Diatrizoate, Methotrexate, Ifosfamide, Ciprofloxacine, Cefuroxime Piperacillin

The following parameters were determined at the beginning of the experiments, in defined time intervals and after 3 weeks: pH-value, redox potential, O_2 concentration, temperature, evaporation rate (gravimetric), the acid consumption for acidification to pH 2; DOC, TIC, oxalate, total N, Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}, NH_4^{+}, Cl^{-}, SO_4^{2-} and PO_4^{3-}. At the end of the experiments the composition of the sediments were examined (after washing with NaOH (at pH 9) and dissolving with HCl (16 %)). In further experiments it was tested if the addition of already stored urine (ratio 1:18) and the addition of urease (1g/L) can accelerate the hydrolysis of urea, which is the main reaction during storage.

2.1.6 Growth-inhibition test and biodegradability

The growth-inhibition test was done according to DIN 38412-37 using micro-titer plates and *Vibrio fischeri*. To each well of the micro-titer plate 40 µl nutrient solution and 100 µl of the compounds (with different concentrations) were pipetted. To some wells 20 µl of a *Vibrio fisheri* suspension were pipetted. The wells without addition of *Vibrio fischeri* are the blank values. At the end all wells were filled up with a 2 % NaCl solution to a final volume of 200 µl. The micro-titer plates were cultivated at 21 ºC for 18 h. In time intervals of 20 min the turbidity of the wells was determined.

The biodegradability of the selected compounds as well as of the transformation products was determined according to DIN EN ISO 9888 (Zahn-Wellens-Test, aerobic biodegradation). In summary: the test compounds were mixed with an inorganic nutrient solution and activated sludge of the waste water treatment plant Ruhleben (Berlin). The biological tests were done at 20-25 ºC in shaded glass bottles. The solution was stirred to be sure that oxygen is not limited. Due the biological effects of the examined compounds the DOC-concentrations desired in the DIN could not be comply. In preliminary tests with a reference compound (aniline) the inhibition effect of the antibiotics to the sludge was studied.

2.1.7 Analytic

The selected compounds were quantified by LC-ESI-MS/MS (HP 1100, Agilent, Waldbronn, Germany; Quattro-LC, Micromass, Manchester, UK, now Waters) using a reversed phase column (Phenomenex: Luna 3µ C18(2); 150×2 mm). The linear gradient elution program is given in Table 3. The flow rate was 0.25 ml/min. The column oven was set to 30ºC and the injection volume was 10 µl.

Table 4: HPLC gradient program.

Time (min)	A: ultra pure water + 0.25 % HCOOH	B: methanol
0	90%	10%
2	90%	10%
10	20%	80%
12	20%	80%
14	90%	10%
25	90%	10%

The LC system was coupled with a orthogonal Z-spray electro spray interface to a mass spectrometer (Quattro-LC;Micromass, Manchester, UK). Drying gas (900 L/h) and nebulizing gas (85L/h) were nitrogen generated from pressurized air (Whatman, Haverhill, MA, USA). The desolvation temperature was 280 ºC and the source temperature was 120ºC. Positive ion as well as negative ion electro spray ionization was used for detection. The capillary voltage was 3.6 / 2.3 kV. The compounds were detected in the selected reaction monitoring (SRM) mode. Argon 5.0 (Messer Griesheim, Germany) was used as collision gas. The pressure in the collision cell was 1.3×10^{-3} mbar. The product ions for the MRM experiments were determined by infusion experiments. The recorded transitions, the cone voltages and the collision energy are given in Table 5. In some cases Iopromide was quantified using the described HPLC system with the same conditions and a UV detector (242 nm). For the detection of unknown compounds the described LC-MS/MS system was used in the scan mode.

Table 5: Selected reaction monitoring conditions for detection of the selected compounds.

compound	transition(s)	cone voltage (V)	collision energy (eV)	ionization mode
Iopromide	792 > 573	35	35	positive
	792 > 559	35	35	
Diatrizoate	615 > 361	30	22	positive
Piperacillin	516 > 233	25	15	negative
	516 > 330	25	15	
Ciprofloxacine	332 > 314	35	28	positive
	332 > 231	35	28	
Cefuroxime	423 > 318	30	9	negative
	423 > 207	30	9	
Methotrexate	455 > 308	25	22	positive
Ifosfamide	261 > 92	30	22	positive
	261> 154	30	22	

The dissolved iron concentration was quantified by atomic absorption spectroscopy (GBC 906AA). After sampling the reactor an aliquot for the iron determination was acidified with hydrogen chloride to pH 2. The DOC was determined by catalytic oxidation with a highTOC (Elementar, Hanau, Germany). The AOI analysis is equal to the AOX determination. The only difference is that the combustion gas is trapped in ultra pure water with a trace of Na_2S and is than analyzed by ion chromatography (Dionex) with UV detection. For details about the AOI analysis sees (Oleksy-Frenzel, Wischnack et al. 1995). Iodide was quantified using the same IC system and the same IC conditions as used for the AOI determination.

Chapter 3

3.1 Results of the kinetic and mechanism experiments

3.1.1 Preliminary tests with Iopromide (reactor type 1)

The first experiments were done in the simple reactor type 1 with water and Iopromide. The type 1 reactor is a simple batch reactor where the reaction mixture is stirred without archiving a homogenous suspension. The reactor is open to the atmosphere and the oxygen concentration during the experiments was 3 - 4 mg/L. The initial concentration of Iopromide was 1.6 g/L. 40 g/L iron was added and the initial pH was 2. Figure 5 shows the concentration of Iopromide, iodide and the pH over the reaction time. The concentration of Iopromide is decreasing with increasing time. At the beginning of the reaction the transformation of Iopromide is very fast and slows down after an hour. After 20 h the Iopromide concentration was below the detection limit.

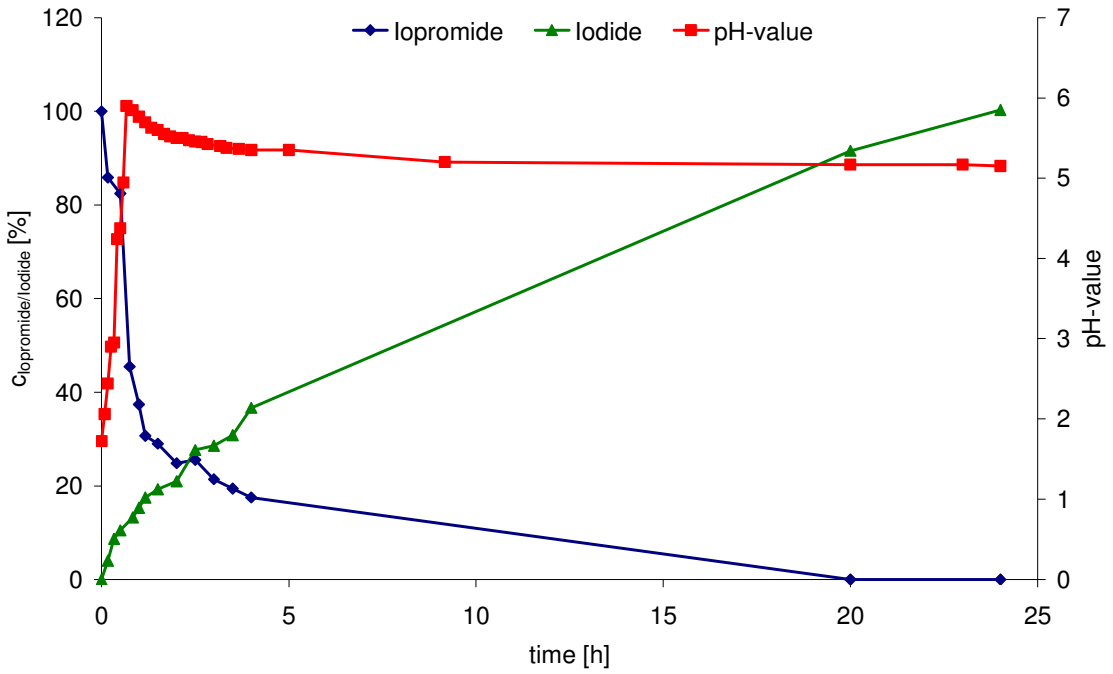

Figure 5: Treatment of Iopromide (1.6 g/L) with zero-valent iron (40 g/L), initial pH = 2, rpm= 200, T = 20 °C; concentration versus time; n = 3.

The increasing iodide concentration indicates that a deiodination of Iopromide occurs as expected based of the iron use for dehalogenation reactions (Gillham and Ohannesin 1994; Focht and Gillham 1995). The fact, that there is an ongoing deiodination after 20 hours when nearly all Iopromide is transformed, indicates that partly deiodinated transformation products are intermediates.

Due to the iron corrosion the pH increases at the beginning of the experiment very fast from the adjusted value of 2 to 6. After that the pH decreases slightly due to the formation of $Fe(OH)_3$ to a constant pH of 5. To study the influence of the pH-value different pH-values were kept constant during the reaction. The results will be discussed using the observed reaction rate constants. For the pH-values 1, 2 and 3 the decrease of the Iopromide concentration can be described by a pseudo first order reaction (equation 9). For the pH-values 4 and 5 the linearization of the zero order reaction (equation 10) fits better (see Figure 6).

$$\frac{dP}{dt} = k_{sa} \cdot \rho_a \cdot P = k_{obs} \cdot P \quad (9) \qquad \frac{dP}{dt} = k_{obs} \quad (10)$$

P: compound concentration [mg/L]

t: time [s^{-1}]

k_{obs}: observed kinetic constant [s^{-1}, pseudo first order reaction and mg L^{-1} s^{-1}, zero order reaction]

In case of the experiments with a free pH-value (not kept constant) the first part of the reaction can be described by a reaction of pseudo first order and than if a pH 5 is reached by a reaction of zero order, indicating that the mechanism has changed. Figure 6 shows the measured Iopromide concentrations in dependence on the pH and the calculated concentration based on the describing observed reaction rate constant (Table 6).

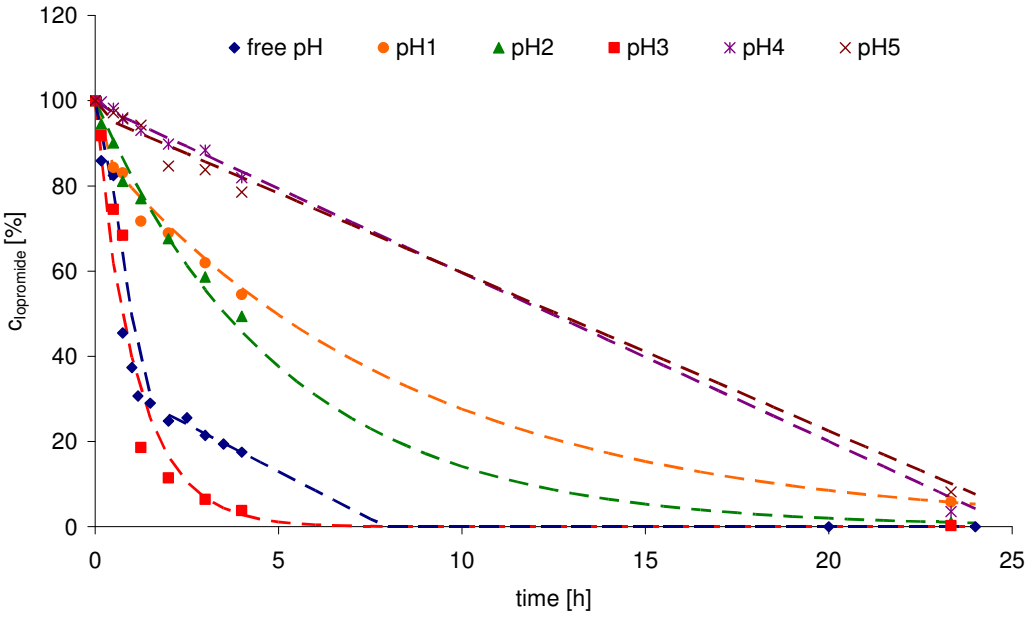

Figure 6: Treatment of Iopromide (1.6 g/L) with zero-valent iron (40 g/L) at different constant pH values, rpm = 200, T = 20 °C; concentration versus time; n = 3.

Obviously, the fastest decrease of the Iopromide concentration can be observed at pH 3 constant. This could be explained by the mechanism of the catalyzed hydrogenation. The Iopromide reacts on the iron surface with adsorbed atomic hydrogen which is formed at low pH-values. The effect that the reaction becomes slower at pH 2 and even more at pH 1 is attributed to the development of an H_2 layer on the iron surface due to the strong formation of H_{ads} and the fast recombination to H_2. The slowest decrease of the Iopromide concentration can be observed at pH 4 and 5. The formation of H_{ads} at these pH-values is much lower and it is more probable that the Iopromide reacts by a direct electron transfer on the iron surface. Another effect at these pH-values is the beginning precipitation of $Fe(OH)_3$ caused by the open system in reactor type 1. The $Fe(OH)_3$ can inhibit the iron surface and slows down the dehalogenation of Iopromide. The good performance at the free pH can be explained by the start pH-value 2 and the fast kinetic until the pH is increased to 5.

Table 6: Observed reaction rate constants for different pH values (constant and not adjusted).

pH- condition	**Reaction order**	**K_{obs}**	**R^2**
Const. pH 1	Pseudo first order	$3.26 * 10^{-5}$ s^{-1}	0.9967
Const. pH 2	Pseudo first order	$5.44 * 10^{-5}$ s^{-1}	0.9992
Const. pH 3	Pseudo first order	$2.45 * 10^{-4}$ s^{-1}	0.9443
Const. pH 4	Zero order	0.016 mg * L^{-1} * s^{-1}	0.9976
Const. pH 5	Zero order	0.015 mg * L^{-1} * s^{-1}	0.9937
Free pH (0 – 90 min)	Pseudo first order	$2.59 * 10^{-4}$ s^{-1}	0.9307
Free pH (> 90 min)	Zero order	0.019 mg * L^{-1} * s^{-1}	0.9477

As already mentioned a release of iodide can be observed although Iopromide is not anymore measurable. The analysis of the transformation products with LC-MS (positive ionization, scan modus) shows the formation and declining of partly deiodinated Iopromide. Iopromide contains 3 iodine atoms and in the reaction solution Iopromide with just two, one or zero iodine atoms were detected (Figure 7). The species distribution is calculated with the ratio of the peak area of the different species and the concentrations of Iopromide, released iodide and adsorbable organic iodine. Despite the poor time resolution it can be seen that the deiodination takes place incremental.

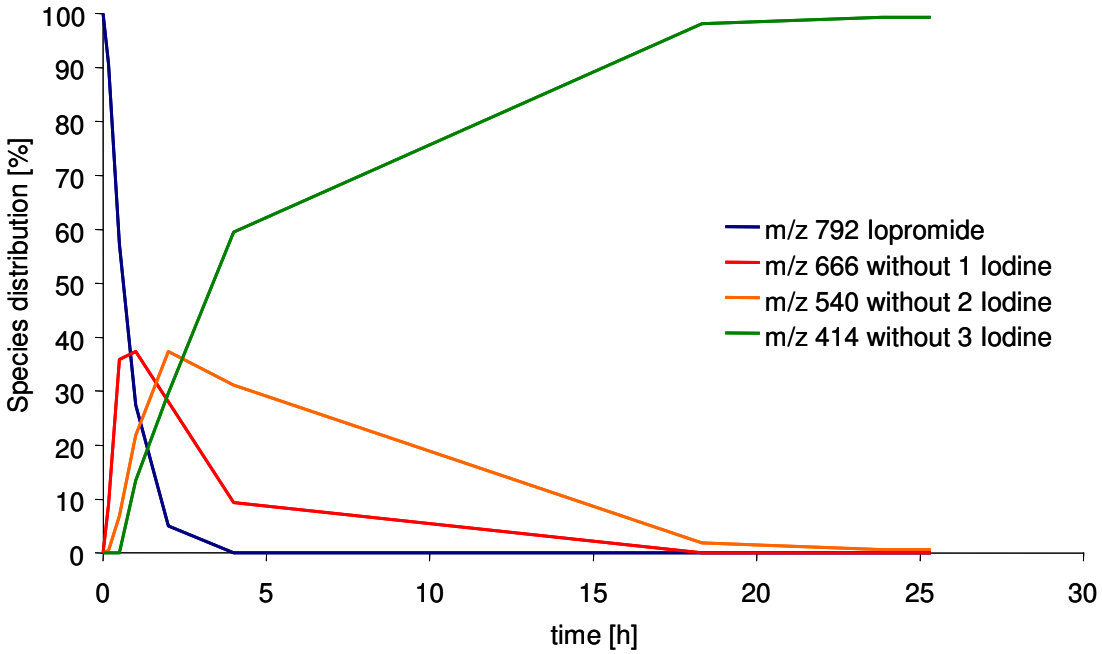

Figure 7: Species distribution versus time obtained by the treatment with zero-valent iron.

In the samples taken after 25 h a further transformation product with a m/z value of 340 is detected. This compound indicates that there is a transformation of the side chains of the complete deiodinated Iopromide (Figure 8).

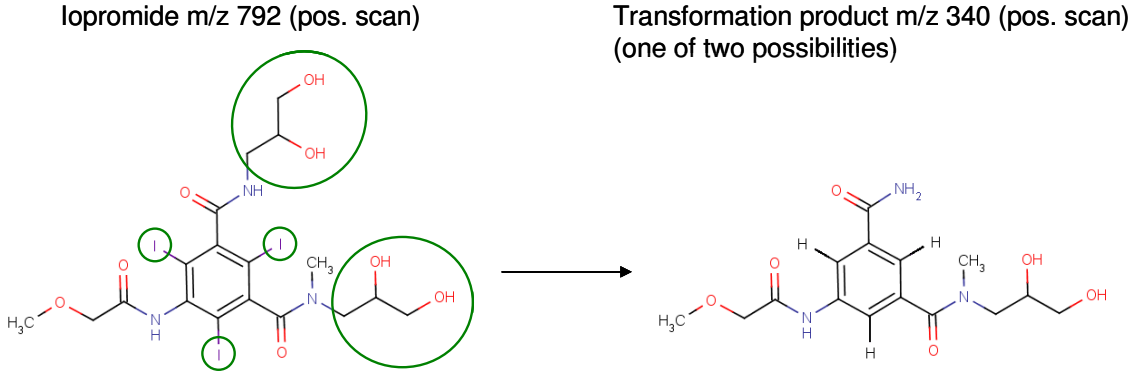

Figure 8: One possible transformation end product for the transformation of Iopromide by zero-valent iron.

The preliminary tests with Iopromide show that the treatment with zero-valent iron leads to a deiodination and a transformation of the side chains. Due to the disadvantages (open system, poor mixing of solution and iron splints) of reactor type 1 all further kinetic studies were done with reactor type 2 (see Chapter 2.1.2.1).

3.1.2 Validation of the analysis

Before starting the kinetic experiments it was tested if the selected compounds are stable at different pH–values (Figure 36, Appendix A7). Furthermore the reproducibility of the quantification was evaluated as well as the influence of dissolved iron on the analysis of the pharmaceuticals and iodide (Figure 37 and 38, Appendix A8-9). The calibrated range for the analytic is 0.05 mg/L to 10 mg/L for the ICM respectively the antibiotics and 0.005 mg/L to 1 mg/L for the cytostatic drugs (Table 19 and 20, Appendix A8).

Ifosfamide (100 % decrease), Piperacillin (100 % decrease) and Cefuroxime (50 % decrease) are not stable at pH 1. Ciprofloxacin is not stable at pH 3 just 60 % of the initial concentration could be detected. Piperacillin is unstable at pH-values higher than 7. The ICM and Methotrexate are stable over the whole pH-range examined. To exclude a concentration decrease due to conditions where the compounds are not stable kinetic experiments were done only with pH-values between 2 and 5.

The reproducibility of the quantification by LC-MS/MS is very good. The selected compounds were dissolved in water and were analyzed 40 times. The initial compound concentration was varied between 0.5 – 100 mg/L. All compounds could be quantified with a standard deviation of less the 15 %. The influence of $FeCl_2$ (50 mg/L) has been tested for the pH-values 3 and 7. Except for the compounds Ciprofloxacine and Methotrexate the iron does not influence the quantification. The decrease of the peak areas of Ciprofloxacin and Methotrexate at pH 7 with iron added can be explained by adsorption onto precipitated iron hydroxide. In case of Methotrexate the standards with iron added at pH 3 show higher peak areas than the standards without iron at pH 7. This indicates that there is a better ionization at lower pH-values. Due to the increasing iron concentration during the experiment the influence of the iron could not be regarded.

3.1.3 Preliminary tests with reactor type 2

The preliminary tests with Iopromide showed that the kinetic of the deiodination depends strongly on the pH-value. Similar to the preliminary tests all selected compounds were treated in the reactor type 2 with iron at different constant pH-values and with an initial pH of 2 which was not kept constant. The initial concentration of the compounds was 100 mg/L for the antibiotics and ICM respectively 10 mg/L for the cytostatic drugs. The added iron concentration was 40 g/L. As found before for Iopromide the maximum of k_{obs} is at pH 3 for all compounds, except in case of Methotrexate. The rate constant of Methotrexate has a minimum at pH 3 but is one order of magnitude higher (Figure 9) as the k_{obs} values of the other compounds.

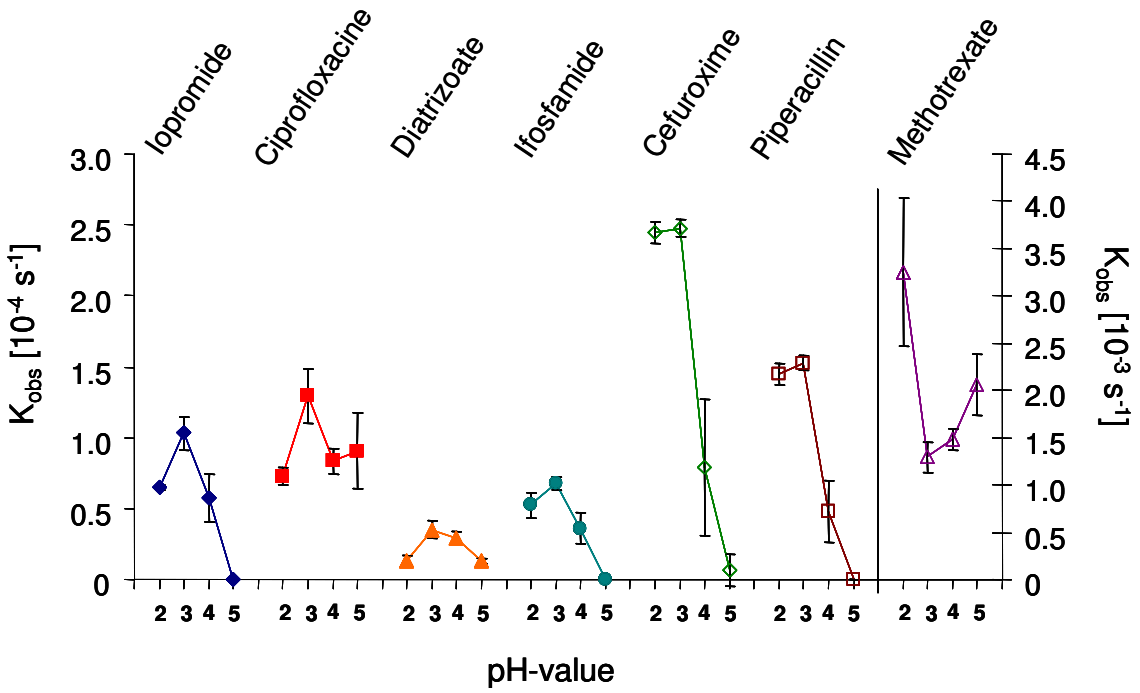

Figure 9: Observed reaction rate constants for the selected compounds for different constant pH values. (40 g Fe^0/L, rpm = 600, T = 20 °C; n = 3).

In case of Methotrexate the increase of the reaction rate constant at pH 2 indicates that another mechanism is responsible for the concentration decrease by the treatment with iron in contrast to the other compounds. The faster kinetic at pH 4 and 5 compared to pH 3 can be explained by adsorption on precipitated iron hydroxide or by interferences during quantification (see above). The compounds with the slowest kinetic are Ifosfamide and Diatrizoate.

The percentage removal rate is higher at pH 3 constant compared to an initial pH of 2 which was not readjusted over the treatment time, except for Diatrizoate and Methotrexate (Figure 10). The removal rate of Diatrizoate is about 6 % higher if the pH is not readjusted. In case of Ifosfamide and Cefuroxime the removal rate is much lower if the pH is not adjusted. In both experiments Methotrexate was not detectable after 8 hours.

Although different initial concentrations were used the removal rates of Iopromide can be compared between the two reactor types used. In reactor type 1 the Iopromide concentration (initial 1.6 g/L) is decreased by more than 90 % within 8 hours using an initial pH of 2 which is not readjusted. Under the same conditions just 75 % are removed in reactor type 2 (initial concentration 100 mg/L). The different removal rates are caused by the different start concentrations and in case of reactor type 2 by a competition about the iron surface with the other compounds and by an accelerating influence of oxygen in case of reactor type 1.

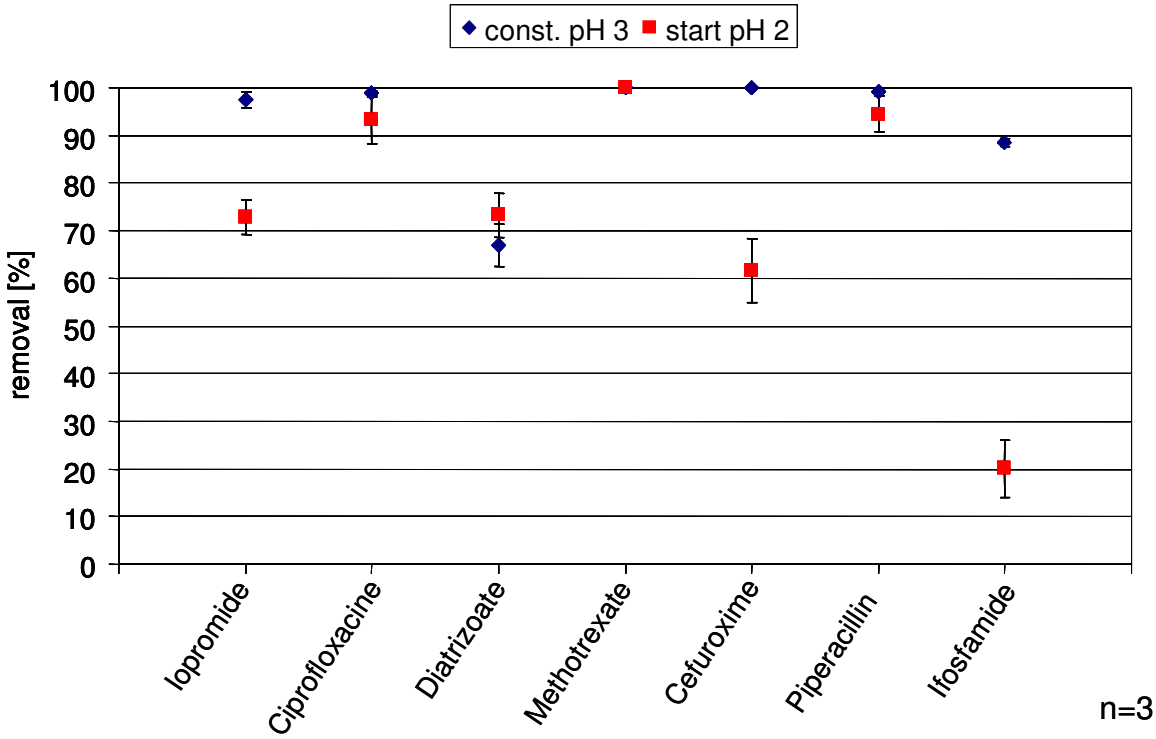

Figure 10: Percentage removal after 8 h for the selected compounds for pH 3 constant and an initial and not readjusted pH of 2. (40 g Fe^0/L, rpm = 600, T = 20 °C; n = 3).

Generally it can be concluded that the removal of the examined compounds is more efficient at constant pH 3 constant.

3.1.3.1 Adsorption / precipitation experiment

The relatively high removal rates observed during experiment with an initial pH of 2 which was not re-adjusted leads to the suggestion that co-precipitation and/or adsorption can additionally be responsible for the concentration decease. Due to the increasing pH-value over time the dissolved iron precipitates and co-precipitation, respectively adsorption of the compounds can occur. Several precipitation experiments were performed to sort out if precipitation and/or adsorption onto the iron hydroxide account to the removal rate.

Flocculation test with $FeCl_3$ (30 mg Fe/L, pH 7) show depending on the compounds different removal rates. The concentration of Methotrexate is decreased by 97 %. The antibiotics Piperacillin, Ciprofloxacine and Cefuroxime are removed by 68.7 %, 40.9 % and 28.6 %. The ICM and Ifosfamide are not removed by flocculation (Table 7). During the experiment with zero-valent iron and a start pH of 2 which is not controlled the iron dissolves as Fe^{2+} and is oxidized to Fe^{3+}. To study the effect of oxidation, which can also be responsible for a transformation by zero-valent iron (see equation 6, page 4) an

experiment with Fe^{2+} ($FeSO_4$, 1 g Fe/L, pH 7) was done. Unfortunately the dosed Fe^{3+} and Fe^{2+} concentrations are very different and thus it is not possible to determine an additional effect of the oxidation $Fe^{2+} \rightarrow Fe^{3+}$. The high Fe^{2+} concentration was chosen because up to 1 g/L iron is dissolved after treatment with Fe^0. The results of these experiments are summarized in Table 7. The removal of the compound Iopromide, Diatrizoate, Ifosfamide, Ciprofloxacine and Methotrexate is improved and no effect is recognized for Piperacillin and Cefuroxime. The higher removal rate with 1 g/L Fe^{2+} is most probably due to the high iron concentration used. At least in experiments at pH 3 constant where flocculation does not occur the removal of the compounds is not attributed to co-precipitation or oxidation of Fe^{2+}.

Table 7: Concentration decrease of the selected compounds due to precipitation.

	30 mg Fe/L ($FeCl_3$)	**1 g Fe/L ($FeSO_4$)**
Compound c_0	**concentration decrease [%]**	**concentration decrease [%]**
Iopromide (100 mg/l)	---	20
Diatrizoate (100 mg/l)	---	15
Ciprofloxacine (100 mg/l)	40.9	98.3
Piperacillin (100 mg/l)	68.7	63.9
Cefuroxime (100 mg/l)	28.6	29.2
Methotrexate (10 mg/l)	97	99
Ifosfamide (10 mg/l)	---	23.6

3.1.3.2 Adsorption

The removal at a free pH is influenced by co-precipitation or adsorption onto precipitated iron hydroxide. To test if there is also an adsorption/co-precipitation process responsible for the removal at constant pH 3 each of the compounds was treated with and without iron and the compound concentration and the DOC-concentration was determined. Without iron the DOC-concentration is constant for all compounds but the compound concentration of the antibiotics decreases by ca. 40 % after 4 hours (Figure 11). This effect validates the results of the preliminary tests that the antibiotics are not stable at acidic conditions (pH < 3). The addition of zero-valent iron leads to a decrease of the DOC-concentration by ca. 30 % for the antibiotics, respectively ca. 40 % for Methotrexate and ca. 10 – 20 % for the ICM and Ifosfamide. The decrease of the compound concentration with values between 80 and 90 % is much higher than the DOC decrease thus there is a transformation of the compounds by the treatment with zero-

valent iron. The decrease of the DOC-concentration can be caused by adsorption onto the iron surface of the compounds and the transformation products or precipitation of less polar transformation products (chemical reduction of functional groups like hydroxyl or carboxylic functional groups). However it is not possible to differentiate and quantify the proportion of adsorption and thus the decrease of the DOC-concentration is not considered for the calculation of the reaction rate constant.

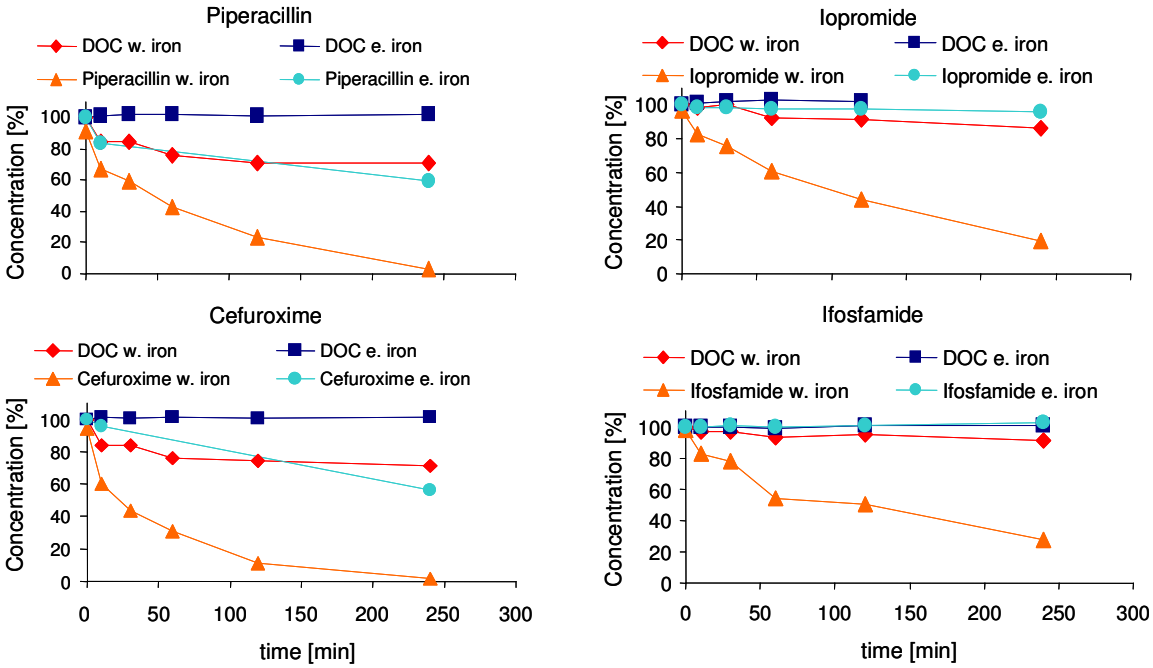

Figure 11: Concentration and DOC decrease versus time of the selected compounds due to precipitation.

3.1.3.3 Influence of the temperature

The temperature is an important factor for the kinetic of chemical reactions. According to the Arrhenius equation an endothermic reaction depends on the temperature. Reactions where an adsorption onto a surface is a prerequisite depend also on the temperature if they are controlled by diffusion. Figure 8 show the k_{obs} values of the treatment with iron at pH 3 constant for different temperatures. The influence of the temperature is only weak, except for Piperacilline and Methotrexate (Figure 12).

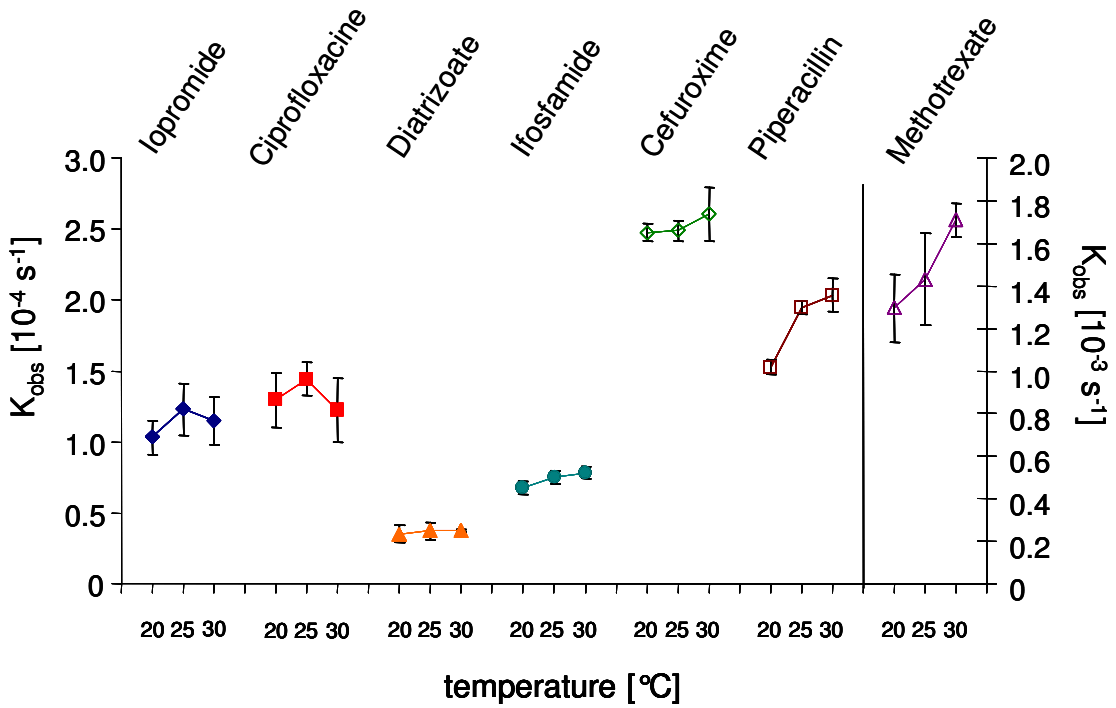

Figure 12: Observed reaction rate constants for the selected compounds in dependence on the temperature. (Fe = 40 g/L, pH = 3 constant, T = 20°C, rpm = 600). n = 3

The observed reaction rate for Piperacillin and Methotrexate increases with increasing temperature. This might indicate that the mechanism for the transformation is different as for the other compounds examined. In case of Methotrexate a different reaction mechanism is also indicated by the different pH dependence of k_{obs} (see page 19).

3.1.3.4 Influence of the stirring speed

The independence between the reaction rate constant and the temperature indicates that adsorption of the compounds onto the iron surface is a prerequisite for the reaction and the speed controlling step is the transport to the iron surface. This supposition is investigated by increasing of the stirring speed with the aim to lower the film layer on the iron surface. The increasing of the stirring speed from 600 to 800 rpm results in a clear acceleration of the kinetic except for Methotrexate (Figure 13). This validates the supposition of a mass transport controlled kinetic and a different reaction mechanism of Methotrexate as already seen before.

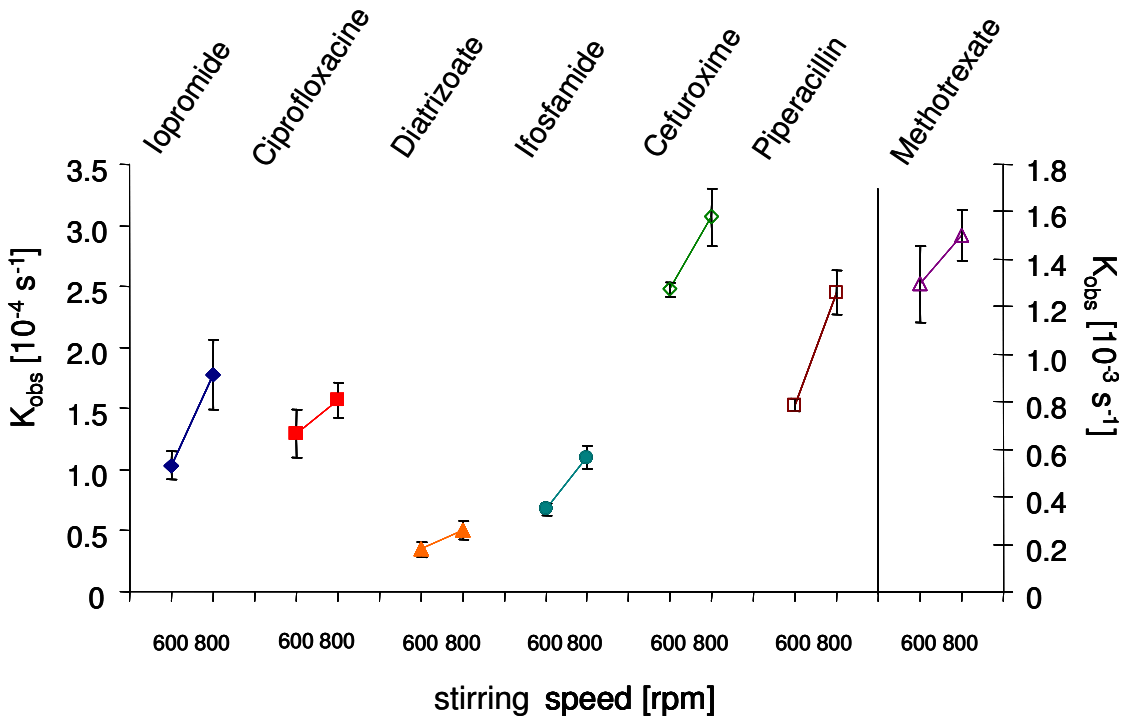

Figure 13: Observed reaction rate constants for the selected compounds in dependence on the stirring speed. (Fe = 40 g/L, pH = 3 constant, T = 20°C) n = 3.

Although the kinetic is faster at a higher stirring speed all further experiments are done at 600 rpm. A higher stirring speed was not used because strong vibration and the formation of high vortices are developed at higher rpm.

3.1.3.5 Influence of the iron surface area

The accelerating influence of the stirring speed on the kinetic is a strong indication that the iron surface has an important impact for the mechanism. Thus increasing the amount of added iron (resulting in a higher iron surface area) should increase the reaction rate constants. This effect can be observed for all compounds up to an iron surface area concentration of 25.6 m^2/g (40 g Fe/L). With higher amounts of added iron the reaction rate stagnates or decreases (Figure 14). This effect could be explained by the special construction of the reactor type 2 where the iron is placed onto the sieve and the solution has to flow through the iron particles. Higher amounts of iron (more than 40 g Fe/L) blockages the sieve and inhibits a good circulatory in the reactor with the result that the whole iron surface can not be used.

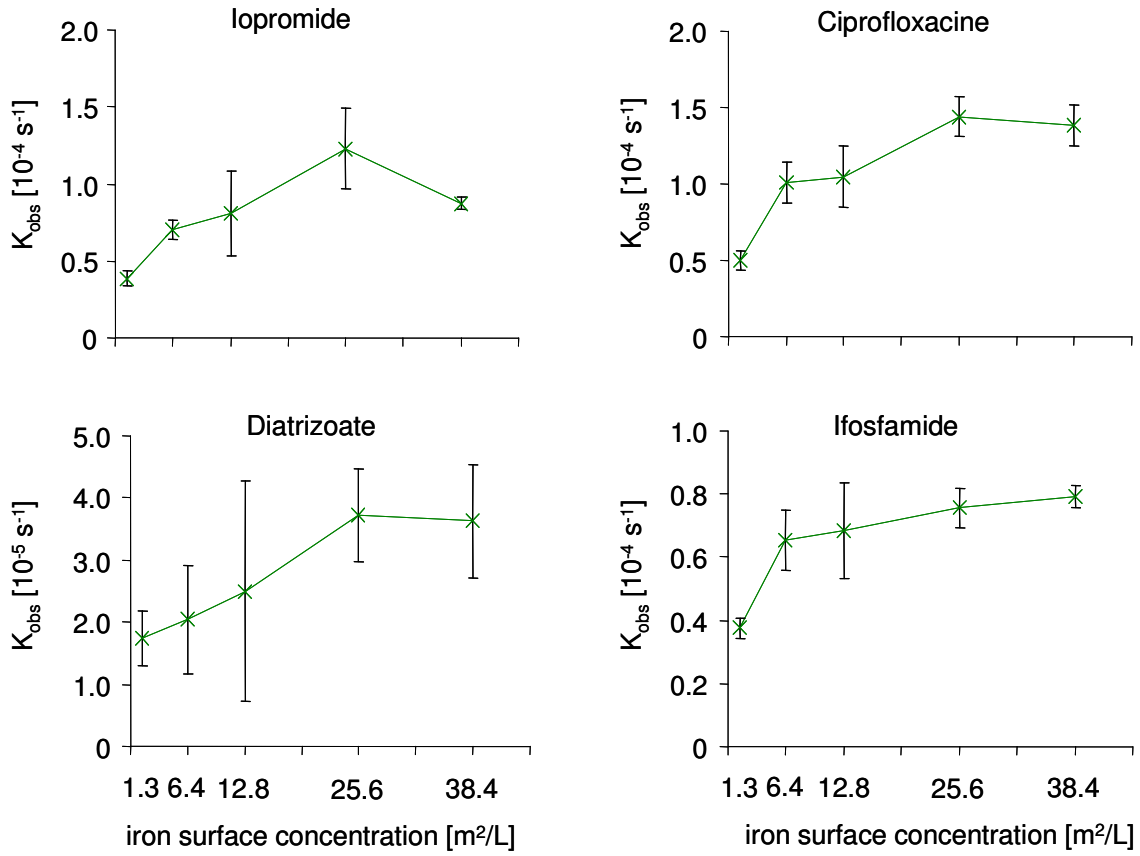

Figure 14: Observed reaction rate constants for the selected compounds in dependence on the iron surface area. (pH = 3 constant, T = 25°C, rpm = 600). n = 3.

3.1.4 Catalytic hydrogenation

The results of the kinetic experiments show that the mechanism for the transformation of the pharmaceuticals is based on a reaction at the iron metal surface. Due to the optimum at pH 3 a reaction with adsorbed atomic hydrogen is very probable. To verify this supposition the selected compounds were hydrogenated with platinum as catalyst. The mechanism of the catalyzed hydrogenation is equal to the mechanism with hydrogen adsorbed onto the iron surface and same transformation products should be produced. Table 8 summarizes the detected transformation products for both reactions (Fe^0 and catalyzed hydrogenation). In most cases same transformation products were detected indicating that a hydrogenation is responsible for the concentration decrease in case of the iron treatment. The mechanism is based on a hydrogenation by atomic hydrogen produced by the reduction of water. The atomic hydrogen is adsorbed onto the iron surface which is the reaction place.

Table 8: Transformation products detected after iron treatment and after catalytic hydrogenation.

Compound	Transformation products
Iopromide	Complete deiodination by treatment with Fe^0 and catalytic hydrogenation. The catalytic hydrogenation leads to only one peak with m/z 414. The treatment with iron leads to two peaks, the main peak has a m/z of 414 and the second of m/z 340 which is most probably the complete deiodinated Iopromide with a transformed side chain (Figure 8).
Diatrizoate	By treatment with Fe^0 the complete deiodinated compound (m/z 237 and m/z 269*) and the corresponding dimere (m/z 473 and 708) were detected within one signal (it is not known if the dimere is produced by the reaction or during ionization for the MS analysis). The catalytic hydrogenation leads to one main signal with the same m/z values as detected after Fe^0 treatment and four further peaks representing the original compound and the partly deiodinated compounds. * Diatrizoate produces an adduct (methanol) in the ESI interface
Methotrexate	The treatment with Fe^0 and the catalytic hydrogenation leads to the same metabolites, one main peak with m/z 280, one peak with m/z 179 and one peak for the original compound.
Ifosfamide	The transformation of the compound is much lower in case of the catalytic hydrogenation than for the Fe^0 treatment. In both reaction solutions a compound with m/z 227 and 274 were detected. The treatment with Fe^0 leads to two further peaks with m/z 241 and m/z 213.
Piperacillin	The catalytic hydrogenation leads in contrast the Fe^0 treatment to many signals in the chromatogram. It was not possible to interpret the mass spectrums. But nevertheless two compounds with m/z 532 and m/z 249 were detectable in both solutions.
Cefuroxime	The catalytic hydrogenation as well as the Fe^0 treatment leads to one transformation product with m/z 380. In case of the catalytic hydrogennation a strong dimerization of the mother compound could be observed. It is not clear if the dimerization occurs during the reaction or in the ESI interface (in case of the Fe^0 treatment the mother compound was not detectable).
Ciprofloxacine	The treatment with Fe^0 and the catalytic hydrogenation leads to a lot of peaks but we could not find any analogy. Maybe there is a stronger transformation by the catalytic hydrogenation than by the treatment with iron.

3.1.5 Experiments with urine

3.1.5.1 Storage of the urine

Fresh urine is an unstable solution with high concentrations of different salts and organic compounds like urea (ca. 15 g/L) or amino acids (ca. 1 g/L). The bacterial hydrolysis of urea is the main reaction which occurs during urine storage (equation 11). Due to that reaction the pH value increases from 6 to 9.

$$NH_2(CO)NH_2 + 2H_2O \rightarrow NH_3 + NH_4^+ + HCO_3^- \qquad (11)$$

The increased pH value leads to a precipitation of struvite (Ronteltap, Maurer et al. 2007; Ronteltap, Maurer et al. 2010), hydroxylapatite and calcite (in case of a high flush water amount, (Udert 2004)) whereby the concentrations of phosphate (ca. 34 %), calcium (ca. 80 %), magnesium (ca. 99 %) and ammonium (ca. 1 %) decrease. The conservation of urine before storage by acidification to pH 2 inhibits completely the bacterial hydrolysis of urea and the concentration of all examined compounds remains constant (Figure 15).

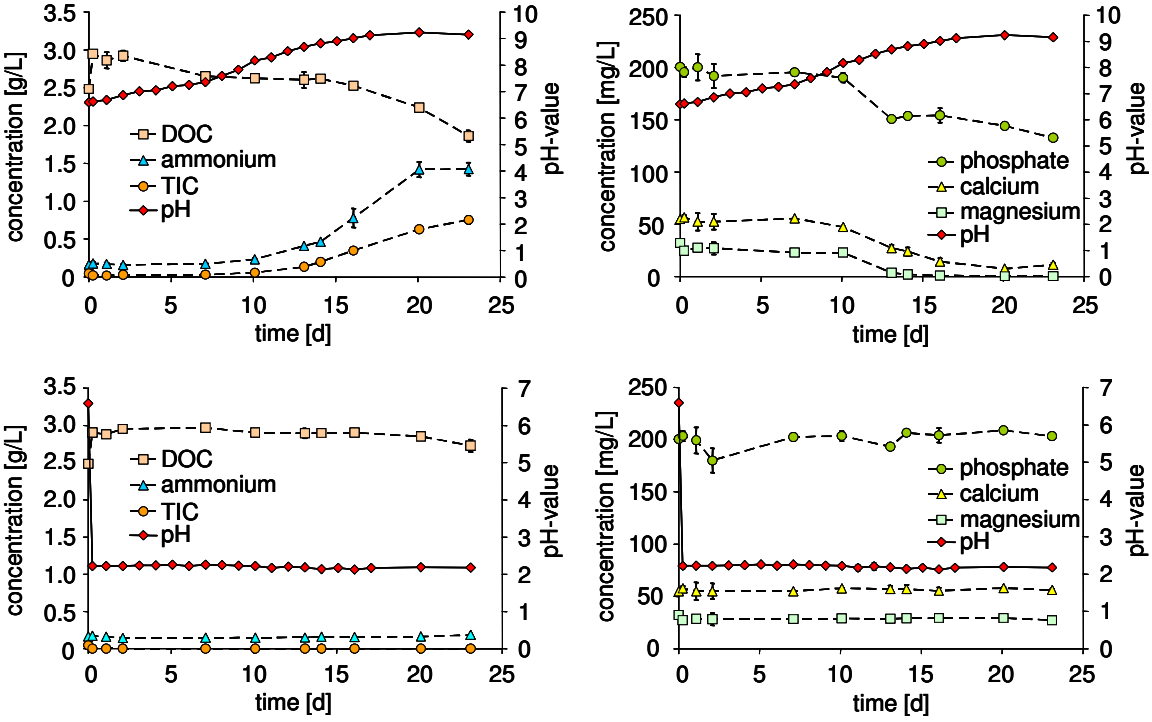

Figure 15: Concentration of urine constituents versus time during storage; n = 2.

Another consequence of the bacterial hydrolysis of urea is an increased acid consumption to acidify the urine after storage. The acid consumption increases from 5 ml/L at the beginning to 35 ml/L at the end of the storage experiment. The increased buffer capacity caused by the increasing ammonium- and carbonic acid concentration is the reason for that. The calculated amount of the NH_3 – alkalinity and the C – alkalinity is presented in Figure 16. The unknown alkalinity is nearly constant over the storage time and consists most probably to 50 % of sulphate and phosphate alkalinity and the remaining 50 % are caused by different organic acids and other organic urine constituents. Is urine conserved (pH 2) before storage nearly no further acid is needed to keep the pH constant. But the acid conditions promote the development of the fungi *Penicillium glaucum* in one of the batches (Figure 35, Appendix A7).

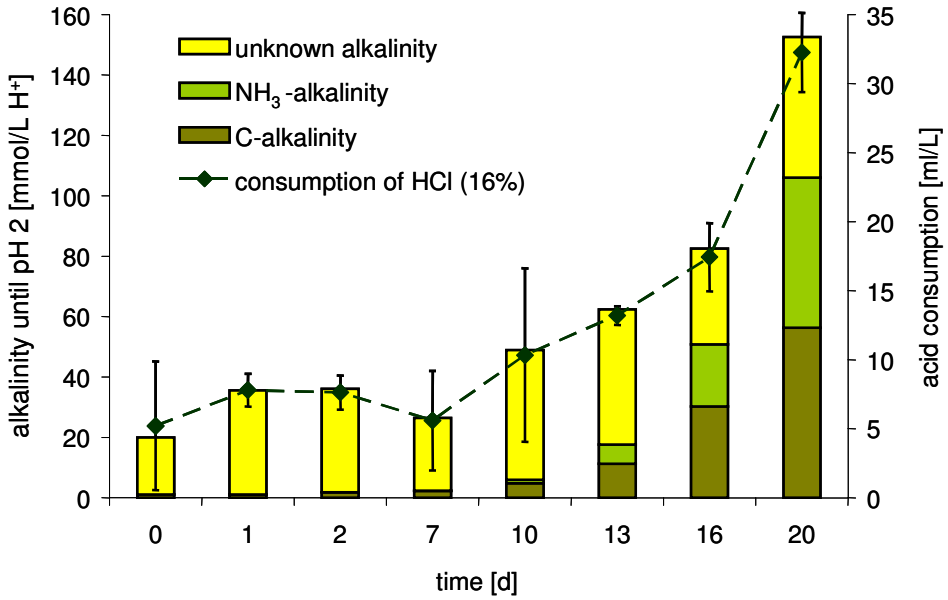

Figure 16: Calculated amount of the NH_3 – alkalinity and the C – alkalinity versus time.

The influence and the behaviour of the selected compounds were studied if un-conserved urine is stored (experiment III, see Methods). The pharmaceuticals inhibit the bacterial activity which is indicated by a delayed hydrolysis of urea compared to the storage test of un-conserved urine without addition of pharmaceuticals (experiment II, see Methods).

The comparison of the pharmaceutical concentration at the beginning and at the end of the storage time show that all compounds except Piperacillin and Cefuroxime stayed in the solution (Figure 17). Additionally no compound could be found in the sediment thus the precipitates are free of the pharmaceuticals what is already found by (Ronteltap, Maurer et al. 2007). Piperacillin and Cefuroxime are not stable at higher pH-values and

thus, the increased pH-value due to the hydrolysis of the urea is responsible for the elimination of the compounds.

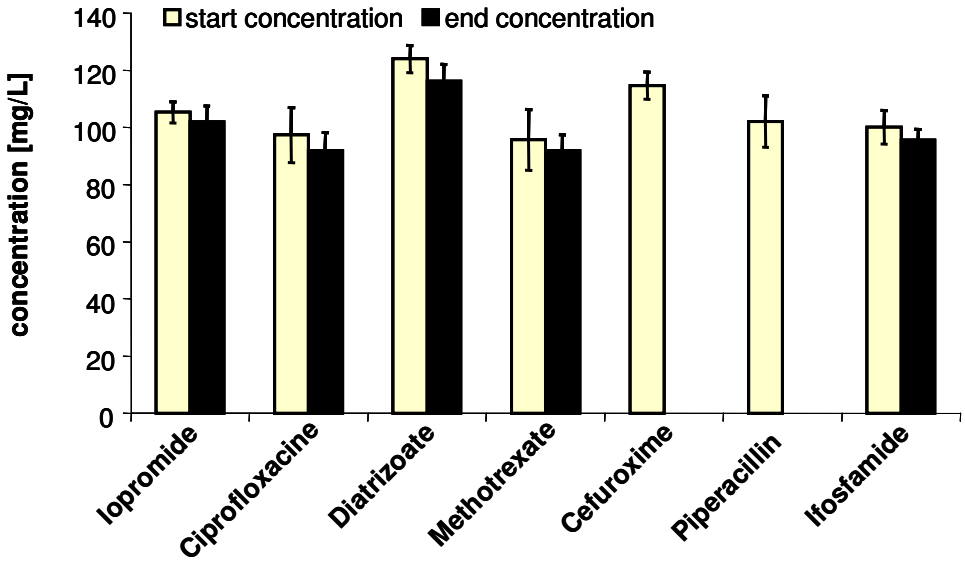

Figure 17: Initial and end concentration of the selected compounds during urine storage, n= 2.

If fresh urine is mixed with a bit of stored un-conserved urine, or if urease is added to fresh urine the hydrolysis of urea can strongly be accelerated. After a few hours the pH has reached a constant value of 9.2 indicating a complete removal of urea (Figure 18).

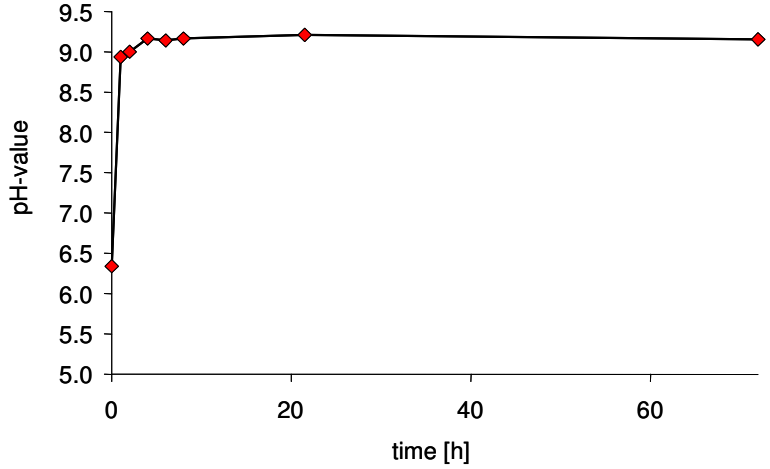

Figure 18: pH versus time during urea hydrolysis.

3.1.5.2 Influence of urine to the reaction rate

The selected pharmaceuticals were dissolved in fresh, acidified urine and were treated with zero-valent iron under conditions which were found to be optimal for the treatment of pure water samples (pH 3, 600 rpm, 25°C and 40 g Fe/L). Figure 19 shows the reaction

rate constant calculated for each compound in the matrices urine and pure water. As expected the reaction rate constants are much lower in the matrix urine.

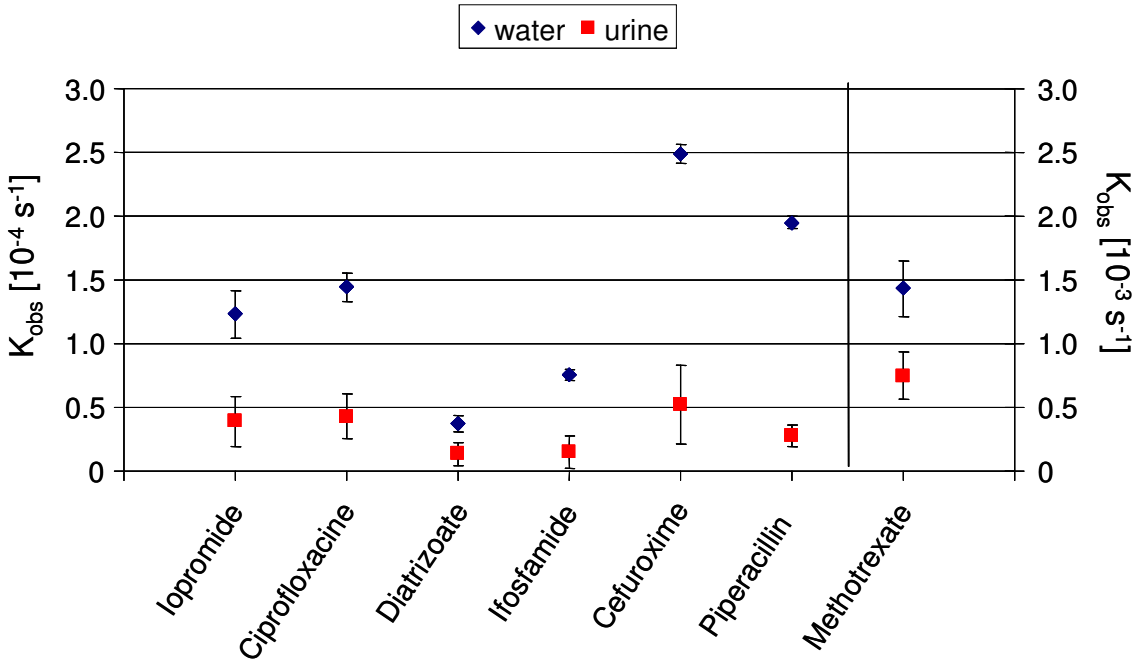

Figure 19: Observed reaction rate constants for the selected compounds dissolved in water and urine. (Fe = 40 g/L, pH = 3 constant, T = 20°C, rpm = 600) n = 3.

Due to the strong decrease of the reaction rate constant in urine the influence of different urine constituents like PO_4^{3-}, SO_4^{2-}, Cl^-, NH_4^+, urea and oxalate were studied. The results are not presented because they show an incoherent picture and it was not possible to draw clear conclusions. Furthermore it was expected that information concerning the mechanism could be obtained. If for the transformation an adsorption onto the iron surface is a prerequisite, than the reaction yield should be lower in the presence of sulphate and phosphate in comparison to chloride, because phosphate and sulphate have a higher affinity to surface complexation with iron oxides. But nevertheless the non-interpretable results support that the hydrogenation by atomic hydrogen represents the mechanism for the transformation of the selected compounds by zero-valent-iron.

The corrosion rate correlating with the reduction of the pharmaceuticals can be expressed by the hydrogen production, the dosed acid which is needed to keep the pH constant and the dissolution rate of Fe^{2+}. Figure 20 show the influence of NaCl (concentrated like in urine), Iopromide and both compounds together on the acid dosage rate. NaCl inhibits the corrosion (less acid is dosed), but the inhibition by Iopromide is much higher. The inhibition of Iopromide and NaCl together is comparable with the inhibition of Iopromide alone. This indicates that the corrosion is much more inhibited by organic than by inorganic compounds.

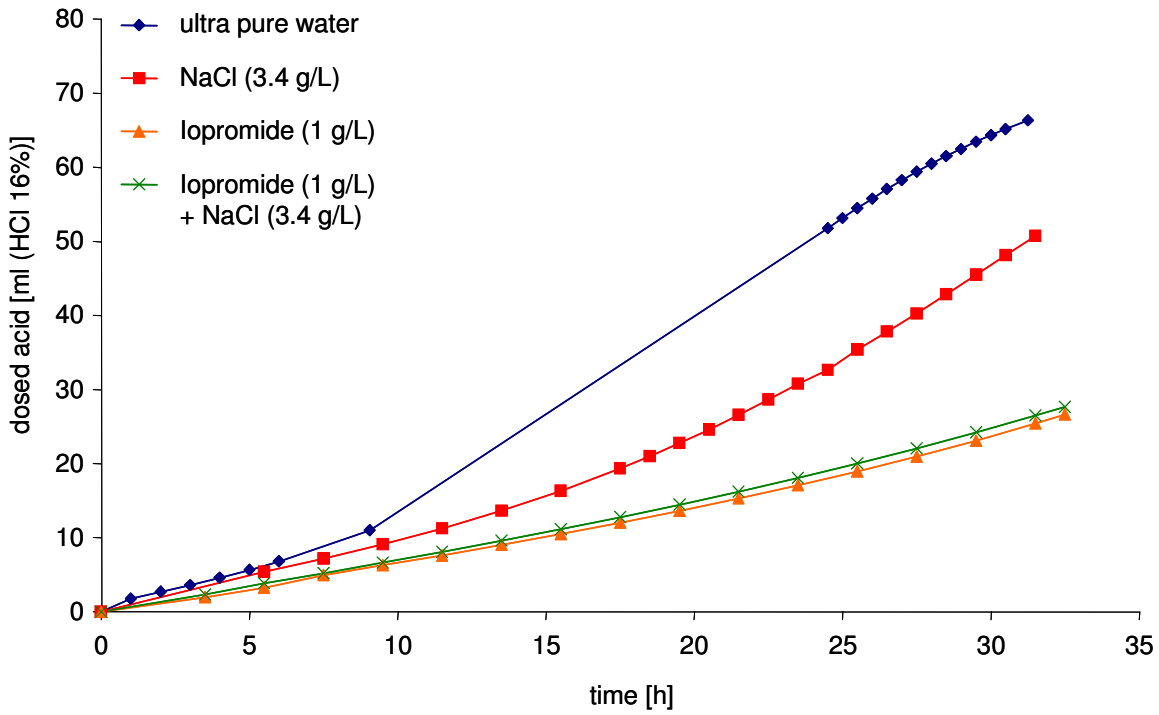

Figure 20: Dosed acid versus time to readjust an initial pH of 3 influenced by NaCl and Iopromide.

Due to this conclusion the influence of urea and glycine as organic urine constituents on the corrosion rate was examined. Figure 21 makes clear that both compounds inhibit the corrosion. Glycine shows a stronger effect than urea even though the concentration is lower. The consideration of the DOC-concentration reveals that adsorption and permanent blockage of urea or glycine are not responsible for the decrease of the corrosion rate. It is much more probable that there is a competition for electrons between the organic compounds and the H^+ on the iron surface. In this case there were less H_{ads}-atoms to react with the pharmaceuticals and additionally a competition for reactive places between organic urine constituents and pharmaceuticals. An indication for the reaction of urea and glycine with electrons of the iron is that the ratio between the molar amount of added H^+ and dissolved Fe^{2+} moves from 2 to amounts smaller than 2. This means Fe^{2+} is dissolved by the reaction with organic compounds. This reaction is slower than the hydrogen corrosion thus the corrosion rate decreases in presence of organic compounds.

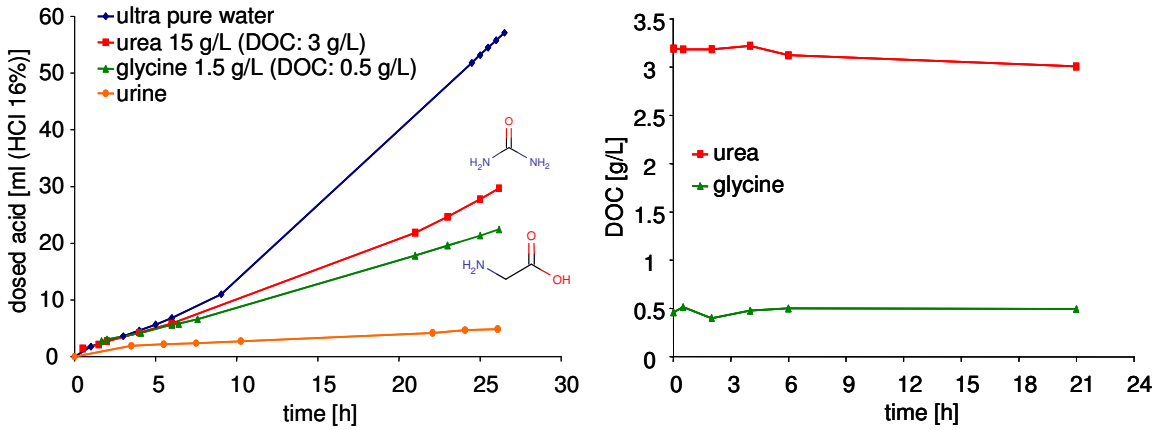

Figure 21: Dosed acid versus time to readjust an initial pH of 3 influenced by the urine constituents urea and glycine versus time respectively DOC-concentration of urea and glycine versus time.

Furthermore it is clear that no single compound like urea (highest concentration in urine) is responsible for the strong decrease of the corrosion rate in urine. Another conclusion is that the reaction rate for the reduction of the pharmaceutical compounds depends strongly on the DOC concentration of the urine.

The addition of Diatrizoate to urine shows an inhibition effect on the corrosion rate (Figure 22). But the percentage effect is lower than the addition of Iopromide or urea and glycine to ultra pure water. The reason for that could be the already low level of the corrosion rate caused by the background compounds of the urine on the one hand and a strong competition for adsorption space on the iron surface with worse adsorption properties of Diatrizoate.

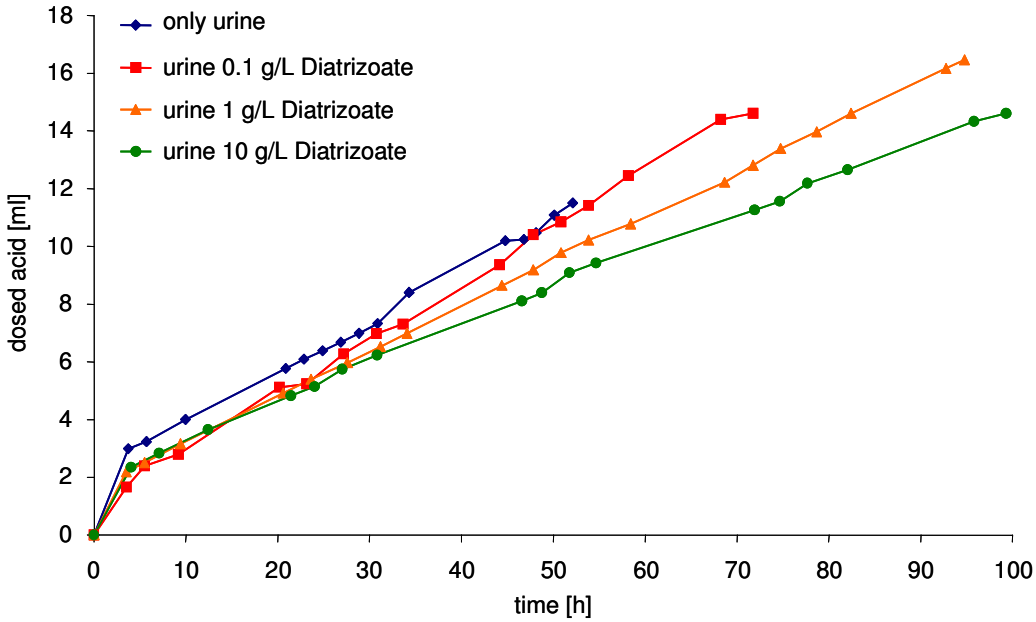

Figure 22: Dosed acid versus time for different concentrations of Diatrizoate in urine.

3.1.6 Summary of the kinetic and mechanism experiments

The seven selected compounds can be transformed by treatment with zero-valent iron in ultra pure water and urine. The decrease of the compound concentrations can be described by a reaction of pseudo first order for pH-values of 3 and lower and by a reaction of zero order for the pH-values 4 and 5 (pH constant). If the pH-value is adjusted to 2 and not kept constant a pseudo first order reaction can be found at the beginning of the reaction changing to zero order if pH-values higher than 4 are reached. The fastest compound concentration decrease in ultra pure water is found at constant pH 3 except for Methotrexate. The temperature has in contrast to the stirring speed a weak influence on the reaction time. An increase of the provided iron surface area accelerates the reaction. These results indicate that the reduction of the compounds is caused by a catalytic reaction with adsorbed atomic hydrogen on the iron surface. This presumption is supported by results of a catalytic hydrogenation with platinum and hydrogen gas where the same transformation products (same m/z values) could be detected as found for the iron treatment. The reaction rate is reduced by the matrix urine. Experiments with different urine constituents show that the corrosion rate, which is related to the reaction rate, is more inhibited by organic than inorganic compounds which is most probably caused by a competition of adsorption places on the iron surface.

3.2 Results of the biological tests

3.2.1 Preliminary considerations

The treatment of the pharmaceuticals with zero-valent iron is performed at pH 3 and is based on the oxidation and dissolution of the iron. Biological tests have to be performed at neutral pH-values thus it is necessary to increase the pH-value. The pH increase results in a precipitation of the dissolved iron. In chapter 3.1.3.1 it is shown that a part of the compound-DOC is removed from the solution by adsorption onto precipitated iron or precipitation of the transformed species if the pH is increased. The treatment of the pharmaceuticals in ultra pure water leads to very high dissolved iron concentrations up to 10 g/L. The precipitation of this huge amount of iron results in a strong removal of the transformed compounds (more than 70 %). Unfortunately it is not possible to identify or differentiate the transformation products thus it is not possible to say if all transformation products are affected equally or if only special fractions are removed. On this account the results of the biological tests with the transformation products are only valid for the residual compounds which remain in the solution.

3.2.2 Luminescence test (DIN EN ISO 11348-3) and Growth-inhibition test (DIN 38412-37)

The growth inhibition test was done with the original compounds and the transformation products after the treatment with zero-valent iron. The test should show if the iron treatment is able to eliminate the biological effects of the antibiotics and cytostatic drugs and if no other toxic compounds are produced. *Vibrio fischeri* was chosen as test organism because one test should be the luminescence test. But it was recognized that the luminescence test is not capable to determine biological effect of the selected compounds. The antibiotics and cytostatic drugs affect the cell division and not metabolic processes which are examined with the luminescence test. Therefore the results of the luminescence test are not considered.

The ICM are known not to be toxic thus, the original compounds were not examined with the toxicity tests. The examination of the deiodinated and eventually existing partly deiodinated species of Iopromide and Diatrizoate show no toxic effects in the examined concentration range (Figure 43, Appendix A13). A surprisingly low toxicity was found for the cytostatic drugs. No toxic effect can be seen for Ifosfamide up to a concentration of 50 mg/L. In case of the antibiotics and Methotrexate the growth inhibition is higher than

50 % in the examined concentration range thus the EC_{50}-values can be calculated (Table 9). Methotrexate is with an EC_{50} of 38.1 mg/L less toxic than the antibiotics Cefuroxime and Piperacillin (ca. 2 mg/L) which are 1000 times less toxic than Ciprofloxacine (2.6 µg/L).

Table 9: Calculated EC_{50} values.

Compound	**EC_{50}**
Methotrexate	38.1 mg/L
Cefuroxime	1.55 mg/L
Piperacillin	2.70 mg/L
Ciprofloxacine	2.60 µg/L

Due to the lack of knowledge about the transformation products the discussion about the toxicity of the transformation products has to be done based on the DOC-concentration. The transformation products of Ifosfamide were examined in a similar DOC-concentration range like the original compound and show no increase of the toxic effect to *Vibrio fischeri* (Figure 23).

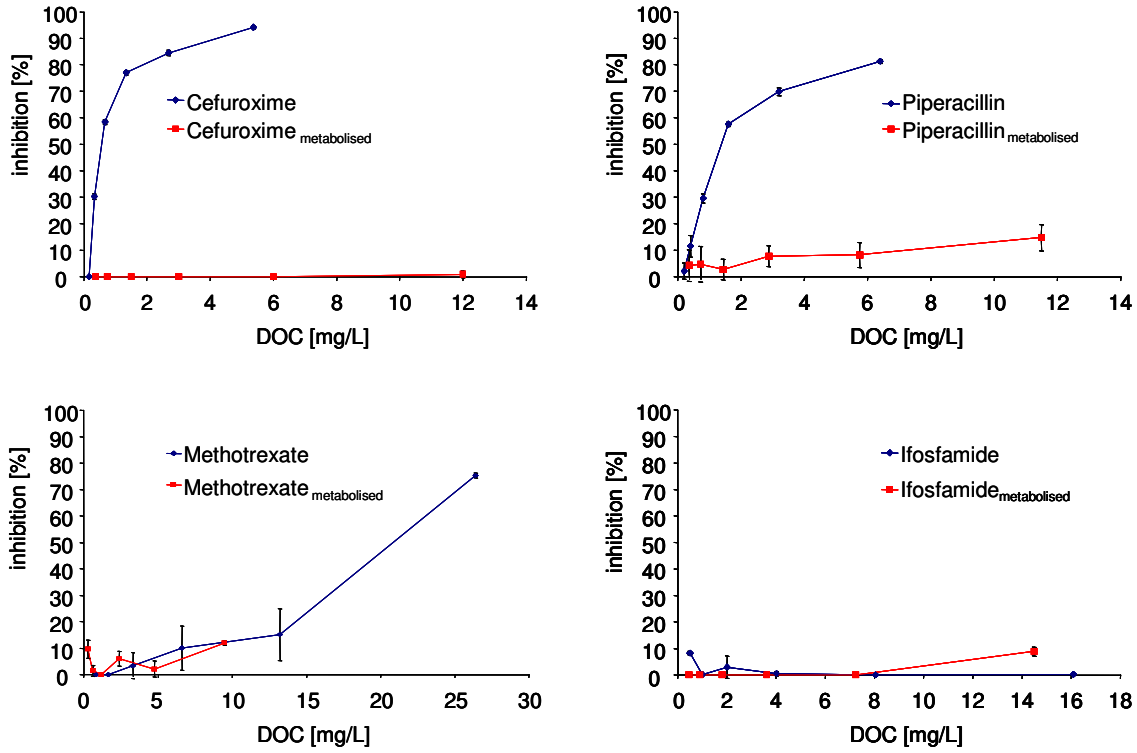

Figure 23: Growth inhibition of *Vibrio fisheri* in dependence of the DOC for the selected compounds and the iron transformation products. n = 2.

The toxic effect of the antibiotics is strong decreased by the treatment with zero-valent iron. Over a wide concentration range the transformation products of Cefuroxime show no growth inhibition. For the transformation products of Piperacillin only a weak inhibition to the test organism was detected. In case of Ciprofloxacin the inhibition is 100 % but it should be mentioned that the examined DOC-concentration was 1000 times higher than in the test done with the original compound (Figure 43, Appendix A10). The inhibition is most probably caused by a residual concentration of Ciprofloxacin (EC_{50} = 2.6 µg/L) which was not transformed. Due to the good adsorption of Methotrexate the DOC-concentration after treatment with iron and removing the dissolved iron was too small to see if there is less toxicity compared to the original compound. However generally it can be said that the treatment with zero-valent iron can decrease the biological activity of the antibiotics and leads not to toxic compounds.

3.2.3 Biodegradation tests

3.2.3.1 Preliminary tests

The growth-inhibition tests have shown that the antibiotics have a strong inhibition effect to *Vibrio fischeri*. The biodegradation tests (Zahn-Wellens-Tests) will be done with activated sludge of the waste water treatment plant Ruhleben (Berlin). Before starting the experiments the inhibition effect of the antibiotics to the organisms of the activated sludge was tested with aniline as reference compound. The goal is to find an appropriate concentration which can be measured (DOC) and leads not to a strong inhibition of the sludge. Table 10 shows an overview of the experiment.

Table 10: Concentrations used for the preliminary tests to evaluate a suitable initial compound concentration for the Zahn-Wellens-Test.

Compound	$DOC_{compound}$ – conc. [mg/L]	Compound conc. [mg/L]	$DOC_{aniline}$ – conc. [mg/L]	Sludge conc. [mg/L]
Ciprofloxacine	10	16.2	20	172.1
	5	8.1	20	172.1
	2.5	4.1	20	172.1
Cefuroxime	10	23.2	20	172.1
	5	11.6	20	172.1
	2.5	5.8	20	172.1
Piperacillin	10	19.5	20	172.1
	5	9.8	20	172.1
	2.5	4.9	20	172.1

An additional batch with only aniline and sludge enables the comparison of the influence of the antibiotics. After an initial lag-phase of two days the DOC-aniline is reduced to a low residual concentration (Figure 24). The residual DOC-concentration of ca. 2.5 mg/L

consists of non-biodegradable compounds added with the sludge and/or aniline, which is not further degradable. For Piperacillin an EC_{50} of 2.7 mg/L was determined with the growth inhibition test (*Vibrio fischeri*) but concentrations up to 4.9 mg/L (2.5 mg/L DOC concentration) do not inhibit the aniline degradation. However after 6 days the DOC concentration corresponds to the sum of the added compound DOC-concentration and the residual aniline DOC amount in case of all experiments and thus, Piperacillin is not biodegradable within 8 days. Same results were found for Cefuroxime (Figure 44, Appendix A11). The strong inhibition effect of Ciprofloxacin *to Vibrio fischeri* can also be seen for the inhibition of the organisms of activated sludge. A concentration of 4 mg/L Ciprofloxacin (2.5 mg/L DOC-concentration) leads to a delay of 4-5 days for a complete aniline degradation. The highest concentration of 16.2 mg/L (10 mg/L DOC-concentration) inhibits the aniline degradation over the 8 days of the experiment. The decrease of the DOC-concentration at the first day is assumed as adsorption of Ciprofloxacin on the sludge due to the good adsorption properties of Ciprofloxacin (Alexy 2003). The experiment done with a ciprofloxacin concentration which is not toxic to the organisms of the activated sludge indicates that ciprofloxacin is not biodegradable because after 8 days the DOC is the sum of the residual aniline and the added compound DOC.

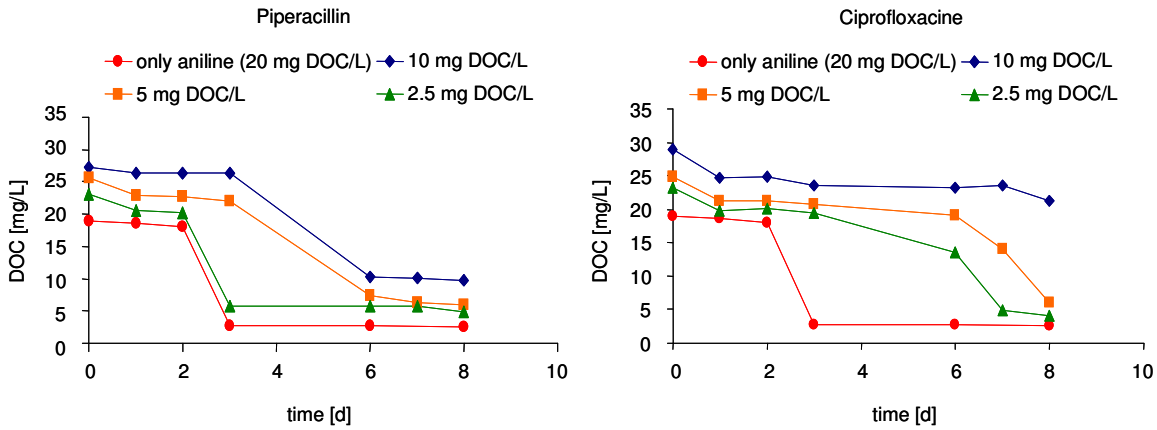

Figure 24: Inhibition of the aniline degradation by the antibiotics, DOC versus time.

Therefore that the cytostatic drugs show less toxicity in the growth inhibition test with *Vibrio fischeri* these compounds are not examined in the preliminary test.

3.2.3.2 Aerobic biodegradation test (Zahn-Wellens-Test DIN EN ISO 9888)

The biodegradation tests (Zahn-Wellens-Test) were done to verify if the selected compounds are better biodegradable after the treatment with zero-valent iron. For that reason the biodegradability of the antibiotics and cytostatic drugs as well as their

transformation products were compared. In case of the ICM which are known to be not biodegradable only the transformation products were tested.

3.2.3.3 Biodegradation of the pharmaceuticals

The DOC-concentration which has to be added according to DIN EN ISO 9888 is in a range of 50 to 400 mg/L. Due to the results of the toxicity tests and the preliminary biodegradation tests a DOC-concentration of ca. 2.5 mg/L for the antibiotics and 8-10 mg/L for the cytostatic drugs were chosen. The added sludge concentration was ca. 300 mg/L for the cytostatic drugs and ca. 117 mg/L for the antibiotics.

The duration of the tests was 28 days. The DOC and the compound concentration were determined. A reference test with aniline shows that the micro organisms of the added activated sludge were active (Figure 45, Appendix A14). A further test with addition of $HgCl_2$ (10 mg/L) was used to be able to recognize an abiotic elimination of the compounds. Figure 25 shows that there is no significant decrease of the DOC-concentration, indicating that the selected pharmaceuticals and/or produced transformation products are not biodegradable as already indicated by the biodegradation test over just 8 days. In case of Ciprofloxacine a small decrease of the DOC-concentration caused by adsorption can be observed during the first three hours. Due to the toxic effect of the pharmaceuticals a release of organic compounds from death micro organisms leads after a few days to an DOC increase which than is reduced again. The same profile is found for the test with added $HgCl_2$.

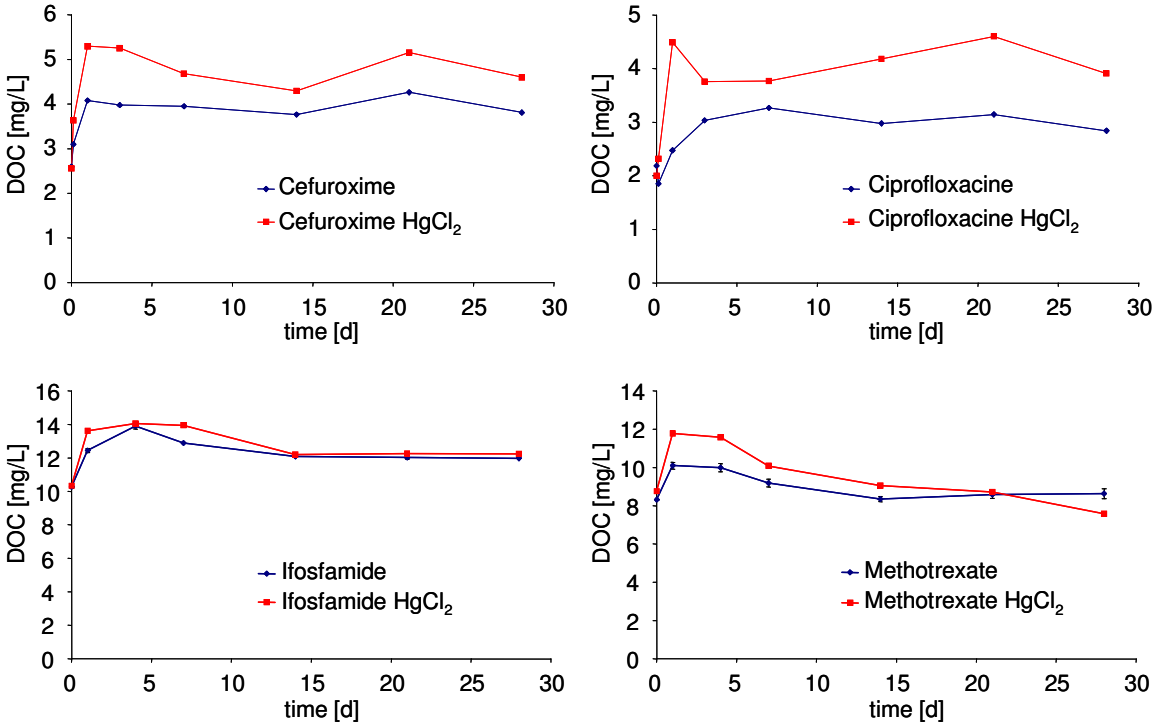

Figure 25: Zahn-Wellens-Test with the selected compounds, DOC versus time.

The behaviour of the compound concentration during the biodegradation test gives more detailed results. Ciprofloxacine has a strong tendency to adsorb onto the sludge (Figure 26) which has already shown by (Alexy 2003). The concentration of Ciprofloxacine is decreased down to 50 % during the first three hours and down to 40 % after one day in case of both tests (with and without $HgCl_2$ addition).

After one day the Ciprofloxacine concentration is just slightly reduced in case of the poisoned test whereas a stronger concentration decrease is recognized in the not poisoned test. The stronger concentration decrease in the not poisoned test can be ascribed to biological transformation, where by the transformation products are not biodegradable due to the constant DOC concentration (see above). In case of Ifosfamide the compound concentration is constant during the complete duration of the test in the poisoned and not poisoned test. Based on this clear result it can be concluded that Ifosfamide is not biodegradable.

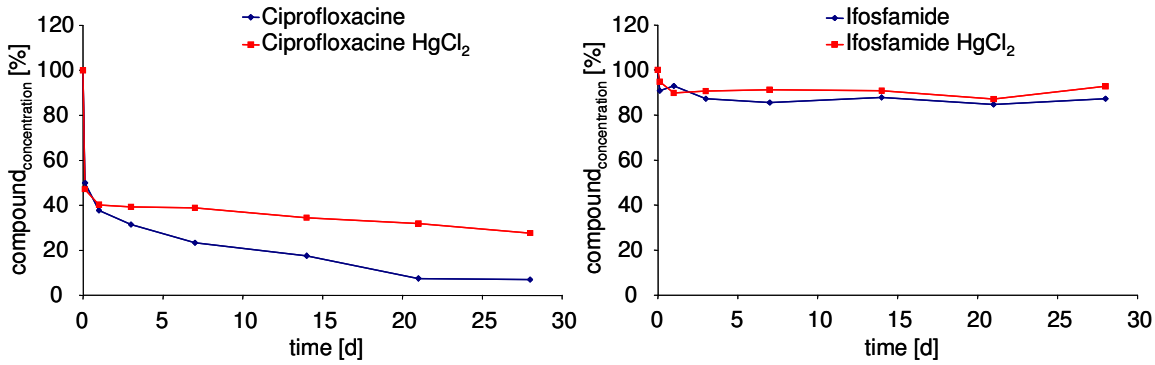

Figure 26: Zahn-Wellens-Test with the selected compounds, compound concentration versus time.

In contrast to Ifosfamide high reduced concentrations for Cefuroxime, Piperacillin and Methotrexate were determined in the biodegradation tests (poisoned and not poisoned test, Figure 47, Appendix A15), indicating a complete abiotic elimination of the compounds. This result is in agreement with a found low biodegradability for ß-lactams, quinolones and sulfonamides and a postulated abiotic elimination (Alexy 2003).

3.2.3.4 Biodegradation of the transformation products

Due to the decreased toxicity of the transformation products produced by the iron treatment the Zahn-Wellens-Test can be done with higher compound, respectively higher DOC-concentrations in contrast to the original compounds. At this point it should be pointed out again that the used concentration for this test is limited by elimination of the transformation products due to adsorption during dissolved iron precipitation which is initiated by raising the pH from 2 to 7. The added sludge concentration for the Zahn-Wellens-Test with the transformation products amounts ca. 200 mg/L.

Compared to the original compounds the DOC of the antibiotic transformation products is decreased up to 50 % (Figure 27) after ca. 15 days. In case of the Ciprofloxacine transformation products adsorption is responsible for the initial DOC decrease during the first day. After one day the DOC is constant until day seven. The DOC decrease down to 5 mg/L starting at day seven is caused by biodegradation by the adapted micro organisms. The residual DOC concentration of 5 mg/L seems to be not biodegradable under the test conditions. The transformation products of the other antibiotics show a continuous DOC decrease to nearly constant amounts of ca. 6 mg/L for Piperacillin and ca. 4.5 mg/L for Cefuroxime. An initial lag-phase is not observed meaning that the bacteria have already appropriate enzymes to degrade the transformation products or the decrease of the DOC-concentration is due to adsorption. In contrast to the antibiotics a DOC concentration increase is recognized in the biodegradation test done with the

transformation products of the ICM. The DOC increase can be caused by toxic transformation products killing the micro organisms followed by a release of soluble organic compounds, as found for the antibiotic and cytostatic drugs in poisoned and not poisoned degradation tests (see above). But keeping in mind that the transformation products of the ICM show no toxic effect (growth inhibition test, see above) the DOC increase is most probably caused by starving bacteria because the transformation products as the only carbon source can not be biologically utilized.

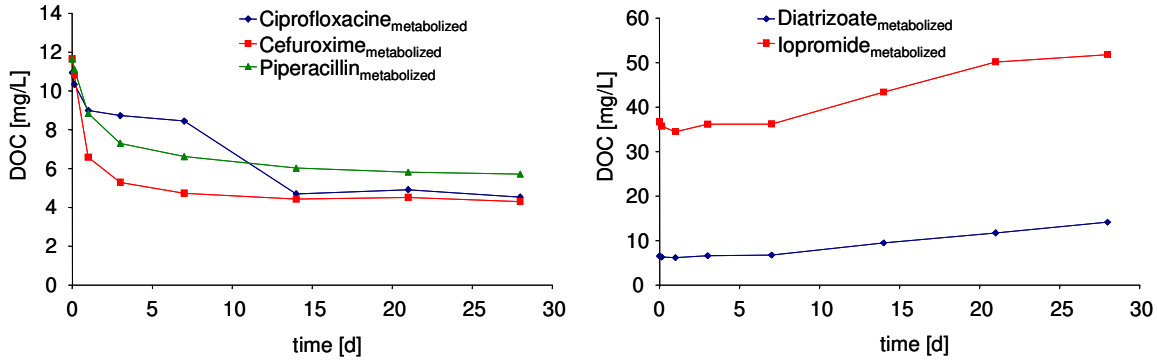

Figure 27: Zahn-Wellens-Test with the transformation products. DOC versus time.

In case of the cytostatic drugs adsorption of the transformation products leads to decreasing DOC-concentrations during the first three hours (Figure 48, Appendix A15). After that the DOC-concentration remains nearly constant, indicating that the compounds are not biodegradable and not toxic.

3.2.3.5 Addition of WWTP influent

The results of the Zahn-Wellens-Test indicate that the transformation products of the ICM and cytostatic drugs are not better biodegradable than the original compounds. To evaluate if the ICM and cytostaic drugs can be degraded by a co-metabolic biodegradation the influent of the waste water treatment plant Ruhleben was added to the Zahn-Wellens-Test. The activated sludge used was from the same waste water treatment plant and thus, the micro organisms are adapted to the same organic compounds and a very fast biodegradation can be expected. The DOC concentration in the blank test (without addition of transformation products) decreases to an amount of ca. 6 mg/L after one day and remains constant for more than 40 days. This amount of not biodegradable DOC is assumed for all batch tests and is demonstrated by a line at 6 mg/L (Figure 28). The second line in each diagram of figure 24 represents the sum of the not biodegradable DOC and the DOC-concentration of the added corresponding transformation products. In case of the antibiotics and the cytostatic drugs the DOC

decrease nearly down to the residual DOC concentration, demonstrating that the compounds are removed. A differentiation between adsorption and biodegradation is not possible. In case of the ICM an increasing DOC-concentration is observed (after one week) again (see above). A DOC concentration increase can be caused by death micro-organisms releasing soluble organic compounds. The death of the organisms can be caused by toxic compounds or by starving if the carbon source is limited, as discussed above. Here, starving bacteria can not be the explanation for the increasing DOC-concentration because in the blank batch test the increase is not observed. For this reason a toxic effect of the ICM transformation products becomes more realistic. (Steger-Hartmann, Lange et al. 2002) examined the toxicity of a transformation product called "free amine" which also can be formed by the treatment with zero-valent iron. He found out that there was only a low short-term toxicity of the primary degradation product ("free amine") and no effects on any of various aquatic species could be found even at concentrations of 1 g L^{-1}. It could be shown that the ICM are deiodinated by the treatment with zero-valent iron and that a further transformation of the side chains is possible. It could be possible that the deiodinated "free amine" is more toxic than an iodinated free amine.

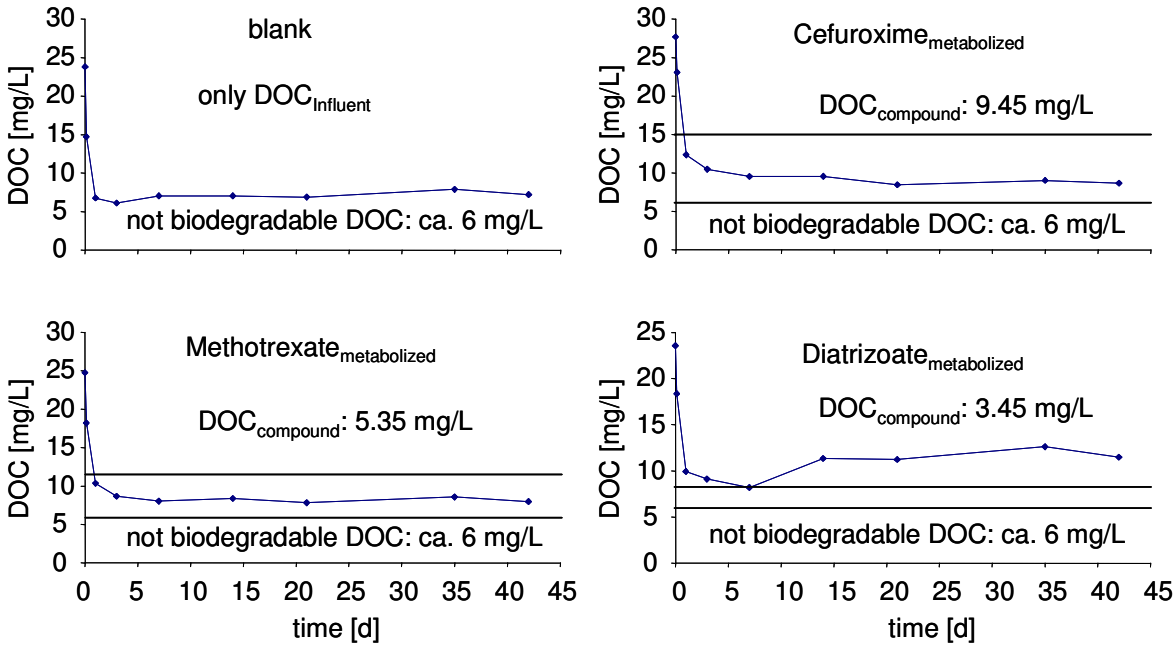

Figure 28: Zahn-Wellens-Test with the iron transformation products and additional biodegradable compounds (influent Ruhleben); DOC versus time.
Line at 6 mg/L: non biodegradable DOC originating from the sludge.
Second line: 6 mg/L DOC plus the initial compound DOC.

3.2.3.6 Decrease of the adsorption

Due to the high concentration of sludge in relation to the added DOC-concentration of transformation products the differentiation of adsorption and biological degradation was not possible. To prevent adsorption a further test was performed and the sludge concentration was decreased from ca. 200 mg/L to ca. 1 mg/L. The transformation products are the only carbon source available for the bacteria. The results show a removal of the DOC-concentration of more than 30 % for all compounds except for the ICM (Figure 29). The ICM show a constant DOC-concentration for the whole test period. Thus there is no better biodegradability of the transformation products than for the ICM themselves. The previously found increase of the DOC-concentration is not apparent due to the small amount of sludge/micro organisms added. This is a further indication for an eventually toxicity of the transformation products of the ICM. Despite the low sludge concentration the transformation products of Ciprofloxacine show an adsorption of ca. 9 % (concentration decrease after a very short time). After that a decrease of the DOC-concentration of ca. 25 % most probably caused by biodegradation can be observed. Such an adsorption can not be seen for the other antibiotics and cytostatic drugs thus in these cases biodegradation is responsible for the decrease of the DOC-concentration. It can be concluded that the transformation products of the antibiotics and cytostatic drugs are better biodegradable than the original compounds.

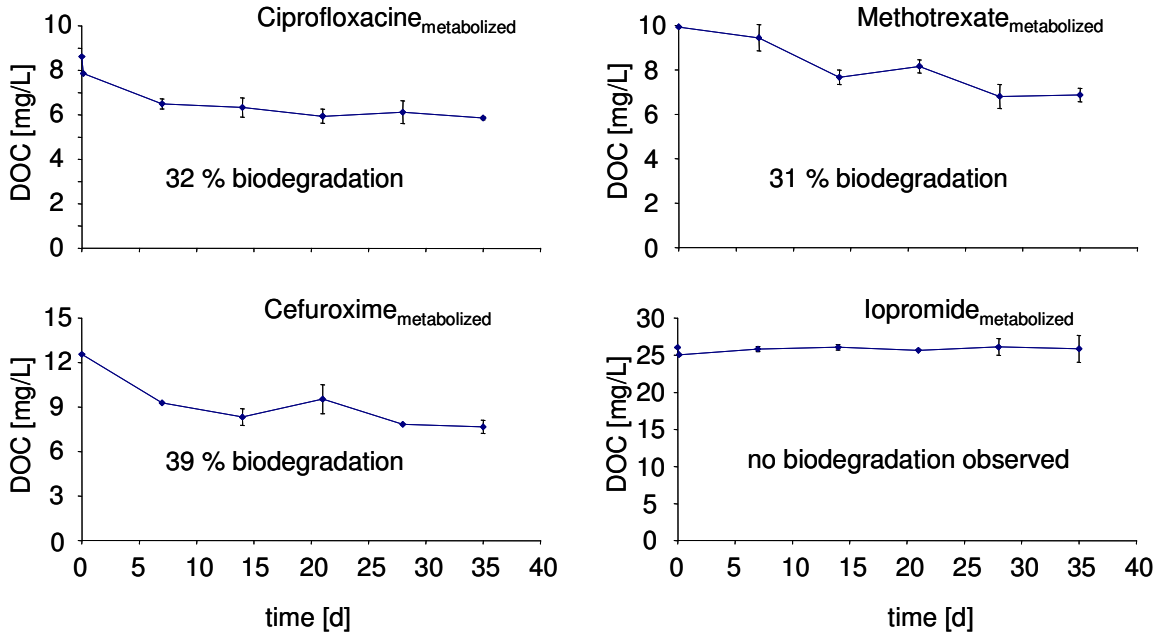

Figure 29: Zahn-Wellens-Test with the transformation products (decrease of the sludge concentration to 1 mg/L); DOC versus time.

3.2.4 Summary of the biological tests

The treatment of the selected compounds with zero-valent iron was done at pH 3. For the biological test the pH has to be increased which result in an iron precipitation and a strong DOC decrease, meaning that some of the transformation products are removed by the precipitation. Due to a strong removal of DOC the biological tests could only be done with the residual compounds remaining in the solution. Thus, the predications of the biological tests are only guilty for the remaining compounds.

The growth inhibition test with *Vibrio fischeri* has shown that the toxicity of the antibiotics can significantly be decreased by treatment with zero-valent iron. Furthermore the results of different modified Zahn-Wellen-Tests demonstrate that the biodegradability of the transformation products of the antibiotics is better than of the original compounds. The cytostatic drugs show an unexpected low toxicity to *Vibrio fischeri* and the transformation products are not more toxic than the original compounds. As found for the antibiotics the transformation products of the cytostatic drugs are better biodegradable than the parent compounds. The transformation products of the ICM show no toxic effects to *Vibrio fischeri* but an increase of the DOC-concentration in the Zahn-Wellens-Tests indicate an eventually increased toxicity and the same low biodegradability as found for the original compounds.

Chapter 4

4.1 Process engineering and cost relevant considerations

As cost relevant aspects for the treatment of urine with zero-valent iron the investment costs for the reactor, a suitable infrastructure (urine separation system), the consumption of energy and material (acid and iron) and costs for the staff are identified. The investment costs and the costs for the staff depend strong on the urine separation system and the kind of reactor used. In the project “Getrennte Erfassung von iodorganischen Röntgenkontrastmitteln in Krankenhäusern” realized by the KWB costs of ca. 7 €/L urine were calculated for a manual collection. These costs can change dramatically if separation toilets are available. Because up to now no well-engineered system is available for the urine separation the collection of urine is not considered for the cost estimation of the treatment.

The consumption of material and energy depends on the reactor type and the treatment conditions. In experiments with Diatrizoate (slowest kinetic of all examined compounds) the influence of the pH-value, the added iron amount and the matrix (fresh or stored urine) on the material consumption was determined. These experiments are done only with urine with a low DOC-concentration (average 2.2 g DOC/L) and an oxygen input during the sampling. The oxygen input leads to a faster kinetic and a higher material consumption due to the higher corrosion rate. It is obvious that the kinetic can be accelerated by using fresh urine, lower pH-values and higher amounts of iron added (Figure 30).

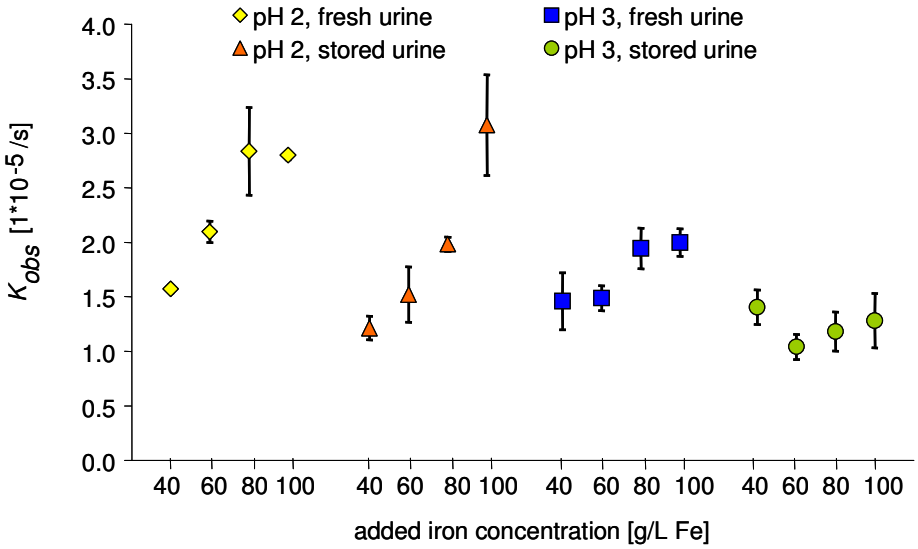

Figure 30: Observed reaction rate constants for the selected compounds for fresh and stored urine at pH 2 and 3 constant. (Fe = 40 g/L, T = 25°C, rpm = 560). n = 3.

These conditions lead to lower reaction times but also to a higher consumption of iron and acid. A better way to compare the conditions is the consideration of the specific consumption. As reference value the time for a 90 percent decrease of the Diatrizoate concentration (c_0: 100 mg/L) is chosen.

Figure 31 show that the differences between the conditions are not very high except for the initial acidification of fresh and stored urine if a 90 % concentration decrease is set at reference. The higher amount of acid used for the initial pH adjustment of stored urine is caused by the increased alkalinity as already discussed in 3.1.5.1. Due to this high acid consumption and the slightly slower kinetic stored urine is not used for further considerations. In fresh urine (or conserved urine acidified to pH 2) it can be seen that the lowest consumption of acid and iron is found for the slowest kinetic at pH 3 and with 40 g Fe^0/L (Figure 30).

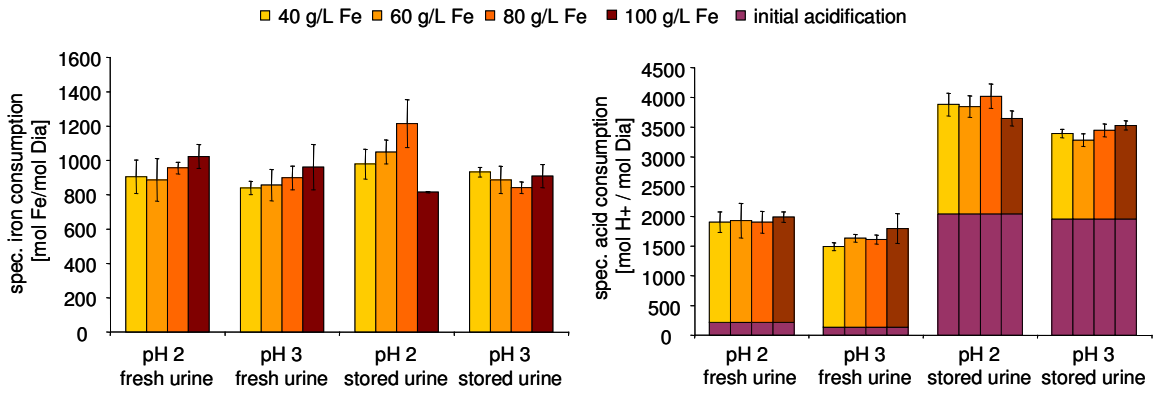

Figure 31: Specific iron and acid consumption for the treatment of fresh and stored urine (T = 25 °C, rpm = 560). n = 3.

In addition to the material consumption the energy expenditure has to be regarded. The calculated power consumption with the used reactor type 2 and a stirring speed of 560 rpm is ca. 1 KW/m^3. The reaction time with the lowest specific material consumption (pH3, 40 g Fe^0/L) is two times higher than at pH 2 and with 100 g Fe^0/L. A cost survey calculated with data for 500 ml urine and 90 percentage transformation of Diatrizoate (100 mg/L) in reactor type 2 is given in Table 11.

Table 11: Material and energy consumption and assumed prices.

parameter	pH 2				pH 3			
	40 g Fe^0/L	60 g Fe^0/L	80 g Fe^0/L	100 g Fe^0/L	40 g Fe^0/L	60 g Fe^0/L	80 g Fe^0/L	100 g Fe^0/L
time [h]	40.85	30.84	22.87	22.56	45.44	43.32	34.59	32.80
dosed HCl [g HCl (33%)/500 ml]	13.61	13.99	13.95	14.72	11.12	12.02	11.93	13.70
dissolved iron [g Fe^{2+}/500 ml]	3.38	3.35	3.68	3.97	3.52	3.28	3.47	3.82
material costs								
costs for HCl (380 €/t) [cent / 500 ml]	0.52	0.53	0.53	0.56	0.42	0.46	0.45	0.52
costs for iron (700 €/t) [cent / 500 ml]	0.24	0.23	0.26	0.28	0.25	0.23	0.24	0.27
sum [cent/500 ml]	0.75	0.77	0.79	0.84	0.67	0.69	0.70	0.79
material costs/m^3 [€/m^3]	15.07	15.33	15.76	16.75	13.38	13.73	13.92	15.76
electricity costs								
electricity costs/m^3 (7 cent/KWh) [cent/m^3]	2.86	2.16	1.60	1.58	3.18	3.03	2.42	2.30
total costs [€/m^3]	17.93	17.48	17.36	18.33	16.56	16.76	16.34	18.06

With the assumed prices (Table 11), the conditions with the slower kinetic and lower material consumption are cheaper than conditions with a shorter runtime. Several parameters can influence the costs. One possibility to reduce the costs is the use of cheaper sulphuric acid instead of hydrochloric acid. Furthermore, the re-use of the iron can also reduce the costs. Due to the elimination of oxide layers on the iron surface during use the re-use of the iron could accelerate the kinetic. An important fact for the treatment is the size of the reactor. It is not possible to scale up the reactor type 2 for higher volume like 100 – 1000 L. The huge amount of particles on the sieve would inhibit the flow of the urine through the iron.

4.1.1 Influence of the acid

The test of sulphuric acid with the same molar H^+-concentration as the hydrochloric (16 %) show that there are no disadvantages concerning the kinetic and the corrosion rate (Figure 32). Thus the costs for the acid can be lowered by using the cheaper sulphuric acid (ca. 117 €/t H_2SO_4 95 %).

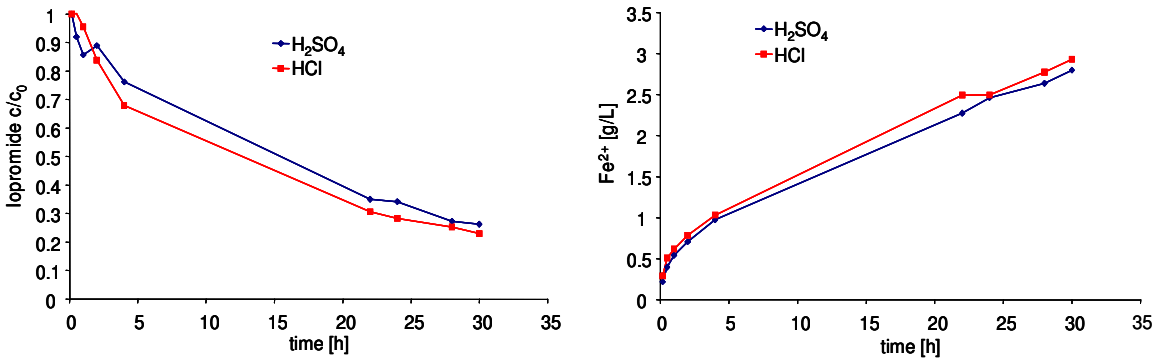

Figure 32: Iopromide and dissolved iron concentration versus time for the use of HCl and H_2SO_4.

The problem of the specific construction of the small reactor type 2 was solved by a simple stirring tank (volume 21 L) with baffles and a propeller stirrer. For a good mixing and turbulence of the iron splints a volume specific power input of 2 kW is needed. The required stirring speed is 1370 rpm. To compare the performance of the reactor type 2 and 3 (21 L) the transformation of Iopromide (100 mg/L) during a re-use experiment of iron was examined. Sulphuric acid was used to get data for a better cost estimation. The experimental conditions were 40 g Fe^0/L and pH 3 and the iron was re-used 3 times. The initial iron amount of each iron re-use experiment was the same and adjusted by adding the consumed iron, based on the dissolved iron concentration after each run. Figure 33 show that the kinetic is faster for reactor type 3 associated with a higher corrosion rate. This can be explained by the higher turbulence and the resulting higher flow on the iron surface. Furthermore it can be seen that the re-use of the iron accelerates the transformation of Iopromide but leads to lower dissolved iron concentrations. The faster kinetic is caused by the elimination of oxide layers on the iron surface (the iron was not pre treated before use). The higher concentration of dissolved iron in the first run can be explained by fine iron dust which is added with the fresh iron and not available in the same amount for the next runs.

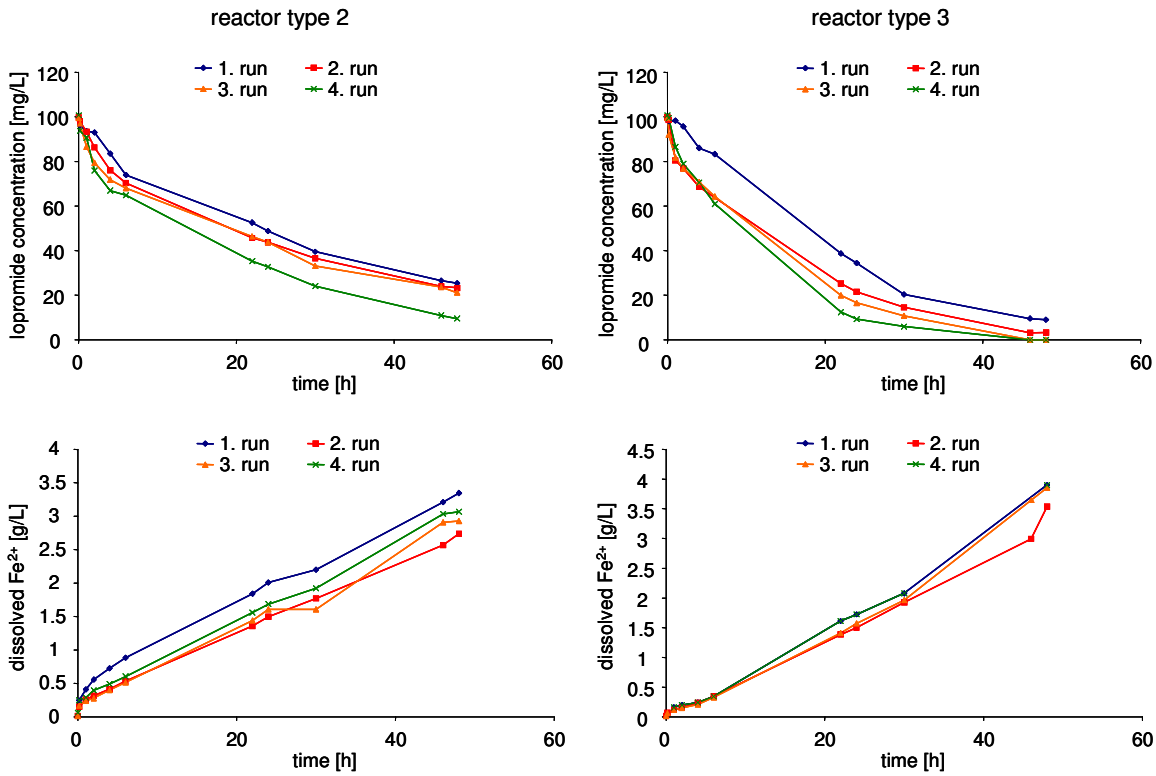

Figure 33: Iopromide and dissolved iron concentration versus time for re-use iron experiments.

New cost estimation has been done with the data of the fourth run of the re-use experiment for the reactor type 3 (Table 12). The chosen reaction time is 46 hours because after that time Iopromide is not detectable and Diatrizoate as the compound with the slowest kinetic is transformed by more than 90 %.

Table 12: Cost estimation

parameter	**data**
time [h]	46
dosed H_2SO_4 [g H_2SO_4 (95%) / L]	7.57
dissolved iron [g Fe^{2+} / L]	3.65
material costs	
costs for H_2SO_4 (117 €/t) [€ / m^3]	0.89
costs for iron (700 €/t) [€ / m^3]	2.56
sum [€ / m^3]	3.44
electricity costs	
electricity costs / m^3 (7 cent/KWh) [€/m^3]	6.44
total costs [€/m^3]	9.88

The usage of H_2SO_4 instead of HCl reduced the material costs but the costs for electricity are increased due to the higher volume specific power input of 2 kW/m^3 for reactor type 3 instead of 1 kW/m^3 for reactor type 2. The electricity costs depend on the duration of the

treatment and thus the costs can be minimized if the conditions are shifted to a treatment with a faster kinetic (lower pH-values, higher amount of added iron).

4.1.2 Economic sense

In Berlin there are 74 hospitals with 19,407 beds (DESTATIS 2008). With an annual usage rate of 82 % (DESTATIS 2008) and ca. 1.5 L urine per bed and day a volume of ca. 8,700 m^3 urine/a is produced. With the presumption that ca. 75 % of the urine can be separated with a complete separation system with modern NoMix-toilets (Lienert and Larsen 2010) a volume of 6,525 m^3 urine/a could be treated. The treatment of this volume induces annual costs of ca. 64,500 € considering the estimated amount of 9.88 €/m^3. Due to the fact that ca. 90 % of the pharmaceutical compounds are discharged by the households an advanced treatment in the waste water treatment plant is necessary to lower the burden of the aquatic environment with biological active trace compounds. In the following the ozonation and the addition of powdered activated carbon (PAC) are compared with focus on money saving potential by a decentralized treatment of hospital urine.

In several studies it could be shown that compared to a lot of other pharmaceuticals and micropollutants more effort is necessary to eliminate the ICM by ozonation (Schumacher 2006), (Bahr 2007), (Putschew, Mlehe et al. 2007) or PAC (Metzger 2008). Additionally the ICM have a high application in hospitals (50 %) and thus can be removed by the separation and treatment of hospital urine. The decentralized treatment has economic sense if the costs for the treatment are lower than the money saving due to the less effort in the waste water treatment plant.

Schumacher 2006 postulated for the WWTP Ruhleben that the oxidation of the ICM (more than 90 %) needs an increase of the ozone concentration from 12 mg/L to 24 mg/L and additional the dosage of 8 mg/L H_2O_2 and the costs increases from 1.4-1.8 cent/m^3 to 3.2-4.1 cent/m^3. Bahr 2007 found an increase of the costs of 0.5 cent/m^3 from 1.7 cent/m^3 to 2.2 cent/m^3 for elimination of the ICM. Metzger 2008 could show that the concentration of added PAC has to be increased from 10 mg/L to 20 mg/L to remove the ICM adequately. The costs for the addition of 10 mg PAC/L are ca. 2 cent/m^3 thus the increase of the costs with the addition of 20 mg PAC/L is not less than 1 cent/m^3. The calculated money saving potential between waste water with and without ICM is shown in Table 13. The assumed waste water volume which has to be treated in Berlin is 224 million m^3/a.

Table 13: Money saving potential for ozonation and addition of PAC in case of a decentralized removal of the ICM.

		aim of the treatment		
source	parameter	removal of most of the pharmaceuticals	additional removal of the ICM	money saving potential by decentralized removal of the ICM
Schumacher 2006	material consumption	1 mg O_3/mg DOC	2 mg O_3/ mg DOC + 8 mg/L H_2O_2	
	operating costs	1.4 - 1.8 cent/m^3	3.2 - 4.1 cent/m^3	3.14 - 5.38 million €/a
Bahr 2007	material consumption	1 mg O_3/mg DOC	1 mg O_3/ mg DOC + 4.8 mg/L H_2O_2	
	operating costs	1.7 cent/m^3	2.2 cent/m^3	1.12 million €/a
Metzger 2008	material consumption	10 mg PAC/L	20 mg PAC/L	
	operating costs	2 cent/m^3	4 cent/m^3	4.48 million €/a

By treating the hospital waste water only 50 % of the ICM can be eliminated. However the treatment costs are only 64.500 €/a thus with the collection and treatment of the urine at all institutions using ICM could double or triple the costs but the money saving potential in the waste water treatment without ICM is still higher.

4.1.3 Summary of the process engineering and cost relevant considerations

The material costs are influenced by the treatment conditions. The specific consumption of iron and acid increase with decreasing pH values which is also valid if the initial iron amount is increased. Decreasing the pH or increasing the amount of added iron result in shorter reaction times and to a reduced energy consumption of the stirrer. It should be possible to find cost optimized treatment conditions in dependence of the prices for iron, acid and electricity. Based on results of an iron re-use experiment with H_2SO_4 and reactor type 3 the calculated costs for 1 m^3 urine are 9.88 €. However in this experiment the treatment conditions were chosen for low specific material consumption and the energy consumption of the stirrer was ignored. Considering the estimated amount of 9.88 €/m^3 the treatment of 6,525 m^3/a (annual volume of hospital urine) induces annual costs of ca. 64,500 €. Assuming that a successful working urine separation system in hospitals and residential physicians is installed the treatment with zero-valent iron deiodinates the ICM and relieve the treatment effort of the WWTP. The money saving potential by that is much higher than the costs for the urine treatment.

Chapter 5

5.1 Conclusion

In the project PharmaTreat it could be shown that the treatment of antibiotics (Ciprofloxacine, Piperacillin and Cefuroxime), cytostatic drugs (Ifosfamide and Methotrexate) and ICM (Iopromide and Diatrizoate) with zero-valent iron leads to transformation products with less biological effects and a better biodegradability (except for the ICM). The treatment conditions with a good ratio of material consumption and treatment time are an acidic pH-value (pH 3) and a moderate amount of added iron (40 g Fe^0/L) in an anaerobic well mixed reactor. The mechanism for the transformation of the compounds under these conditions is most probably the reaction with adsorbed atomic hydrogen at the iron surface. An important requirement for the treatment of hospital urine is an efficient separation system. Due to an increasing buffer capacity by hydrolysis of urea if urine is stored for an economic treatment it is necessary to acidify the urine after separation as fast as possible. The calculated price of 9.88 €/m^3 urine can be decreased by optimizing the reactor and the treatment conditions considering the prices of iron, sulphuric acid and electricity. The treatment of urine with zero-valent iron is much more expensive than the treatment of waste water with ozon or PAC, but the volume of urine which has to be treated is much lower than the volume of waste water and thus there is a huge money saving potential in case of advances waste water treatments techniques if for example the ICM are removed before the waste water enter the WWTP.

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Appendix A

Compound selection

Table 14: Annual consumption of antibiotics (Charité 2006)

antibiotics	consumption kg/a	categories
Piperacillin	385	Acylaminopenicillin
Ampicillin	130	Aminopenicillin
Cefuroxime	126	Cephalosporins
amoxicillin	119	β-Lactam-antibiotic
Clindamycin	75	Lincosamide
Ciprofloxacine	75	Fluoroquinolones
Cefotiam	73	Cephalosporins
Sulbactam	55	ß-lactamase-inhibitor
Co-trimoxazol	55	Trimethoprim and Sulfamethoxazole (1:5)
Ceftriaxon	46	Cephalosporins
Ceftazidim	46	Cephalosporins
Metronidazol	44	Nitroimidazole
cefazolin	44	Cephalosporins
Vancomycin	34	Glykopeptid-antibiotic
Meropenem	30	β-Lactam-Antibiotika
Flocloxacillin	30	Fluoroquinolones
Cefotaxim	19	Cephalosporins
Fosfomycin	16	-
Clarithromycin	13	Makrolide-antibiotic
Erythromycin	10	Makrolide-antibiotic

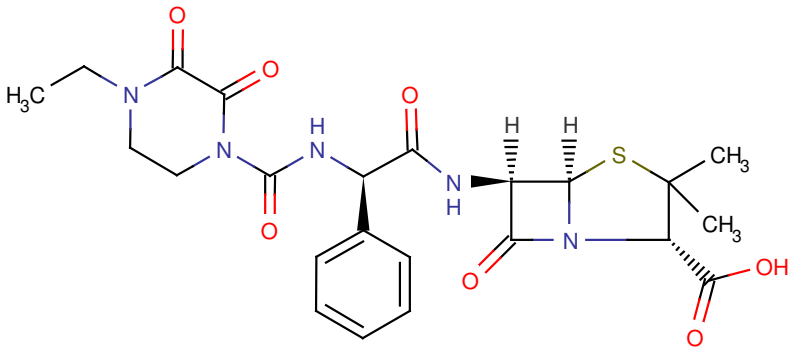
Table 15: Annual consumption of cytostatic drugs (Charité 2006)

cytostatic drug	consumption kg/a	categories
Ifosfamide	7	Oxazaphosphorin
Fluorouracil	6	Antimetabolit
Cytarabin	4	Cytosinanalog
Cyclophosphamide	3	Oxazaphosphorin
Methotrexate	3	Antimetabolit
Hydroxycarbamide	3	Ribonukleotid-Reduktase Hemmstoff
Treosulfan	3	Akylsulfonate
Mitotan	2	Mitotane

The compounds Piperacillin, Cefuroxime, Ciprofloxacine, Ifosfamide and Methotrexate were selected. Additionally Iopromide and Diatrizoate were examined.

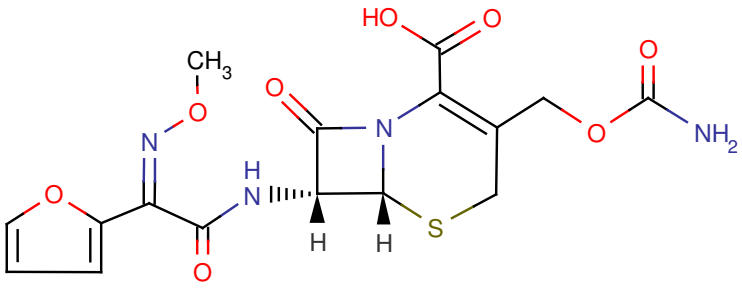
Compound characteristics

Piperacillin



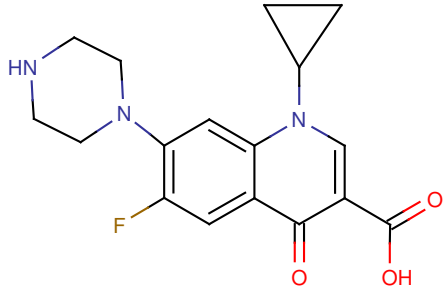
parameter	data
molecular formula	C23-H26-N5-O7-S-Na [49]
molar mass	539.54 g/mol [49]
carbon content	51.20%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	in water (20 °C) 207 mg/L [87]
elimination	60-80 % in first 24h unchanged in urine
further details	No retention in the WWTP (Feldmann 2005)

Cefuroxime



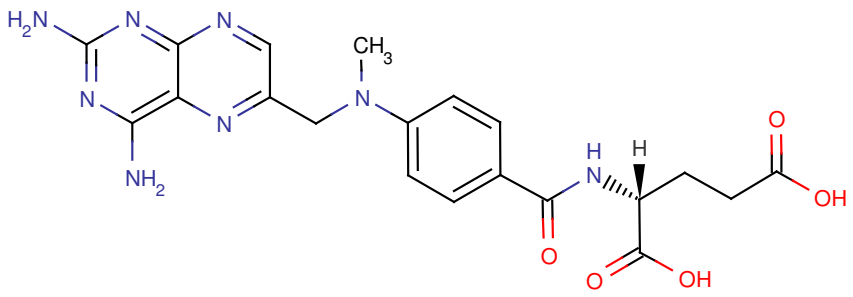
parameter	data
molecular formula	C16-H15-N4-O8-S-Na [86]
molar mass	446.37 g/mol [86]
carbon content	43.05%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	in water (20 °C) 145 mg/L
elimination	89 % in the first 8h unchanged in urine
further details	---

Ciprofloxacine



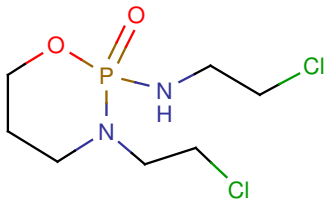
parameter	data
molecular formula	C17-H18-N3-O3-F [38]
molar mass	331.35 g/mol [38]
carbon content	61.61%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	in water (20°C) 30 g/L
elimination	26,9 % in the first 24 h unchanged in urine
further details	retention in WWTP: 25-75% (Heberer, Mechlinski et al. 2004) 40-79% (Feldmann 2005) ~83% (Golet, Xifra et al. 2003)

Methotrexate



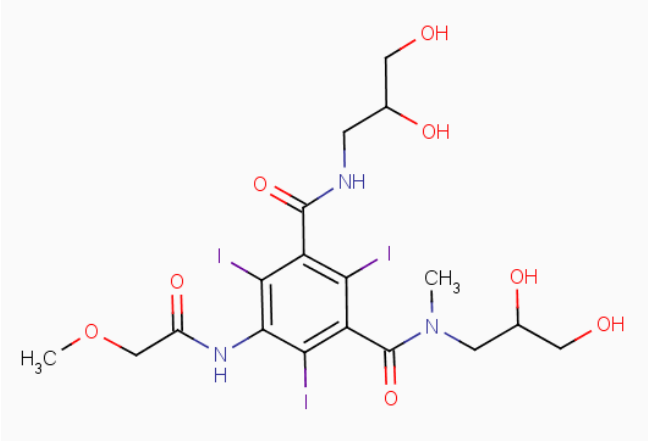
parameter	data
molecular formula	C20-H22-N8-O5
molar mass	454.45 g/mol
carbon content	52.80%
aggregate state	solid, powder
colour	yellow
purity	> 99 %
solubility	in water (25°C) 2,600 mg/L
elimination	80-90 % in first 24 h unchanged in urine
further details	ca. 1 µg/L in sewage effluent (Aherne, English et al. 1985)

Ifosfamide



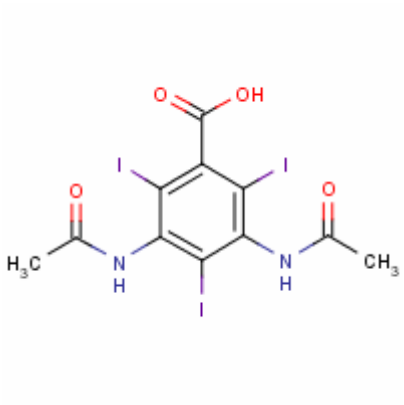
parameter	data
molecular formula	C7-H15-Cl2-N2-O2-P
molar mass	261.09 g/mol
carbon content	32.20%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	in water (25°C) 3,780 mg/L
elimination	12-18 % in 72 h unchanged in urine
further details	Surface water: -180 ng/L WWTP influent: 0.007-0.04 µg/L WWTP effluent: 0.01-2.9 µg/L (Schneider 2005)

Iopromide



parameter	data
molecular formula	C18-H24-I3-N3-O8
molar mass	791.1 g/mol
carbon content	27.30%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	---
elimination	complete unchanged in 24 h
further details	detected concentrations > 0.1µg/L ((Putschew and Jekel 2001))

Diatrizoate



parameter	data
molecular formula	C11-H9-I3-N2-O4
molar mass	613.9 g/mol
carbon content	21.50%
aggregate state	solid, powder
colour	white
purity	> 99 %
solubility	---
elimination	complete unchanged in 24 h
further details	detected concentrations > 1µg/L (Ivashechkin 2005)

Urine collection


Figure 34: Pictures of the urine collection at the department of water quality control.

Table 16: normal concentrations of fresh urine (Udert 2004).

parameter	unit	fresh urine
pH	-	6.2
total nitrogen	gN/L	9.2
total ammonium	mgN/L	480
urea	gN/L	7.6
sulphate	mgSO4/L	748
total phosphate	mgP/L	740
calcium	mg/L	180
magnesium	mg/L	100
sodium	g/L	2.7
potassium	g/L	2.2
chloride	g/L	3.8
TIC	mgC/L	0
CSB	gO2/L	8.2

Table 17: measured concentrations of collected urine.

parameter	unit	fresh urine (n=16)	
		average	+/-
pH	-	6.5	0.4
total nitrogen	gN/L	3.7	543
total ammonium	mgN/L	111	41
sulphate	mgS/L	448	139
phosphate	mgP/L	172	73
calcium	mg/L	62	27
magnesium	mg/L	28	7
chloride	g/L	2.1	634
TIC	mgC/L	42	41
DOC	gC/L	2.4	510

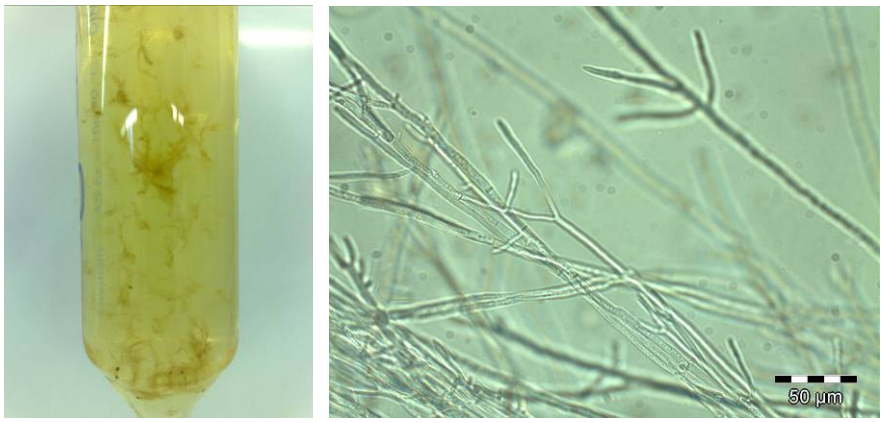


Figure 35: Fungal infestation in acidified urine batches (potential *Penicillium glaucum*).

Validation of the reactor type 3

Variation of the stirring speed

The calculated stirring speed for the complete suspension of iron particles in reactor type 3 is 1373 rpm. To test if the calculated stirring speed is sufficient to suspend all iron particles the stirring speed was changed and the parameter suspension (observation), reaction rate (100 mg/L Iopromide) and corrosion rate were compared (Table 18).

Table 18: Variation of the stirring speed to test the particle suspension

Parameter	**Data**		
Stirring speed [rpm]	1080	1370	1500
Volume specific power input [kW / m^3]	1	2	2.6
k_{obs} [10^{-5} s^{-1}]	2.59	3.08	3.43
acid consumption [ml/h]	10.3	15.4	16.7
DOC-concentration of the urine [mg/L]	1.24	1.6	1.67
Suspension	the bigger particles could not be suspended and stayed at the bottom of the reactor	all particles could be suspended	all particles could be suspended

The stirring speed of 1370 rpm is high enough to suspend all iron particles in reactor type 3. A lower stirring speed leads to an incomplete suspension of the bigger particles and a decrease of the reaction rate despite less DOC-concentration. An increase of the stirring speed leads to an increase of the rate constant as discussed in the kinetic results (3.1.3.4). The observed suspension at 1500 rpm is similar to 1370 rpm.

Validation of the analysis

Compound stability at different pH-values

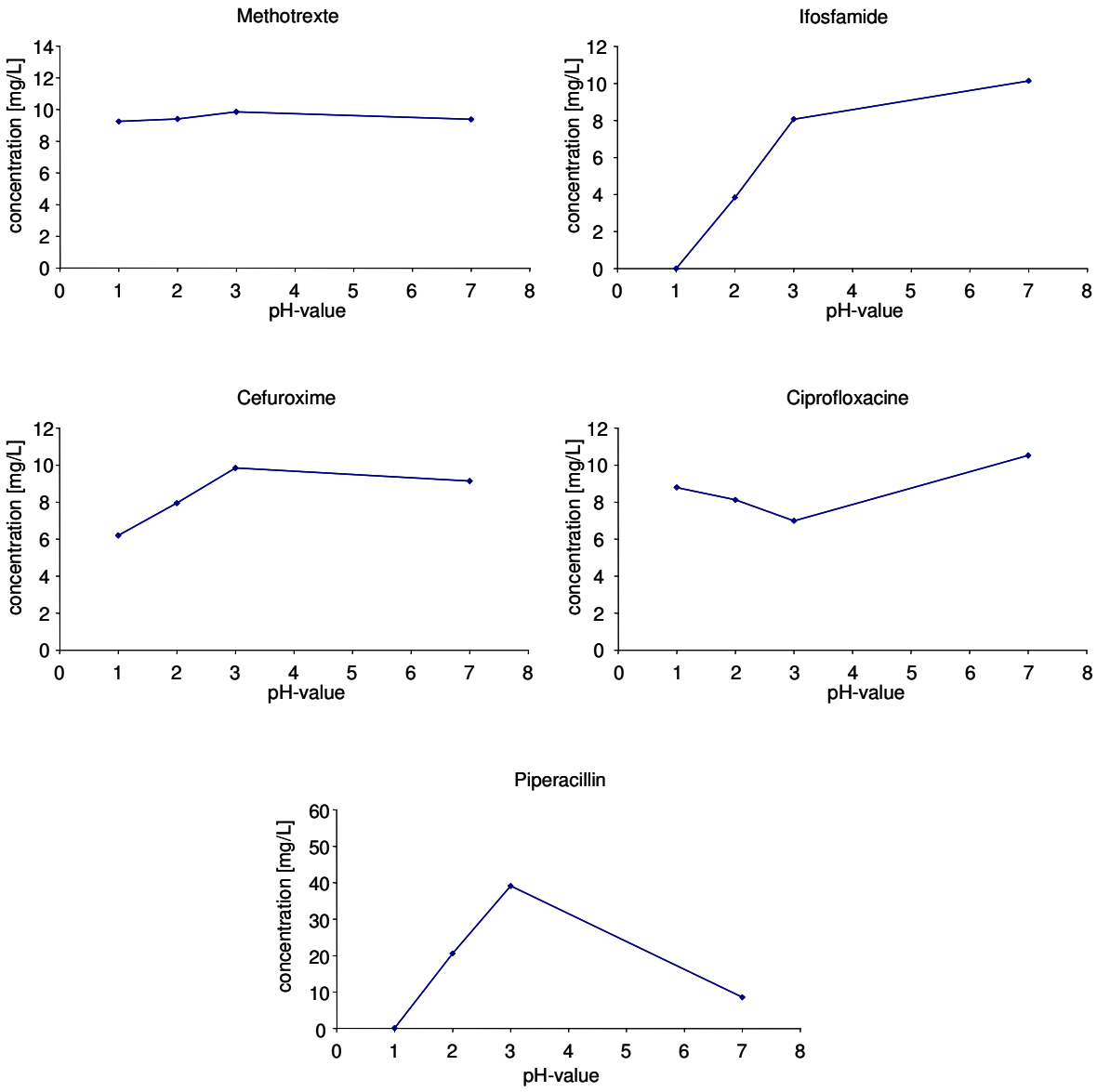


Figure 36: Influence of different pH-values to the compound stability (c_0 = 10; 50 mg/L, after 24 h).

The ICM are not estimated but no pH-effects could be observed in the preliminary tests with Iopromide.

Calibration

Table 19: Calibration of Iopromide / iodide in UPW and urine (LC-UV).

compound	calibration range	UPW (n = 10)		calibration range	urine (n = 8)	
	[mg/L]	equation	R^2	[mg/L]	equation	R^2
Iopromide	0.5 - 100	y = 52.313x + 4.1007	0.9999	0.5 - 100	y = 49.947x + 3.1545	0.9999
Iodide	0.5 - 40	y = 14.648x - 0.9141	0.9999	---	---	---

Table 20: Calibration of the pharmaceuticals in UPW and urine (LC-MS).

compound	calibration range	UPW (n = 29)		calibration range	urine (n = 5)	
	[mg/L]	equation	R^2	[mg/L]	equation	R^2
Methotrexate	0.005 - 1	y = 52862x + 603.02	0.9993	0.005 - 1	y = 25146x + 161.14	0.9997
Ifosfamide	0.005 - 1	y = 76795x + 1589.7	0.9978	0.005 - 1	y = 38630x + 6456.9	0.9978
Iopromide	0.05 - 10	y = 4314.1x + 440.06	0.9989	0.05 - 10	y = 2792x + 223.21	0.9992
Diatrizoate	0.05 - 10	y = 1080.8x + 64.018	0.9993	0.05 - 10	y = 655.14 + 15.668	0.9967
Ciprofloxacine	0.05 - 10	y = 30716x + 2491.2	0.9999	0.05 - 10	y = 29323x - 1171.3	0.9993
Piperacillin	0.05 - 5	y = 19026x + 3302.5	0.9949	0.05 - 1	y = 19804x + 392.17	0.9992
	5 - 10	y = 10694x + 44034		1 - 10	y = 7958.4x + 16293	0.9674
Cefuroxime	0.05 - 5	y = 7192.7x + 1174.1	0.9953	0.05 - 1	y = 4739.2x + 49.069	0.9999
	5 - 10	y = 4459.8 + 14503		1 - 10	y = 2688.8x + 2876.7	0.9899

Influence of dissolved iron

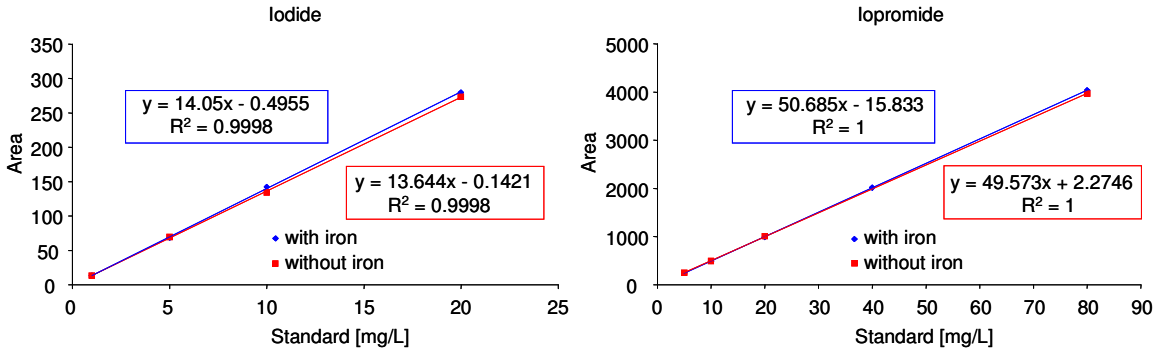


Figure 37: Influence of dissolved iron to the analytic of iodide and Iopromide (LC-UV).

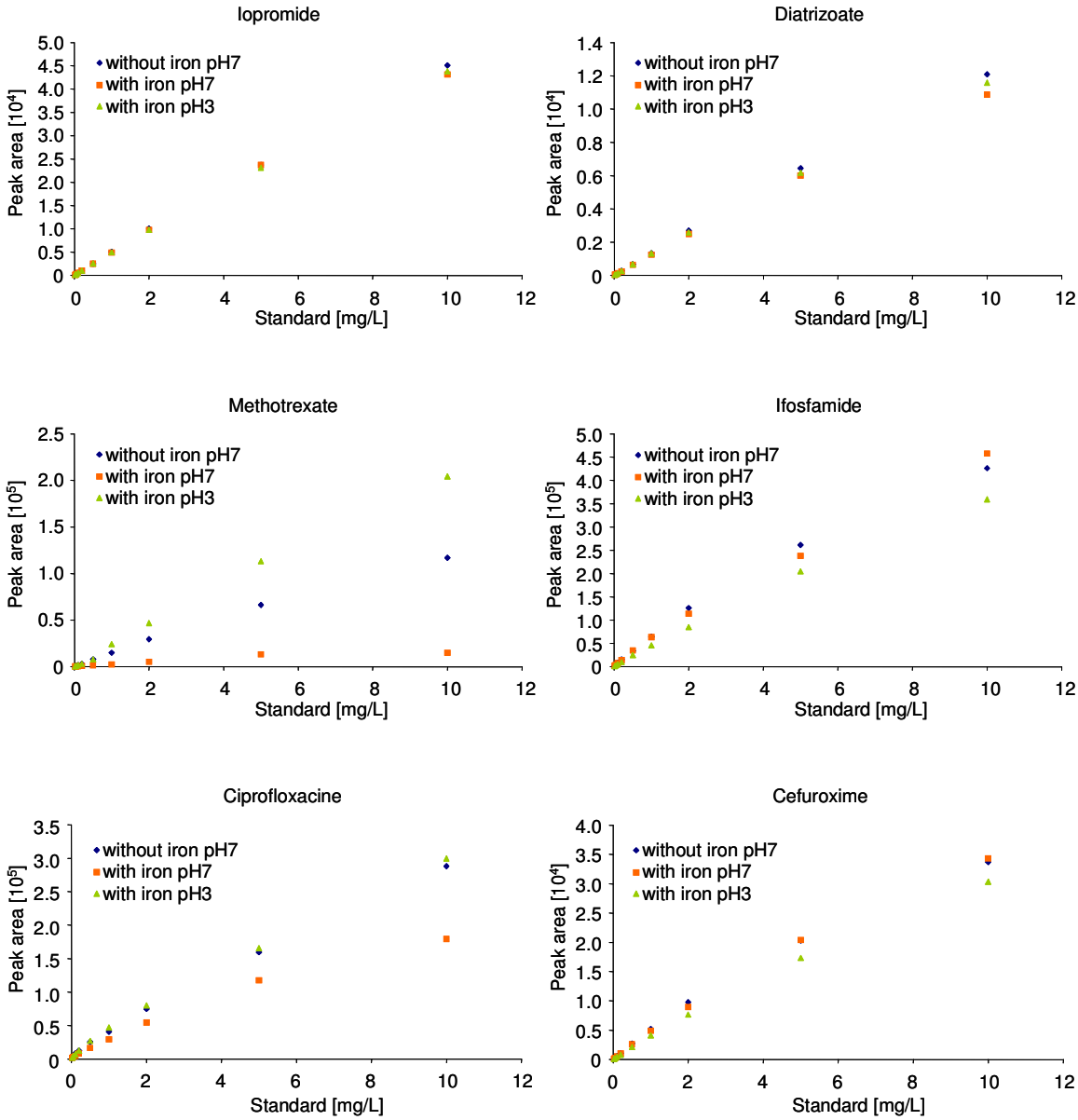


Figure 38: Influence of dissolved iron to the analytic of the pharmaceuticals (LC-MS).

Measurement of the redox potential

The redox potential was examined with a pE-meter WTW pH 330 and an electrode InLab501 Redox. The experiments were done in a reactor type 2 but without a gas tight bearing for the stirrer. Thus there was an aerated system. The redox potential is an important parameter for the discussion of redox reactions. Unfortunately the measurement of the redox potential is difficult and needs a long time to find the equilibrium. The environment in the batch reactor is changing over the time. Another point is that the redox potential of the bulk solution is most probably different to the redox

potential at the iron surface area. Due to these reasons the measurement of the redox potential is questionable. However in Figure 39 – 42 few results of the measurement of the redox potential are shown.

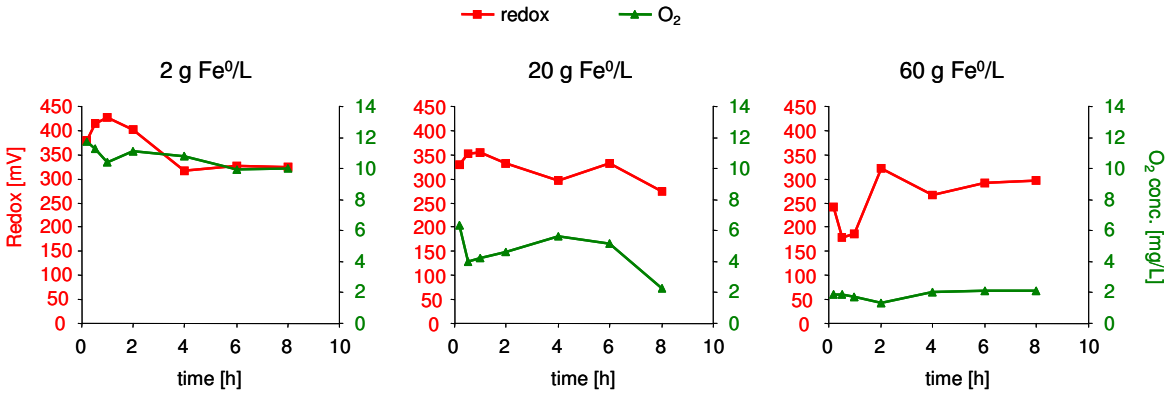


Figure 39: Redox potential and oxygen concentration in dependence of the iron amount used (pH 3, 25°C, 600 rpm, UPW with pharmaceuticals)

It can be seen that a higher amount of iron used leads to lower concentrations of dissolved oxygen due to the consumption during the corrosion. The redox potential shows only a weak dependency on the different amounts of iron and the resulting different concentrations of oxygen. The pharmaceuticals (100mg/L each antibiotic and ICM and 10 mg/L each cytostatic drug) have a higher influence to the redox potential. In Figure 40 it can be seen that the redox potential in ultra pure water is 50 – 100 mV higher than in ultra pure water with pharmaceuticals.

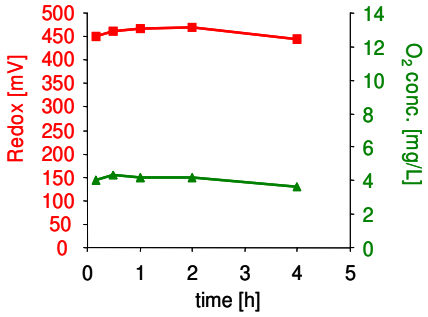


Figure 40: Redox potential and oxygen concentration in UPW (pH 3, 25°C, 600 rpm, 40 g Fe^0/L)

In Figure 41 the influence of dissolved iron (Fe^{2+} and Fe^{3+}; both 1 g/L) shows that there is no difference in the redox potential but a higher corrosion rate with Fe^{3+}. Furthermore it can be seen that EDTA has a high influence to both the corrosion rate and the redox potential. The redox potential is much lower and decreases over the time and the corrosion rate is much higher than in pure water without EDTA. This effect can be

explained by the complexation of iron on the iron surface and as result a better transfer of Fe^{2+} to the solution.

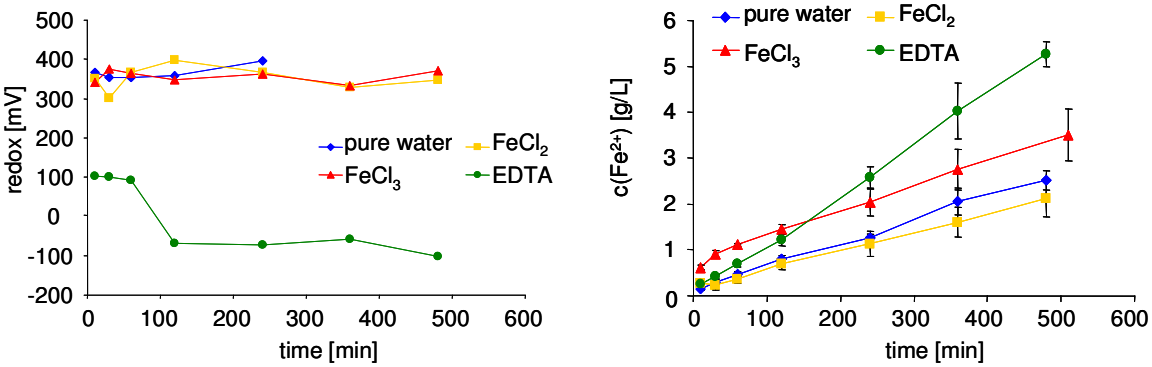


Figure 41: Redox potential and iron dissolution in dependence of the addition of Fe^{2+}, Fe^{3+} and EDTA (pH 3, 25°C, 600 rpm, 40 g Fe^0/L, UPW)

The matrix urine influences the corrosion rate and the degradation of the pharmaceutical compounds. However there is no significant correlation between the redox potential of the bulk solution, the corrosion rate and the reaction rate of the pharmaceuticals.

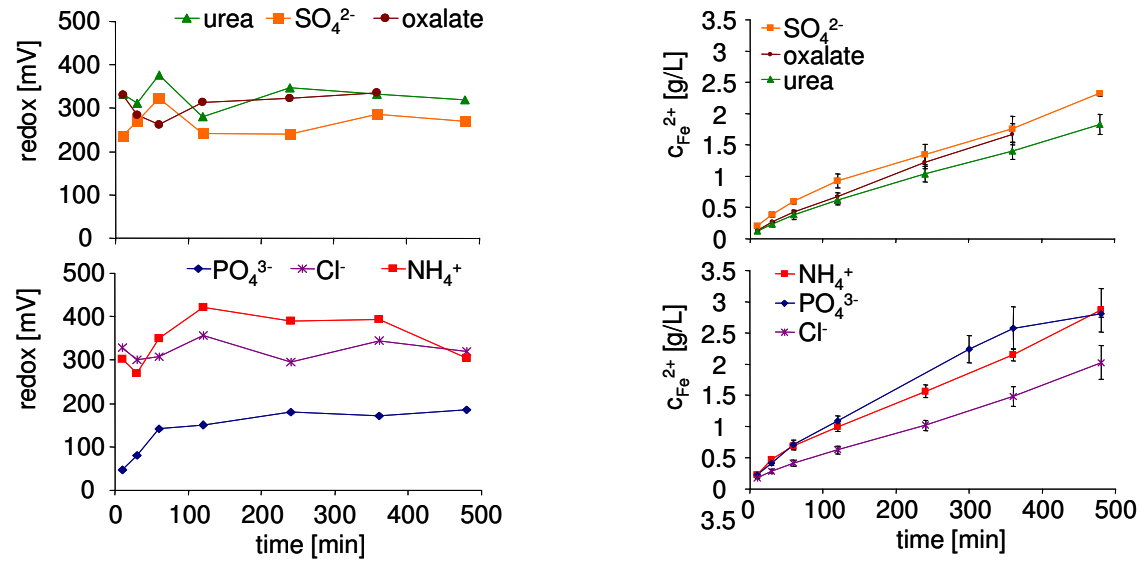


Figure 42: Redox potential and iron dissolution in dependence of the addition of urea, SO_4^{2-}, oxalate, PO_4^{3-}, Cl^-, NH_4^+ in typical urine concentrations (pH 3, 25°C, 600 rpm, 40 g Fe^0/L, UPW with pharmaceuticals)

Toxicity and biodegradation tests

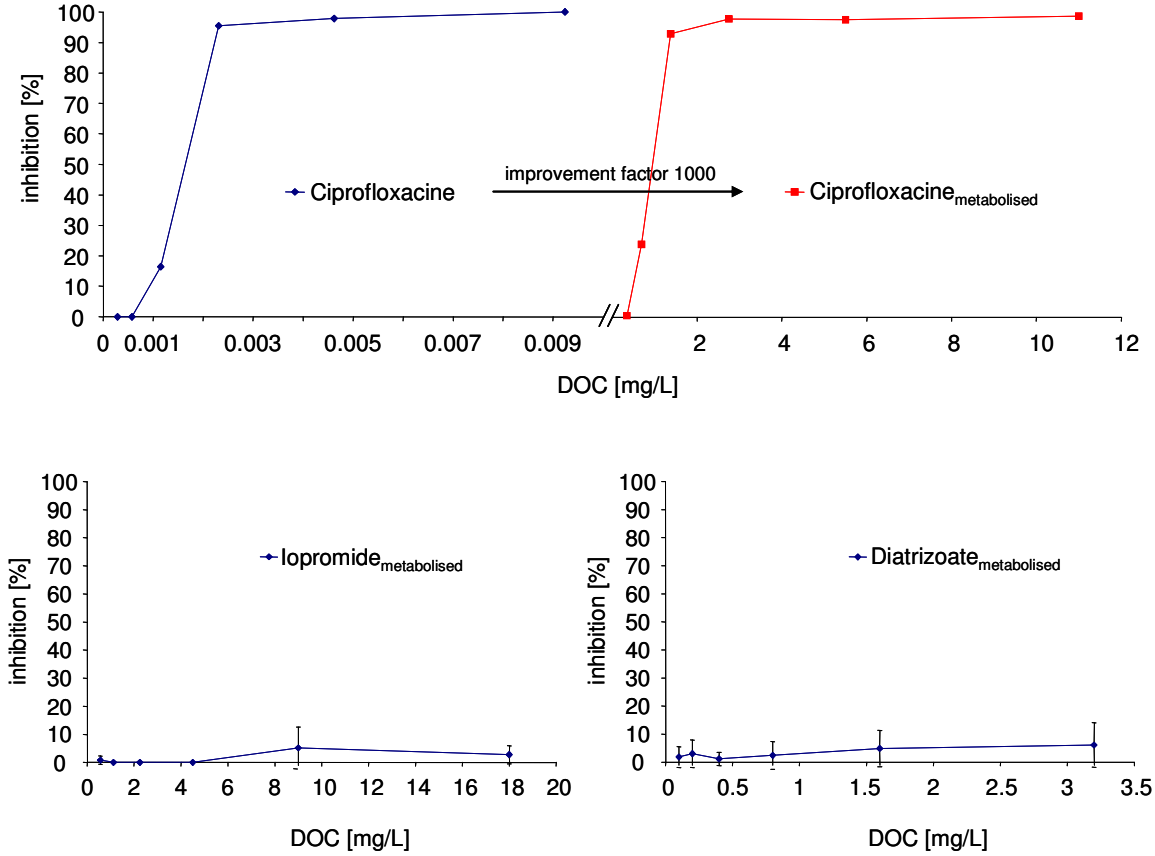


Figure 43: Inhibition effect of the transformation products to *Vibrio fisheri* (growth inhibition test).

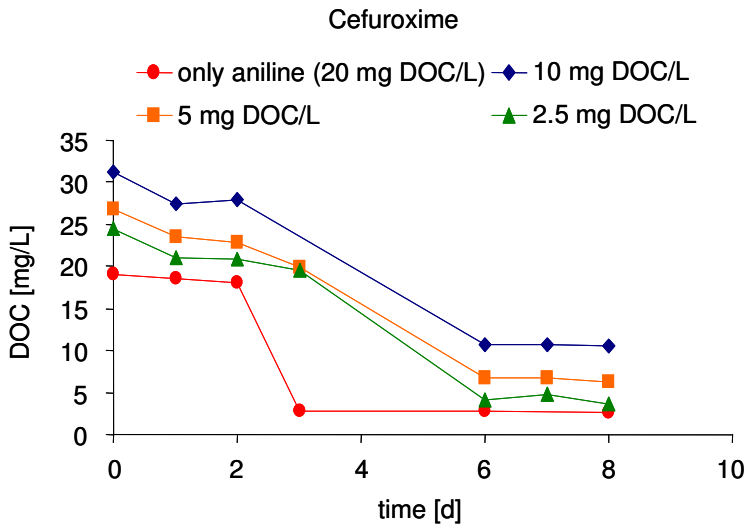


Figure 44: Inhibition of the aniline degradation by Cefuroxime, DOC versus time.

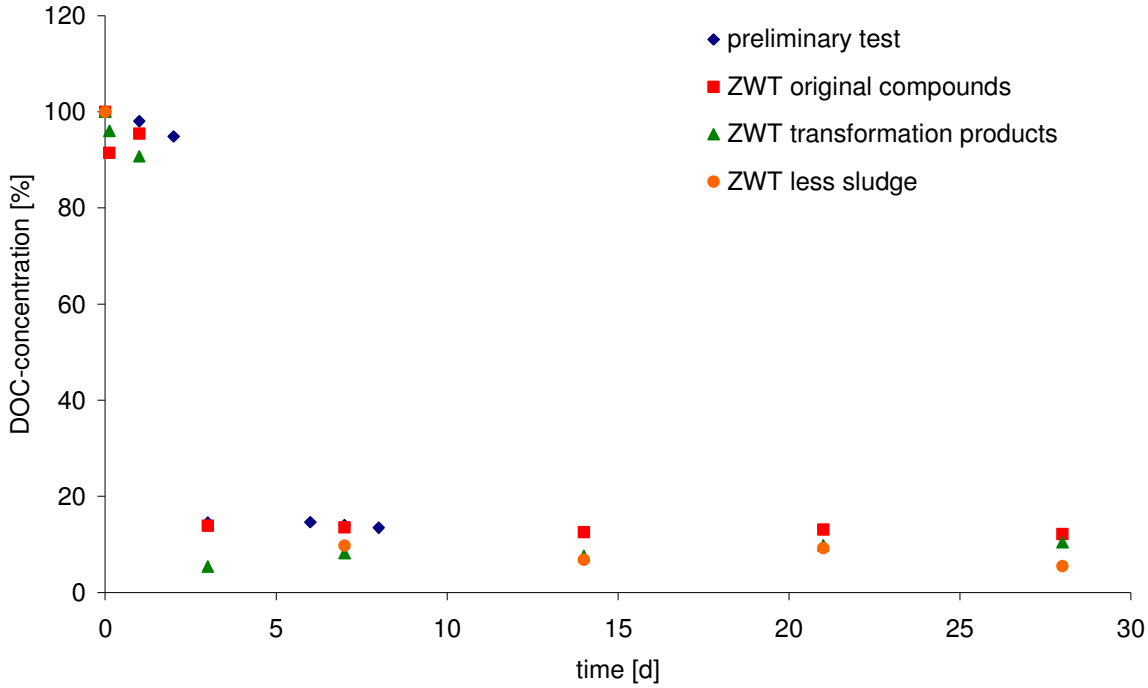


Figure 45: Aniline degradation in % versus time (as sludge control in the different experiments).

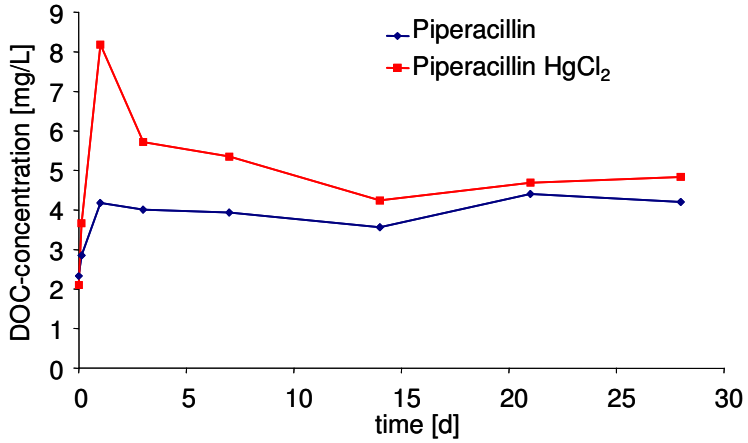
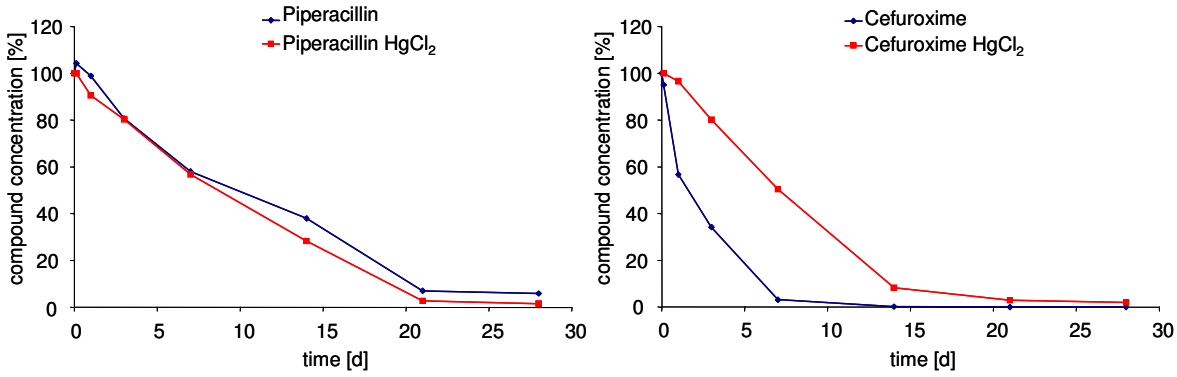


Figure 46: DOC-degradation of Piperacillin versus time (ZWT).



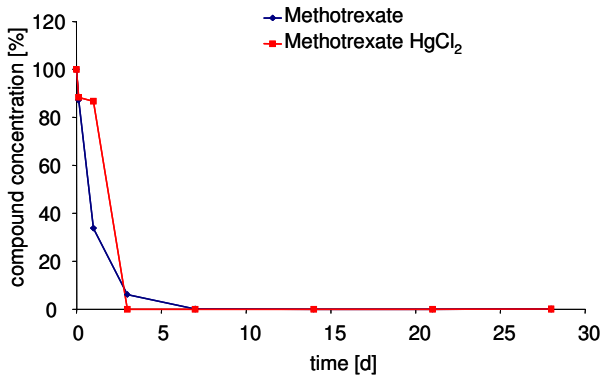


Figure 47: Decrease of the compound concentration in % versus time in the ZWT with and without $HgCl_2$.

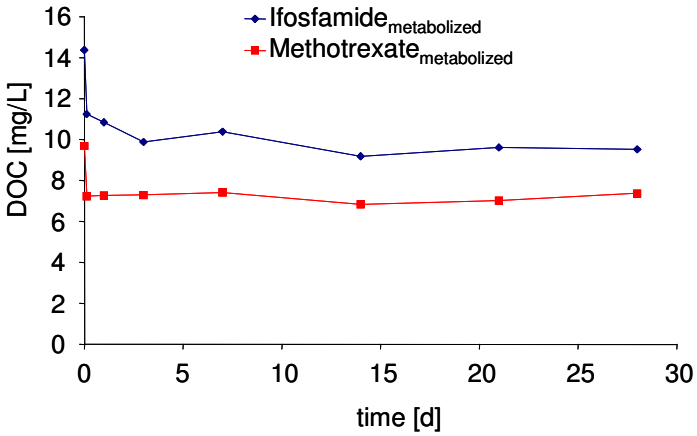


Figure 48: ZWT with the transformation products of Ifosfamide and Methotrexate. DOC versus time.

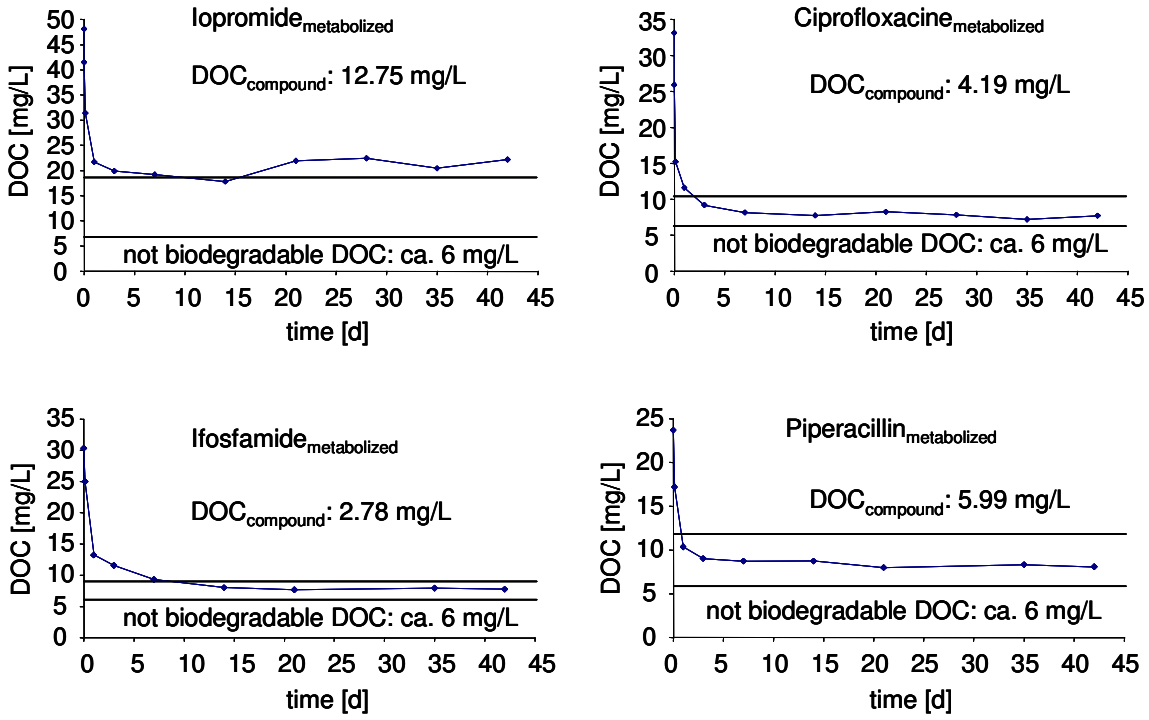


Figure 49: ZWT with the transformation products of the pharmaceuticals and additional biodegradable compounds (influent Ruhleben); DOC versus time.
Line at 6 mg/L: non biodegradable DOC originating from the sludge.
Second line: 6 mg/L DOC plus the initial compound DOC.

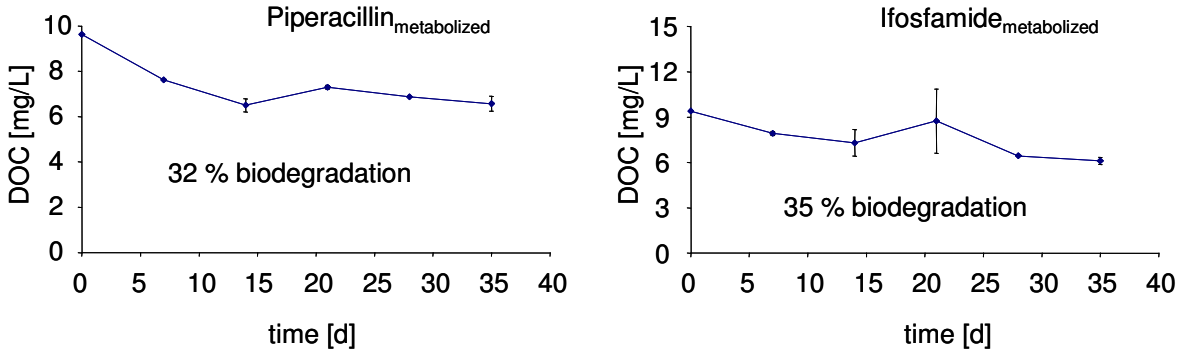


Figure 50: ZWT with the transformation products (decrease of the sludge concentration to 1 mg/L); DOC versus time.