

Detoxification of Diclofenac - A Comparison between Oxidative and Reductive Degradation Processes

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Abstract Reductive degradation / dehalogenation of diclofenac (DCF) — one of the most commonly used anti-inflammatories — occurs efficiently at moderately elevated temperatures between 300°C and 500°C with zero valent iron (iron powder) in a nitrogen atmosphere. The proton donors tested were ethanol and water. The observed production of phenol and cresol and other dehalogenation products indicates that the reaction is not simple pyrolysis, but is rather a reduction. No halogenated organic products were observed. In contrast, oxidative degradation of DCF — for example, electrochemical oxidation or oxidation with ozone or H₂O₂ — led to predominantly chlorinated products. All products resulted were tested via gas chromatography-mass spectrometry (GC-MS).

Keywords: reductive dehalogenation, diclofenac, zero-valent iron

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1. Introduction

Diclofenac (DCF), a nonsteroidal anti-inflammatory drug used for the treatment of pain and inflammation, can also help relieve the symptoms of arthritis, swelling and joint pain [1]. However, diclofenac may also cause serious effects on the stomach and intestines, including bleeding and perforation [2]. In Germany alone 90 t are used annually, of which 63t enters the waste water after being excreted in urine [3].

The exceptional use of DCF and its release into the environment may pose risks to human health and aquatic environments. Although the ecotoxicity of DCF is quite low, prolonged exposure increases the environmentally relevant concentration with considerable negative effects on the environment.

In analytical and environmental chemistry, two strategies are followed: (1) The fast and sensitive detection of DCF using chromatographic and electrochemical methods, and (2) the degradation and removal of residual DCF from aqueous systems. In this paper we focus on the degradation aspects.

A data search on DCF in the SciFinder database returned approximately 30,000 references. Amongst the medical and analytical aspects, there are four principal degradation methods: oxidative, reductive, photocatalytic processes and ultrasound irradiation.

In this article we restrict ourselves to oxidative and reductive processes, because these methods seem to be the most promising for degrading DCF on an industrial scale.

The most frequently used and most versatile analytical methods for studying the degradation products are HPLC and GS-MS [4].

1.1. Oxidative Degradation of DCF

In a review article, Klavarioti et al. [5] summarised the oxidation methods that can remove residual pharmaceuticals such as diclofenac from aqueous systems. Besides electrochemical oxidation processes [6,7,8,9], the methods of choice are Fenton oxidation [10,11,12,13,14] and heterogeneous photo(electro)catalysis [15,16,17,18,19]. Advanced oxidation with H₂O₂ and ozone have been investigated by Vogna et al. [20], Zwiener and Frimmel [21], Hikmat et al. [22] and Giri et al. [23]. These authors proposed different reaction pathways depending on the oxidant; however, in each case C-N cleavage resulted.

In this article we will show that oxidative degradation of DCF may not be a successful route for detoxifying DCF because dichloroaniline and other chlorinated products result, which are much more toxic than DCF itself. A realistic detoxification is the complete reductive dehalogenation as shown by Aristov and Habekost [24] for polychlorinated biphenyl and by Habekost and Aristov [25] for polybrominated flame retardants.

1.2. Reductive Degradation of DCF

To completely detoxify halogenated organic waste, exposing the waste to heated iron in an anaerobic environment can be sufficient. The products of the reductive dehalogenation reactions are halides and halogen-free organics. In this paper we demonstrate this with DCF. The work presented here expands on previous results of our laboratory on the dehalogenation of PCBs and polybrominated diphenylethers [24,25]. There the PCBs were pre-mixed with toluene or slake lime that acted as the proton donors for the reduction. Here we

show that ethanol and water or a mixture can also act as proton donors. We tested the procedure on DCF to determine whether it would also dehalogenate completely and “cleanly” to benign products.

The work presented here is valuable because it shows, in contrast to the oxidative methods cited above, that DCF can be eliminated in a technologically simple, fast and inexpensive fashion, without special reagents, and with a reaction time that is within seconds rather than hours.

2. Experimental

Analytical instruments:

GC-MS: The products were analysed with GC-MS. Experimental conditions were: GC: Hewlett Packard 5890 with RTX-35, 30 m, 0.32 μm column, temperature ramping: 50°C, then 15°C/min to 280°C, 10 min isotherm. MSD: Hewlett Packard 5972, autosampler: Hewlett Packard 6890, column: RTX-35; carrier gas: He 5.0. Ionisation in EI mode.

Cyclic voltammetry: Potentiostat (μ -STAT 400, DropSens), screen-printed electrodes (SPE) (carbon nanotubes decorated with nano-Au: CNT-GNT, DropSens).

UV-VIS: UV-VIS spectrometer (Perkin Elmer Lambda XLS+).

Spectroelectrochemical setup: A fibre passed the light from the spectrometer (Kontron 432) through the transparent SPE (DRP AUTR 10, DropSens) fixed in the transmission cell with focusing lens and fibre optics (DRP-TRANSCCELL, DRP-CLENS, DRP-TFIBER, DRP-RPROBE, DropSens).

A second fibre opposite guided the beam into a photomultiplier (Hamamatsu, R4220P with power supply: MH5781). The first fibre consisted of six single fibre bundles around one reflection fibre that collected the reflected light beam to control the incident light intensity via another photomultiplier.

Ozonisation: Ozone generator Model 500 (Fischer Technology, Germany); ozone output: 5 g/h.

3. Results and Discussion

Electrochemical oxidation

The DCF solution (100 mL of a 0.1 mol/L in ethanol) was acidified with some drops of sulphuric acid (0.1 mol/L) to enhance the conductivity at $\text{pH} \approx 4$. The electrolysis was carried out for 30 min with platinum mesh electrodes (area $\approx 4 \text{ cm} * 4 \text{ cm}$) by constant stirring at voltages of 8–10 V (current $\approx 50 \text{ mA}$).

Cid-Ceròn et al. (2016) proposed that substituted anilines such as nitroaniline or dichloroaniline are one of the electrochemical oxidation products. They claimed that the experimental evidence gives stronger support to dichloroaniline.

We recorded the UV-VIS spectrum during the electrolysis. Therefore, we could simultaneously detect the absorption of DCF (about 290 nm) and the formation of the reaction product (Figure 1). The spectrum shows absorption bands around 290 nm (DCF) and around 450 nm. The absorption at 450 nm increases with increasing electrolysis time. However, 2,6-dichloroaniline does not absorb at 450 nm.

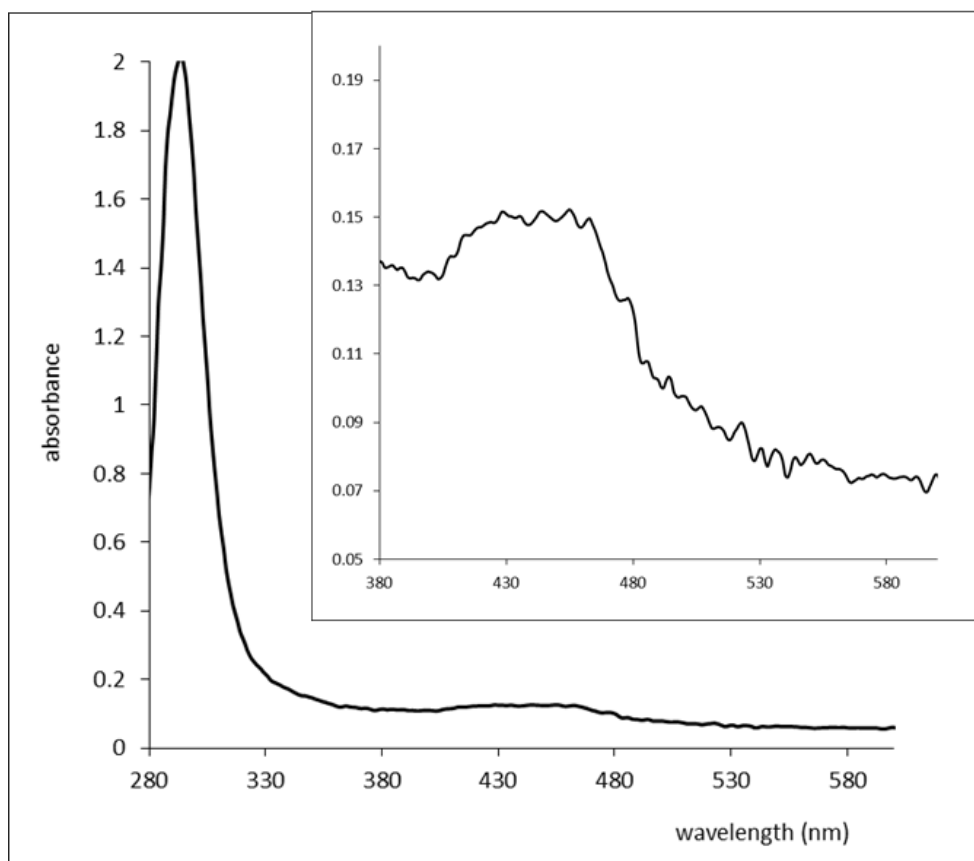


Figure 1. Absorption of DCF at 290 nm and the reaction product (after electrolysis) at 450 nm (insert)

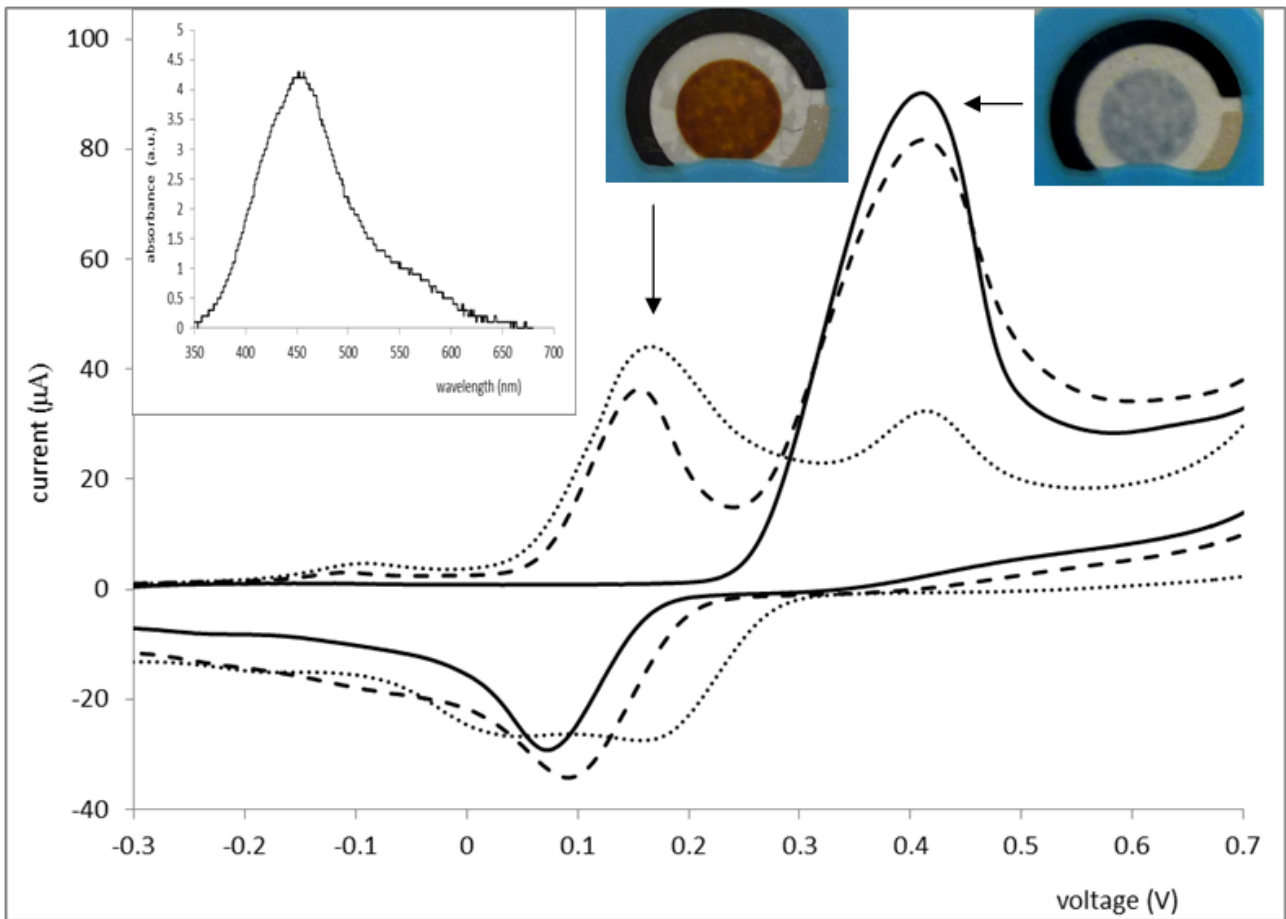


Figure 2. Three consecutive cyclic voltammograms of 100 $\mu\text{mol/L}$ diclofenac in $(\text{NH}_4)_2\text{HPO}_4$. Working electrode: DRP ATR 10. Solid line: first CV, dotted line: third CV. Insert: Spectrum of the reaction product of DCF at 0.55 V

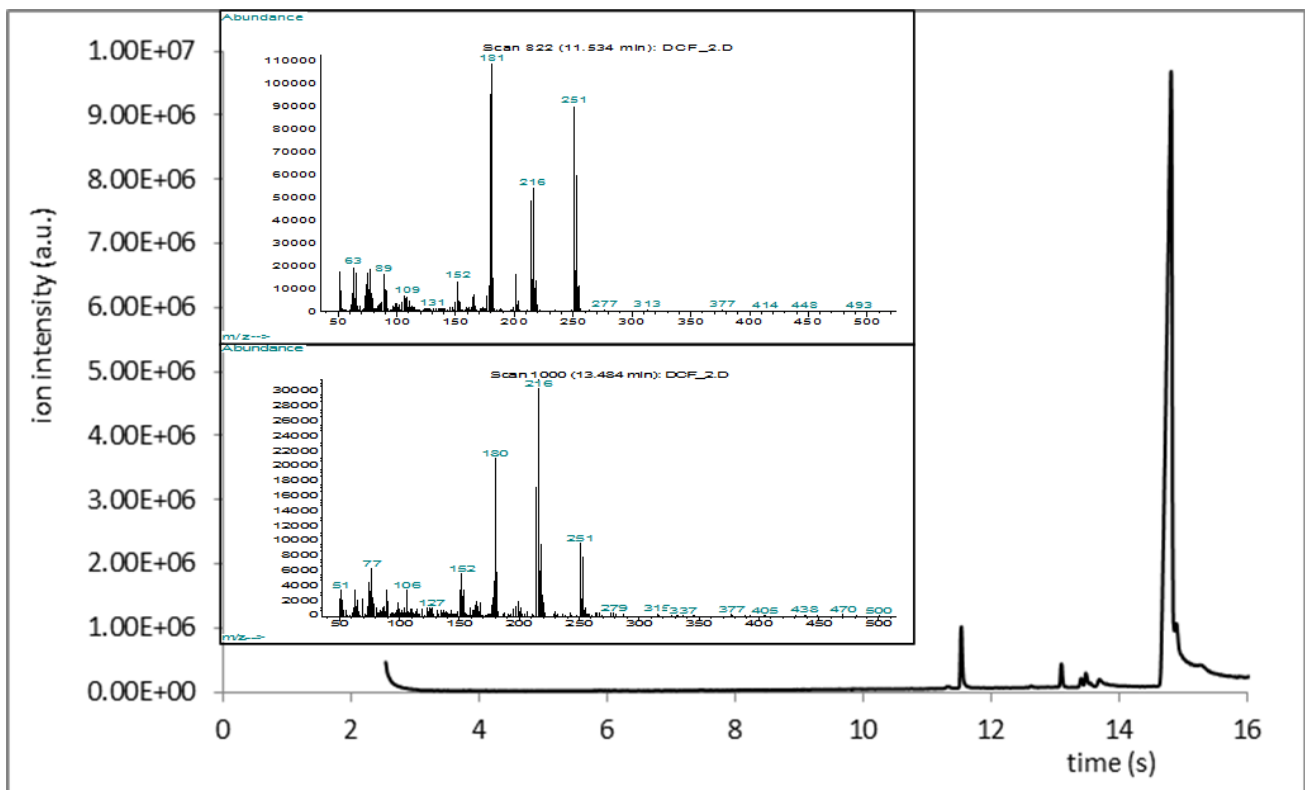


Figure 3. Gas chromatogram of DCF after electro-oxidation. Peak 14.8: DCF. Insert: EI-MS of peaks 11.554 and 13.484. The fragmentation pattern of mass 251 indicates that the molecule must contain two chlorine atoms: Loss of one and two chlorine atoms leads to the fragments 216 amu and 181 amu

3.1. Spectroelectrochemical Measurements

In cyclic voltammetry (CV) the electrochemical reaction of DCF can be directly observed. Figure 2 shows the cyclic voltammogram and the changing colour of the (transparent gold) working electrode for three CV scans. The colour of the working electrode changes from grey to brown. This reflects the CV. The oxidation peak of DCF appears at 0.4 V only in the first CV. The reduction peak (0.1 V) has a comparable low intensity. This implies an EC mechanism (electron transfer followed by chemical reaction) as proposed already by Cid-Cerón et al. (2016). After the first CV the anodic current peak decreases, and a new redox-couple results (0.15 V and 0.1 V). The insert of Figure 2 shows the spectrum of the reaction product of DCF after electrolysis at 0.55 V. The value $\lambda_{\max} \approx 450$ nm corresponds to the spectrum after electrochemical decomposition.

For identifying the products of the electrochemical and spectroelectrochemical measurements, we recorded the GC-MS. The GC-MS (Figure 3) indicates that DCF decomposes electrochemically only to a low extent. The main secondary products are substances that contain two chlorines. Although the substances could not be precisely identified from the Wiley and NIST data libraries, the fragmentation patterns of the products from the parent peak indicate cleavage of one and two chlorines (see insert of Figure 1). It is obvious that decarboxylation occurs during the electro-oxidative process (main ion: 251: -COOH, main fragments: 216: -COOH and -Cl, 201: -COOH, -Cl and -CH₃, 181: -COOH and -Cl₂, 166: -COOH, -Cl₂ and -CH₃).

Therefore, we suggest that the substance that absorbs around 450 nm is not dichloroaniline but is rather the decarboxylation product of DCF.

3.2. Ozonisation

The DCF solution in ethanol was bubbled with ozone for about 30 min. We took into account that ozone also oxidizes the solvent. However, the advantage of this

chemical system is that the products can be directly injected into the GC-MS without any pretreatment.

In contrast to electro-oxidation, dichloroaniline is one of the main products of ozonisation (see GC-MS in Figure 4). Additional substances are dichlorobenzene, dichloronitrobenzene and other dichlorinated compounds.

3.3. Reaction with H₂O₂

The DCF solution in ethanol was mixed with 10 mL of 30% destabilised H₂O₂ and stirred for about 30 min. Similar results are obtained as with ozone (Figure 5).

As a summary, electrochemical oxidation of DCF and oxidation with ozone or H₂O₂ leads to products that are more toxic than DCF itself. Therefore, oxidation is not a satisfactory strategy for detoxifying DCF.

3.4. Gas phase reduction

The experimental apparatus and methods have been described in detail by Aristov and Habekost [24]. Briefly, for dehalogenation, a 10 mL portion of DCF in a mixture of ethanol and water (50:50, 0.1 mol/L) was injected via a syringe into a heated steel pipe (V2A steel, 18 mm diameter, 700 mm length) containing 20 g iron powder (1–10 μ m, Merck 1.03819) dispersed through 0.5 g quartz wool. The iron powder was otherwise not pre-treated. The gas-phase products were transported by the nitrogen carrier gas (at about 10 mL/min flow rate) and condensed in an ice-table salt cooled test tube. The dwell time in the reactor was about 15 to 20 s.

Figure 6 shows the results at different temperatures (300°C, 400°C and 500°C). The GC-MS spectrum is quite different from those spectra shown above: No chlorinated products are detectable. DCF decomposes almost entirely in the reductive atmosphere at temperatures above 300°C. The main products are phenol (3.1), cresol (3.8), dimethylphenol (4.6), quinoline derivatives (6.4) and indole derivatives (10.8). The peak at 12.8 cannot be assigned, but the molecule does not contain chlorine.

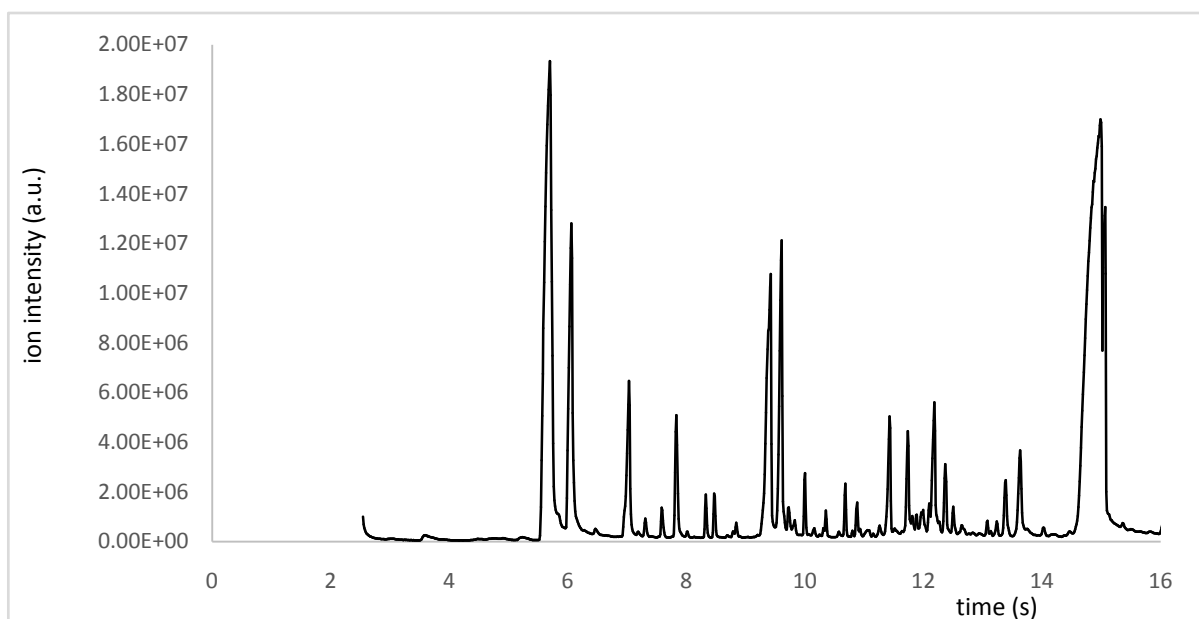


Figure 4. GC-MS of DCF after ozonisation: Peak 5.6: dichloroaniline; peak 6.05: dichloroaniline derivatives; peak 7.02: dichloronitrobenzene; peaks around 9: all dichlorinated benzene or aniline derivatives

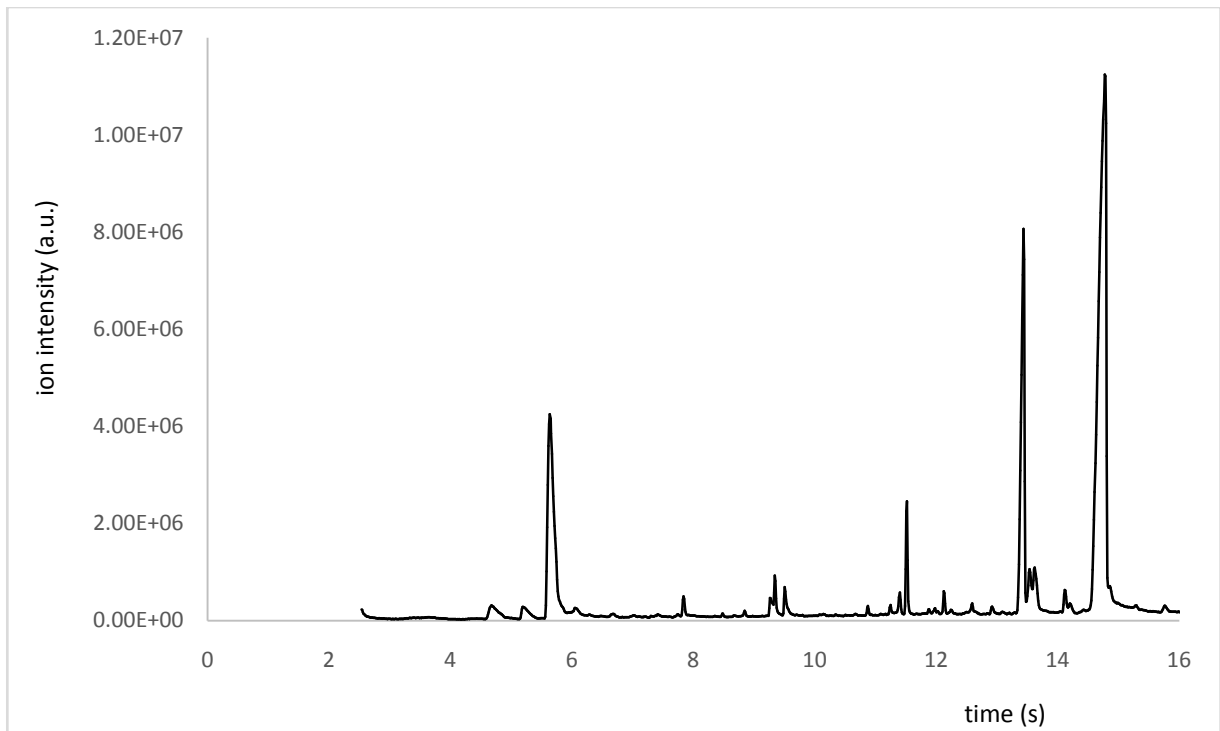


Figure 5. GC-MS of DCF after treatment with H_2O_2 : Peak 4.9: monochloroaniline; peak 5.1: dichlorophenol; peak 5.6: dichloroaniline; peaks around 9: dichlororbenzene derivatives; peaks around 11: dichlorophenyl-benzene; peak 13.5: decarboxylated DCF

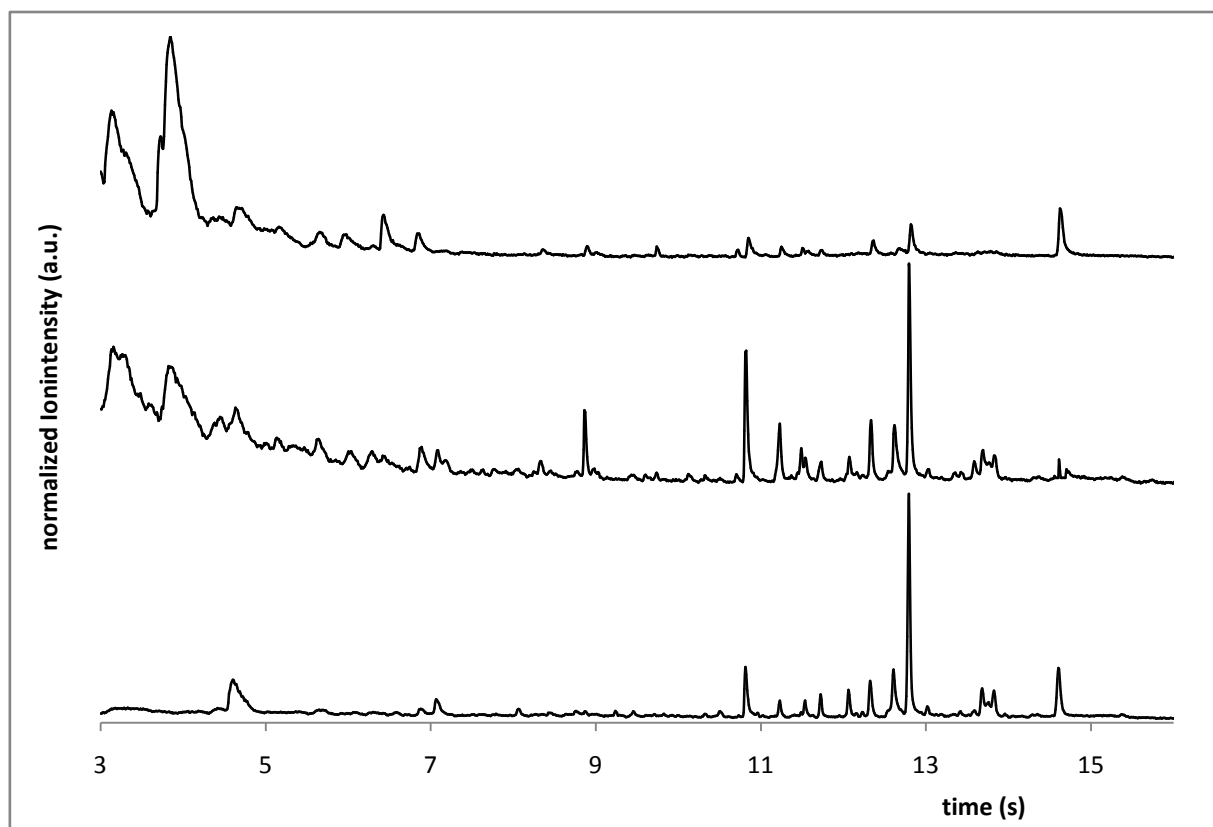


Figure 6. GC-MS of DCF after reductive dehalogenation at different temperatures (bottom: 300°C, middle: 400°C and top: 500°C)

4. Conclusion

We can conclude that reductive degradation of DCF occurs efficiently at temperatures between 300°C and 500°C with zero valent iron in a nitrogen atmosphere. The proton donors are ethanol and water. The production of phenol, cresol and other dehalogenation products indicate

that the reduction of DCF leads to less toxic substances. In contrast, since oxidative degradation of DCF leads to predominantly chlorinated products during the period investigated, it is not suitable as a detoxification method.

Further work is planned to show whether the reductive dehalogenation used is also applicable for determining diclofenac in waste water.

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