Degradation of Tamoxifen During Ozonation: pH Dependency

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Summary: Ozonation is one of the recommended technologies for the removal of micropollutants from wastewater effluents in Germany. Although a wide range of micropollutants is sufficiently removed, transformation processes and products for most compounds are not sufficiently investigated yet. Therefore we determine these processes for the endocrine disruptive pharmaceutical tamoxifen to gain further information on the chemical processes during ozonation and possible effects of the transformation products onto the aquatic environment.

Keywords: Ozone, Tamoxifen, Wastewater

Introduction: Anthropogenic compounds (e.g., pharmaceuticals) are present in almost all surface waters receiving wastewater treatment effluents, which can affect aquatic organisms e.g., as endocrine disruptors. Additionally these compounds might represent a threat to the human population receiving drinking water from affected surface waters if not removed by an adequate treatment process. (Hübner et al. 2015)

Ozonation and adsorption using activated carbon are considered as effective methods for the removal of most micropollutants in wastewater treatment (von Gunten 2003).The anti-estrogenic pharmaceutical Tamoxifen is used for cancer therapy (Zheng et al. 2007). Due to its endocrine activity it might have an effect on the development of single organisms as well as whole populations when emitted into the environment. Roberts and Thomas (2006) found Tamoxifen in concentrations of up to 369 ng L^{-1} in the effluent of a municipal wastewater treatment plant. This gives an average environmental input of 31 g day^{-1} from a single wastewater treatment plant into the river Tyne, England. The river itself contained 27-212 ng L^{-1}. (Roberts and Thomas 2006)

The aim of this work is to determine the influence of pH on the reaction kinetics of tamoxifen and ozone, and the formation of transformation products.

Material and Methods: Ozone is produced onsite with an ozone generator (Oxygen feed gas O_2: 99.999%). The reaction kinetics are determined for the oxidation of tamoxifen (Alfa Aesar, 98+ %) by ozone at pH 2 to pH 12. HPLC-UV and HPLC-ESI-MS are used for quantification of tamoxifen and for the determination of transformation products. This will allow the determination of the fractions of each transformation product over the whole range.

Results and discussion: Ozone and tamoxifen react rapidly ($k_{O3,\ Tamoxifen} = 3.56x10^6\ m^1s^{-1}$) at a pH of 7.1 (Chen et al. 2008). On the other hand, pH dependency of the reaction kinetics is yet not determined but can be expected since ozone can attack tamoxifen at two different reactive sites (see Figure 1). The first site is the olefin double bond and the second site is the tertiary amine.

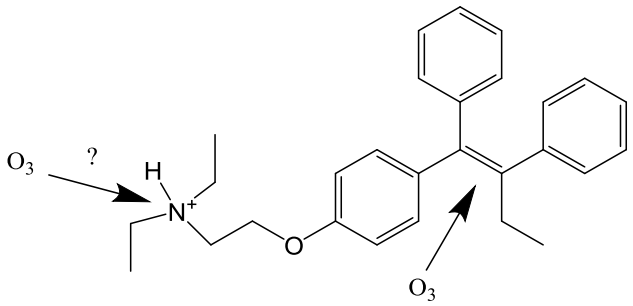

Figure 1 Structure of tamoxifen and predicted sites reactive to ozone at pH 7.

The main reaction site of ozone at a pH of 7.1 is the olefin double bond. The reaction of ozone and the amine is here not prominent due to the low pK_b value (≈4) of tertiary amines. The protonated amines show nearly no reactivity toward ozone whereas the free electron pair of the deprotonated amine can react rapidly with ozone (von Gunten 2003). As a consequence the reaction kinetics will increase with increasing pH. Also the transformation products will differ in structure. The attack of ozone at the amine is of major interest since the tertiary amine is responsible for the interaction with the estrogen receptors (Zheng et al. 2007).

This shows that the pH dependency of the reaction is essential to assess the reaction kinetics correctly and to determine the structure of the transformation products. Based on our experience we also assume that the endocrine activity is not completely removed if the tertiary amine is not oxidized. Hence the transformation products would still represent a threat when released into the aquatic environment even though tamoxifen itself may not be further detectable.

It can be concluded that the influence of the pH determines the reaction kinetics as well as the formed transformation products. These effects are investigated in the present study, for assessing environmental impact of tamoxifen related transformation products.

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