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Advanced oxidation processes for the removal of residual non-steroidal anti-inflammatory pharmaceuticals from aqueous systems

Ling Feng

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Ling Feng. Advanced oxidation processes for the removal of residual non-steroidal anti-inflammatory pharmaceuticals from aqueous systems. Earth Sciences. Université Paris-Est; Università degli studi (Cassino, Italie), 2013. English. NNT: 2013PEST1109 . tel-00952080

HAL Id: tel-00952080

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**ADVANCED OXIDATION
PROCESSES FOR THE REMOVAL OF
RESIDUAL NON-STEROIDAL ANTI-
INFLAMMATORY
PHARMACEUTICALS FROM
AQUEOUS SYSTEMS**

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This research was conducted under the auspices of the Erasmus Mundus Joint Doctorate Environmental Technologies for Contaminated Solids, Soils, and Sediments (ETeCoS3) and University of Paris-Est.

Joint PhD degree in Environmental Technology



Docteur de l'Université Paris-Est
Spécialité : Science et Technique de l'Environnement



Dottore di Ricerca in Tecnologie Ambientali



Degree of Doctor in Environmental Technology

Thèse – Tesi di Dottorato – PhD thesis

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**Advanced oxidation processes for the removal of residual non-steroidal
anti-inflammatory pharmaceuticals from aqueous systems**

To be defended December 2nd, 2013

In front of the PhD committee

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Erasmus Joint doctorate programme in Environmental Technology for Contaminated Solids, Soils and Sediments (ETeCoS³)



Dedication

The thesis is dedicated to my parents. They give me the encouragements to study abroad and make me realize there are more important things in the world and never fear yourself from the uncertainty you created. All their encouragement and careness kept me working and enjoying this 3 years study.

Acknowledgement

I am so honored to have this opportunity to study in the Laboratoire Géomatériaux et Environnement under the grant agreement FPA no. 2010-0009 of Erasmus Mundus Joint Doctorate programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments).

I am very grateful to my thesis advisor Mehmet Oturan for his insight, kind support, also with his guidance of my work and valuable suggestions and comments on my thesis and papers, thanks so much again for all your work and help.

I am very thankful to my Co-supervisor Eric van Hullebusch, who puts a lot of effort to help me on starting the project, my paper writing, and endless concerns on my work during this three years study.

I am grateful to Dr. Nihal Oturan and all the members in my lovely lab, thanks for all of you valuable suggestions, friendly welcome and nice working environment, which help me work happily and being more confident in the future work.

My internship in the Florida State University with Dr. Michael J. Watts and University of South Florida with Dr. Daniel Yeh, and University of Cassino with Giovanni Esposito was very inspiring and fruitful. Only all you kindly and useful suggestions and warmly help makes me achieve the goals.

Thanks for my parents who encourage me in all my university study, supporting me with all their love which make me stronger.

Thanks to all the people I met during my three years study abroad, thanks for all your kindly help, support and suggestions, thanks again!

Abstract

The thesis mainly focused on the implementation of advanced oxidation processes for the elimination of three non-steroidal anti-inflammatory drugs-ketoprofen, naproxen and piroxicam in waters. The three compounds are among the most used medicines, whose presence in waters poses a potential ecotoxicological risk. Due to the low pharmaceuticals removal efficiency of traditional wastewater treatment plants, worldwide concerns and calls are raised for efficient and eco-friendly technologies. Advanced oxidation processes, such as ozonation-biofiltration, electro-Fenton and anodic oxidation processes, which attracted a growing interest over the last two decades, could achieve almost complete destruction of the pollutants studied.

Firstly, removal of selected pharmaceuticals from tap water was investigated by electrochemical advanced oxidation processes “electro-Fenton” and “anodic oxidation” with Pt or boron-doped diamond anode and carbon felt cathode at lab-scale. Removal rates and mineralization current efficiencies under different operational conditions were analysed. Meanwhile, intermediates produced during the mineralization were also identified, which helps to propose plausible oxidation pathway of each compound in presence of $\bullet\text{OH}$. Finally, the evolution of the global toxicity of treated solutions was monitored using Microtox method, based on the fluorescence inhibition of *Vibrio fischeri* bacteria.

In the second part, the three nonsteroidal anti-inflammatory molecules added in organics-free or surface water were treated under varying ozone treatment regimes with the quite well established technology ozone/biofiltration. A bench-scale biological film was employed to determine the biodegradability of chemical intermediates formed in ozonized surface water. Identification of intermediates formed during the processes and bacterial toxicity monitoring were conducted to assess the pharmaceuticals degradation pathway and potential biological effects, respectively.

Keywords: Advanced Oxidation Processes; Electro-Fenton; Anodic Oxidation; Ozonation; Biofiltration; Ketoprofen; Naproxen; Piroxicam.

Résumé

La thèse a porté principalement sur la mise en œuvre de procédés d'oxydation avancée permettant l'élimination de trois anti-inflammatoires non stéroïdiens, le kétoprofène, le naproxène et le piroxicam dans l'eau. Ces trois composés sont parmi les médicaments les plus utilisés, dont la présence dans les eaux naturelles présente potentiellement un risque toxicologique. En raison de la faible efficacité d'élimination des produits pharmaceutiques par les stations traditionnelles de traitement des eaux usées, les scientifiques se sont mis à la recherche de technologies de traitements efficaces et respectueuses de l'environnement. Les procédés d'oxydation avancée, comme l'ozonation-biofiltration, l'électro-Fenton et l'oxydation anodique peuvent permettre d'atteindre la destruction presque complète des polluants étudiés et de ce fait ils ont suscité un intérêt grandissant au cours des deux dernières décennies.

Tout d'abord, ce travail s'intéresse à l'élimination de certains produits pharmaceutiques dans des solutions synthétiques préparées dans l'eau de robinet à l'aide des procédés électro-Fenton et oxydation anodique dans une cellule électrochimique équipée d'une anode de platine ou de diamant dopé au bore et d'une cathode de feutre de carbone. Cette étude a été menée à l'échelle du laboratoire. Les vitesses d'élimination des molécules pharmaceutiques ainsi que le degré de minéralisation des solutions étudiées ont été déterminées sous différentes conditions opératoires. Pendant ce temps, les sous-produits de l'oxydation générés au cours de la minéralisation ont également été identifiés, ce qui nous a permis de proposer les voies d'oxydation possible pour chaque composé pharmaceutique en présence du radical hydroxyl $\bullet\text{OH}$. Enfin, l'évolution de la toxicité au cours des traitements a été suivie en utilisant la méthode Microtox, basée sur l'inhibition de la fluorescence des bactéries *Vibrio fischeri*.

Dans la deuxième partie de ce travail de thèse, les trois anti-inflammatoires non stéroïdiens ont été ajoutés dans une eau déminéralisée ou dans une eau de surface. Ces eaux ont été traitées à l'aide de différentes doses d'ozone; puis le traitement à l'ozone a été combiné à un traitement biologique par biofiltration. Un biofilm biologique déposé à la surface d'un filtre de charbon actif a été utilisé pour déterminer la biodégradabilité des sous-produits d'oxydation formés dans les eaux de surface ozonée. L'identification des intermédiaires formés lors des processus de traitement et des contrôles de toxicité bactérienne ont été menés pour évaluer la voie de dégradation des produits pharmaceutiques et des effets biologiques potentiels, respectivement.

Mots Clés: Procédés d'Oxydation Avancée; Electro-Fenton; Oxydation Anodique;
Ozonation; Biofiltration; Ketoprofen; Naproxène; Piroxicam

Abstract

Dit proefschrift was voornamelijk gericht op de implementatie van geavanceerde oxidatie processen voor de verwijdering van drie niet-steroïdale anti-inflammatoire geneesmiddelen uit water: ketoprofen, naproxen en piroxicam. Deze drie stoffen behoren tot de meest gebruikte geneesmiddelen, en hun aanwezigheid in water vormt een potentieel ecotoxicologisch risico. Door het lage verwijderingsrendement van de traditionele afvalwaterzuivering voor deze farmaceutische stoffen is er wereldwijd zorg vanwege hun potentiële toxiciteit en vraag naar efficiënte en milieuvriendelijke verwijderingstechnologieën. Geavanceerde oxidatie processen, zoals ozonisatie-biofiltratie, electro-Fenton en anodische oxidatie processen kregen in de afgelopen twee decennia een groeiende belangstelling en zouden een bijna volledige verwijdering van de bestudeerde verontreinigende stoffen kunnen bereiken.

Ten eerste werd de verwijdering van de geselecteerde geneesmiddelen uit leidingwater onderzocht door de elektrochemische geavanceerde oxidatieprocessen "electro-Fenton" en "anode oxydatie" met Pt of boor gedoteerde diamant anode en koolstof kathode op laboratoriumschaal. Verwijderingsnelheden en mineralisatie efficiënties werden geanalyseerd onder verschillende operationele omstandigheden. Tussenproducten geproduceerd tijdens de mineralisatie werden ook geïdentificeerd, wat hielp om de oxidatie pathway van elke verbinding in de aanwezigheid van $\cdot\text{OH}$ te reconstrueren. Tenslotte werd de evolutie van de globale toxiciteit van behandelde oplossingen gemonitord met behulp de Microtox methode, gebaseerd op de fluorescentie remming van *Vibrio fischeri* bacteriën.

In het tweede deel werden de drie niet-steroïde anti-inflammatoire stoffen toegevoegd aan organische-vrij water of oppervlaktewater dat werd behandeld onder wisselende ozon regimes met de gevestigde "ozon/biofiltratie" technologie. Een bench-scale biofilm werd gebruikt om de biologische afbreekbaarheid van chemische tussenproducten gevormd in geozoniseerde oppervlaktewater te bepalen. Tussenproducten gevormd tijdens het proces werden geïdentificeerd om de afbraakroute van de farmaceutische producten te bepalen en bacteriële toxiciteit werd gemonitord om mogelijke biologische effecten te evalueren.

Trefwoorden: Geavanceerde Oxidatie Processen; Electro-Fenton; Anode Oxydatie, Ozonisatie, Biofiltratie; Ketopofen, Naproxen, Piroxicam.

Astratto

Il presente lavoro di tesi è centrato sull'implementazione di processi di ossidazione avanzata per la rimozione dalle acque di tre farmaci non steroidei antinfiammatori: ketoprofene, naproxene e piroxicam. I tre composti sono tra i medicinali più usati e la loro presenza in acqua pone un rischio potenziale di tipo ecotossicologico. A causa delle ridotte efficienze di rimozione degli impianti tradizionali di trattamento delle acque reflue nei confronti di tali composti farmaceutici, si è resa necessaria la ricerca di nuove tecnologie più efficienti e eco-sostenibili. I processi di ossidazione avanzata, come ozonizzazione-biofiltrazione, elettro-Fenton e ossidazione anodica, che hanno riscontrato un crescente interesse negli ultimi due decenni, sono in grado di degradare in maniera quasi completa i suddetti inquinanti.

Pertanto nella tesi è stato studiato, in primo luogo, l'impiego dei processi di ossidazione elettrochimica avanzata electro-Fenton e ossidazione anodica per la rimozione dei prodotti farmaceutici dall'acqua di rubinetto, usando Pt o boron-doped diamond come anodo e carbon felt come catodo, in scala di laboratorio. In particolare sono state esaminate le velocità di rimozione e le efficienze di mineralizzazione ottenute in condizioni operative diverse. Allo stesso tempo sono stati identificati i composti intermedi prodotti nel corso della mineralizzazione per individuare dei percorsi di ossidazione plausibili per ogni composto in presenza di $\bullet\text{OH}$. Inoltre l'evoluzione della tossicità globale delle soluzioni trattate è stata monitorata utilizzando il metodo Microtox, basato sull'inibizione della fluorescenza dei batteri *Vibrio fischeri*.

Nella seconda parte della tesi i tre composti antinfiammatori non steroidei aggiunti ad acque prive di sostanza organica o acque superficiali sono stati trattati con la tecnologia già affermata dell'ozonizzazione/biofiltrazione. Una pellicola biologica in scala banco è stata impiegata per determinare la biodegradabilità degli intermedi chimici prodotti nell'acqua superficiale ozonizzata. L'identificazione degli intermedi formati durante i processi ossidativi e il monitoraggio della tossicità batterica sono stati condotti, rispettivamente, per valutare i percorsi di degradazione dei composti farmaceutici e i potenziali effetti biologici.

Parole chiave: Processi di Ossidazione Avanzata; Electro-Fenton, Ossidazione Anodica, Ozonizzazione, Biofiltrazione; Ketoprofen, Naproxene, Piroxicam.

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Author

List of Publications

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List of abbreviation

| | |
|------------------|---|
| AO | anodic oxidation |
| AOPs | advanced oxidation processes |
| BAC | biological activated carbon |
| BDD | boron doped diamond |
| BOD ₅ | biochemical oxygen demand (mg L ⁻¹) |
| BOM | biodegradable organic matter |
| BPA | Bisphenol A |
| CAS | conventional activated sludge plant |
| COD | chemical oxygen demand (mg L ⁻¹) |
| DOC | dissolved organic carbon (mg L ⁻¹) |
| EAOPs | electrochemical advanced oxidation processes |
| EBCT | empty bed contact time |
| EC ₅₀ | half maximal effective concentration for 50% reduction of the response during exposition to a drug (mg L ⁻¹) |
| EF | electro-Fenton |
| ESI-MS | electrospray ionization - mass spectrometry |
| GAC | granular activated carbon |
| GC-MS | gas chromatography mass spectrometry |
| GDEs | gas diffusion electrodes |
| HPLC | high performance liquid chromatography |
| LC ₅₀ | median lethal dose required to kill 50% of the members of a tested population after a specified test duration (mg L ⁻¹) |
| LC-MS | liquid chromatography - mass spectrometry |
| LP/MP UV | low /medium pressure ultraviolet |
| MBR | membrane bioreactor |
| NSAIDs | nonsteroidal anti-inflammatory drugs |
| NOEC | no observed effect concentration |
| •OH | hydroxyl radicals |
| PEF | photoelectro-Fenton |
| Pt | platinum |
| RO | reverse osmosis |
| SEC | supporting electrolyte concentration |

| | |
|-------------|--|
| SPEF | solar photoelectro-Fenton |
| TOC | total organic carbon (mg L ⁻¹) |
| TYPE II LAB | de-ionized water |
| WWTPs | wastewater treatment plants |

Chapter 1. General Introduction

Chapter 1 General Introduction

1.1 Background

Pharmaceuticals with different physicochemical and biological properties and functionalities already have been largely consumed over the last 50 years. These compounds are most notably characterized by their more or less specific biological activity and low micro-biodegradability feature. As the fate of pharmaceuticals in environment shows, most of them are discarded in their original chemical structures or metabolites via toilet (human only can metabolize a small percentage of the medicines), or production facilities, hospitals, and private household into the municipal sewers. Others from solid waste landfill or manure waste could enter into the water cycle, due to their nonadsorbed polar structure [1-3].

The traditional wastewater treatment plants are mostly not designed to deal with polar micropollutants such as pharmaceuticals. With the respect of pharmaceutical characteristic being resistant to microbial degradation, low removal percentages are performed in the secondary treatment in traditional water treatments. Such final effluents containing residual pharmaceuticals are discharged into natural surface water bodies (stream, river or lake).

Low removal efficiency of pharmaceuticals by conventional wastewater treatment plants requests for more efficient technologies and nowadays research on advanced oxidation processes (AOPs) have become a hot topic. AOPs, rely on the destruction of pollutants by highly reactive oxidant species, such as hydroxyl radical ($\bullet\text{OH}$), ion superoxide ($\text{O}_2^{\bullet-}$), hydroperoxyl radical (HO_2^{\bullet}), and organic peroxide radical (ROO^{\bullet}). These oxidants can highly react with a wide range of organic compounds in a non-selective oxidation way. The target compounds could be quickly and efficiently converted into small inorganic molecules such as CO_2 and H_2O . However, with the great power of the AOPs, the utilization of such processes in water treatments has not been applied in a large number because of the high costs of chemical reagents inputs or extra demanding of pre or after treatment. However, due to the request of clean and safe water sources, the interests of applying AOPs for wastewater treatment is rising in different countries.

The advanced treatment applied in wastewater treatment plants is called the tertiary treatment step. Wet oxidation, ozonation, Fenton process, sonolysis, homogeneous ultraviolet irradiation, and heterogeneous photo catalysis using semiconductors, radiolysis and a number of electric and electrochemical methods are

Chapter 1 General Introduction

classified in this context. As researches in different water matrix showed, ozonation, Fenton process and related systems, electrochemistry, heterogeneous photocatalysis using TiO₂/UV process and H₂O₂/UV light process seem to be most popular technologies for pharmaceuticals removal from wastewater effluents.

1.2 Problem Statement

Most of the traditional wastewater treatment plants (WWTPs) are especially not designed with tertiary treatment step to eliminate pharmaceuticals and their metabolites [4]. WWTPs therefore act as main pharmaceuticals released sources into environment. The released pharmaceuticals into the aquatic environment are evidenced by the occurrence of pharmaceuticals up to $\mu\text{g L}^{-1}$ level in the effluent from medical care units and sewage treatment plants, as well as surface water, groundwater, and drinking water [5-9]. It is urgent to supply the adapted technologies to treat the pharmaceuticals in WWTPs before releasing them into natural water system.

Nevertheless, increased attention is currently being paid to pharmaceuticals as a class of emerging environmental contaminants [10]. Because of the presence of the pharmaceuticals in the aquatic environment and their low volatility, good solubility and main transformation products dispersed in the food chain, it is very important to investigate their greatest potential risk on the living organisms [11-13]. Since the pharmaceuticals are present as a mixture with other pollutants in the waste and surface waters, effect as synergistic or antagonistic can occur as well [14, 15]. Therefore, their long-term effects have also being taken into consideration [16].

In the last years, European Union [17] and USA [18] have taken action to establish regulations to limit the pharmaceuticals' concentrations in effluents to avoid environmental risks. The focuses are on the assessments of effective dose of pharmaceuticals for toxicity in industrial effluents or surface water. In 2011, the World Health Organization (WHO) published a report on pharmaceuticals in drinking-water which reviewed the risks to human health associated with exposure to trace concentration of pharmaceuticals in drinking-water [19].

The trace level concentration of pharmaceuticals in aquatic environments results from ineffective removal of traditional water treatments processes. Therefore, to overcome the shortcomings, developments of more powerful and ecofriendly techniques are of great interests. Electrochemical advanced oxidation processes (EAOPs), as a

Chapter 1 General Introduction

combination of chemical and electrochemical methods, are mainly developed to oxidize the pollutants at the anodes or by the improvement of classic Fenton process [20]. This latter process favors the production of $\bullet\text{OH}$, which are capable of oxidizing almost all the organic and inorganic compounds in a non-selective way [21, 22].

The former one, as anodic oxidation (AO), oxidizes the pollutants directly by the adsorbed $\bullet\text{OH}$ formed at the surface of anode from water oxidation (Eq. (1.1)), with no need of extra chemical reagents in contrast to Fenton related processes [3]. The nature of anodes material greatly influences the performance of AO. With the techniques' development, a boron-doped diamond (BDD) thin film anode, characterized by its higher oxygen overvoltage, larger amount production and lower adsorption of $\bullet\text{OH}$, shows a good organic pollutants removal yield [23]. AO process with BDD has been conducted with tremendous removal efficiency on pharmaceuticals.



Indirect oxidation as the electro-Fenton (EF) generates the H_2O_2 by the reduction of oxygen in an acidic medium at cathode surface (Eq. (1.2)) [24]. Then, the oxidizing power is enhanced by the production of $\bullet\text{OH}$ in bulk solution through Fenton reaction (Eq. (1.3)). This reaction is catalyzed from electrochemical re-generation of ferrous iron ions (Eq. (1.4)) [25].



In an undivided cell system, the two oxidation mechanisms can coexist during the process. However, parasitic or competitive reactions also occur during the procedure [26, 27].

Otherwise, ozonation is one of the most popular AOPs, using the oxidative power of ozone (O_3) and producing extra $\bullet\text{OH}$ as oxidant, that has been widely applied for drinking water production [28, 29]. It has been proved that natural organic matter biodegradability and an efficient inactivation of a wide range of microorganisms could be achieved by ozonation via ozone or $\bullet\text{OH}$ [30]. At present, ozonation is the only AOPs that have been applied at full-scale for the degradation of pharmaceuticals still

Chapter 1 General Introduction

remaining in the wastewater effluents before discharge in the environment. This technology was shown to reduce of effluent toxicity after ozone treatment [31-33].

Biodegradable organic compounds generated by AOPs can be an energy and carbon sources for the heterotrophic bacteria and may cause serious problem of bacterial regrowth in the drinking water distribution system. This makes the combination of AOPs and microbiological treatments as an attractive and economical way for the purification of water treatments.

Biofiltration systems are operated robustly and constructed simply with low energy requirements [34]. This technology has been used for many years for water treatments, proved to be able to significantly remove natural organic matter, ozonation by-products, disinfection by-products precursors as well as pharmaceuticals [34, 35-40]. Among the media for the biofiltration, the one with a larger attachment surface for the microbial biofilm and the one with the higher adsorption capacity for organic compounds such as granular activated carbon (GAC) is mostly utilized [35, 36].

1.3 Goal of the Research

As world concerned pollutants, three molecules of anti-inflammatory and analgesic pharmaceuticals - ketoprofen, naproxen and piroxicam were selected for this study. The selection was under the consideration of their detection frequency, ecotoxicity, removal rate in wastewater treatment plants and other oxidation techniques (see chapter 2) [3]. The efficient technologies promoted for the removal of these compounds are powerful EAOPs (EF and AO) and popular ozonation/biofiltration system.

The general research objective for this study is to find out the removal efficiency of the EAOPs and ozonation/biofiltration system. The emphases is on optimizing the parameters with the consideration of both degradation and mineralization rate of pharmaceuticals. Likewise, the kinetic study for three compounds oxidized by $\bullet\text{OH}/\text{O}_3$ was also conducted by competition method in order to determine the absolute kinetic constant. Finally, oxidation intermediates and end-products (aromatic compounds, carboxylic acids and inorganic ions) were determined during the mineralization for the selected pollutants degradation pathways by EAOPs and ozonation processes.

Specific research objective of this study is on the toxicity of treated solution to assess the ecotoxicity of the treatment processes. The intent of application of ozonation

Chapter 1 General Introduction

followed by biofiltration is to find the economical and ecofriendly energy input for drinking water treatment plants. With the investigation of the mineralization pathway and study of toxicity evolution during the processes operation, a deep understanding of pharmaceuticals removal from aquatic environment is expected to be achieved.

All the work above is intended to cope with water problems with removal of pharmaceuticals and to select the right method or most often the right combination of methods for an ecofriendly application in water treatments.

1.4 Research Questions

Considering the potential ecotoxicological risk of pharmaceuticals in aquatic environment and the need to develop efficient technologies for the removal of these pollutants, AOPs (i.e. EF, AO and ozonation) were studied. The present thesis aims at the determination of the kinetics, mechanisms, and evolution of the toxicity of pharmaceuticals in the treated solutions.

The following matters are the main questions to be answered in this thesis:

1. What are the optimal operational parameters allowing to reach the best removal rate to achieve energy saving? Which process has better performance, and what is the reason for that?
2. How the oxidants react with the pharmaceuticals? What kinds of intermediates will be produced during the mineralization process? Whether the mechanisms of pharmaceuticals oxidized by EAOPs can be proposed?
3. How the toxicity values change during the EAOPs processes? What is the explanation for the results?
4. Whether the combination of biofiltration with ozone treatment can improve the removal of these organic micropollutants and decrease the toxicity in treated water? In what kind of situation it works?
5. With all the questions being answered, can this study help to reach a successful elimination of the pollutants and a low cost demand for per m³ water treated for the application? If not, what kind of other solutions or perspective can be addressed to accelerate the implementation of AOPs/EAOPs at full-scale?

1.5 Outline of the Thesis

The whole thesis is divided into the following main sections.

Chapter 1 General Introduction

In the chapter 2, a literature review summarizes the relevant removal of pharmaceuticals by AO and EF processes. The frequent detection and negative impact of pharmaceuticals on the environment and ecology are clarified. Therefore, efficient technologies as EAOPs (i.e AO and EF) for the removal of anti-inflammatory and analgesic pharmaceuticals from aqueous systems are well overviewed as prospective technologies in water treatments.

The chapter 3 is the research of comparison of EF and AO processes on ketoprofen removal. Ketoprofen is not efficiently removed in wastewater treatment plants. Its frequent detection in environment and various treatment efficiencies make it chosen as one of the pollutants investigated in this work. The results show promising removal rates and decreasing toxic level after treatment.

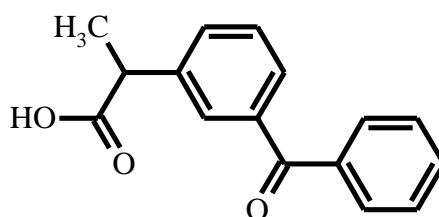


Fig. 1.1. Chemical structure of ketoprofen

Naproxen has been widely consumed as one of the popular pharmaceuticals. More researches have revealed its high level of detected concentration in environment and toxic risk on living species. In the chapter 4, the removal of naproxen from aqueous medium is conducted by EF process to clarify the effect of anode material and operating conditions on removal. It can be concluded that high oxidizing power anode can achieve better removal rate.

Then, different processes as EF and AO with same electrodes are compared in electrochemical oxidation of naproxen in tap water in the chapter 5. It is showed, under the same condition, the removal rate is better by EF than that of AO.

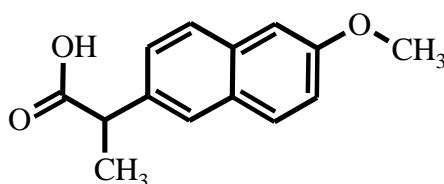


Fig. 1.2. Chemical structure of naproxen

Chapter 1 General Introduction

In the chapter 6, as one popular medicine used for almost 30 years, the degradation of piroxicam by EF and AO processes is performed. The research is divided into 4 parts: 1. The optimization of the procedure in function of catalyst concentration, pH, air input and current intensity applied on both degradation (HPLC) and mineralization (TOC) rate; 2. The kinetic constant of reaction studied between pollutant and $\cdot\text{OH}$ (competition kinetics method); 3. Intermediates formed during the mineralization (HPLC, standard material) and pathway proposed by the intermediates produced and related paper published; 4. The evolution of the toxicity (Microtox method) of the solution treated.

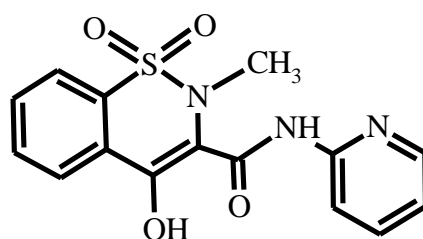


Fig. 1.3. Chemical structure of piroxicam

Chapter 7 is about the removal of pharmaceuticals cytotoxicity with ozonation and BAC filtration. The experiments are set-up to optimize the parameters involved for removal of the three compounds. Afterwards, O_3/O_3 and H_2O_2 oxidized solutions are treated by biological activated carbon (BAC). Later, oxidation intermediates identified by electrospray ionization mass spectrometry and *Vibrio fischeri* bacterial toxicity tests are conducted to assess the predominant oxidation pathways and associated biological effects.

General discussion is presented in chapter 8. Firstly, the overall results of the research are discussed. Except the work of this thesis, perspective of the future work of AOPs on removal of persistent or trace pollutants is proposed. Lastly, the conclusion of the all work of this thesis is given.

Chapter 1 General Introduction

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Chapter 2. Review Paper

Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced processes. A review

This chapter has been published as:

Feng, L., van Hullebusch, E.D., Rodrigo, M.A., Esposito, G. and Oturan, M.A. (2013) Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced oxidation processes. A review. Chemical Engineering Journal 228, 944-964.

Chapter 2: Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced processes. A review

Abstract:

Occurrence of pharmaceuticals in natural water is considered as an emerging environmental problem owing to their potential toxicological risk on living organisms even at low concentration. Low removal efficiency of pharmaceuticals by conventional wastewater treatment plants requests for a more efficient technology. Nowadays research on advanced oxidation processes (AOPs) have become a hot topic, because these technologies have been shown to be able to oxidize efficiently most organic pollutants until mineralization to inorganic carbon (CO₂). Among AOPs, the electrochemical advanced oxidation processes (EAOPs), and in particular, "anodic oxidation" and "electro-Fenton", have demonstrated good prospective at lab-scale level for the abatement of pollution caused by the presence of residual pharmaceuticals in waters. This paper reviews and discusses the effectiveness of electrochemical EAOPs for the removal of anti-inflammatory and analgesic pharmaceuticals from aqueous systems.

Keywords: Pharmaceuticals; Emerging Pollutants; NSAIDs; EAOPs; Hydroxyl Radicals; Anodic Oxidation; Electro-Fenton; Degradation; Mineralization.

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2.1 Introduction

In 1899, the first anti-inflammatory drug, aspirin (acetylsalicylic acid, $C_9H_8O_4$), was registered and produced extensively by German Bayer Company. During the following years, many other nonsteroidal anti-inflammatory drugs (NSAIDs) were developed and marketed. Nowadays, this group of medicines includes more than one hundred compounds and they are known to be largely used throughout the world as inflammatory reducer and pain killer. From the chemical structure point of view, they consist of an acidic moiety attached to a planar, aromatic functionality (Fig. 2.1). Mechanistically, they inhibit the cyclooxygenase (COX) enzymes, which convert arachidonic acid to prostaglandins, thromboxane A₂ (TXA₂) and prostacyclin, reducing consequently ongoing inflammation, pain and fever.

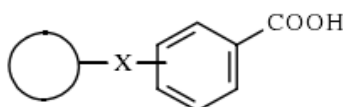
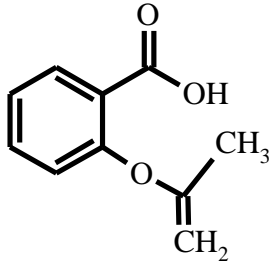
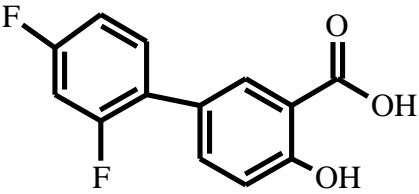


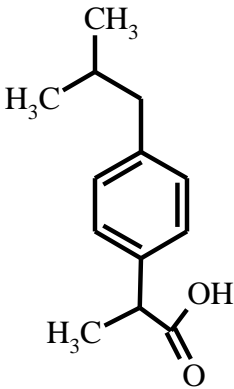
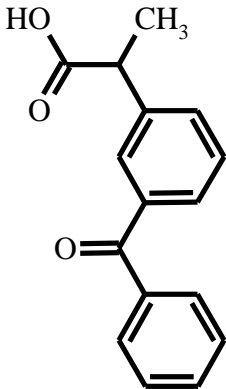
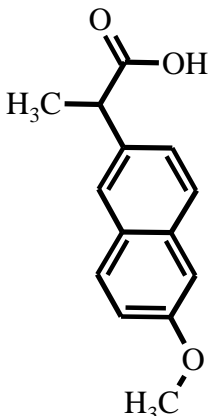
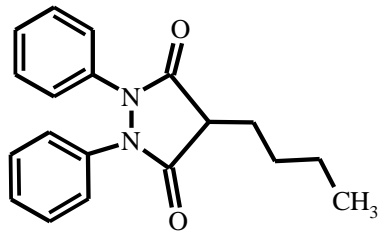
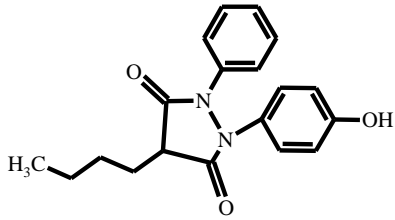
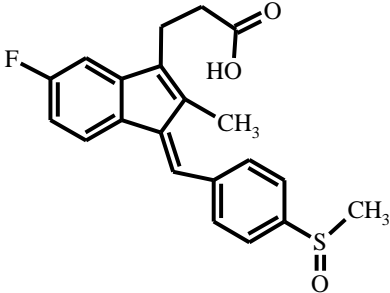
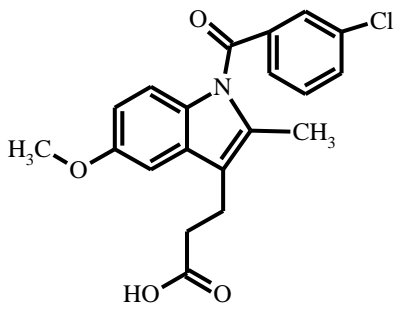
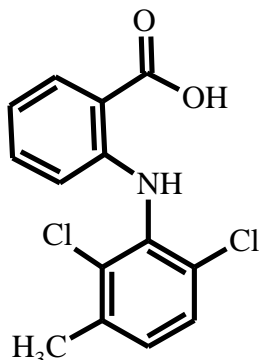
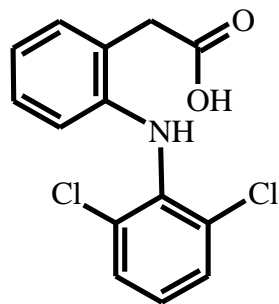
Fig. 2.1. General structure of NSAIDs

In Table 2.1, it is shown a classification of NSAIDs according to their chemical structure. This table also shows the most frequently detected pharmaceuticals in environment.

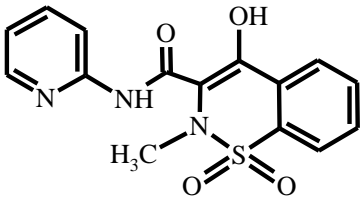
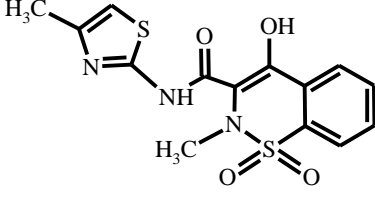
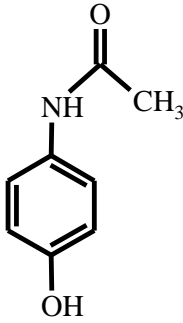
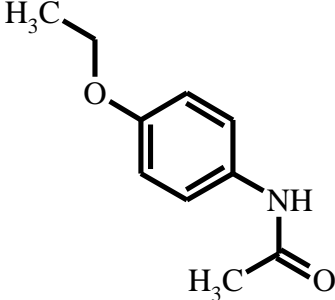
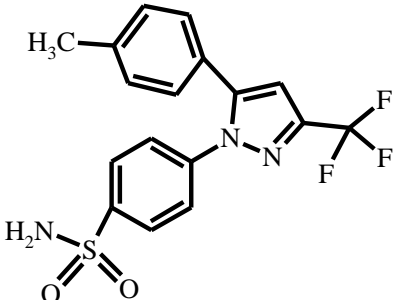
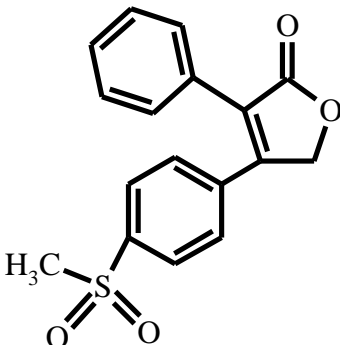
Table 2.1. Classification of NSAIDs.

| 1 | Non-selective COX Inhibitors/General Structure | Typical Molecules | |
|---|--|--|--|
| | Salicyliclates / Derivatives of 2-hydroxybenzoic acid (salicylic acid), strong organic acids and readily form salts with alkaline materials | Aspirin  | Diflunisal  |

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| | | | |
|--|--|---|---|
| <p>Propionic Acid Derivatives / Characterized by the general structure Ar-CH(CH₃)-COOH, often referred to as the “profens” based on the suffix of the prototype member</p> | <p>Ibuprofen</p>  | <p>Ketoprofen</p>  | <p>Naproxen</p>  |
| <p>Phenylpyrazolones / Characterized by the 1-aryl-3,5-pyrazolidinedione structure</p> | <p>Phenylbutazone</p>  | <p>Oxyphenbutazone</p>  | |
| <p>Aryl and Heteroarylacetic Acids / Derivatives of acetic acid, but in this case the substituent at the 2-position is a heterocycle or related carbon cycle</p> | <p>Sulindac</p>  | <p>Indomethacin</p>  | |
| <p>Anthranilates / N-aryl substituted derivatives of anthranilic acid which itself is a bioisostere of salicylic acid</p> | <p>Meclofenamate</p>  | <p>Diclofenac</p>  | |

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| | | |
|---|--|---|
| <p>Oxicams / Characterized by the 4-hydroxybenzothiazine heterocycle</p> | <p>Piroxicam</p>  | <p>Meloxicam</p>  |
| <p>Anilides / Simple acetamides of aniline which may or may not contain a 4-hydroxy or 4-alkoxy group.</p> | <p>Paracetamol</p>  | <p>Phenacetin</p>  |
| <p>2 Selective COX II Inhibitors / All are diaryl-5-membered heterocycles.</p> | <p>Celecoxib</p>  | <p>Rofecoxib</p>  |

There are more than 30 million people using NSAIDs every day. The consumption in USA, United Kingdom, Japan, France, Italy and Spain has increased largely at a rate of 11.9% each year, which means a market rising from 3.8 billion dollar in 1998 to 11.6 billion dollar in 2008. Following data from French Agency for the Safety of Health Products (Agence Française de Sécurité Sanitaire des Produits de Santé, AFSSAPS 2006), the consumed volumes of pharmaceuticals differ significantly in different countries. Thus, in USA, about 1 billion prescriptions of NSAIDs are made every year. In Germany, more than 500 tons of aspirin, 180 tons of ibuprofen and 75 tons of diclofenac were consumed in 2001 [1]. In England, 78 tons of aspirin, 345 tons of ibuprofen and 86 tons of diclofenac were needed in 2000 [2], while 400 tons of

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aspirin, 240 tons of ibuprofen, 37 tons of naproxen, 22 tons of ketoprofen, and 10 tons of diclofenac were consumed in France in 2004. The amount of paracetamol manufactured was 1069 ton in Korea in 2003 [3].

Since such a large amount of pharmaceutical compounds are consumed every year, significant unused overtime drugs, including human (household, industry, hospitals and services) and veterinary (aquaculture, livestock, and pets) medical compounds, are released into environment continuously. A small part of unused or expired drugs is gathered to be incinerated. However a large part, in the form of original drugs or metabolites, is discarded to waste disposal site or flushed down via toilet (human body only metabolizes a small percentage of drug) into municipal sewer in excrement. As an example, in Germany, it is estimated that amounts of up to 16 000 tons of pharmaceuticals are disposed from human medical care and 60–80% of those disposed drugs are either washed off via the toilets or disposed of with normal household waste each year [4, 5]. Much of these medicines escape from being eliminated in wastewater treatment plants (WWTPs), because they are soluble or slightly soluble, and they are resistant to degradation through biological or conventional chemical processes. In addition, medicines entering into soil system, which may come from sewage sludge and manure, are not significantly adsorbed in the soil particles due to their polar structure. Therefore, they have the greatest potential to reach significant levels in the environment. Ground water for drinking water production may be recharged downstream from WWTPs by bank filtration or artificial ground water [6-9], making NSAIDs entering into the drinking water cycle that could be used for the production of drinking water. Consequently, it is reported NSAIDs are detected on the order of ng L^{-1} to $\mu\text{g L}^{-1}$ in the effluent of sewage treatment plants and river water [9-12]. All discharge pathways above mentioned act as entries of pharmaceuticals into aquatic bodies, waters and potable water supplies [13] (Fig. 2.2).

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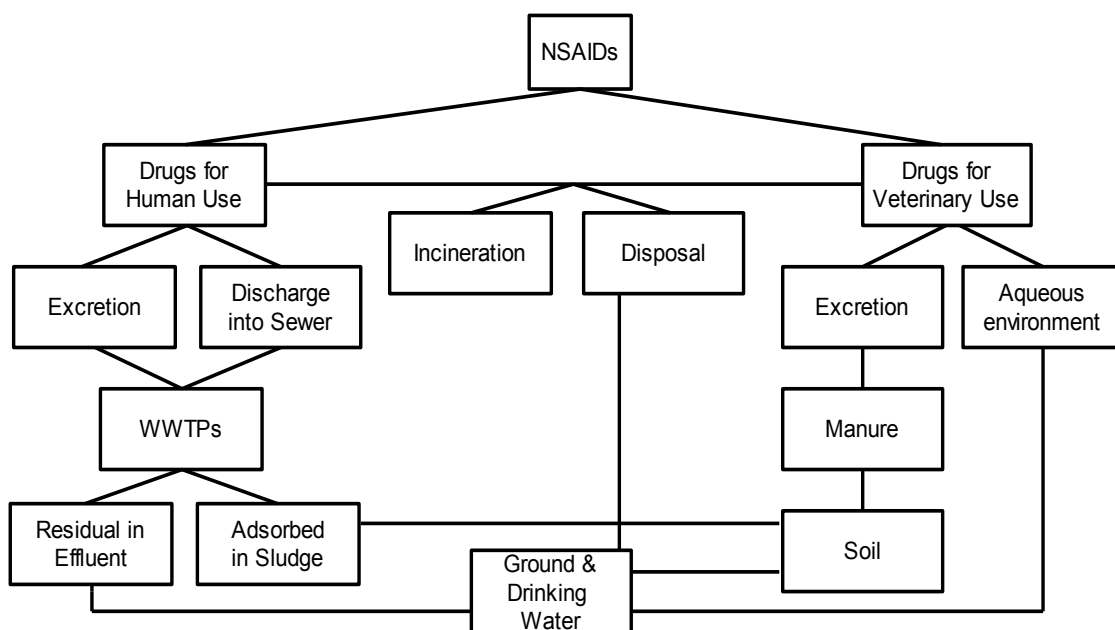


Fig. 2.2. Pathway for the occurrence of pharmaceuticals in aqueous environment (adapted from [14] with Copyright from 2011 American Chemical Society).

The pharmaceuticals are specially designed against biological degradation. This means that they can retain their chemical structure long enough to exist in human body, and mostly released into environment in original form. It is known that pharmaceuticals may not only target on specific metabolic pathways of humans and domestic animals but also have effect on non-target organisms, even at very low concentrations [15-19]. In 2011, the World Health Organization (WHO) published a report on pharmaceuticals in drinking-water which reviewed the risks to human health associated with exposure to trace concentrations of pharmaceuticals in drinking-water, raising the fear that the continuous input of pharmaceuticals may pose a potential risk for the organisms living in terrestrial and aquatic environment [20]. Inflammatory drugs, such as ibuprofen, naproxen, diclofenac and ketoprofen, which exist in effluents of WWTPs and surface water, being discharged without the use of appropriate removal technologies, may cause adverse effects on the aquatic ecosystem [21, 22], and it has been considered as an emerging environmental problem. Recent studies had confirmed that the decline of the population of vultures in the India subcontinent was related to their exposure to diclofenac residues [23, 24]. Furthermore, it is accepted that the co-existence of pharmaceuticals or other chemicals (so-called drug “cocktail”) brings more complex toxicity to living organisms [25] that is uneasily to be forecasted and resolved. For example, the investigation of the combined occurrence of diclofenac, ibuprofen,

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naproxen and acetylsalicylic acid in water demonstrates synergistic effect on toxicity [39]. This fact has resulted in raising concerns about the recent elimination efficiency of pharmaceuticals in environment, and the need for the assessment of safety of drinking water, reclaimed, reused wastewater, and aquatic ecosystems.

Considering that conventional wastewater treatment processes display sometime poor removal efficiency for pharmaceuticals, this paper gives a quick overview of removal efficiency of some NSAID's that were investigated in the literature. Then, in the frame of this review, among the different Advanced Oxidation Processes (AOPs) available, the interest of using electrochemical advanced oxidation processes (in particular anodic oxidation and electro-Fenton) for the removal of NSAID's is discussed. These technologies are still at a very early stage compared with other AOPs (i.e. ozonation, Fenton or UV/H₂O₂) [26-30] with most studies found in the literature carried out at the lab-scale. However, as it will be discussed in this paper, they show a very promising potential and very soon scale up and effect of actual matrixes of water will become hot topics.

2.2 Anti-inflammatory and analgesic drugs discussed in this review

The NSAIDs constitute a heterogeneous group of drugs with analgesic, antipyretic and anti-inflammatory properties that rank intermediately between corticoids with anti-inflammatory properties on one hand, and major opioid analgesics, on the other. Considering the contamination level of anti-inflammatory and analgesic drugs in aqueous environment, aspirin, ibuprofen, ketoprofen, naproxen, diclofenac, paracetamol and mefenamic acid can be considered as the most significant ones. Their main physicochemical characteristics are given in Table 2.2. Such molecules have also been shown to be poorly removed or degraded by conventional water treatment processes in contrast to results obtained by application of AOPs.

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Table 2.2. Basic information of selected NSAIDs.

| NSAIDs | Formula | Mass (g mol ⁻¹) | CAS No. | pKa | Solubility (mg L ⁻¹) | log Kow | log Koc | Ref. |
|----------------|--|--------------------------------|------------|------|-------------------------------------|------------|------------|------------|
| Aspirin | C ₉ H ₈ O ₄ | 180.0 | 50-78-2 | 3.50 | 4600 | 1.20 | 1.0 | [31,32,39] |
| Diclofenac | C ₁₄ H ₁₁ Cl ₂ NO ₂ | 296.2 | 15307-79-6 | 4.91 | 2 | 4.51 | 1.9 | [33-35] |
| Ibuprofen | C ₁₃ H ₁₈ O ₂ | 206.3 | 15687-27-1 | 4.15 | 21 | 4.51 | 2.5 | [33-35] |
| Ketoprofen | C ₁₆ H ₁₄ O ₃ | 254.3 | 22071-15-4 | 4.45 | 51 | 3.12 | 2.5 | [32,33] |
| Mefenamic acid | C ₁₅ H ₁₅ NO ₂ | 241.3 | 61-68-7 | 5.12 | 20 | 5.12 | 2.7 | [33,36] |
| Naproxen | C ₁₄ H ₁₄ O ₃ | 230.3 | 22204-53-1 | 4.15 | 144 | 3.18 | 2.5 | [32,33] |
| Paracetamol | C ₈ H ₉ NO ₂ | 151.2 | 103-90-2 | 9.38 | 1290 0 | 0.46 | 2.9 | [37,38] |

Data of solubility at 20°C

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Aspirin, 2-acetoxybenzoic acid, is one of the most popular pain killers, this compound, as well as its derivatives, is known to exhibit high toxicity to a wide range of aquatic organisms in water bodies [39, 40].

Diclofenac, 2-[2-(2,6-dichlorophenyl)aminophenyl] ethanoic acid, commonly used in ambulatory care, has a highest acute toxicity [21, 41, 42]. This medicine and its metabolites are the most frequently detected NSAIDs in water, because they could resist biodegradation in the WWTPs effluents. It was investigated that prolonged exposure at the lowest observed effect concentration (LOEC) of $5 \mu\text{g L}^{-1}$, leads to impairment of the general health of fishes, inducing renal lesions and alterations of the gills [43].

Ibuprofen, (RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid, hugely global consumed, has a high acute toxicity, which was suspected of endocrine disrupting activity in human and wildlife [44, 45]. Quite similar toxicological consequences in aquatic environment have been shown by the intermediates formed by biological treatment [46].

Ketoprofen, (RS)-2-(3-benzoylphenyl)propanoic acid, is metabolized mainly in conjugation with glucuronic acid (a cyclic carboxylic acid having structure similar to that of glucose) and excreted mainly in the urine (85%) [47]. Surveys of livestock carcasses in India indicated that toxic levels of residual ketoprofen were already present in vulture food supplies [48].

Naproxen, (+)-(S)-2-(6-methoxynaphthalen-2-yl)propanoic acid, is widely used in human treating veterinary medicine [49], with a chronic toxicity higher than its acute toxicity shown by bioassay tests. It was also shown that the by-products generated by photo-degradation of naproxen were more toxic than itself [50].

Mefenamic acid, 2-(2,3-dimethylphenyl)aminobenzoic acid, has potential contamination of surface water, it is of significant environmental relevance due to its diphenylamine derivative [47].

Paracetamol, N-(4-hydroxyphenyl)acetamide, is one of the most frequently detected pharmaceutical products in natural water [51]. As an example, it was detected in a concentration as high as $65 \mu\text{g L}^{-1}$ in the Tyne river (UK) [52]. In addition, by chlorination in WWTPs, two of its identified degradation compounds were transformed into unequivocally toxicants [53].

2.3 Conventional wastewater treatment on anti-inflammatory and analgesic drugs

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Conventional wastewater treatment consists of a combination of physical, chemical, and biological processes. There are four removal stages: preliminary treatment, primary treatment, secondary treatment, tertiary treatment and/or advanced wastewater treatment. Preliminary treatment is used for removal of coarse solids and other large materials often found in raw wastewater, intended to reduce oils, grease, fats, sand, and grit, done entirely mechanically by means of filtration and bar screens. Primary treatment is performed to remove organic suspended solids and a part of the colloids, which is necessary to enhance the operation and maintenance of subsequent treatment units. Secondary treatment is designed to substantially degrade the organic content of the sewage, usually using microorganisms in the purification step; in tertiary treatment step, the stronger and more advanced treatment is applied. This tertiary treatment and/or advanced wastewater treatment is employed when specific wastewater constituents which cannot be removed by secondary treatment must be removed such as phosphorus or pharmaceuticals. Therefore, biological and physicochemical processes could be applied. For instance, for the removal of pharmaceuticals residues, ozonation is currently used at full-scale [54] and the final effluent can be discharged into natural surface water bodies (stream, river or lake).

Wastewater treatment plants are not specifically designed to deal with highly polar micro pollutants, like anti-inflammatory and analgesic drugs (Table 2.3). It is assumed that pharmaceuticals are likely to be removed by adsorption onto suspended solids or through association with fats and oils during aerobic and anaerobic degradation, and chemical (abiotic) degradation by processes such as hydrolysis [55, 56]. A recent study on the elimination of a mixture of pharmaceuticals in WWTPs including the beta-blockers, the lipid regulators, the antibiotics and the anti-inflammatory drugs exhibited removal efficiencies below 20% in the WWTPs [57].

Table 2.3 gives also information on environmental toxicity of the listed NAISDs. Chronic toxicity investigations could lead to more meaningful ecological risk assessment, but only a few chronic toxic tests for pharmaceuticals have been operated. In this context, Ferrari et al. [58] tested the ecotoxicological impact of some pharmaceuticals found in treated wastewaters. Higher chronic than acute toxicity was found for carbamazepine, clofibrac acid, and diclofenac by calculating acute EC_{50} /chronic NOEC (A/C) ratios for *Ceriodaphnia dubia*, for diclofenac, clofibrac acid, and carbamazepine, while the chronic toxicity was conducted as 0.33 mg L⁻¹ compared

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with 66.4 mg L^{-1} in acute toxicity for naproxen by *Daphnia magna* and *Ceriodaphnia dubia* (48 h/21days).

Regarding NSAIDs, ibuprofen, ketoprofen, diclofenac, and naproxen are highly hydrophilic compounds due to their pKa ranging between 4.1 and 4.9; consequently their elimination on sorption process is so inefficient and it mainly depends on chemical or biological processes [2]. Consequently, removal results are very dissimilar. Thus, in previous studies shown in the literature about treatability with conventional technologies, it was found that after being treated in a pilot-scale sewage plant [59], approximately 95% of diclofenac was not eliminated, while ibuprofen concentration decreased down to 40% of its original concentration. Better results were obtained in other study, in which about 90% of ibuprofen was successfully transformed to hydroxyl and carboxyl derivatives [2]. However, results have to be carefully interpreted because in literature [60], it was also pointed that some of these metabolites maybe hydrolyzed and converted to the parent compound again. Another work pointed that an efficient elimination of ibuprofen and naproxen depends on the applied hydraulic retention times in WWTPs, with a considerable improvement by applying hydraulic retention times longer than 12 hours in all the processes [36]. Regarding other NSAIDs, the efficiency of ketoprofen removal in WWTPs varied from 15-98% [61] and the data on the elimination of mefenamic acid by standard WWTP operations are controversial. Aspirin can be completely biodegradable in laboratory test systems, but with a removal of 80-98% in full-scale WWTPs owing to complex condition of practical implication [62-65]. Consequently, the removal rate varies in different treatment plants and seasons, from “very poor” to “complete”, depending strongly on the factors, like the nature of the specific process being applied, the character of drugs or external influences [66]. It had been reported that diclofenac, ibuprofen, ketoprofen and naproxen were found in the effluents of sewage treatment plants in Italy, France, Greece and Sweden [2], which indicated the compounds passed through conventional treatment systems without efficient removal, and were discharged into surface waters from the WWTP effluent (Fig. 2.2), entering into surface waters, where they could interrupt natural biochemistry of many aquatic organisms [67].

Hence, from the observation mentioned above, common WWTPs operations are found insufficient for complete or appreciable elimination of these pharmaceuticals from sewage water which make anti-inflammatory and analgesic drugs remain in the aqueous phase [5, 68] at concentration of $\mu\text{g L}^{-1}$ to ng L^{-1} in aquatic bodies. It was

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reported that the drug could be stable and remains nearly at the same concentration in the plant influent, effluent and downstream [69].

Considering the uncertainty of treatment in the WWTPs and potential adverse effect of original pharmaceuticals and or their metabolites on living organisms at very low concentrations [40,70], more powerful and efficient technologies are required to apply in treatment of pharmaceuticals

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Table 2.3. The detected concentration and frequency of NSAIDs in WWTP influent/effluent, surface water and their toxicity data.

| Drug | WWTP influent ($\mu\text{g L}^{-1}$) & Frequency of detection | WWTP effluent ($\mu\text{g L}^{-1}$) & Frequency of detection | Removal rate % | Surface water ($\mu\text{g L}^{-1}$) | Acute toxicity (EC ₅₀ mg L ⁻¹) Daphnia Algae Fish | Acute toxicity (LC ₅₀ mg L ⁻¹) Daphnia Algae Fish | Ref. |
|----------------|---|---|----------------|--|--|--|-------------------------|
| Aspirin | 100/100 | 0.05-1.51/93 | 81.0 | < 0.05/100 | 88, 107, - | 141.0, -, 178 | [39, 66, 71] |
| Diclofenac | 0.10-4.11/96 | 0.04-1.95/86 | 34.6 | 0.001-0.07/93 | 5057, 2911, 532 | 22.4, 14.5, - | [39, 71-75] |
| Ibuprofen | 0.17-83.50/100 | < 95/89 | 74.2 | n.d.-0.20/96 | 38, 26, 5 | 9.1, 7.1, 173 | [33, 67, 71-74, 76, 32] |
| Ketoprofen | >0.32/93 | 0.14-1.62/82 | 31.1 | < 0.33/ - | 248, 16, 32, | 64.0, -, - | [71, 74, 78, 79] |
| Mefenamic acid | 0.14- 3.2/50 | 0.09-2.4/75 | 40.0 | -/20 | 20, 4.33 - | - | [71, 72, 32] |
| Naproxen | 1.79-611/96 | 0.17-33/96 | 81.6 | n.d-0.04/93 | 15, 22, 35 | 43.5, 320, 560 | [39, 63, 71-73] |
| Paracetamol | -/100 | 6.9/100 | 40.0 | 10/89 | 41, 2549, 258 | 9.2, 134, 378 | [62, 80, 67, 81, 82] |

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2.4 Advanced Oxidation Processes on anti-inflammatory and analgesic drugs

WWTPs usually do not reach complete removal of pharmaceuticals and therefore behave as an important releasing source of pharmaceuticals into environment. The implementations of sustainable technologies are imposed as possible solutions for the safe reclamation of high-quality treated effluent.

(AOPs) are therefore particularly useful for removing biologically toxic or non-degradable molecules such as aromatics, pesticides, dyes and volatile organic compounds potentially present in wastewater [83-88], getting more and more interests compared to conventional options, being treated as promising powerful and environmentally friendly methods for treating pharmaceuticals and their residues in wastewater [89-91]. The destruction reaction involves different oxidant species, like hydroxyl radicals ($\bullet\text{OH}$) and other strong oxidant species (e.g. $\text{O}_2\bullet$, $\text{HO}_2\bullet$, and $\text{ROO}\bullet$) produced *in situ* in reaction media. Hydroxyl radical ($\bullet\text{OH}$), produced via hydrogen peroxide, leaving “green” chemicals oxygen gas and water as by-products, has a high standard reduction potential ($E^0_{(\bullet\text{OH}/\text{H}_2\text{O})} = 2.8 \text{ V/SHE}$), which is known as the second strongest oxidizing agent just after fluorine. It can highly react with a wide range of organic compounds, regardless of their concentration. A great number of methods are classified under the broad definition of AOPs, as wet oxidation, ozonation, Fenton process, sonolysis, homogeneous ultraviolet irradiation, and heterogeneous photocatalysis using semiconductors, radiolysis and a number of electric and electrochemical methods [92]. AOPs are able to destruct the target organic molecules via hydroxylation or dehydrogenation, and may mineralize all organics to final mineral products as CO_2 and H_2O [92, 93].

2.5 Electrochemical Advanced Oxidation Processes

Among the AOPs, EAOPs were extensively studied during the last decade at lab-scale and several interesting works were published with perspective for up scaling as pilot-plant in the near future [92, 94-97]. In EAOPs, hydroxyl radicals can be generated by direct electrochemistry (anodic oxidation, AO) or indirectly through electrochemically generation of Fenton's reagent. In the first case $\bullet\text{OH}$ are generated heterogeneously by direct water discharge on the anode while in the last case $\bullet\text{OH}$ are generated homogeneously via Fenton's reaction (electro-Fenton, EF). Both processes are widely applied to the treatment of several kind of wastewater with an almost

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mineralization efficiency in most cases. They can be applied in a variety of media and volumes; also can eliminate pollutants in form of gas, liquid, and solid.

The use of electricity for water treatment was first suggested in 1889 [98]. Since then, many electrochemical technologies have been devised for the remediation of wastewaters [99-101], like anodic oxidation (AO), electro-Fenton (EF), photoelectro-Fenton (PEF), and sonoelectro-Fenton [102], providing valuable contributions to the protection of the environment through implementation of effluent treatment and production-integrated processes. The non-selective character of $\bullet\text{OH}$ helps to prevent the production of unwanted by-products that could minimize waste, making them as promising technologies to treatment of bio-refractory compounds in waters [103, 104].

Regarding the literature discussing the applications of EAOPs, most studies only pay attention to the mineralization of a specific organic molecule, and very few are paying attention to the removal of a specific organic molecule from wastewater matrices. Therefore, it is worth to distinguish between studies intended to determine if a technology is suitable to degrade a specific pollutant and studies performed with complex aqueous matrices (e.g. wastewater).

In the first case, the main information that can be obtained is the reaction kinetics mechanisms of the oxidation process (in particular the occurrence of intermediates that could be even more hazardous than the parent molecule) and the possibility of formation of refractory or more toxic by-products. Inappropriate intermediates or final products may inform against the application of the technology just with the data obtained in this first stage of studies.

In the second case (assessment of the technology efficiency in a real with a real aqueous matrix), although the presence of natural organic matter or some inorganic species such as chloride ion, can affect the reaction rate and process efficacy (since part of $\bullet\text{OH}$ is consumed by these organics), a complete characterization of the wastewater is generally difficult, since a complex matrix can contain hundreds of species. In this case, the main results are related to the operating cost and to the influence of the matrix composition on process effectiveness.

Nowadays, most EAOPs are within the first stage of development and far away for the pre-industrial applicability. Thus, as it is shown in this manuscript, most studies focused on the evaluation of intermediates and final products; and only few of them can

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be considered as second-stage studies, trying to determine the effect of the aqueous matrices.

2.5.1 Anodic oxidation Processes

Anodic oxidation can be defined as an electrochemical technology that is able to attain the oxidation of pollutants from water or wastewater, either by direct or by mediated oxidative processes originated on the anode surface of an electrochemical cell. This means that these oxidative-processes should not necessarily be carried out on the anode but just initiated on its surface. As a consequence, this treatment combines two main type of processes [96].

- Heterogeneous oxidation of the pollutants on the anode surface. This is a complex process which consists of a series of simpler processes: transport of the pollutants from the bulk to the surface of the electrode, adsorption of the pollutant onto the surface, direct electrochemical reaction by electron transfer to the pollutant, desorption of products and transport of oxidation products to the bulk;
- Homogeneous oxidation of pollutants in the bulk by oxidants produced on the anode surface from components of the electrolyte. These oxidants can be produced by the heterogeneous anodic oxidation of water or ions contained in the water (or dosed to promote their production) and their action is done in the bulk of the electrochemical cell.

One of these oxidants is the hydroxyl radical. Its occurrence can be explained as a first stage in the oxidation of the water or of hydroxyl ions (Eqs. (2.1) and (2.2)), in which no extra chemical substances are required.



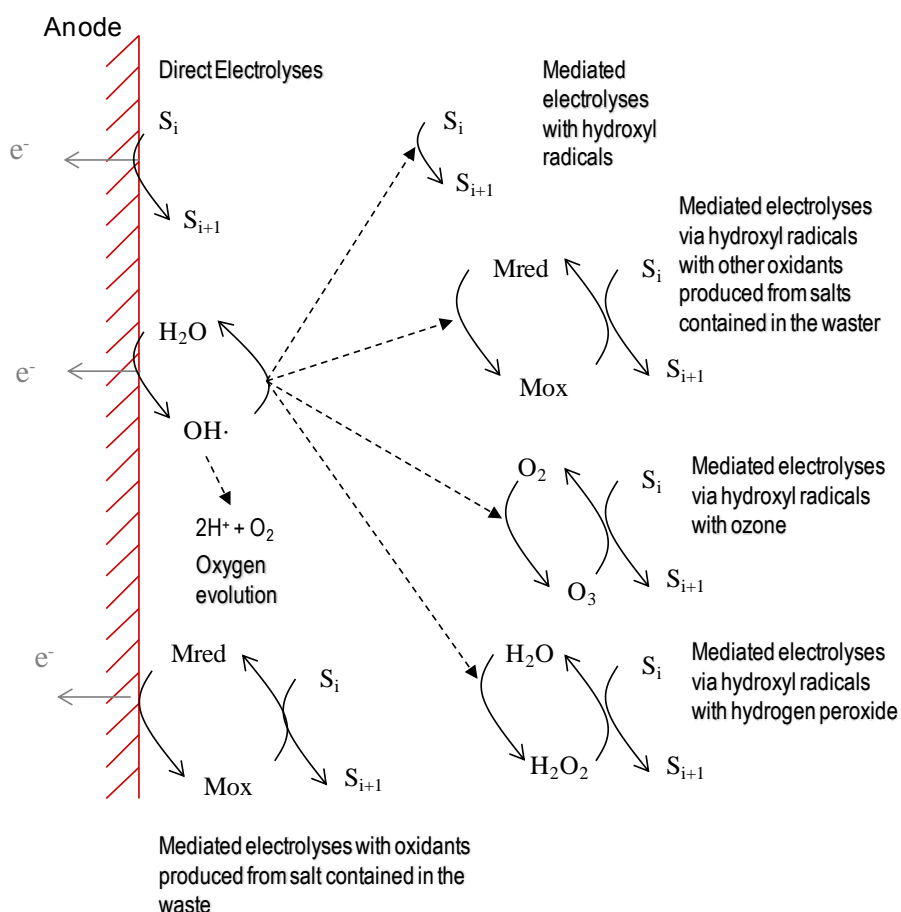
Production of this radical allowed to consider anodic oxidation as an AOP [105]. The significant role of hydroxyl radicals on the results of AO process has been the object of numerous studies during the recent years [106]. The short average lifetime of hydroxyl radicals causes that their direct contribution to anodic oxidation process is limited to the nearness of the electrode surface and hence, in a certain way, it could be considered as a heterogeneous-like mediated oxidation process. Thus, it is very difficult to discern the contribution between direct oxidation and mediated oxidation in the

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treatment of pollutants, the kinetic of both processes being mass-transport controlled [107].

However, the extremely high oxidation capacity of hydroxyl radicals makes them promote the formation of many other oxidants from different species contained in the wastewater and this effect converts the surface-controlled quasi-direct electrochemical process into a significantly much more efficient volumetric-oxidation process. Thus, it has been demonstrated the production of persulfates, peroxyphosphates, ferrates and many other oxidants using anodic oxidation processes [108] and it has also been demonstrated their significant effects on the improvement of the remediation efficiency [109]. Synergistic effects of all these mechanisms can explain the good efficiencies obtained in this technology in the removal of pollutants and the huge mineralization attained as compared with many other AOPs [110, 111].

Figure 2.3 shows a brief scheme of the main processes which should be considered to understand an anodic oxidation process.



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Fig. 2.3. A simple description of the mechanisms occurred during anodic oxidation of a pollutant. (Adapted from ref [112] with Copyright from 2009 Wiley).

Two points are of particular importance in understanding of AO process: electrode material and cell design. The first one is important, because it may have a significant influence on the direct oxidation of a given organic pollutant (i.e. catalytic properties related to adsorption or the direct electron transfer processes) and on the production of oxidants, which can extend the oxidation of pollutants to the bulk of the treatment. The second one is also very important, particularly in the treatment of pollutant at low concentrations, such as the typically assessed in this study, because the kinetics of these processes is mass-transfer controlled. A good mechanical design, which promotes turbulence and modifies the key factors that limit the rate of oxidation, can increase the efficiency of processes. However, as it is going to be discussed during this section, removal of pharmaceutical compounds from water and wastewater is still in an earlier lab scale stage and optimization of the cell design is usually done in later scale up studies. Single flow or complete-mixed single-compartment electrochemical cells are proper cells to assess the influence of the electrode material at the lab scale, but in order to apply the technology in a commercial stage, much more work has to be done in order to improve the mechanical design of the reactor [113]. For sure, it will become into a hot topic once the applicability at the lab scale has been completely demonstrated.

Regarding the anode, material is the key point in the understanding of this technology, and two very different behaviors are described in the literature for the oxidation of organic pollutants [114]. Some types of electrode materials lead to a very powerful oxidation of organics with the formation of few intermediates and carbon dioxide as the main final product while others seems to do a very soft oxidation. Although not yet completely clear, because a certain controversy still arises about mechanisms and even about the proposed names for the two types of behaviors (they have been called active vs. non active, high-oxygen vs. low-oxygen overvoltage electrodes, etc.), interaction of hydroxyl radicals formed during the electrochemical process with the electrode surface could mark the great differences between both behaviors and just during the treatments with high oxidation-efficiency materials, hydroxyl radicals can be fully active to enhance the oxidation of pollutants. In that case, hydroxyl radicals do not interact strongly with the surface, but they promote the

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hydroxyl radical mediated oxidation of organics and also the production of many other more-stable oxidants (which help to produce a volumetric control of the kinetics).

Graphite and other sp^2 carbon based electrodes, and also many metal (i.e. Pt, Ti/Pt), some metal oxide electrodes (i.e. IrO_2 , RuO_2) and mixed metal oxide electrodes (containing different Ir, Ru, Mo oxides) behave as low-efficiency electrodes for the oxidation of organics. These anodes promote a soft oxidation of organics, with a great amount of intermediates (most aromatics treated by these anodes are slowly degraded due to the generation of hardly oxidizable carboxylic acids [115]), with small mineralization rates and in some cases (particularly, under high concentration of pollutants) with production of polymers. This produces a very low current efficiency and consequently small perspectives of application [114]. Low efficiencies are even more significant with the use of carbon-based materials because during the electrochemical process they can also be electrochemically incinerated (transformed into carbon dioxide) when high voltages are required to oxidize organic pollutants. The reaction of heterogeneously formed $\bullet OH$ at a low-efficiency anode (M) from water oxidation is commonly represented by Eq. (2.3), where the anode is represented as MO, indicating the inexistence of hydroxyl radicals as free species close to the anode surface: this means that the oxidation is carried out through a higher oxidation state of the electrode surface caused by hydroxyl radicals but not directly by hydroxyl radicals.



Other metal oxide and mixed metal oxide electrodes (those containing PbO_2 and/or SnO_2) and conductive-diamond electrodes (particularly the boron doped diamond (BDD) electrodes) behave as high-efficiency electrodes for the oxidation of organics. They promote the mineralization of the organics with an efficiency only limited by mass transport control, and usually very few intermediates are observed during the treatment. As a consequence, AO, determined mainly on the power required for driving the electrochemical process, can be performed at affordable costs with such electrodes, without the common AOP drawbacks, being considered as a very useful technique [115-117]. Among these electrodes, metal oxides are not stable during polarity reversal, and they can even be continuously degraded during the process, which cause negative influence on the practical application of electrochemical wastewater treatment (such as the occurrence of lead species in the water). For this reason, just conductive-diamond electrodes are being proposed for this application. However, it is important to take into

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account that conductive-diamond is not a unique material, but many types of materials are included into this denomination with significantly different behaviors [118], depending on the substrate (Ti, p-Si, Nb, etc), doping compound (N, F) and concentration level, sp^3 - sp^2 ratio, etc. This explains some contradictory results shown in literature when generalizations are done. BDD is the most common conductive-diamond electrode and the only type used in the studies shown in this work. The reaction of heterogeneously formed $\bullet\text{OH}$ at a high efficiency anode (M) from water oxidation is commonly represented by Eq. (2.4), indicating the occurrence of hydroxyl radicals as free species close to the anode surface.



2.5.1.1 Anodic oxidation for degradation of analgesic and anti-inflammatory pharmaceuticals

Research on the degradation of pharmaceutical products is still at a very early lab-scale stage and far from the commercial application. Many studies have focused on the degradation of analgesic and anti-inflammatory pharmaceuticals from synthetic water solutions, trying to increase the knowledge about the fundamentals of the process and in particular about the main intermediates, taking into account that those intermediates can be even more hazardous or persistent than the parent compound.

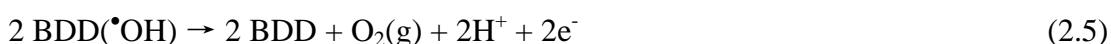
A pioneering contribution was the oxidation of aspirin with platinum and carbon fiber (modified manganese-oxides) electrodes, looking for a partial degradation of pharmaceutical molecules in order to increase the biodegradability of industrial wastewaters [119].

However, the development of BDD anodes and the huge advantages of this electrode as compared with others [120] make that most of the works published in the literature have focused on this material (or in the comparison of performance between diamond and other electrodes). A first work reporting the use of anodic oxidation with BDD electrodes was done by the Brillas' group [121] and the focus was on the oxidation of paracetamol (acetaminophen). It was found that anodic oxidation with BDD was a very effective method for the complete mineralization of paracetamol up to 1 g L^{-1} in aqueous medium within the pH range 2.0–12.0. Current efficiency increased with raising drug concentration and temperature and decreased with current density, showing a typical response of a diffusion controlled process. In this work, Pt was also

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used as anode for comparison purposes. It was found that anodic oxidation with Pt had much lower oxidizing power and yielded poor mineralization.

After that initial work, Brillas et al. [122] studied degradation of diclofenac in aqueous medium by anodic oxidation using an undivided cell with a Pt or BDD anode. It was demonstrated that diclofenac was completely depleted by AO with BDD even at the very high concentrations assessed (175 mg L⁻¹). Only some carboxylic acids were accumulated in low concentrations and oxalic and oxamic were found to be the most persistent acids. Comparative treatment with Pt gives poor decontamination and great amounts of malic, succinic, tartaric and oxalic acids. The reaction of diclofenac followed pseudo-first-order kinetics. For BDD, TOC and drug decays were enhanced with increasing current, although efficiency in terms of the use of current decreased significantly due to the promotion of side reactions, such as oxidation of BDD([•]OH) to O₂ (Eq. (2.5)), production of hydrogen peroxide (Eq. (2.6)) and destruction of hydrogen peroxide by hydroxyl radicals (Eq. (2.7)).



The formation of different oxidants was also suggested in Brillas's work (Eqs. (2.8)-(2.10)). As stated in other works, the effect of these oxidants is very important but contradictory: they are less powerful than hydroxyl radicals; however, their action is not limited to the nearness of the electrode surface but to the whole volume of reaction.



It is worth to take into account that they can be produced by direct electron transfer (as indicated in the previous equations) or by the action of hydroxyl radicals as shown below (Eqs. (2.11)-(2.13) for peroxosulfates) and (Eqs. (2.14)-(2.16) for peroxophosphates) [112].



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This helps to understand that their effect on the whole process efficiency is very important and that it is indirectly related to the production of hydroxyl radicals on the surface of anode during anodic oxidation processes.

In all cases, chloride ion was released to the medium during the electrolysis of diclorofenac. This behavior seems to be characteristic of electrochemical treatment of chlorinated-organics and it is very important because hazardousness of the non-chlorinated intermediates is usually smaller than those of the parent compounds. Thus, dechlorination has been found in the literature to be characteristic of many anodic oxidation treatments of wastewaters [123, 124], although it is normally explained in terms of a cathodic reduction of the organic rather than by anodic processes.

The anodic oxidation of diclorofenac with BDD was also studied by Zhao et al. [125]. Results showed that with 30 mg L⁻¹ initial concentration of diclofenac, anodic oxidation was effective in inducing the degradation of diclofenac and degradation increased with increasing applied potential. Mineralization degree of 72% of diclofenac was achieved after 4 h treatment with the applied potential of 4.0 V. The addition of NaCl produced some chlorination intermediates as dichlorodiclofenac and led to a less efficient decrease in the mineralization. Regarding mechanisms, it was proposed that oxidative degradation of diclofenac was mainly performed by the active radicals produced in the anode with the application of high potential. At the low applied potential, direct electro-oxidation of diclofenac did not occur although there was observed an anode oxidation peak in the cyclic voltammetry curve. The main intermediates including 2,6-dichlorobenzamine (1), 2,5-dihydroxybenzyl alcohol (2), benzoic acid (3) and 1-(2,6-Dichlorocyclohexa-2 4-dienyl) indolin-2-one (4) were identified. These aromatic intermediates were oxidized gradually with the extension of reaction time, forming small molecular acids. The proposal degradation pathway of diclofenac (Fig. 2.4) was provided.

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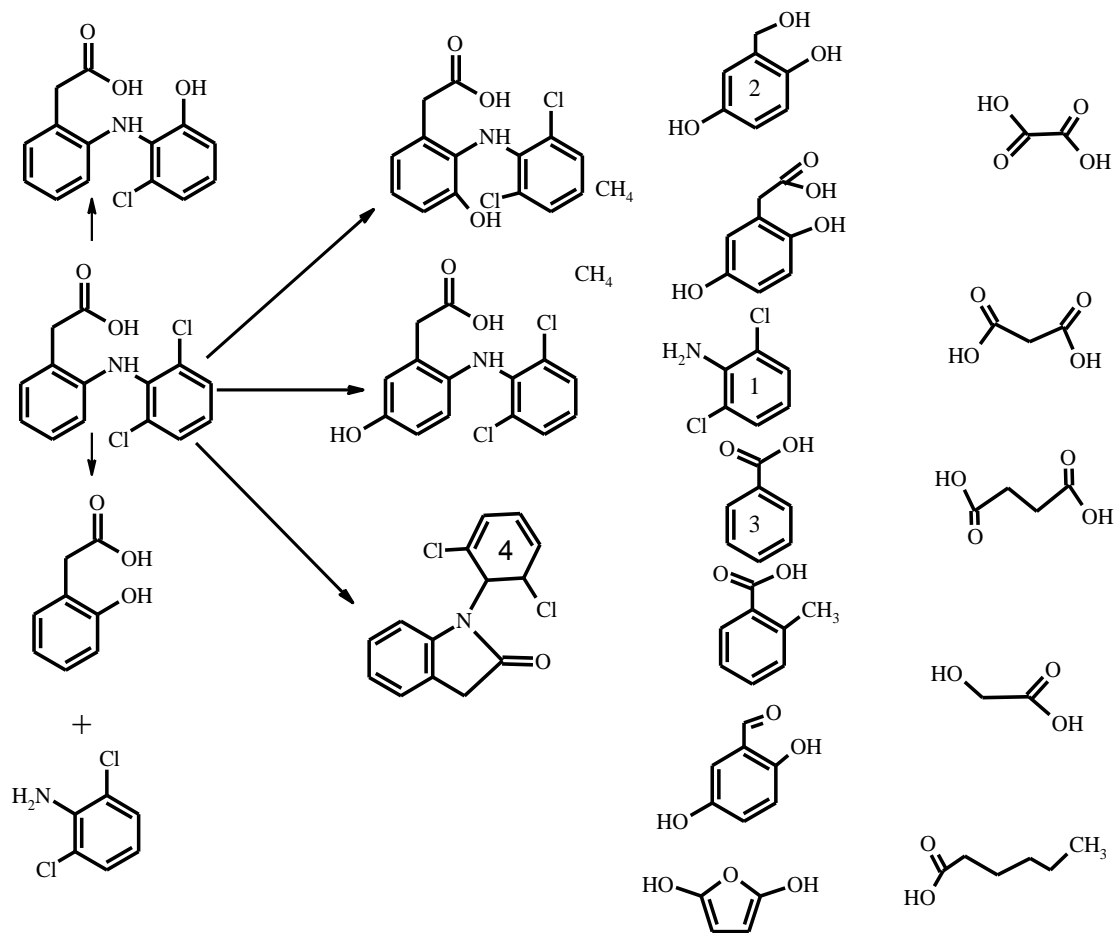


Fig. 2.4. Proposed electro-oxidation degradation pathway of diclofenac (Adapted from ref [125] with Copyright from 2009 Elsevier).

Another interesting comparative work was done by Muruganathan et al. [126]. The studies of anodic oxidation with BDD or Pt electrodes on ketoprofen revealed that ketoprofen was oxidized at 2.0 V by direct electron transfer and the rate of oxidation was increased by increasing the current density, although the mineralization current efficiency dropped, which was better at lower current density at 4.4 mA cm⁻². This behavior was the same observed by Brillas with diclofenac and paracetamol [121, 122], and it could be explained in terms of a mass transfer control of the process. Thus, the degradation of ketoprofen was found to be current controlled at initial phase and became diffusion controlled process beyond 80% of TOC removal. The importance of the electrolyte was also assessed in this study. It was found that TOC removal was much higher with electrolytes containing sulfates, suggesting an important role of mediated oxidation. Figure 2.5, was obtained from the results shown in that work, indicating that the oxidation of ketoprofen follows a pseudo-first-order kinetic and that kinetic rate is

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clearly dependent on the nature of the electrolyte. The high mineralization in the presence of SO_4^{2-} could be explained by *in situ* generation of $\text{S}_2\text{O}_8^{2-}$ and sulfate radical as shown in Eqs. (2.9), (2.12) and (2.13) [127].

The oxidants are either consumed for the degradation of ketoprofen molecule or coupled with water molecule to form peroxomonosulfuric acid (H_2SO_5) which in turn can produce H_2O_2 [128].

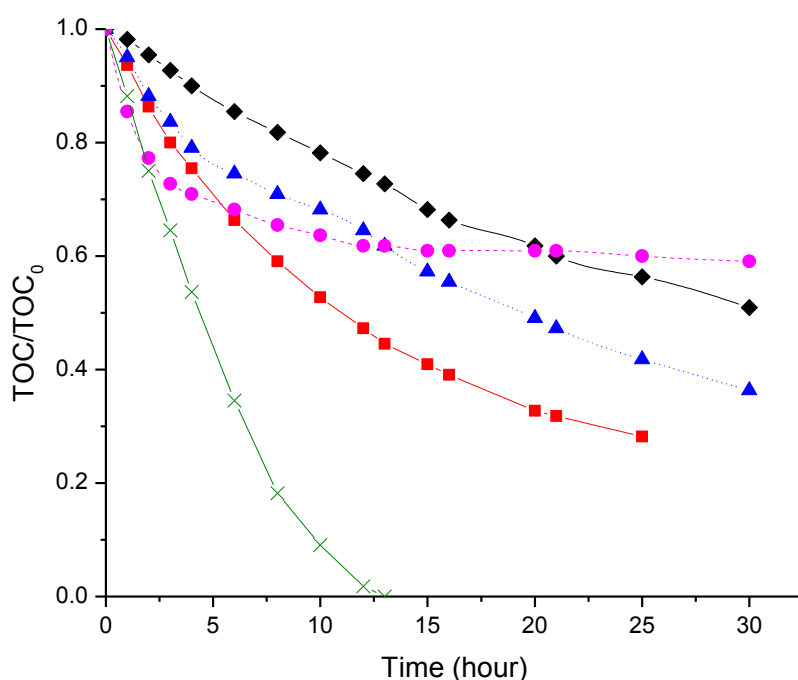


Fig. 2.5. Effect of supporting electrolyte on TOC removal (electrolyte concentration: 0.1 M, ketoprofen: 5 mM, initial pH: 6.00, T: 25 °C, applied current density: 8.8 mA cm⁻², (◆) BDD–NaCl, (*) BDD–Na₂SO₄, (■) BDD–NaNO₃, (●) Pt–NaCl, (▲) Pt–Na₂SO₄. (Adapted from ref [126] with permission of copyright 2010 Elsevier).

Comparing the performance of both electrodes, as expected, BDD is always more efficient than Pt. However, it was found that the initial rate of mineralization was better on Pt anode compared to BDD in the presence of NaCl although a significant concentration of refractory compounds were found with the Pt anodic oxidation and at larger oxidation times mineralization obtained by BDD are clearly better.

The negative effect of chloride observed for the degradation of ketoprofen with BDD anode was also observed by Zhao et al. ([125]) for diclofenac degradation with

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BDD electrode in aqueous solution. This observation is important because chlorides are known to be electrochemically oxidized to hypochlorite, which may act as an oxidation mediator.



However, the lower efficiency obtained in that media suggest that these oxidants are not very efficient. This can be easily explained taking into account that the final product in the oxidation of chlorides with BDD is not hypochlorite but perchlorate [129]. The formation of these species can be explained in terms of the oxidation of chloride and oxoanions of chlorine by hydroxyl radicals, according to Eqs. (2.18)-(2.21).



The oxidation of ketoprofen using anodic oxidation with BDD electrodes was also studied by Domínguez et al. [130]. In that work, experiments were designed not to assess the mechanisms of the process but to optimize the process and study the interaction between the different operative parameters. Accordingly, from the significance statistical analysis of variables carried out, it was demonstrated that the most significant parameters were current intensity, supporting electrolyte concentration and flow rate. The influence of pH was very small. This marks the importance of mass transfer control in these processes, influenced by current density and flow rate, in particular taking into account the small concentrations assessed. It also shows the significance of mediated oxidation processes, which are largely affected by the supporting electrolyte concentration. More recently, Loaiza-Ambuludi et al. [131] reported the efficient degradation of ibuprofen reaching almost total mineralization degree of 96% using BBB anode. In addition to the determination of second order rate constant $k_2 = 6.41 \times 10^9 \text{ L mol}^{-1} \text{ s}^{-1}$, by competitive kinetic method, four aromatic intermediates (i.e. *p*-benzoquinone, 4-isobutylphenol, 1-(1-hydroxyethyl)-4-isobutylbenzene, and 4-isobutylacetophenone) were detected by GC-MS analysis from treated solution.

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A last comparative work on the anodic oxidation of analgesic and anti-inflammatory pharmaceuticals in synthetic water solutions was done by Ciríaco et al. [132]. In this case, two electrodes with an expected high efficiency in the removal of organics (BDD and Ti/Pt/PbO₂) were compared for the treatment of ibuprofen at room temperature under galvanostatic conditions. As expected, results showed a very good efficiency, with removals of COD between 60% and 95% and mineralization (TOC removal) varying from 48 to 92%, in 6 h experiments. The efficiency was found to be slightly higher with BDD at lower current density and similar for both anodes at 30 mA cm⁻².

2.5.1.2 Enhancement of the degradation of analgesic and anti-inflammatory pharmaceuticals by photoelectrochemical processes

As stated before, most of the research works published in the recent years focused on the assessment of electrochemical technologies with synthetic solutions which contain much higher concentration of analgesic and anti-inflammatory pharmaceuticals than those in which they are found in the environment and that are only representative of industrial flow. Hence a typical concentrations found in those assessments are within the range 1-100 mg organic L⁻¹ which are several folds above the typical value found in a wastewater or in a water reservoir. This means that although conclusions about mineralization of the analgesic and anti-inflammatory pharmaceuticals and intermediates are right, mass transfer limitations in anodic oxidation processes will be more significant in the treatment of an actual wastewater and, even more, in the treatment of actual ground or surface water. Consequently, current efficiencies will be significantly lower than those reported in literature due to the smaller organic load. This effect of the concentration of pollutant was clearly shown in the treatment of RO concentrates generated in WWTPs [133], and it has been assessed in many papers about other pharmaceutical products [134-136], in which it is shown the effect of the concentration during the anodic oxidation of solutions of organics covering a range of initial concentrations of 4 orders of magnitude. In these papers, it has been observed that the same trends are reproduced within the four ranges of concentration without significant changes, except for the lower charges required to attain the same change for the smaller concentrations. This observation confirms that some of conclusions obtained in the more concentrated range of concentrations can be extrapolated to other less concentrated ranges of concentrations in the removal of pharmaceutical products.

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The expected effect of mass transfer limitations on the efficiency of this processes (and hence on the economy) made researchers look for improvements of the anodic oxidation processes. Thus, an additional improvement in the results attained by anodic oxidation is obtained when light irradiation or ultrasounds are coupled to the anodic oxidation. In the first case, it is due to the promotion of the formation of hydroxyl radicals; in the second one, it is because of the enhancement of additional mass transfer. To the author's knowledge, no works have been found regarding the removal of anti-inflammatory and analgesic drugs by sono-enhanced anodic oxidation, although this technique seems to obtain great advantages in the destruction of other emerging pollutants [136].

Regarding photo-electrochemical processes, some pioneering works have been published. For improving the efficiency of anodic oxidation, Zhao et al. [137], deposited Bi_2MoO_6 onto a BDD surface to assess the degradation of ibuprofen and naproxen. Anodic oxidation was performed in a cylindrical quartz reactor, in which the solution was irradiated with a 150W Xe lamp (wavelength above 420 nm). Bi_2MoO_6 can absorb visible light near 460 nm and it is a visible-light driven photocatalyst for O_2 evolution from an aqueous solution. Results showed that ibuprofen and naproxen both can be degraded via photoelectrocatalytic process under visible light irradiation. The degradation rates of these molecules in the combined process were larger than the sum of photocatalysis and anodic oxidation. The ibuprofen and naproxen were also efficiently mineralized in the combined process. Hu et al. [138] developed a novel magnetic nanomaterials-loaded electrode for photoelectrocatalytic treatment. The degradation experiments were performed in a quartz photo reactor with 1.0×10^{-3} mol L^{-1} diclofenac. Magnetically attached $\text{TiO}_2/\text{SiO}_2/\text{Fe}_3\text{O}_4$ electrode was used as the working electrode, a platinum wire and a saturated calomel electrode as the counter electrode and reference electrode, respectively. A 15 W low pressure Hg lamp with a major emission wavelength of 253.7 nm was used. The result of degradation efficiency with different techniques indicated that after 60 min UV irradiation, 59.1% of diclofenac was degraded, while efficiency reached 77.3% by employing $\text{TiO}_2/\text{SiO}_2/\text{Fe}_3\text{O}_4$ electrode. When applied + 0.8 V and UV irradiation simultaneously on the magnetically attached $\text{TiO}_2/\text{SiO}_2/\text{Fe}_3\text{O}_4$ electrode, the degradation efficiency of diclofenac was improved to 95.3% after 45 min treatment, but the COD removal efficiency was only 47.8% after 45 min, less than half of the degradation efficiency, due

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to the slow mineralization of diclofenac and difficult removal intermediates were quickly formed during the photo-electrochemical processes.

Further examples of the anodic oxidation application for the removal of NSAIDs are depicted in table 2.4.

2.5.1.3. Application of anodic oxidation for the removal of pharmaceuticals from aqueous systems

From the results obtained in the works described above, it can be stated that anodic oxidation is a very promising technology for the removal of analgesic and anti-inflammatory pharmaceuticals from water, in particular when using BDD electrodes. There is a strong influence of the supporting electrolyte, which account for the significance of mediated oxidative processes. The significant reduction in the hazard of the intermediates caused by dechlorination (most likely caused by a cathodic reduction process) seems to be also a good feature of the technology. The weak point of this research is the high concentrations of organics tested, far away from the concentration levels measured in a typical wastewater or in a water reservoir, but it should be taken into account that research is not focused on real applications but on a preliminary assessment of the technology.

Although some studies of oxidative degradation were carried out on different pharmaceuticals by various AOPs [139, 140], few studies have been done regarding the removal of analgesic and anti-inflammatory pharmaceuticals from water in actual matrixes. Initially, strong differences are expected because of the different range of concentration and the huge influence of the media composition [141]. Regarding this fact, there is a very interesting work about the application of anodic oxidation with BDD anodes for the treatment of reverse osmosis (RO) concentrates generated in WWTPs [133]. In this study, a group of 10 emerging pollutants (including two analgesic and anti-inflammatory pharmaceuticals) were monitored during the anodic oxidation treatment. Results obtained demonstrated that in the removal of emerging pollutants in actual matrixes, electrical current density in the range 20-100 A m⁻² did not show influence likely due to the mass transfer resistance developed in the process when the oxidized solutes are present in such low concentrations. Removal rates fitted well to first order expressions, being the average values of the apparent kinetic constant for the electro-oxidation of naproxen $4.4 \times 10^{-2} \pm 4.5 \times 10^{-4} \text{ min}^{-1}$ and for ibuprofen 2.0×10^{-2}

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min^{-1} . Emerging pollutants contained in the concentrates were almost completely removed, with removal percentages higher than 92% in all the cases after 2 h oxidation.

Other interesting work [142] was not focused on the treatment of urban wastewaters but on the treatment of an actual industrial wastewater produced in a pharmaceutical company. This wastewater had a concentration as high as 12000 ppm COD and consisted of a mixture of different solvents and pharmaceutical species. Results demonstrate that complete mineralization of the wastewater can be obtained using proper operation conditions, showing the good prospects of this technology in actual matrix when using BDD anodes. However nothing was stated about cost, which is a very important point for the future application of this technology. This has been clearly stated for other technologies such as photocatalytic reactor membranes, nonthermal plasma advanced oxidation process [143] and ozone, $\text{O}_3/\text{H}_2\text{O}_2$ [144] and UV/ H_2O_2 [145]. Regarding this point, it is worth to take into account another work [146] that assessed the operating and investment cost for three different AOP (Fenton, Ozonation and Anodic Oxidation) applied in the treatment of many types of wastewater. This work was not focused on wastewater produced in pharmaceutical industries but it assesses others with a similar behavior. Results showed that from the mineralization capability, anodic oxidation clearly overcomes ozonation and Fenton because it was the only technology capable to abate the organic load of the wastewater studied down to almost any range of concentration while the other technologies lead to the formation of refractory COD. However, within the range of concentrations in which the three technologies can be compared, Fenton oxidation was the cheaper and ozonation was much more expensive than anodic oxidation. This means that anodic oxidation could compete with them in many actual applications and that scale-up studies is a very interesting hot topic now to clarify its potential applicability.

Another interesting work on applicability of anodic oxidation [109] make a critical analysis of the present state of the technology and it clearly states the range of concentrations in which this technology is technically and economically viable and give light on other possible drawbacks which can be found in scale-up assessments. It is also important to take into account that energy supply to electrochemical systems can be easily made with green energies and this has a clear influence on operating cost as it was recently demonstrated for anodic oxidation [147].

Regarding other applications of anodic oxidation, and although it is not the aim of this review, it is important to mention analytical methods. Over the last years, electrode

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materials have been proposed for the anodic oxidation of analgesic and anti-inflammatory pharmaceuticals looking for new more accurate analytical techniques based on the electrochemical behavior of a given analgesic and anti-inflammatory pharmaceutical on a particular anode surface. Accordingly, these works focused more on the description of electrochemical characterization techniques than on bulk electrolysis results. Good examples are the studies about the oxidation of hispanone with Pt-Ni [148], piroxicam with glassy carbon anode [149], mefenamic acid, diclofenac, and indomethacin with alumina nanoparticle-modified glassy carbon electrodes [150], aspirin with cobalt hydrotalcite-like compound modified Pt electrodes [151], aspirin and acetaminophen with cobalt hydroxide nanoparticles modified glassy carbon electrodes [152], mefenamic acid, diclofenac, and indomethacin with alumina nanoparticle-modified glassy carbon electrodes [153], mefenamic acid and indomethacin with cobalt hydroxide modified glassy carbon electrodes [154].

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Table 2.4. Anodic oxidation (AO) process applied on anti-inflammatory and analgesic drugs

| Pharmaceutical investigated | Anodic and processes | oxidation and likely | Matrix | Results obtained | Ref. |
|-----------------------------|--|----------------------|--------|--|-------|
| Aspirin | Pt or steel as cathode, plates of Pt or carbon fiber as anodes. 0.1 NH ₂ SO ₄ or 0.1 N NaOH as supporting electrolyte concentration (SEC) | | Water | The progressive oxidation increased biological availability. | [119] |
| Diclofenac | Pt/stainless steel and BDD/stainless steel cells, added 0.05 M Na ₂ SO ₄ without pH regulation or in neutral buffer medium with 0.05 M KH ₂ PO ₄ + 0.05 M Na ₂ SO ₄ + NaOH at pH 6.5, 35°C | | | AO with Pt: 1) acidified the solution, lead to good mineralization degree; 2) gave poor decontamination at low contents of the drug; 3) high amounts of malic, succinic, tartaric, oxalic acids, NH ₃ ⁺ produced. AO with BDD: 1) the solution became alkaline, only attained partial mineralization; 2) total mineralization of low contents of the drug; 3) increased current accelerated the degradative process, but decreased its efficiency; 4) produced small extent of some carboxylic acids but a | [122] |

BDD or Ti/Pt/PbO₂ as anodes and stainless steel foils as cathodes, 0.035 M Na₂SO₄ as SEC, at 22-25 °C

larger persistence of oxalic and oxalic acids, NH₃⁺ and NO⁻ released. The diclofenac decay always followed a pseudo first-order reaction; aromatic intermediates identified as 2-hydroxyphenylacetic acid, 2,5-dihydroxyphenylacetic acid, 2,6-dichloroaniline and 2,6-dichlorohydroquinone (Fig. 2.5); chloride ion was lost in all cases.

COD removed between 60 and 95% and TOC varying from 48 to 92% in 6 h experiments, with higher values obtained with the BDD electrode; both electrodes gave a similar results in general current efficiency and mineralization current efficiency for 20 mA cm⁻² but a very different one at 30 mA cm⁻²; BDD has a slightly higher combustion efficiency at lower current density and equal to 100% for both anodes at 30 mA cm⁻². [132]

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| | | | | |
|------------|---|-----------------|--|-------|
| | Photoelectrocatalysis (PEC); a working electrode: TSF (magnetic $\text{TiO}_2/\text{SiO}_2/\text{Fe}_3\text{O}_4$ loaded), a counter electrode: Pt, and a reference electrode: a 15 W low pressure Hg lamp emitting at 253.7 nm | Distilled water | After 45 min treatment, 95.3% of diclofenac was degraded on the magnetically attached TSF electrode, providing a new strategy for preparing electrode with high stability. | [138] |
| Ketoprofen | Single compartment with two-electrode cell (BDD) at 25 °C, pH = 3-11, current intensity (J) = 0-320 mA cm^{-2} , SEC: $[\text{Na}_2\text{SO}_4] = 0.05\text{-}0.5 \text{ mol L}^{-1}$, solution flow rate (Qv) = 1.42 and 8.34 cm min^{-1} | Millipore water | Optimum experimental conditions: pH: 3.99, Qv: $1.42 \text{ cm}^3 \text{ min}^{-1}$, J: 235 mA cm^{-2} using a SEC: 0.5 mol L^{-1} . | [130] |
| | BDD/Pt electrode with reference electrode Hg/HgCl, KCl at 25°C | Distilled water | <i>In situ</i> generation of $\bullet\text{OH}$, S_2O_8^- , and active chlorine species, as Cl_2 , HOCl, OCl $^-$ degraded ketoprofen to CO_2 and H_2O ; poor mineralization at both BDD and Pt anodes in the presence of NaCl as SEC, while complete mineralization was achieved using Na_2SO_4 as | [126] |

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SEC.

| | | | |
|----------------------------|--|---------------------------|---|
| Paracetamol | graphite bar as Millipore cathode and BDD/Pt as anode, 0.05 M Na ₂ SO ₄ as SEC, at pH = 2.0- 12.0 , at 25–45 °C, paracetamol < 1 g L ⁻¹ | water | Mineralization process [121] accompanied with release of NH ₄ ⁺ and NO ⁻ ; the current efficiency increased with raising drug concentration and temperature; oxalic and oxamic acids were detected as ultimate products,; completely removed with Pt and its kinetics followed a pseudo-first-order reaction with a constant rate independent of pH. |
| Mefenamic acid, Diclofenac | A reference electrode: Ag/AgCl, 3M KCl and a counter electrodes: Pt, glassy carbon or an alumina nanoparticle-modified GC as the working electrode, at physiological pH | Phosphate buffer solution | The drugs were [150] irreversibly oxidized on bath electrodes via an anodic peak and the process was controlled by diffusion in the bulk of solution; alumina nanoparticles (ANs) increased the oxidation current, and lowered the peak and onset potentials, had an electrocatalytic effect, both kinetically and thermodynamically. |

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| | | |
|---------------------------------|---|---|
| <p>Ibuprofen & Naproxen</p> | <p>A counter-electrode: Millipore Pt, a working electrode: Bi₂MoO₆ particles deposited onto BDD surface, and a reference electrode: SCE; 0.1 mg L⁻¹ Na₂SO₄ as SEC, applied bias potential: 2.0 V</p> | <p>Ibuprofen and naproxen [137] can be rapidly degraded via combined electro-oxidation and photocatalysis process under visible light irradiation, in which degradation is larger than the sum of photocatalysis and electro-oxidation processes, also efficiently mineralized. The main intermediates of ibuprofen degradation were detected, phenol (C₆H₆O) and 1,4-benzenecarboxylic acid (COOHC₆H₆COOH) and small molecular acids including 2-hydroxyl–propanoic acid (CH₃COHCOOH), hydroxyl–acetic acid (CH₂OHCOOH), pentanoic acid (COO(CH₂)₂CHOOH), and malonate (COOHCH₂COOH).</p> |
| | <p>Two circular secondary electrodes and effluent stainless steel of cathode, current WWTP density values ranging from 20 to</p> | <p>Apparent kinetic constants [133] (s⁻¹) and removal % at 2 h of ibuprofen: 2 x 10⁻² and 55.1%; and naproxen: 4.4 x 10⁻² ± 4.5 x 10⁻⁴ and 94.9%; ibuprofen was</p> |

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200 A m⁻² at 20 °C

most resistant compound to electrochemical treatment. The current density and initial concentration level of the compounds did not exert influence on the electrooxidation and kinetics; appropriate operational conditions attained concentration was lower than the standards for drinking water established in European and EPA regulations.

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2.5.2. Electro-Fenton process

Electro-Fenton (EF) process, which can be defined as electrochemically assisted Fenton's process, is one of the most popular techniques among EAOPs. A suitable cathode applied to be fed with O₂ or air reduces dioxygen to superoxide ion (O₂^{•-}), leading to the formation of H₂O₂ continuously in an acidic medium (Eq. (2.22)). Catalysts such as Fe²⁺, Fe³⁺, or iron oxides react with H₂O₂ (Eq. (2.23)), following Fenton's reaction to yield [•]OH radicals. Fe³⁺ ions produced by Fenton's reaction are electrochemically reduced to Fe²⁺ ions (the Fe³⁺/Fe²⁺ electrocatalytic system), which catalyze the production of [•]OH from Fenton's reaction [92, 155]. On the other hand, molecular oxygen can also be produced in the anodic compartment simply by the oxidation of water with Pt or other low O₂ overvoltage anodes (Eq. (2.25)).



Then the generated strong oxidant radical ([•]OH) can either dehydrogenate unsaturated compounds (RH) or hydroxylate aromatic pollutants (Ar) or other compounds having unsaturated bonds until their overall mineralization (conversion into CO₂, H₂O and inorganic ions). The oxidation of organic pollutants by EF process can be visualized in the catalytic cycle of Fig. 2.6b.

In EF process, several operating parameters involved in process (Fig. 2.6a), such as O₂ feeding, stirring rate or liquid flow rate, temperature, solution pH, applied current (or potential), electrolyte composition, and catalyst and initial pollutant concentration influence the degradation and/or mineralization efficiency. The optimized works have been done to find best experimental conditions, which are operating at high O₂ or air flow rates, high stirring or liquid flow rate, temperatures in the range of 25-40 °C, solution pH near 3.0, and optimized Fe²⁺ or Fe³⁺ concentration (0.05-0.2 mM) to obtain the maximum [•]OH production rate in the bulk [84, 156] and consequently pollutant removal efficiency.

Three and two-electrode divided and undivided electrolytic cells are chosen to utilize in EF process. Cathode materials are mostly carbon-felt [157] or gas diffusion

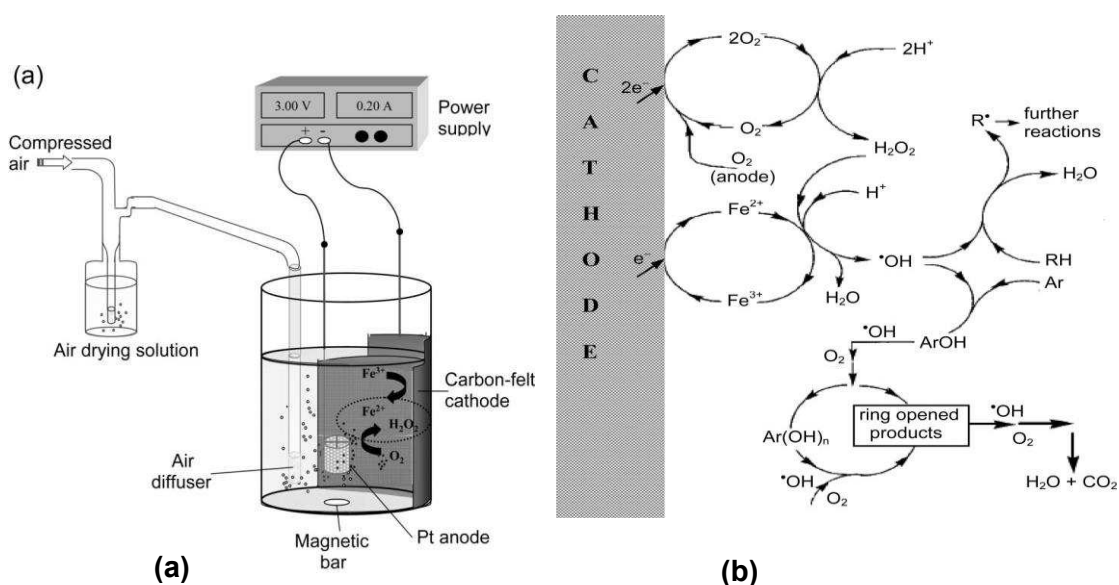
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electrodes (GDEs) [158], however other materials such as graphite [159], reticulated vitreous carbon (RVC) [160], activated carbon fiber (ACF) [161], and carbon nanotubes (NT) [162] are also studied. The classical anode is Pt while metal oxides, such as PbO_2 [163], SnO_2 [164], DSA [165] (mixed metal oxide anodes) were also employed in EF processes. Recently the BDD anode revealed to have better characteristics as anode material, therefore BDD is usually chosen as anode materials [97].

The significant enhancement of electro-Fenton process has been achieved in the replacement of the classical anode Pt by the emergent anode BDD. Except the generation of supplementary heterogeneous hydroxyl radicals, BDD($\bullet\text{OH}$) could provide additional homogeneously $\bullet\text{OH}$ in bulk solution (Eq. (2.3)). The extra advantages of application of BDD in the treatment are: i) higher oxidizing power of BDD($\bullet\text{OH}$) than others $\text{M}(\bullet\text{OH})$ for its larger O_2 overvoltage (Eq. (2.4)); ii) high oxidation window (about 2.5 V) makes it oxidizing the organics directly.

The usual application of EF in experiment can be seen in Fig. 2.6a.

Electro-Fenton process was successfully applied to removal of organic pollutants from water with high oxidation and/or mineralization rates, mainly by Oturan's and Brillas' groups. The removal from water of several organic pollutants such as pesticide active ingredients [166-170], pesticide commercial formulations [171], synthetic dyes [163, 172-174], pharmaceuticals [104, 156, 175, 176], industrial pollutants [177], landfill leachates [178, 179], etc., was thoroughly studied with almost mineralization efficiency in each case, showing that the electro-Fenton process can be an alternative when conventional treatment processes remain inefficient.



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Fig. 2.6. (a): Sketch of a bench-scale open and stirred two electrode undivided tank reactor with a 60 cm² carbon-felt cathode fed with compressed air utilized for the EF treatment of organic solutions and **(b):** Schematic representation of the main reactions involved in the EF process in a divided cell. RH is an unsaturated compound that undergoes dehydrogenation, while Ar is an aromatic pollutant that is hydroxylated. Reprinted with permission from ref [165]. Copyright 2002 Elsevier.

2.5.2. 1 Application to the removal of NSAIDs

Although the electro-Fenton process has been successfully applied to the treatment of a very large group of organic pollutants during the last decade, studies on NSAIDs are scarce, unlike the anodic oxidation process. Preliminary work dealing with the electro-Fenton process on pharmaceutical residues was started by Oturan et al. using a divided cell with a mercury pool as cathode under air bubbling [180, 181] Reactivity of several NSAIDs, including, among others, salicylic acid (aspirin), ketoprofen, diclofenac, naproxen, sulindac, and proxicam with electrochemically generated $\bullet\text{OH}$ was investigated at pH 4 and 7 showing that all NSAID tested behave as $\bullet\text{OH}$ scavengers with high reactivity, rate relative constant of the reaction between NSAIDs and $\bullet\text{OH}$ ranging between 1.0 – 1.9 times compared that of salicylic acid ($k = 2.2 \times 10^{10} \text{ L mol}^{-1} \text{ s}^{-1}$) [143].

These studies investigated also the product distribution of salicylic acid, showing that the main reaction was the successive hydroxylation of parent molecule leading to the formation of 2,3-, 2,4-, 2,5- and 2,6-dihydroxybenzoic acids, 2,3,4-, 2,3,5- and 2,4,6-trihydroxybenzoic acids, the major hydroxylation products being the 2,3-dihydroxybenzoic acid (35%) and 2,5-dihydroxybenzoic acid (10%). Determination of rate constants of formed hydroxylated derivatives of salicylic acid showed that they are more or as well as reactive than the parent molecule; for example the rate constant of hydroxylation of 2,4,6-trihydroxybenzoic acid was found three time higher than that of salicylic acid. These findings showed that hydroxylated products are able to react with $\bullet\text{OH}$ until oxidative breaking of aromatic ring leading to the formation of short-chain carboxylic acids which can be mineralized in their turn by further reactions with $\bullet\text{OH}$. As regards the ketoprofen, three hydroxylated derivatives (2-hydroxy, 3'-hydroxy and 4'-hydroxy ketoprofene) are found as main oxidation products.

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More recently, Brillas' group carried out a number of reports on the electro-Fenton treatment of several pharmaceuticals and in particular some NSAIDs such as paracetamol [182, 183], salicylic acid [184] and ibuprofen [185], using undivided cell equipped with a GDE as cathode, the anode being Pt or BDD. Results on oxidation kinetics and mineralization power of the process confirm the superiority of BDD compared to Pt as anode in all cases. Higher removal rates were obtained as the current density increased due to the enhancement of generation rate of homogeneous ($\bullet\text{OH}$ produced in the bulk) and heterogeneous (BDD($\bullet\text{OH}$) generated at the anode surface) hydroxyl radicals. Almost total mineralization was found for paracetamol, salicylic acid and ibuprofen with BDD anode while mineralization efficiency remained low with Pt anode confirming the interest of the BDD anode as a better alternative in electro-Fenton process. The mixture of Fe^{3+} and Cu^{2+} as catalyst was found to have positive synergetic effect on mineralization degree.

2.5.2.2 Electro-Fenton related processes

EF lays the foundation for a large variety of related processes, which aim at minimizing or eliminating the drawbacks of individual techniques or enhancing the efficiency of the EF process by coupling with other methods, including UV-irradiation combined technologies, like photoelectro-Fenton (PEF) [186] and solar photoelectro-Fenton (SPEF) [93]; coagulation involved methods as peroxi-coagulation (PC) [165]; UV-irradiation with coagulation (photoperoxi-coagulation (PPC)) [187]; and ultrasonic coupled with electro-Fenton (sonoelectro-Fenton (SEF)) [163]. There are other combined Fenton processes as Fered-Fenton [188], electrochemical peroxidation (ECP) [189], anodic Fenton treatment (AFT) [190], and plasma-assisted treatments [191]. Electrocoagulation and internal micro-electrolysis processes can be applied as pre-treatments to deal with high organic loads, are the most straightforward and cheap ones, while Photoelectrocatalysis (PEC) and plasma technologies are complex and need expensive accessories [92].

Photoelectro-Fenton and solar photoelectro-Fenton at constant current density were studied by Skoumal et al. [185]. The degradation of ibuprofen solution at pH 3.0 was performed in a one-compartment cell with a Pt or BDD anode and an O_2 diffusion cathode. It was found the induced sunlight strongly enhanced generation of $\bullet\text{OH}$ via PEF reaction, ascribed to a quicker photodegradation of Fe(III) complexes induced by the UV intensity supplied by sunlight. Mineralization rate was increased under UVA

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and solar irradiation by the rapid photodecomposition of complexes of Fe (III) with acidic intermediates. SPEF with BDD was the most potent method, giving 92% mineralization with a small proportion of highly persistent final by-products formed during the process preventing total mineralization. Higher mineralization with BDD than Pt means the use of a BDD anode instead of Pt yielded much more oxidation power in this procedure. The decay of ibuprofen followed a pseudo-first-order kinetics by using BDD ($\cdot\text{OH}$), Pt ($\cdot\text{OH}$) and/or $\cdot\text{OH}$ formed homogeneously in the bulk, and current density and UV intensity influenced significantly its destruction rate.

The author of this study identified aromatic intermediates (Fig. 2.7), such as 1-(1-hydroxyethyl)-4-isobutylbenzene, 4-isobutylacetophenone, 4-isobutylphenol and 4-ethylbenzaldehyde. The carboxylic acids such as pyruvic, acetic, formic and oxalic were identified as oxidation by-products. Oxalic acid was the ultimate by-product and the fast photo decarboxylation of its complexes with Fe(III) under UVA or solar irradiation contributes to high mineralization rate.

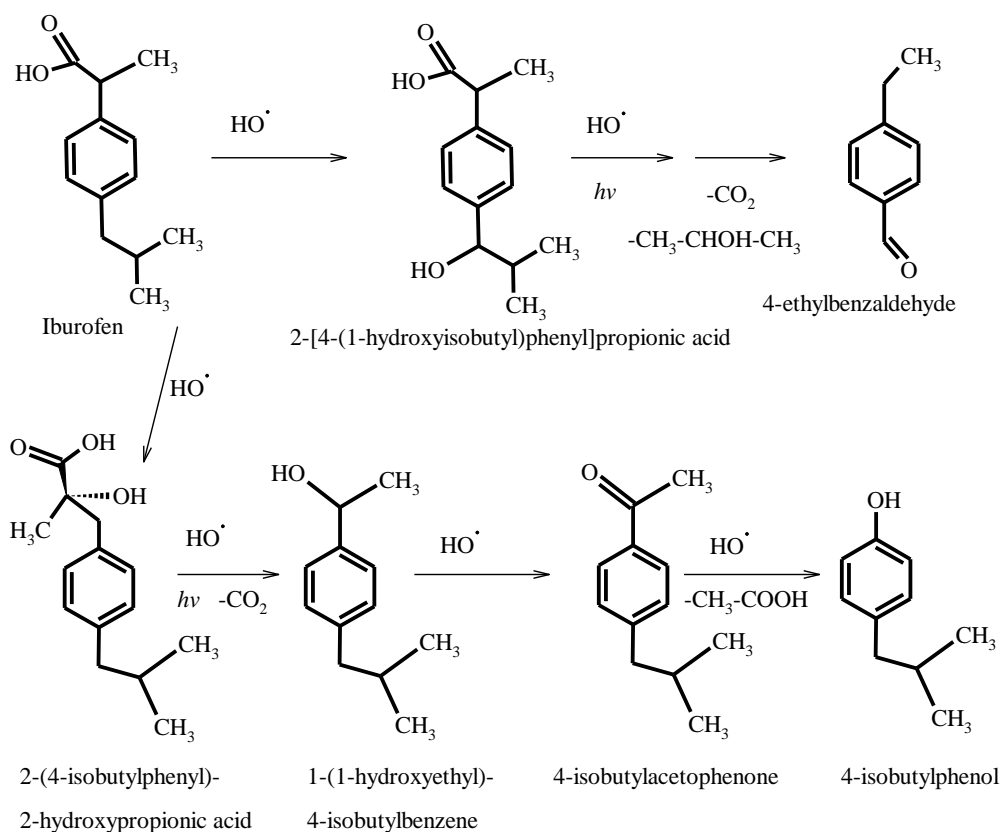


Fig. 2.7. Proposed reaction scheme for the initial degradation of ibuprofen by EF and PEF. The sequence includes all aromatics detected, along with hypothetical intermediates within brackets. Pt ($\cdot\text{OH}$) and BDD ($\cdot\text{OH}$) represent the hydroxyl radical

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electrogenerated from water oxidation at the Pt and BDD anode, respectively, and $\bullet\text{OH}$ denotes the hydroxyl radical produced in the medium. Adapted with permission from reference of [185]. Copyright 2010 Elsevier.

The operational factor, as Fe^{2+} content, pH and current density on PEF degradation also had been studied. For the SPEF degradations, the best operating conditions were achieved using Fe^{2+} between 0.2 and 0.5 mM, pH 3.0 and low current density. Thus, during the SPEF-BDD treatment of ibuprofen, 86% mineralization in 3 h was achieved at solution close to saturation with 0.5 mM Fe^{2+} and 0.05 M Na_2SO_4 at pH 3.0 and 6.6 mA cm^{-2} with an energy cost as low as 4.3 kW hm^{-3} . With the results obtained, PEF methods have the higher oxidation power in comparison to EF process in the case of gas diffusion cathode.

Fenton and electro-Fenton processes treatment on paracetamol was investigated by application of anodes as mesh-type titanium metal coated with $\text{IrO}_2/\text{RuO}_2$ and cathodes as stainless steel. The effect of operating parameters on degradation were investigated and compared; Fe^{2+} concentration had great influence on the degradation rate, followed by H_2O_2 concentration and pH [192].

The opposite result was obtained that electro-Fenton treatment of paracetamol was more efficient than the photoelectro-Fenton method in wastewater, though the differences of removal efficiencies are negligible [193]. Considering the energy consumption (additional UVA irradiation for PEF), the electro-Fenton processes are more suitable and economical. The processes were designed by using a double cathode electrochemical cell, and the results showed that initial Fe^{2+} concentration, H_2O_2 concentration and applied current density all positively affected the degradation efficiency while Fe^{2+} concentration has most significant influence on the efficiency. The removal efficiency of paracetamol was all above 97% and COD removal above 42% for both methods operated at optimum conditions.

Finally a degradation pathway was proposed. Hydroquinone and amide were produced by $\bullet\text{OH}$ attack in the para position. The amide is further degraded till finally turned into nitrates. On the other hand, the hydroquinone is converted into benzaldehyde which oxidized to benzoic acid, following further degradation into short chain carboxylic acids (Fig. 2.8).

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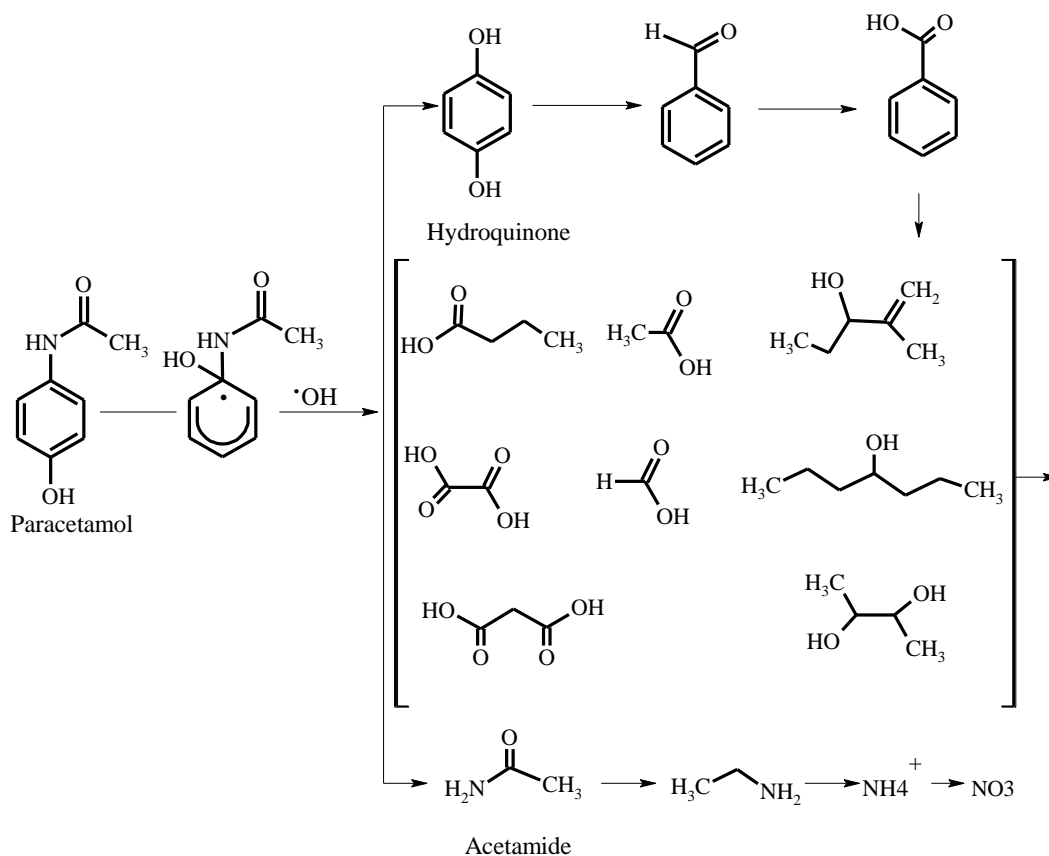


Fig. 2.8. Proposed degradation pathway for paracetamol (Adapted [193] with permission from Copyright 2012 Elsevier).

2.5.2.3 Application of electro-Fenton related processes for removal of pharmaceuticals from aqueous solutions

Sonoelectro-Fenton (SEF) processes, have received intensive attention recently [102]. Ultrasounds applied to aqueous solutions leads to the formation of cavitation bubbles; a fast pyrolysis of volatile solutes takes place and water molecules also undergo thermal decomposition to produce H^+ and $\cdot\text{O}$; then reactive radicals formed from water decomposition in gas bubbles, together with thermal decomposition, due to the acoustic energy concentrated into micro reactors, enhancing the reaction with $\cdot\text{OH}$ by ultrasound irradiation. It is not only the additional generation of $\cdot\text{OH}$ by sonolysis from reaction to accelerate the destruction process, but also the bubbles produced in solution help the transfer of reactants Fe^{3+} and O_2 toward the cathode for the electrogeneration of Fe^{2+} and H_2O_2 , as well as the transfer of both products to the solution increasing $\cdot\text{OH}$ production in Fenton's reaction,



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where))) denotes the ultrasonic irradiation. Simultaneously $\bullet\text{OH}$ is produced in the medium by electro-Fenton process via electrochemically induced Fenton's reaction. There are more interests in the development on this technique [194, 195].

Fered-Fenton process is another one of the Fenton family methods, in which both H_2O_2 and Fe^{2+} are simultaneously added to the solution. Unlike the electro-Fenton process, Fenton's reagent is externally added to the solution to be treated; nevertheless Fenton reaction is catalysed electrochemically by regeneration of Fe^{2+} ion (catalyst). The Fenton reaction takes place with the production of $\bullet\text{OH}$ and Fe^{3+} ions (Eq. (2.23)). Formed Fe^{3+} is cathodically reduced to Fe^{2+} (Eq. (2.24)) in order to catalyse Fenton's reaction [196-198]. The oxidation can be also occurred at anode when the adequate is selected.



Electrochemical peroxidation (ECP), is a proprietary process that utilizes sacrificial iron electrodes for Fe^{2+} electro generation and $\bullet\text{OH}$ formed from Fenton's reaction with added or cathodically generated H_2O_2 [187, 189]



With voltage applied to steel electrodes, Fe^{2+} is produced, and then the presence H_2O_2 (added or cathodically generated) leads to the formation of $\bullet\text{OH}$ from the Fenton's reaction (Eq. (2.24)).

The major advantage of ECP process is the reaction above that allows the recycle of $\text{Fe}^{3+}/\text{Fe}^{2+}$ (Eq. (2.28)).

Plasma can be defined as the state of ionized gas consisting of positively and negatively charged ions, free electrons and activated neutral species (excited and radical). It is classified into thermal (or equilibrium) plasma and cold (or non-equilibrium) plasma. For thermal plasma, the energy of this plasma is extremely high enough to break any chemical bond, so that this type of plasma can significantly removes most organic, while the cold plasma easily generate electric discharges under reduced pressure, such as high-energy electrons, $\bullet\text{OH}$, $\bullet\text{H}$, $\text{O}\bullet$, and $\text{O}_2\bullet^-$, as well as long-lived active molecules such as O_3 , H_2O_2 , excited-state neutral molecules, and ionic species, which can oxidize organic pollutants. Plasma-assisted treatments, with the addition of Fe^{2+} or Fe^{3+} to the aqueous medium, can produce extra $\bullet\text{OH}$ with extra

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generated H_2O_2 , accelerating the degradation rate of organics. However, excessive energy is required for expensive and complex accessories application.

ECP process combined with a more inexpensive biological treatment in practical application can reduce the toxicity of suspended solids and effluent, improving the quality of the treated water for potential reuse. A practical application of electrochemical process on wastewater treatment plants [199] was performed as pre-electrochemical treatment for a post-biological treatment in a flow cell. The electrochemical experiment contained the working electrode (graphite felt), which was separated from the two interconnected carbon-graphite plate counter electrode compartments by cationic exchange membranes. A good homogeneity of the potential distribution in the three dimensional working electrode was obtained when the graphite felt was located between two counter electrodes. The saturated calomel electrode as reference electrode was positioned in the middle of the felt. The electrolyte solution (0.05 M Na_2SO_4 containing the insecticide phosmet) was percolated the porous electrode with a constant flow rate. For biological treatment, activated sludge issued from a local wastewater treatment plant was used at 30 °C and pH 7.0.

From the results, electrolysis led to a decrease of the toxicity EC_{50} value and an increase of biodegradability; during activated sludge culture, an almost total mineralization of the electrolyzed solution was recorded. It was noticed that the high cathodic potential used made another reduction occur; the reduction of water could lead to hydrogen production. The faradic yield was therefore very low (below 10%) and can be less cost effective. For this purpose, application of higher hydrogen overvoltage electrolytes, the optimization of flow rate in the percolation cell as well as the thickness of the graphite felt and reuse of the acclimated activated sludge for successive experiments could be helpfully considered to enhance the efficiency and reduce the process duration; all of these work will be helpful as a guide for the treatment of real polluted wastewater afterwards.

To the best of our knowledge, there are no detailed studies on economic assessment of this technology taking into account operating and investment cost that permitting to compare with other AOPs. However, a recent work conducted by one of the author of this paper [200] focused on the mineralization of a synthetic solution of the pharmaceutical tetracycline by EF process, showed that the operating electrical energy consumption is significantly lower compared to that obtained in other assessments done in the recent literature for other EAOPs. Thus, the 1.1 kWh/g TOC removed obtained

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for the removal of tetracycline during electro-Fenton treatment compares favorably with the 1.8 kW h/g TOC obtained in the degradation of a dye with anodic oxidation [202] and with the 2.9 or 2.2 kW h/g TOC removed obtained in the removal of phenol by a single electrochemical and an photoelectrochemical process, respectively, in very similar conditions (range of concentration of pollutant) [203].

2.6. Conclusions and suggestions for future research

A large part of the pharmaceuticals is excreted in original form or metabolite into environment due to the low removal efficiency of standard WWTPs on such compounds. This combined with the special effects of pharmaceuticals on target even unintended organisms at low doses, makes it urgent to develop more efficient technologies for their elimination.

AOPs, designed to eliminate in source persistent or toxic organic xenobiotic present in small volumes, avoiding their release into the natural water streams and could be applied for treating pharmaceutical residues and pharmaceutical wastewaters. Indeed, the application of typical AOPs would become technically and economically difficult or even impossible once the environmentally dangerous persistent organic pollutants are diluted in large volumes. However, with the advanced feature and developed improvement, the AOPs and in particular the EAOPs, overcoming the usual reluctance to electrochemistry approach, could be applied as a plausible and reliable alternative promising method to treat pharmaceutical containing wastewaters. In the case of applicability of EAOPs for wastewater volumes EAOPs were successfully used as bench-scale post-treatment to reverse osmosis concentrates [201] or nano-/ultra-filtration concentrates [178].

In this review, the applicability of EAOPs for the removal of NSAIDs, which are mostly consumed and detected in environment, was discussed. From the focus of recent researches, it is clear that the most frequently removed NSAIDs by EAOPs are ibuprofen, paracetamol and diclofenac. The elucidation of the reaction pathways, by-products generated during the treatment and their toxicities are another important consideration of electrochemical treatments. Aromatic intermediates produced from pharmaceutical residues in primary stage have significant influence on increase/decrease toxicity of solution, after while the short chain carboxylic acids generated in following steps could influence the TOC abatement. This technology was largely investigated at lab-scale; the next steps are: design of a pilot-scale reactor, investigation of the

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operational as well as the influent parameters, such as: pH, inorganic salts (ions from the supporting electrolyte or already present in wastewater), presence of natural organic matter, catalyst concentration, and temperature on the treatment efficiency. These new tests to be carried out at pilot-scale will determine if lab-scale research can be transposed to pilot-scale to show feasibility of using EAOPs for industrial scale reactor. In addition, several researchers have interest on the new materials applied to enhance the performance and efficiency of the NSAIDs elimination process. Significant progress has been evidenced from the development of novel electrodes and membranes and the amelioration of the reactor setup. For instance, the use of BDD anode gives high mineralization efficiency when applied under optimal conditions.

Process pre-modelling and pollutant behaviour prediction are helpful for the economical and practical application of EAOPs in real wastewater treatment. They can be used to optimize the operational parameters of the process, as pH, current applied, catalyst concentration, UV length, supporting electrolyte, nature of electrode (either cathode or anode material). UVA and solar irradiation applied in electrochemical processes could make the decomposition processes more rapid.

Concerning the economic aspects, cheap source of electrical power by using sunlight-driven systems is considered as an economical application. Combination of other technologies is also practical in industrial treatment, which could provide a significant savings of electrical energy on the overall decontamination process. For example, it has been demonstrated [\[143\]](#) the feasibility and utility of using an electro-oxidation device directly powered by photovoltaic panels to treating a dye-containing wastewater. Further reductions in electrode price and use of renewable energy sources to power the EAOPs will enhance the development of more sustainable water treatment processes.

Acknowledgements

Ling Feng is a Doctoral research fellow of the Erasmus Mundus Joint Doctorate programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA no. 2010-0009.

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Chapter 3. Research Paper

Degradation of anti-inflammatory drug ketoprofen by electro-oxidation: comparison of electro-Fenton and anodic oxidation processes

The results of this section were concluded in the paper:

Feng, L., Oturan, N., van Hullebusch, E.D., Esposito, G. and Oturan, M.A. Degradation of anti-inflammatory drug ketoprofen by electro-oxidation: comparison of electro-Fenton and anodic oxidation processes. *Accepted in Current Organic Chemistry*

Chapter 3: Degradation of anti-inflammatory drug ketoprofen by electro-oxidation: comparison of electro-Fenton and anodic oxidation processes

Abstract

The electrochemical degradation of the non-steroidal anti-inflammatory drugs ketoprofen in tap water has been studied using electro-Fenton (EF) and anodic oxidation (AO) processes with Pt and BDD anodes and carbon felt cathode. Fast degradation of the drug molecule and mineralization of its aqueous solution were achieved by BDD/carbon-felt, Pt/carbon felt and AO with BDD anode. Obtained results showed that oxidative degradation rate of ketoprofen and mineralization of its aqueous solution increased by increasing applied current. Degradation kinetics well fitted to a pseudo-first-order reaction. Absolute rate constant of the oxidation of ketoprofen by electrochemically generated hydroxyl radicals was determined to be $(5.4 \pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ by using competition kinetics method. Several reaction intermediates such as 3-hydroxybenzoic acid, pyrogallol, catechol, benzophenone, benzoic acid and hydroquinone were identified by HPLC analyses. The formation, identification and evolution of short-chain aliphatic carboxylic acids like formic, acetic, oxalic, glycolic and glyoxylic acids were monitored with ion-exclusion chromatography. Based on the identified aromatic/cyclic intermediates and carboxylic acids as end-products before mineralization, a plausible mineralization pathway was proposed. The evolution of the toxicity during treatments was also monitored using Microtox method, showing a faster detoxification with higher applied current values.

Keywords: Ketoprofen; Electro-Fenton; Anodic Oxidation; Hydroxyl Radicals; Mineralization; Toxicity.

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3.1 Introduction

The non-steroidal anti-inflammatory drugs (NSAIDs) are designed against biological degradation that they can keep their chemical structure long enough to last in environment. A large number of reports revealed their presence and that of their metabolites in the wastewater treatment effluents, surface and ground water, due to their widely use since several decades ago [1-4]. Some of them are in the high risk that may cause adverse effects on the aquatic ecosystem [5-7]. It was shown that prolonged exposure to the chemicals as NSAIDs is expected to affect the organism health [8]. Due to the low removal efficiency of the wastewater treatment plants (WWTPs) on pharmaceuticals compounds, and in particular, NSAIDs accumulated in natural waters [9-11].

Ketoprofen, 2-(3-benzoylphenyl) propanoic acid), is categorized as a pharmaceutically active compound. It has high hydrophilic ability due to its pKa (i.e. 4.45), making the elimination on sorption process in WWTPs inefficient; its elimination being mainly dependent to chemical or biological process used [12]. Therefore the removal efficiency of ketoprofen in WWTPs varied from 15 to 98% [11]. The unstable removal rate varies in different treatment plants and seasons, from “very poor” to “complete”, depending strongly on the nature of the specific processes being applied. Due to the inefficient removal from WWTPs, ketoprofen remains in water stream body at concentration from ng L^{-1} to $\mu\text{g L}^{-1}$ [13].

Various treatment methods were explored to remove NSAIDs from water, while advanced oxidation processes (AOPs) that involves in situ generation of hydroxyl radicals ($\bullet\text{OH}$) and/or other strong oxidant species, have got more interest as promising powerful and environmentally friendly methods for treating pharmaceuticals and their residues in wastewater [14-16]. Among the AOPs, electrochemical advanced oxidation processes (EAOPs), with attractive advantages, being regarded as the most perspective treatments, especially in eliminating the low concentration pollutants [17-20]. The EAOPs are able to generate the strong oxidizing agent $\bullet\text{OH}$ either by direct oxidation of water (anodic oxidation, AO) [21, 22], or in the homogeneous medium through electrochemically generated Fenton's reagent (electro-Fenton (EF) process) [17, 23]. $\bullet\text{OH}$ s thus generated are able to oxidize organic pollutants until their ultimate oxidation state, c.a., mineralization to CO_2 , water and inorganic ions [17, 24].

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In AO, heterogeneous hydroxyl radicals $M(\bullet\text{OH})$ are generated by electrochemical discharge of water (Eq. (3.1)) or OH^- (Eq. (3.2)) on a high O_2 evolution overvoltage anode (M). In the case of the boron doped diamond (BDD) film anode, $\bullet\text{OH}$ s are physisorbed and therefore more easily available compared, for example, to Pt anode on which $\bullet\text{OH}$ s are chemisorbed [25].



In contrast, homogeneous hydroxyl radicals ($\bullet\text{OH}$) are generated by electro-Fenton process in the bulk solution via electrochemically generated Fenton's reagent (mixture of $\text{H}_2\text{O}_2 + \text{Fe}^{2+}$), which leads to the formation of the strong oxidant from Fenton's reaction (Eq. (3.3)):



One of the main advantages of this process is the electrocatalytic and continues regeneration of ferrous iron ions from Fe^{3+} produced by Fenton's reaction according to the following reaction [26]:



In this work, the degradation of the anti-inflammatory drug ketoprofen was carried out, for the first time, by EAOPS anodic oxidation and electro-Fenton with Pt and BDD anodes. Different operating parameters influencing the oxidation power of the processes and its mineralization efficiency during treatment of ketoprofen aqueous solutions were investigated. Apparent and absolute rate constants of the oxidation of ketoprofen by $\bullet\text{OH}$ were determined. The aromatic/cyclic reaction intermediates were identified by HPLC analysis. The formation of short-chain carboxylic acids as end-products before complete mineralization was monitored by ion exclusion chromatography. Combining by TOC measurements, these data allowed a plausible mineralization pathway for ketoprofen by $\bullet\text{OH}$ proposed.

3.2 Materials and methods

3.2.1 Chemicals

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The pharmaceutical-ketoprofen (2-[3-(benzoyl) phenyl] propanoic acid, (C₁₆H₁₄O₃), sodium sulfate (supporting electrolyte), anhydrous Na₂SO₄ (99%), and acetic acid (glacial p.a. C₂H₄O₂) were supplied by Sigma-Aldrich. Sulfuric acid (ACS reagent grade, 98%), Iron (II) sulfate heptahydrate (catalyst, 99%), 4-*p*-hydroxybenzoic acid (as competition substrate in kinetic experiments), methanol (for HPLC analysis grade), aromatic intermediates: benzophenone (C₁₃H₁₀O), phenol (C₆H₆O), 3-hydroxybenzoic acid (C₇H₆O₃), benzoic acid (C₇H₆O₂), catechol (C₆H₆O₂), pyrogallol (C₆H₆O₃), hydroquinone (C₆H₆O₂) and carboxylic acids: acetic (C₂H₄O₂), glyoxylic (C₂H₂O₃), oxalic (C₂H₂O₄), formic (CH₂O₂), glycolic (C₂H₄O₃) acids were purchased from Acros Organics in analytical grade. All other products were obtained with purity higher than 99%.

Ketoprofen solutions of concentration 0.198 mM were prepared in tap water, and all other stock solutions were prepared with ultra-pure water obtained from a Millipore Milli-Q-Simplicity 185 system with resistivity > 18 MΩ cm at 25 °C. The pH of solutions was adjusted using analytical grade sulfuric acid or sodium hydroxide (Acros).

3.2.2 Electrochemical cell and apparatus

Experiments were carried out in a 250 mL open, undivided cylindrical glass cell of inner diameter of 7.5 cm at room temperature, equipped with two electrodes. The working electrode (cathode) was a 3D carbon-felt (18.0 cm × 6.0 cm × 0.6 cm, from Carbone-Lorraine) placed on the inner wall of the cell, covering the total internal perimeter. The anode was a 4.5 cm² Pt cylindrical mesh or a 24 cm² BDD thin-film deposited on both sides of a niobium substrate, centered in the electrolytic cell. 0.05 M Na₂SO₄ was introduced to the cell as supporting electrolyte. Prior to electrolysis, compressed air at about 1 L min⁻¹ was bubbled for 5 min through the solution to saturate the aqueous solution and reaction medium was agitated continuously by a magnetic stirrer (800 rpm) to make mass transfer to/from electrodes. For the electro-Fenton experiment, the pH of the medium set to 3.0 by using 1.0 M H₂SO₄, and was measured with a CyberScan pH 1500 pH-meter from Eutech Instruments, and an adequate concentration of FeSO₄·7H₂O was added to initial solutions as source of Fe²⁺ as catalyst.

The currents of 100-2000 mA were applied for degradation and mineralization kinetics, by-product determination and toxicity experiments. The current and the amount of charge passed through the solution were measured and displayed

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continuously throughout electrolysis by using a DC power supply (HAMEG Instruments, HM 8040-3).

3.2.3 Analytical measurements

3.2.3.1 High performance liquid chromatography (HPLC)

The determination of decay kinetics of ketoprofen and identification of its aromatic intermediates, as well as the measure of the absolute rate constants for oxidation of ketoprofen were monitored by high performance liquid chromatography (HPLC) using a Merck Lachrom liquid chromatography equipped with a L-2310 pump, fitted with a reversed phase column Purospher RP-18, 5 μm , 25 cm x 4.6 mm (i.d.) at 40° C and coupled with a L-2400 UV detector selected at optimum wavelengths of 260 nm. Mobile phase was consisted of a 49:49:2 (v/v/v) methanol/water/acetic acid mixtures at a flow rate of 0.7 mL min⁻¹. Carboxylic acid compounds produced during the processes were identified and quantified by ion-exclusion HPLC using a Supelcogel H column (ϕ = 4.6 mm x 25 cm), column at room temperature at λ = 210 nm. 1% acetic acid solution at a flow rate of 0.2 mL min⁻¹ was performed as mobile phase solution.

In the analysis, all the injection volume was 20 μL and measurements were controlled through EZChrom Elite 3.1 software. The identification and quantification of the intermediates were conducted by comparison of the retention time with that of authentic substances.

3.2.3.2 Total organic carbon (TOC)

The mineralization reaction of ketoprofen by hydroxyl radicals can be written as follows:



The mineralization degree of initial and electrolyzed samples was monitored by the abatement of their total organic carbon content, determined on a Shimadzu VCSH TOC analyzer. The carrier gas was oxygen with a flow rate of 150 mL min⁻¹. A non-dispersive infrared detector, NDIR, was used in the TOC system. Calibration of the analyzer was attained with potassium hydrogen phthalate (99.5%, Merck) and sodium hydrogen carbonate (99.7%, Riedel-de-Haën) standards for total carbon (TC) and inorganic carbon (IC), respectively. Reproducible TOC values with $\pm 1\%$ accuracy were found using the non-purgeable organic carbon method.

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The mineralization current efficiency (MCE in %) at a given electrolysis time t (h) was calculated according to the following equation [27]:

$$\text{MCE} = \frac{n F V_s \Delta(\text{TOC})_{\text{exp}}}{4.32 \times 10^7 m I t} \times 100 \quad (3.6)$$

where n is the number of electrons consumed per molecule mineralized (72), F is the Faraday constant (96487 C mol^{-1}), V_s is the solution volume (L), $\Delta(\text{TOC})_{\text{exp}}$ is the experimental TOC decay (mg L^{-1}), 4.32×10^7 is a homogenization factor ($3600 \text{ sh}^{-1} \times 12,000 \text{ mg mol}^{-1}$), m is the number of carbon atoms of ketoprofen (16) and I is the applied total current (0.1-2A).

3.2.3.3. Toxicity tests

For testing the potential toxicity of ketoprofen and of its reaction intermediates, the measurements were carried out with the bioluminescent marine bacteria *Vibrio fischeri* (Lumistox LCK 487), provided by Hach Lange France SAS, by means of the Microtox[®] method, according to the international standard process (OIN 11348-3). The two values of the inhibition of the luminescence (%) were measured after 5 and 15 min of exposition of bacteria to treated solutions at $15 \text{ }^\circ\text{C}$. The bioluminescence measurements were realized on solutions electrolyzed at several constant current intensities ($I = 100, 300 \text{ mA}$), and on a blank ($C_0 = 0 \text{ mg L}^{-1}$).

3.3 Results and discussion

3.3.1 Effect of experimental parameters on the electrochemical treatments efficiency

Among different operating parameters affecting the efficiency of the electro-Fenton process, the most important are applied current intensity, catalyst concentration, solution pH, temperature, and electrode materials [17, 28-31]. The solution pH value is now well known as 3.0 [32], and room temperature is convenient to the process since higher temperature lower the O_2 solubility and can provoke H_2O evaporation. Regarding electrodes materials, carbonaceous cathode and BDD anode were shown to be better materials [17, 33]. Thus, we will discuss the effect of other parameters in the following subsections.

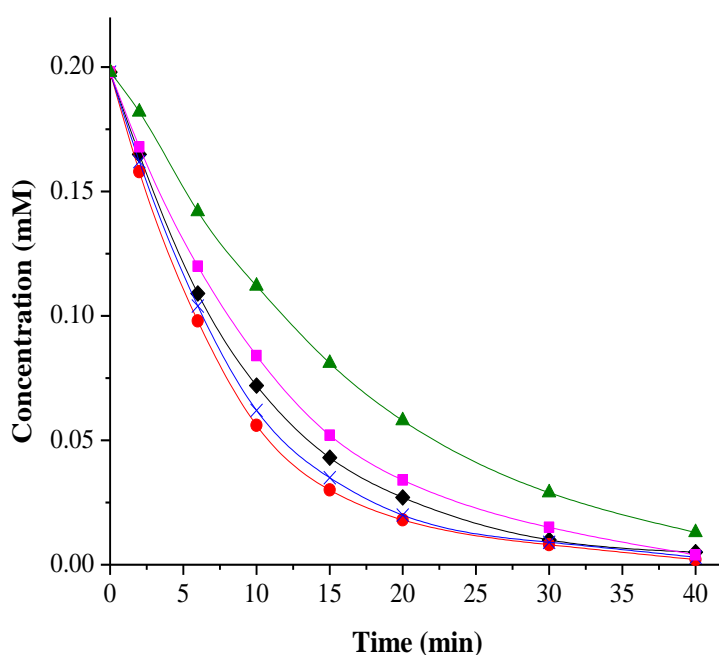
3.3.1.1 Effect of catalyst (Fe^{2+}) concentration on degradation kinetics of ketoprofen

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Catalyst concentration (i.e. Fe^{2+}) is an important parameter influencing process efficiency, particularly in the case of Fe^{2+} as catalyst [17, 28]. Figure 3.1 shows the degradation of a 101 mg L^{-1} (0.198 mM) ketoprofen in aqueous solution of pH 3, as function of time in electro-Fenton experiments using Pt/carbon felt cell at a current intensity of 100 mA with different catalyst concentrations ranging from 0.05 to 1 mM.

At optimum pH condition (pH = 2.8-3.0), Fenton process take place according to equation (3.3) [17, 29, 34] to generate $\bullet\text{OH}$ s that react with ketoprofen. Thus the rate of $\bullet\text{OH}$ generation is controlled by the rate of the electrochemical generation of Fe^{2+} from Eq. (3.4).

Figure 3.1 shows that decay of concentration of ketoprofen was fastest for 0.1 mM Fe^{2+} concentration. The degradation rate decreased with increasing Fe^{2+} concentration up to 1 mM. The degradation was significantly slowed down with 1.0 mM Fe^{2+} ; 80 min were necessary for completed oxidation of ketoprofen while 50 min were enough with 0.1 mM Fe^{2+} . There was no much considerable change in the oxidative degradation rate for Fe^{2+} concentration values between 0.1 and 0.2 mM, while the concentration of 0.05 mM implied a slower degradation rate compared to 0.1 mM. According these data, the catalyst concentration of 0.1 mM was chosen as the optimum value under our experimental conditions and was used in the rest of the study.



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Fig. 3.1. Effect of Fe^{2+} (catalyst) concentration on the degradation kinetics of ketoprofen (C_0 : 0.198 mM) in tap water medium by electro-Fenton process with Pt anode at 100 mA and pH 3. $[\text{Fe}^{2+}]$: 0.05 mM (◆); 0.1 mM (●); 0.2 mM (×); 0.5 mM (■); 1.0 mM (▲); $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L.

The reason for lower efficiency when increasing Fe^{2+} concentration can be related to the enhancement of the wasting reaction (Eq. (3.7)) between Fe^{2+} and $\bullet\text{OH}$ for which reaction rate is enhanced by increasing the concentration of ferrous ion. The increase of the rate of reaction (3.7) means the wasting more $\bullet\text{OH}$ by this parasitic reaction decreasing the efficiency of oxidation of ketoprofen [35, 36]



3.3.1.2 Influence of the applied current intensity on degradation rate

The applied current intensity is one of main parameter of process efficiency in AO and EF process, since the generation of hydroxyl radicals is governed by this parameter through Eqs. (3.1), (3.3), (3.4) and (3.8):



To clarify the effect of applied current intensity on the degradation kinetics, experiments were set-up with 0.198 mM ketoprofen by using electro-Fenton process with Pt (EF-Pt) and BDD (EF-BDD), and AO with BDD (AO-BDD) anodes versus carbon felt cathode for the applied currents values ranging from 100 to 2000 mA (Fig. 3.2). The oxidative degradation rate of ketoprofen was found to increase with increasing applied current intensity due to the production of homogeneous $\bullet\text{OH}$ at higher extent from Eq. (3.3) (at bulk of solution) and heterogeneous Pt($\bullet\text{OH}$) or BDD($\bullet\text{OH}$) at the anode surface. High current intensity promotes generation rate of H_2O_2 from Eq. (3.8) and Fe^{2+} from Eq. (3.4), leading to the formation of more $\bullet\text{OH}$ from Eq. (3.3) on the one side, and that of Pt($\bullet\text{OH}$) and/or BDD($\bullet\text{OH}$) from Eq. (3.1) on the other side [17, 24, 37].

Complete degradation of ketoprofen was achieved at 50, 40 and 30 min of electrolysis for 100, 200 and 500-2000 mA current intensity, respectively, in EF-Pt cell. The treatment time required for EF-BDD cell was 20 min for 2000 mA, 30 min for 500 to 1000 mA and 50 min for 100 mA. The relatively lower degradation kinetics of EF-Pt cell can be explained by enhancement of the following parasitic reaction (Eq. (3.9)), the increasing applied current, harms the accumulation of H_2O_2 in the medium. In the case

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of EF-BDD cell, generation of more BDD(\bullet OH) at high current values compensates the loss of efficiency in the bulk.

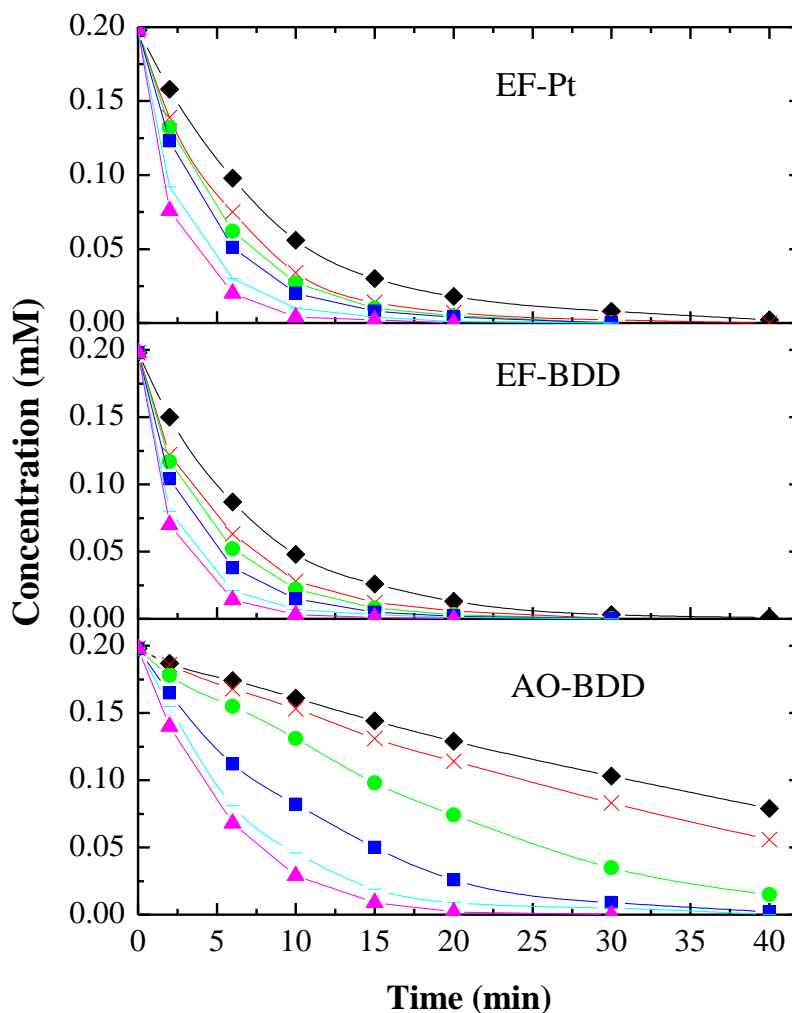


Fig. 3.2. Effect of current intensity on the degradation kinetics of ketoprofen in tap water medium by different electrochemical processes: 100 mA (\blacklozenge); 300 mA (\times); 500 mA (\bullet); 750 mA (\blacksquare); 1000 mA (\square); 2000 mA (\blacktriangle). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L; electro-Fenton: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0; Anodic oxidation at pH 7.5.

In contrast to EF, degradation kinetics of ketoprofen was significantly lower, in all applied currents for AO-BDD cell. The time required for complete transformation of ketoprofen ranged from 140 to 30 min for applied current values from 100 to 2000 mA respectively. Comparing the electrolysis time for 2000 mA, one can conclude that

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hydroxyl radicals are predominantly formed at anode surface (Eq. (3.1)) rather than Fenton reaction. The requirement for complete degradation of aqueous solution of 0.198 mM ketoprofen at a moderate current value of 300 mA was 30, 40, 120 min with EF-BDD, EF-Pt and AO-BDD processes, respectively, we can conclude that the oxidation power of the tested EAOPs ranged in the sequence EF-BDD > EF-Pt > AO-BDD. The ketoprofen concentration decay was well fitted to a pseudo-first order reaction kinetics in all cases. Therefore, the apparent rate constants of the oxidation reaction of ketoprofen by hydroxyl radicals were determined by using the integrated equation of first-order reaction kinetics law. The results displayed in Table 3.1 (obtained from Fig. 3.2) at the same current intensity, confirm that the oxidation ability follows the order: EF-BDD > EF-Pt > AO-BDD (Table 3.1), indicating the BDD anode has a larger oxidizing power than Pt anode in EF process.

Table 3.1. Apparent rate constants of degradation of KP at different current intensities in tap water medium by electrochemical processes.

| mA | EF-Pt | EF-BDD | AO-BDD |
|------|--|--|--|
| 100 | $k_{app} = 0.114$ ($R^2 = 0.993$) | $k_{app} = 0.135$ ($R^2 = 0.998$) | $k_{app} = 0.035$ ($R^2 = 0.984$) |
| 300 | $k_{app} = 0.170$ ($R^2 = 0.997$) | $k_{app} = 0.182$ ($R^2 = 0.995$) | $k_{app} = 0.036$ ($R^2 = 0.995$) |
| 500 | $k_{app} = 0.190$ ($R^2 = 0.996$) | $k_{app} = 0.216$ ($R^2 = 0.998$) | $k_{app} = 0.068$ ($R^2 = 0.96$) |
| 750 | $k_{app} = 0.206$ ($R^2 = 0.988$) | $k_{app} = 0.228$ ($R^2 = 0.994$) | $k_{app} = 0.107$ ($R^2 = 0.987$) |
| 1000 | $k_{app} = 0.266$ ($R^2 = 0.997$) | $k_{app} = 0.284$ ($R^2 = 0.959$) | $k_{app} = 0.153$ ($R^2 = 0.998$) |
| 2000 | $k_{app} = 0.338$ ($R^2 = 0.995$) | $k_{app} = 0.381$ ($R^2 = 0.971$) | $k_{app} = 0.214$ ($R^2 = 0.984$) |

3.3.1.3 Effect of pH and introduced air on the AO process

The pH of the solution is well known to influence the rate of Fenton and electro-Fenton process [17, 32]. In contrast, there are inconsistent values reported in the literature for AO process [38-40]. Therefore, the effect of pH on the treatment of ketoprofen still needed to be examined. For this, AO treatments of 250 mL 0.198 mM

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ketoprofen solution (corresponding to 38.4 mg L^{-1} TOC) was carried out at 300 mA, and at pH values of 3.0, 7.5 (natural pH) and 10.0. Results indicated that the solution pH influenced significantly the ketoprofen degradation in AO process. Figure 3.3a shows the faster decrease of ketoprofen concentration at pH 3.0, followed by pH 7.5 (without adjustment), which was slightly better than pH 10. Compared to the literature [38-40], one can conclude that the optimized pH value in of AO treatment depends on the nature of pollutant under study.

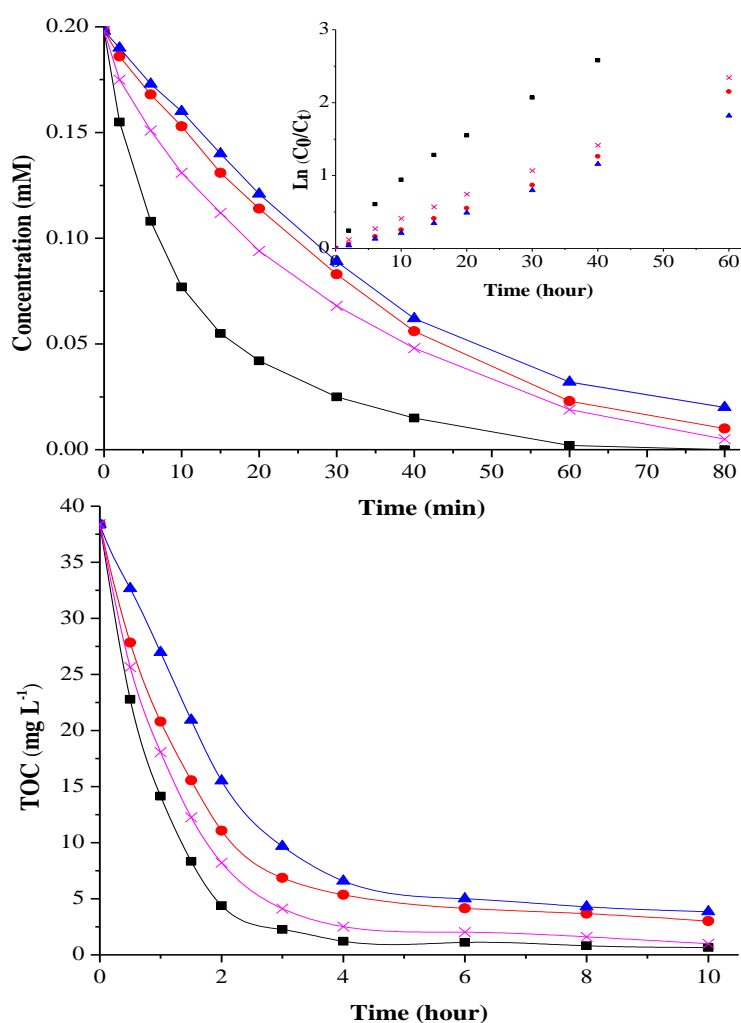


Fig. 3.3. Effect of pH and air bubbling on the degradation kinetics and mineralization degree of ketoprofen in tap water medium by AO at 300 mA: pH = 7.5 (●); pH = 3 without introduced air (×); pH = 10 (▲); pH = 3 (■); C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L.

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Experiments regarding the effect of introduced compressed air on the removal of ketoprofen in AO process at pH of 3 were then performed. Results obtained were expressed in TOC removal terms and show that continuous air input significantly influenced the mineralization degree of ketoprofen. The mineralization rate was much better at pH 3 with continuous air bubbling through the solution than that at pH 3 without air input, followed by the values obtained at pH 7 and 10 (Fig. 3b). TOC removal was fast at beginning 4 h, which reached 96.9% (pH 3.0 with air bubbling), 93.4% (pH 3.0 without air bubbling), 86.1% (pH 7.5) and 82.8% (pH 10.0), respectively, being then slower on longer treatment times, due to the formation of recalcitrant end products such as carboxylic acids [41, 42]. This results show that O₂ play a significant role in the oxidation mechanism.

3.3.2 Kinetic study of ketoprofen degradation

The absolute (second order) rate constant (k_{KP}) of the reaction between ketoprofen and $\bullet\text{OH}$ was determined by the competition kinetics method selecting *p*-hydroxybenzoic acid (*p*-HBA) as standard competitor [43], since its absolute rate constant is well established as $k_{p\text{-HBA}}$: $2.19 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [44]. The electro-Fenton treatment was performed with both compounds in equal molar concentration (0.2 mM) and under the same operating conditions ($I = 100 \text{ mA}$, $[\text{Fe}^{2+}] = 0.1 \text{ mM}$, $\text{Na}_2\text{SO}_4 = 100 \text{ mM}$, $\text{pH} = 3.0$, $V = 250 \text{ mL}$). To avoid the influence of their intermediates produced during the process, the kinetic analysis was performed at the early time of the degradation.

During the treatment, hydroxyl radicals concentration is considered as practically constant due to its high destruction rate and very short life time, which can not accumulate itself in the reaction solution [20]. The absolute rate constant for the k_{KP} was then calculated following the Eq. (3.10) [43, 45].

$$\frac{k_{KP}}{k_{p\text{-HBA}}} = \ln \frac{[\text{KP}]_0}{[\text{KP}]_t} / \ln \frac{[p\text{-HBA}]_0}{[p\text{-HBA}]_t} \quad (3.10)$$

where the subscripts 0 and t are the reagent concentrations at time $t = 0$ (initial concentration) and at any time t of the reaction.

$\ln ([\text{KP}]_0/[\text{KP}]_t)$ and $\ln ([p\text{-HBA}]_0/[p\text{-HBA}]_t)$ provides a linear relationship, then the absolute rate constant of oxidation of ketoprofen with $\bullet\text{OH}$ can be calculated from the slope of the integrated kinetic equation, which was well fitting ($R^2 = 0.999$). The

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value of k_{KP} was then determined as $5.4 (\pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$. This value is lower than that reported by Real and al. [46] ($8.4 (\pm 0.3) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$), obtained during photo-Fenton treatment of ketoprofen. We did not find any other data in the literature for comparison.

3.3.3 Effect of current intensity on the mineralization of ketoprofen aqueous solutions

The mineralization degree is considered as an indicator of the efficiency of the treatment by AOPs. To investigate the effects of applied current intensity on the mineralization degree of ketoprofen aqueous solution, several experiments were performed in similar experimental condition. The EF and AO treatments of 250 mL, 0.198 mM ketoprofen solution (corresponding to 38.4 mg L^{-1} TOC) with 0.1 mM Fe^{2+} at pH 3.0 were comparatively tested for the different systems to clarify their relative mineralization power. A range of current intensity 100 mA - 2000 mA was investigated.

A progressive mineralization of the drug solution with prolonging electrolysis time to 360 min was found in all cases, while the solution pH decayed up to 2.7 - 2.8 owing to the production of acidic by-products (see Fig. 3.6).

Figure 3.4a shows that, EF-Pt reached 91% TOC removal at 300 mA and 94% at 2000 mA, while EF-BDD reached 97% TOC removal at 300 mA and almost 100% TOC removal at 2000 mA at the end of electrolysis. The great mineralization power of EF-BDD is related to the production of supplementary, highly reactive BDD($\bullet\text{OH}$) on the cathode compared to Pt anode. In contrast, AO-BDD reached 89% and 95% TOC removal at 300 and 2000 mA at the end of electrolysis. Higher mineralization degrees obtained by EF process can be explained by the quicker destruction of ketoprofen and by-products with homogeneous $\bullet\text{OH}$ generated from Fenton's reaction (Eq. (3.3)). The oxidation reaction takes place in the mass of hole volume of the solution, while in AO, oxidation rate of ketoprofen is depended to the transfer rate to the anode. After 2 hours of treatment, the percentage of TOC removal rised from 79% to 96% for EF-Pt, from 94% to 99% for EF-BDD and from 71% to 93% for AO process at 300 and 2000 mA applied currents, respectively, due to higher amount of $\bullet\text{OH}$ produced with higher applied current. These results confirm again the order of mineralization power in the sequence $\text{AO-BDD} < \text{EF-Pt} < \text{EF-BDD}$.

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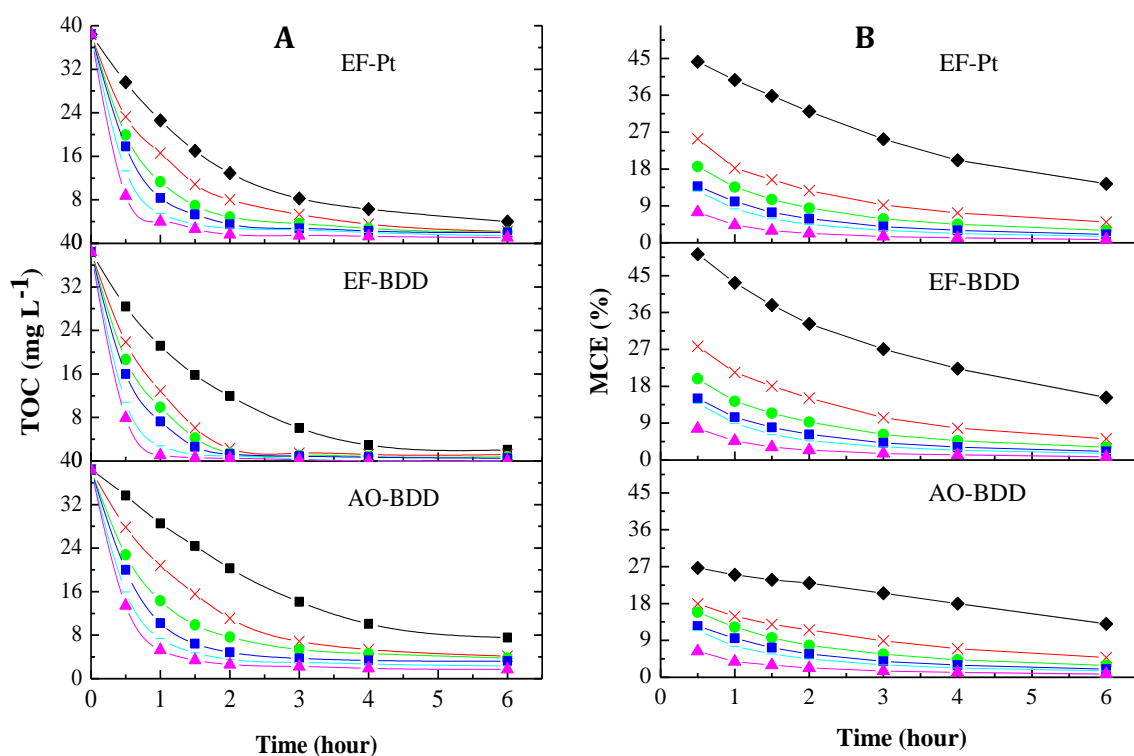


Fig. 3.4. Effect of applied current on the mineralization efficiency (in terms of TOC removal) (a), and MCE (b) during treatment of 0.198 mM ketoprofen in tap water medium by EAOPs: 100 mA (◆); 300 mA (×); 500 mA (●); 750 mA (■); 1000 mA (▬); 2000 mA (▲). [Na₂SO₄]: 50 mM; V: 0.25 L. EF: [Fe²⁺]: 0.1 mM; pH: 3.0. AO: pH 7.5.

The evolution of the mineralization current efficiency (MCE) with electrolysis was shown on Fig. 3.4b. Highest MCE values were obtained at lowest current density in different cell configuration, as MCE decreased with current intensity increased. Similarly, the MCE of EF was better than AO, and that of EF-BDD were better than EF-Pt. There was an obvious difference on MCE between current density of 100 and 300 mA, while not too much from 300 to 2000 mA. In all the case, the MCE < 51% was obtained, and decreased gradually along the electrolysis time. The progressive decrease in MCE on longer treatment time can be explained by the low organic concentration, the formation product more difficult to oxidize (like carboxylic acids) and enhancement of parasitic reactions [17, 34, 47].

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3.3.4 Formation and evolution of aromatic and aliphatic by-products

The identification of the reaction intermediates from oxidation of ketoprofen was performed at a lower current intensity of 60 mA, which allowed accumulation of formed intermediates and their easy identification. Figure 5 shows that the aromatic intermediates were formed at the early stage of the electrolysis in concomitance with the disappearance of the parent molecule.

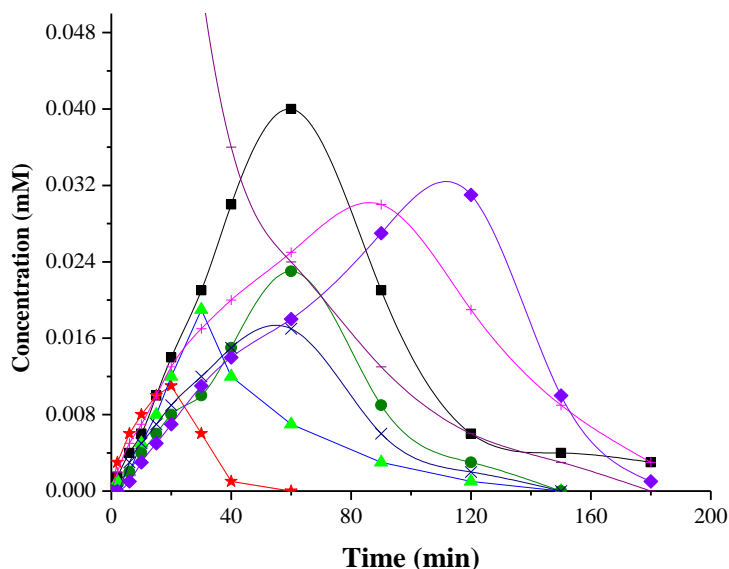


Fig. 3.5. Time course of the concentration of the main intermediates accumulated during degradation of ketoprofen in tap water medium with EF-Pt: benzophenone (■); phenol (☆); 3-hydroxybenzoic acid (▲); benzoic acid (+); catechol (●); pyrogallol (×); hydroquinone (◆); ketoprofen (-). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. Electro-Fenton: $[\text{Fe}^{2+}]$: 1 mM; pH: 3.0; current density: 60 mA.

Phenol appeared at early electrolysis time, and its concentration reached a maximum value of 0.011 mM at 20 min, then decreased to non-detected level at 60 min. 3-Hydroxybenzoic acid, pyrogallol and catechol, attained their maximum concentration of 0.019, 0.017, 0.023 mM at 30, 60 and 60 min, respectively, then they are no longer detected after 150 min. Benzophenone, benzoic acid and hydroquinone reached their concentration peaks at 0.021, 0.03 and 0.031 mM at 90, 90 and 120 min, respectively, and still could be detected when ketoprofen was totally degraded (Fig. 3.5). EF-Pt and EF-BDD treatments were performed at current density of 100 mA to monitor the main short chain carboxylic acids formed during electrolysis. Figure 6 displays the formation

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and time-course of short chain-chain carboxylic acids generated during electrolysis. It can be observed that evolution of main carboxylic acids produced by EF-BDD and EF-Pt has similar trends. Glyoxylic and formic acids had a high accumulation and long resistance in EF-Pt treatment, oxalic and acetic acids were persistent during the whole processes, while glycolic acid reached its maximum concentration in 15 min, and then disappeared immediately. Generated C-4 acids like as succinic and malic acids were observed at very low concentration (< 0.005 mM) in EF-BDD, but at relatively high concentration in EF-Pt experiment (malic acid attained its maximum concentration of 0.087 mM). These acids were slowly destroyed in EF-Pt while their destruction was much quicker in EF-BDD.

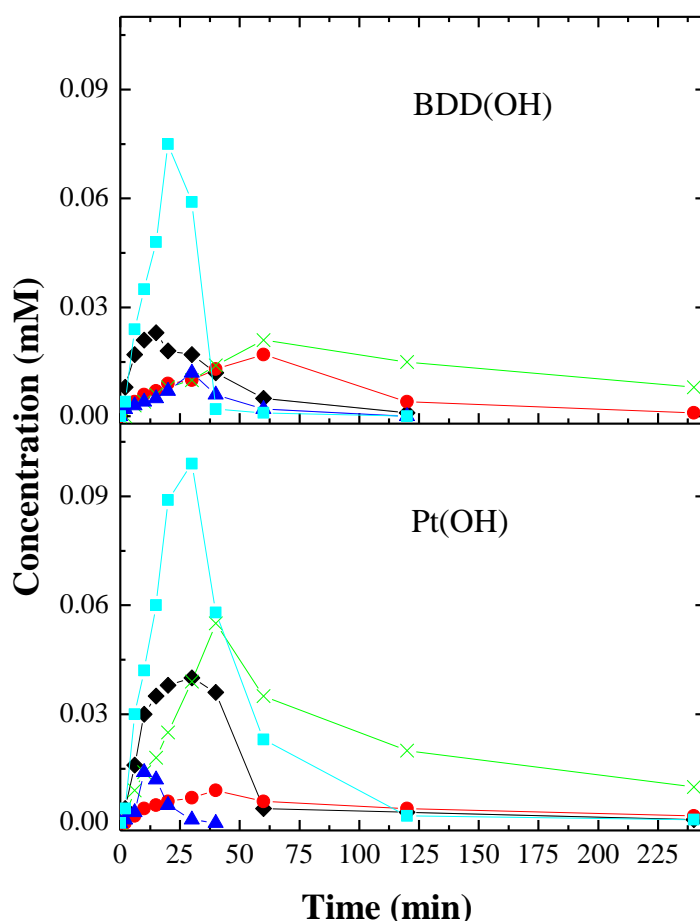


Fig. 3.6. Time course of the concentration of the main carboxylic acid intermediates accumulated during EAOPs treatment at 300 mA of ketoprofen in tap water medium; acetic (●); glyoxylic (■); oxalic (×); formic (◆); glycolic (▲). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. Electro-Fenton: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0.

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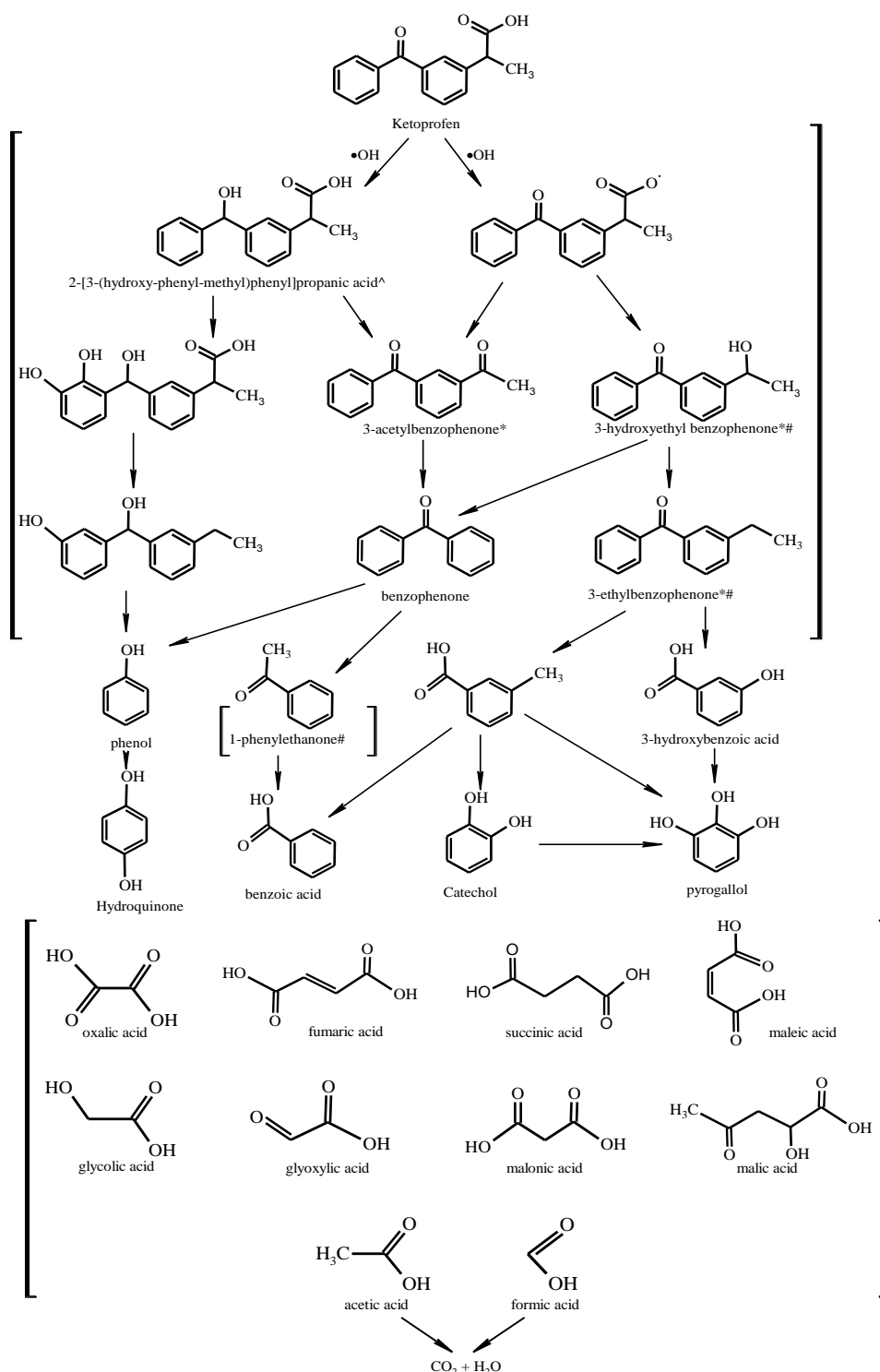


Fig. 3.7. Plausible reaction pathway for mineralization of ketoprofen in aqueous medium by $\bullet\text{OH}$. Product marked * [51], # [53] and ^ [52] are identified and reported already by using other AOPs than EAOPs.

The identification of the degradation by-products allowed us to propose a plausible reaction pathway for mineralization of ketoprofen by $\bullet\text{OH}$ generated from

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EAOPs studied (Fig. 3.7). The reaction could happen by addition of $\bullet\text{OH}$ on the benzoic ring (hydroxylation) or by H atom abstraction reactions from the side chain propionic acid group. The compounds present in [] in the mineralization pathway had been detected as by-products from the literature [48-50]. These intermediates were then oxidized to form polyhydroxylated products that underwent finally oxidative ring opening reactions leading to the formation of aliphatic compounds. Mineralization of short-chain carboxylic acids constituted the last step of the process as showed by TOC removal data (Fig. 3.4).

3.3.5 Toxicity tests

The evolution of toxicity during EF treatment of ketoprofen of the solution at two different current intensities (100 and 300 mA) was investigated over 120 min electrolysis. A 15 min exposure of *Vibrio fischeri* luminescent bacteria to the ketoprofen solutions was monitored by Microtox[®] method (Fig. 3.8). The global toxicity (% luminescence inhibition) was increased quickly at the early treatment time, indicating the formation of intermediates more toxic than ketoprofen. Figure 8 exhibits several peaks due to the degradation primary intermediates and formation to secondary/tertiary intermediates than can be more or less toxic and then previous intermediates. After about 50 min, the samples displayed a lower percentage of bacteria luminescence inhibition compared to the initial condition, which clearly shows the disappearance of toxic intermediate products.

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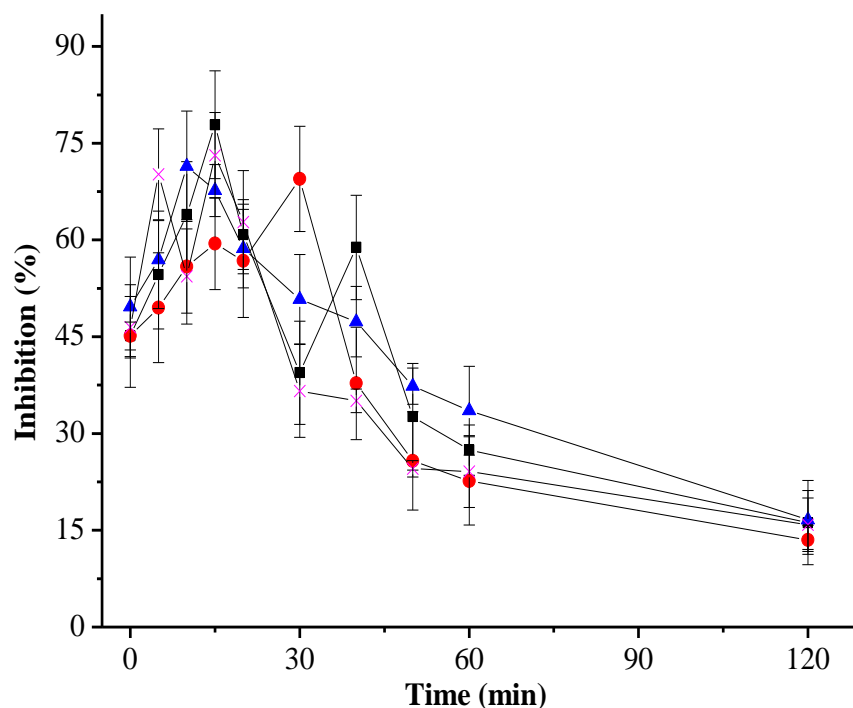


Fig. 3.8. Evolution of the solution toxicity during the treatment of ketoprofen aqueous solution by inhibition of marine bacteria, *Vibrio fisheri* luminescence (Microtox® test) during ECPs of KP in tap water medium: (▲): EF-BDD (100 mA); (×): EF-BDD (300 mA); (■): EF-Pt (100 mA); (●): EF-Pt (300 mA). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. EF: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0.

It was observed no much inhibition difference between treatment by EF-BDD and EF-Pt, while luminescence inhibition lasted longer for smaller current values. The shift of luminescence inhibition peaks with the current intensity was attributed to formation rate of the $\bullet\text{OH}$ in function of current value as explained in § 3.3.1.2. After 120 min treatment, the low % luminescence inhibition is related to formed carboxylic acids which are biodegradable.

3.4 Conclusion

The complete removal of the anti-inflammatory drug ketoprofen from water was studied by electrochemical advanced oxidation EF and AO. The effect of operating conditions on the process efficiency, such as catalyst (Fe^{2+}) concentration, applied current value, nature of anode material, solution pH were studied. While the by-products produced and micro-toxicity of the solution during the mineralization of ketoprofen, have been conducted. From the obtained results, we can conclude that:

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1. The fast degradation rate of ketoprofen by electro-Fenton was displayed at 0.1 mM of Fe^{2+} (catalyst) concentration. Further increase in catalyst concentration results in decrease of oxidation rate due to enhancement of the rate of the wasting reaction between Fe^{2+} and $\cdot\text{OH}$.

2. The oxidation power and the removal ability of ketoprofen was found to be followed the sequence AO-BDD < EF-Pt < EF-BDD, indicating higher oxidation power of BDD anode compared to Pt anode. The similar trend was also observed in the mineralization treatments of ketoprofen aqueous solution.

3. Solution pH and air bubbling through the solution affect greatly the oxidation/mineralization efficiency of the process.

4. The absolute (second order) rate constant of the oxidation reaction of ketoprofen was determined as $(5.4 \pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ by using competition kinetic method.

5. High TOC removal (mineralization degree) values were obtained using high applied current values. A complete mineralization (nearly 100% TOC removal) was obtained at 2 h using EF-BDD at 2 A applied current.

6. The evolution of global toxicity of treated solutions highlighted the formation of more toxic intermediates at early treatment time, while it was removed progressively by the mineralization of aromatic intermediates.

Finally the obtained results show that the EAOPs, in particular electro-Fenton process with BDD anode and carbon felt cathode, are able to achieve a quick elimination of the ketoprofen from water.

Acknowledgements

Ling Feng is a Doctoral research fellow of the Erasmus Mundus Joint Doctorate programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA no. 2010-0009.

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Chapter 4. Research Paper

Electro-Fenton removal of naproxen from aqueous medium: effect of anode material and operating conditions

Chapter 4: Electro-Fenton removal of naproxen from aqueous medium: effect of anode material and operating conditions

Abstract

The removal of non-steroidal anti-inflammatory drug naproxen in tap water by hydroxyl radicals ($\bullet\text{OH}$) formed by electro-Fenton process was conducted either with Pt or BDD anodes and a 3D carbon felt cathode. 0.1 mM ferrous ion was proved to be the optimized dose to reach the best naproxen removal rate in electro-Fenton process. Both degradation and mineralization rate increased with increasing applied current intensity. The degradation of naproxen by $\bullet\text{OH}$ vs. electrolysis time was well fitted to a pseudo-first-order reaction kinetic. An almost complete mineralization was achieved under optimal catalyst concentration and applied current values. Considering efficiency of degradation and mineralization of naproxen, electro-Fenton process with BDD anode exhibited better performance than that of Pt anode. The absolute rate constant of the second order kinetic of the reaction between naproxen and $\bullet\text{OH}$ was evaluated by competition kinetics method and the value $(3.67 \pm 0.3) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$ was obtained. Identification and evolution of the intermediates, as aromatic compounds and carboxylic acids, were deeply investigated, leading to the proposition of oxidation pathway for naproxen. The evolution of the degradation products and solution toxicity were determined by monitoring the luminescence of bacteria *Vibrio fischeri* (Microtox method).

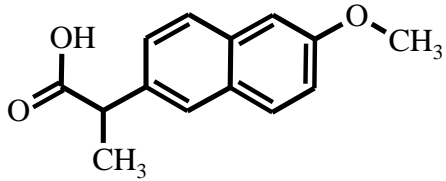
Keywords: Naproxen; Electro-Fenton; BDD Anode; Degradation Pathways; By-products; Toxicity

Chapter 4: Electro-Fenton removal of naproxen from aqueous medium: effect of anode material and operating conditions

4.1 Introduction

It is reported that more than 2000 pharmaceuticals are consumed in the international pharmaceutical market in Europe [1]. Among these pharmaceuticals, non-steroidal anti-inflammatory drugs (NSAIDs) are used by more than 30 million people every day. It was confirmed that 400 tons of aspirin, 240 tons of ibuprofen, 37 tons of naproxen, 22 tons of ketoprofen, 10 tons of diclofenac were consumed in France in 2004 (AFSSAPS 2006). The frequent detection of these compounds in environment [2-4] is due to the continuous input and inefficiency of the wastewater treatment plants. Their potential risks on living organisms in terrestrial and aquatic environments are well documented by literatures and public concern are rising accordingly [5-7].

Table 4.1. Basic physicochemical parameters of naproxen [8, 9].

| Naproxen | Formula: C ₁₄ H ₁₄ O ₃ | Structure |
|--|---|---|
| Mass (g mol ⁻¹): 230.3 | CAS No.: 22204-53-1 |  |
| Log K _{oc} : 2.5 | Log K _{ow} : 3.18 | |
| Solubility (at 20°C): 144 mg·L ⁻¹ | Concentration in WWTPs: < 32 μg L ⁻¹ [10-12] | |

Naproxen, 6-methoxy- α -methyl-2-naphthalene acetic acid, is widely used as human and veterinary medicine [13]. This compound occurs frequently in wastewater treatment plants (WWTPs) effluents (96% of occurrence) and surface water [14-16] (Table 4.1). The detected concentrations are more than 10 times than the threshold value suggested by the European Medicine Agency (EMA) [17]. Chronic toxicity higher than its acute toxicity was also confirmed by bioassay tests [18], which may be due to the stability of the chemical structure (i.e., naphthalene ring) (Table 4.1). Other researchers considered naproxen as micropollutant due to its trace concentration level in bile of wild fish organisms living in lake, which is receiving treated wastewater discharged from municipal wastewater treatment plants [19].

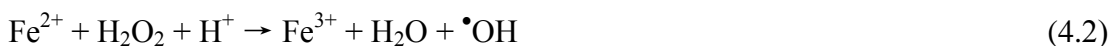
Due to low efficiency of conventional wastewater treatment plants in the elimination of pharmaceuticals [20-22], several recent studies focused on developing more efficient processes for the complete removal of pharmaceuticals present in wastewater after conventional treatments [23-27]. Among these processes, advanced oxidation processes (AOPs) are attracting more and more interests as an effective

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method [28-31], which are mostly used for removing biologically toxic or recalcitrant molecules. Such processes, may involve different oxidant species produced by *in situ* reactions, particularly hydroxyl radicals ($\bullet\text{OH}$ s) and other strong oxidant species (e.g. $\text{O}_2\bullet^-$, $\text{HO}_2\bullet$, and $\text{ROO}\bullet$). Hydroxyl radical ($\bullet\text{OH}$) is a strong oxidizing agent ($E^0 = 2.8$ vs. ENH at pH 0), able to react with a wide range of organic compounds in a non-selective oxidation way, causing the organic pollutant's ring opening, regardless of their concentration [32, 33].

Among AOPs, electrochemical advanced oxidation processes (EAOPs) are being regarded as the most perspective treatments for removing persistent organic micropollutants [11, 12, 34-37]. Generally, EAOPs can be carried out directly (forming of $\bullet\text{OH}$ at the anode) or indirectly (using the Fenton's reagent partially or completely generated from electrode reactions) by electrochemical oxidation through reduction electrochemically monitored Fenton's reaction [38].

Electro-Fenton (EF) treatment [39, 40, 41], is improved from classical Fenton's reagent process, with a mixture of iron salt catalyst (ferrous or ferric ions) and hydrogen peroxide (oxidizing agent), producing hydroxyl radicals in which the reaction is catalysed via a free radical chain. A suitable cathode fed with O_2 or air reduce dioxygen to a superoxide ion ($\text{O}_2\bullet^-$) to generate H_2O_2 continuously. The process can occur in homogeneous or heterogeneous systems and has been known as a powerful process for organic contaminants (Eqs. (4.1)-(4.4)) [42, 43].



On the other hand, supplementary $\bullet\text{OH}$ s can be formed at the anode surface from oxidation of water (Eqs. (4.5) and (4.6)) directly without addition of chemical substances [44].



This extra oxidant production on the anode surface enhances the decontamination

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of organic solutions which possess much greater degradation ability than similar advanced oxidation and Fenton processes alone.

As there is scarce research (except the work done in Ref. [41]) of the elimination on naproxen by EAOPs, this work aims at studying the effect of anode materials on EF removal efficiency of naproxen in tap water. For clearly understanding the efficiency of the electrochemical oxidation set-ups, the influence of experimental variables (such as current density and catalyst concentration) on elimination of naproxen was also investigated. The mineralization of treated solutions, the decay kinetics of naproxen, as well as the generated carboxylic acids were monitored. Based on these by-products, a reaction sequence for naproxen mineralization was proposed. Finally, the evolution of the toxicity of intermediates produced during processes was monitored.

4.2 Materials and methods

4.2.1 Materials

Naproxen powder was purchased from Sigma-Aldrich and used without further purification. Sodium sulfate (Na_2SO_4) was chosen as supporting electrolyte and iron (II) sulfate heptahydrate ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$) as catalyst. *p*-hydroxybenzoic acid (*p*-HBA, $\text{C}_7\text{H}_6\text{O}_3$) was used as competition substrate in kinetic experiment. Aromatic intermediates: 3-hydroxybenzoic acid ($\text{C}_7\text{H}_6\text{O}_3$), 1-naphthalenacetic ($\text{C}_{12}\text{H}_{10}\text{O}_2$), phenol ($\text{C}_6\text{H}_6\text{O}$), 1,5-dihydroxynaphthalene ($\text{C}_{10}\text{H}_8\text{O}_2$), 2-naphthol, catechol ($\text{C}_6\text{H}_6\text{O}_2$), benzoic acid ($\text{C}_7\text{H}_6\text{O}_2$), phthalic acid ($\text{C}_8\text{H}_6\text{O}_4$), pyrogallol ($\text{C}_6\text{H}_6\text{O}_3$), phthalic anhydride, hydroquinone ($\text{C}_6\text{H}_6\text{O}_2$), and carboxylic acids: formic (CH_2O_2), acetic ($\text{C}_2\text{H}_4\text{O}_2$), glycolic ($\text{C}_2\text{H}_4\text{O}_3$), glyoxylic ($\text{C}_2\text{H}_2\text{O}_3$), oxalic ($\text{C}_2\text{H}_2\text{O}_4$), malic ($\text{C}_4\text{H}_6\text{O}_5$) acids, were purchased from Acros Organics in analytical grade. All other products were obtained with purity higher than 99%.

Naproxen solutions were prepared in tap water. The pH of solutions was adjusted using analytical grade sulfuric acid or sodium hydroxide.

4.2.2 Electrolytic systems

Experiments were performed at room temperature ($23 \pm 2^\circ\text{C}$) in an open, cylindrical and one-compartment cell of inner diameter of 7.5 cm, with a working volume of 250 mL. A 3D carbon-felt (18.0 cm \times 6.0 cm \times 0.6 cm, from Carbone-Lorraine, France) was placed beside the inner wall of the cell as working electrode,

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surrounding the counter electrode centered in the cell, either as a 4.5 cm high Pt cylindrical mesh anode or a 24 cm² BDD thin-film anode (double side coated on niobium substrate from CONDIAS, Germany). Compressed air was bubbled through the solution with a flow rate of 1 L min⁻¹. Solution was agitated continuously by a magnetic stirrer (800 rpm) to ensure mass transfer during the whole process. A DC power (HM 8040-3) was used to monitor electrochemical cell and carry out electrolyses at constant current. 0.05 M Na₂SO₄ was induced to the solution as supporting electrolyte. As well known for electro-Fenton process, the best parameter of pH for the medium was adjusted to 3.0 by H₂SO₄ with a CyberScan pH 1500 meter. An adequate dose of FeSO₄ 7H₂O was added into initial solutions as catalyst.

4.2.3 Apparatus and analytical procedures

Naproxen and its aromatic intermediates were monitored by high performance liquid chromatography (HPLC). Mobile phase for analyses was a mixture of 69:29:2 (v/v/v) methanol/water/acetic acids at a flow rate of 0.2 mL min⁻¹. The measurement was carried out by a Purospher RP-18: 5 μm, 25 cm × 3.0 mm (i.d.) column, coupled with an L-2400 UV detector under the optimum setting at 240 nm and 40°C. The identification and quantification of carboxylic acid compounds as end by-products produced during the electrochemical processes were monitored by ion-exclusion HPLC with a Supelcogel H column (4.6 mm × 25 cm). For the detection, the mobile phase solution was 1% H₃PO₄ solution, and UV length was fixed to 210 nm. The by-products were analyzed by comparison of retention time with that of pure standard substances under the same conditions. For the analysis, all the injection volume was 20 μL and measurements were controlled through EZChrom Elite 3.1 software.

The mineralization degree of samples was determined on a Shimadzu VCSH TOC analyser, as the abatement of total organic content. Reproducible TOC values with ±2% accuracy were found using the non-purgeable organic carbon method.

The test of potential toxicity of naproxen and its intermediates was conducted following the international standard process (OIN 11348-3), by the inhibition of the luminescence (%) of bioluminescent marine bacteria *V. fischeri* (Lumistox LCK 487, Hach Lange France SAS) by Microtox[®] method. The value of the inhibition of the luminescence (%) was measured after 15 min of exposition of bacteria to treated solutions at 15°C. The bioluminescence measurements were performed on solutions

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electrolyzed at several constant current intensities ($I = 100, 300$ mA), and on blank ($C_0 = 0$ mg L⁻¹ naproxen).

4.3 Results and discussion

4.3.1 Influence of iron concentration on naproxen electro-Fenton removal

Catalyst concentration is an important parameter in the EF processes which is strongly influencing organic pollutants removal efficiency [43]. The electro-Fenton experiments at a low current intensity (i.e. 100 mA) with Pt/carbon felt cell (EF-Pt) were performed with 45.6 mg L⁻¹ naproxen solution (0.198 mM), in order to determine the optimal catalyst concentrations for naproxen degradation by EF process.

The degradation curves of naproxen by $\bullet\text{OH}$ within electrolysis time followed pseudo-first-order reaction kinetics, whose rate expression can be given by the following [45]:

$$\ln(C_0/C_t) = k_{\text{app}} t \quad (4.7)$$

which k_{app} is apparent (pseudo-first-order) rate constant, and C_0 and C_t are the concentrations of naproxen at the beginning and at the given time t , respectively.

Table 4.2 shows the apparent rate constants (k_{app}) of naproxen at various Fe^{2+} concentrations. The degradation curves (data not shown) were fitting well as showed by the R-squared values above 0.987. The apparent rate constants reported in Table 4.2 shows that ferrous ion concentration significantly influenced the removal rate of naproxen by electro-Fenton treatment. A ferrous ion concentration of 0.1 mM shows the highest k_{app} value followed by that of 0.05 mM and 0.2 mM. However, higher ferrous ion concentrations (i.e. 0.5 mM and 1 mM) displayed lower k_{app} value, which means that the naproxen removal rate decreased with increasing ferrous ion concentration from 0.2 to 1 mM. This is an indication that optimized iron concentration for electro-Fenton on naproxen removal was fluctuating from 0.05 mM to 0.2 mM, while 0.1 mM is the best concentration in our experimental conditions. It can be seen from Eqs. (4.2) and (4.3) that with the increase of ferrous ion concentration, more $\bullet\text{OH}$ and $\text{HO}_2\bullet$ could be produced which enhance the removal rate of naproxen. However, if higher ferrous ion concentration is added, these extra ions will be reacting with $\bullet\text{OH}$ (see Eq. (4.8)), and therefore leads to lower naproxen removal efficiency [46, 47].



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Consequently, an optimal 0.1 mM of ferrous ion concentration has been used for the further experiments.

Table 4.2. Apparent rate constant of naproxen oxidation by $\bullet\text{OH}$ at different concentration of ferrous ion in tap water medium by EF process.

| Fe^{2+} k_{app} & R^2 | 0.05 mM | 0.1 mM | 0.2 mM | 0.5 mM | 1 mM |
|---------------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| $y = a \times x$ | $y = 0.116 \times x$ | $y = 0.135 \times x$ | $y = 0.107 \times x$ | $y = 0.076 \times x$ | $y = 0.074 \times x$ |
| R^2 | 0.991 | 0.998 | 0.989 | 0.987 | 0.992 |
| K_{app} (min^{-1}) | 0.116 | 0.135 | 0.107 | 0.076 | 0.074 |

4.3.2 Kinetics of naproxen degradation and mineralization efficiency

As another important parameter in the EF process (Eq. (4.1), (4.2), (4.4), and (4.5)), the influence of current intensity ranging from 100 to 2000 mA was determined for EF processes with Pt (EF-Pt) or BDD (EF-BDD) anodes versus carbon felt cathode by monitoring the degradation and mineralization of 0.198 mM naproxen (Fig. 4.1.A). The removal rate of naproxen and its mineralization were found increased by increasing applied current value, which resulted from more amount of $\bullet\text{OH}$ generated in the medium by higher current that could accelerate the H_2O_2 formation rate (Eq. (4.1) and (4.5)) and regeneration of Fe^{2+} (Eq. (4.4)) to promote the $\bullet\text{OH}$ generation (Eq. (4.3)).

The degradation of 0.198 mM naproxen was achieved at electrolysis time of 40 and 30 min at 300 mA current intensity, in contrast to 10 and 5 min at 2000 mA current intensity, under EF-Pt and EF-BDD processes, respectively (Fig. 4.1.A). The monitoring of the mineralization process shows that the naproxen mineralization efficiency by EF process rapidly increased with increasing current intensity and then reached a steady state value afterwards (Fig. 4.1.B). The removal percentage is 84.6% and 97.2% at 100 mA, while 92.1% and 96.5% at 2000 mA in 4 and 8 h electrolysis with EF-Pt and EF-BDD processes, respectively.

All the degradation curves of naproxen decreased exponentially in all the current values and it fitted well the pseudo-first-order reaction kinetic (Fig. 4.1.A). The apparent rate constants k_{app} of naproxen oxidation by EF process at current intensity of 300 mA and 1000 mA are presented in Table 4.3. From the results, it is clear that removal of naproxen by EF-BDD process has a higher rate than that of EF-Pt process. The great mineralization power of EF-BDD is related to the production of

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supplementary, highly reactive BDD(\bullet OH) produced at the anode surface compared with Pt anode [48]. The oxidation rate of naproxen at 1000 mA current intensity is almost 3 times higher than that of 300 mA current intensity.

Table 4.3. Apparent rate constants for oxidative degradation of naproxen at 300 mA and 1000 mA current intensity by EF process with BDD or Pt anodes.

| Processes \ Current | 300 mA | 1000 mA |
|---------------------------------|------------------------------------|------------------------------------|
| EF-Pt | $y = 0.147 \times x / R^2 = 0.996$ | $y = 0.451 \times x / R^2 = 0.997$ |
| K_{app} (min^{-1}) | 0.190 | 0.593 |
| EF-BDD | $y = 0.185 \times x / R^2 = 0.981$ | $y = 0.779 \times x / R^2 = 0.999$ |
| K_{app} (min^{-1}) | 0.185 | 0.779 |

On the other hand, the mineralization reaction of naproxen can be written as follows:



The mineralization current efficiency (MCE in %) is an indicator for acknowledgement of the capacity of current intensity application, can be calculated by following formula at a given electrolysis time t (h) as [49]:

$$\text{MCE} = \frac{nFV_s\Delta(\text{TOC})_{\text{exp}}}{4.32 \times 10^7 mIt} \times 100 \quad (4.10)$$

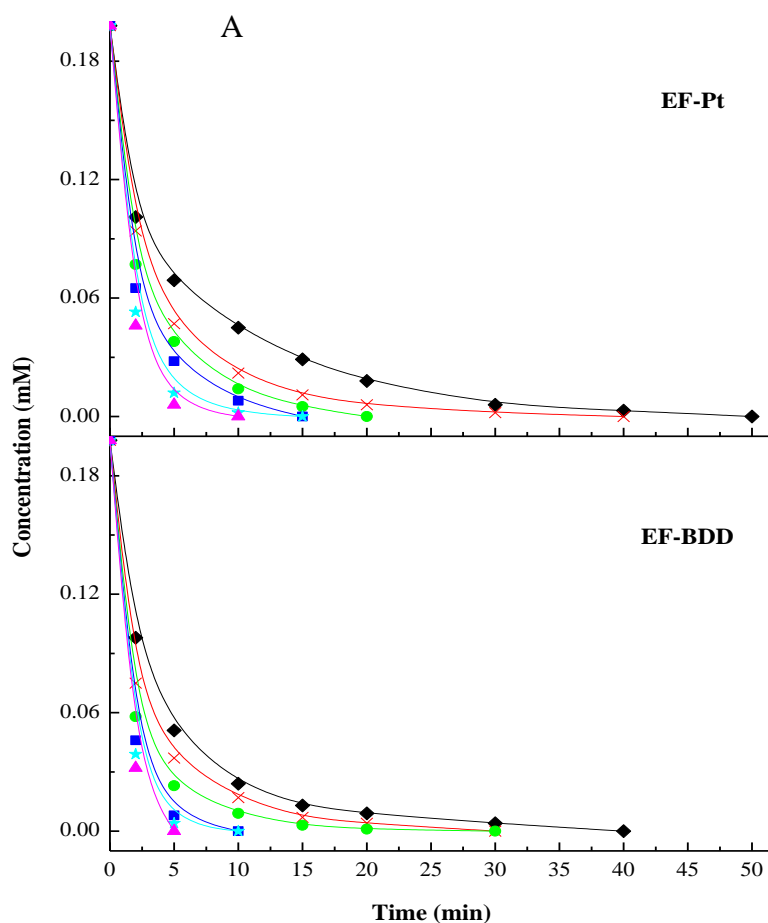
where n is the number of electrons consumed per molecule mineralized (i.e. 64), F is the Faraday constant (96487 C mol^{-1}), V_s is the solution volume (L), $\Delta(\text{TOC})_{\text{exp}}$ is the experimental TOC decay (mg L^{-1}), 4.32×10^7 is a homogenization factor ($3600 \text{ sh}^{-1} \times 12,000 \text{ mg mol}^{-1}$), m is the number of carbon atoms of naproxen (14) and I is the applied current intensity (0.1-2 A).

Figure 4.1.B shows the evolution of MCE curves as function of electrolysis time at different current intensity. It can be seen from this figure that MCE values decreased with increasing current intensity and the lower current intensity achieved the highest MCE value in all EF processes (Fig. 4.1.B). There was an obvious difference on MCE value between current density of 100 and 300 mA. However, no big difference from current density of 300 to 2000 mA was noticed. The lower MCE value of higher current intensity can be the completion between formation of H_2O_2 (Eq. (4.1)) with parasitic

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reaction of the hydrogen gas evolution ($2 \text{H}_2\text{O} + 2 \text{e}^- \rightarrow \text{H}_2 (\text{g}) + 2 \text{OH}^-$) [50]. MCE value got its peak of 28.24% and 42.62% in 1.5 and 1 h electrolysis by EF-Pt and EF-BDD processes. Lower MCE value appeared at the ending electrolysis time indicated that more hardly oxidizable by-products such as short-chain carboxylic acids are formed and accumulated in the electrolyzed solution, as showed later in Fig. 4.2.

The comparison with the different material anodes shows that, EF process with BDD had higher removal ability in degradation, mineralization and MCE than that with Pt, due to more reactive $\cdot\text{OH}$ produced thanks to larger oxidizing power ability [51].



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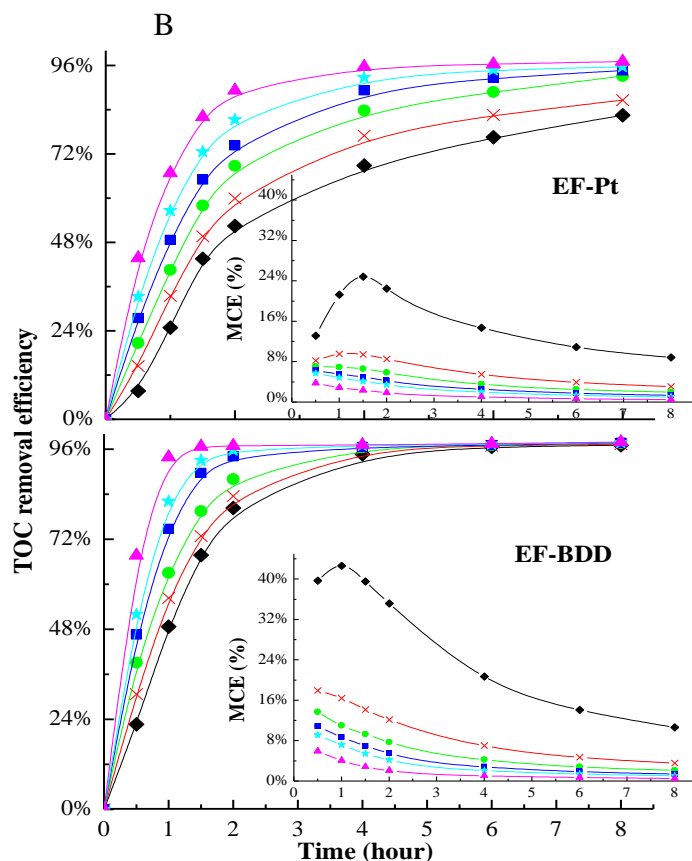


Fig. 4.1. Effect of applied current intensity on degradation (A), mineralization and MCE (%) (B) of naproxen in tap water by electro-Fenton process with Pt or BDD anodes. 100 mA (◆); 300 mA (×); 500 mA (●); 750 mA (■); 1000 mA (★); 2000 mA (▲); $C_0 = 0.198$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; $[\text{Fe}^{2+}] = 0.1$ mM; pH = 3.0.

4.3.3 Kinetic study of naproxen oxidation

The absolute (second order) rate constant (k_{NAP}) of the reaction between naproxen and $\bullet\text{OH}$ was determined by the competition kinetics method selecting p-hydroxybenzoic acid (p-HBA) as standard competitor [52], since its absolute rate constant is well established as $k_{\text{p-HBA}}$: $2.19 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [53]. The electro-Fenton treatment was performed with both compounds in equal molar concentration (0.2 mM) and under the same operating conditions ($I = 100$ mA, $[\text{Fe}^{2+}] = 0.1$ mM, $\text{Na}_2\text{SO}_4 = 50$ mM, pH = 3.0, $V = 250$ mL). To avoid the influence of their intermediates produced during the process, the kinetic analysis was performed at the early time of the oxidation process. During the electrochemical treatment, $\bullet\text{OH}$ cannot accumulate itself in the reaction solution due to its high disappearance rate and very short life time. Therefore the steady state approximation can be applied to its concentration. Taking into account

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this hypothesis, the pseudo-first-order rate law can be applied to naproxen and p-HBA decay [54]. From these pseudo-first-order kinetic law expressions, the following equation can be obtained to calculate the absolute rate constant for oxidation of naproxen by $\bullet\text{OH}$.

$$\frac{k_{\text{NAP}}}{k_{\text{p-HBA}}} = \frac{\text{Ln} \frac{[\text{NAP}]_0}{[\text{NAP}]_t}}{\text{Ln} \frac{[\text{p-HBA}]_0}{[\text{p-HBA}]_t}} \quad (4.11)$$

where the subscripts 0 and t indicate the reagent concentrations at time $t = 0$ (initial concentration) and at any time of the reaction.

$\text{Ln}([\text{NAP}]_0/[\text{NAP}]_t)$ and $\text{Ln}([\text{p-HBA}]_0/[\text{p-HBA}]_t)$ provides a linear relationship, then the absolute rate constant of naproxen oxidation with $\bullet\text{OH}$ can be calculated from the slope of the integrated kinetic equation, which is well fitting ($R^2=0.998$). The value of k_{NAP} was determined as $3.67 (\pm 0.03) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$. This value is lower than the data reported for naproxen oxidation by Fenton's reagent as $9.6 (\pm 0.5) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$ [55], and UV photolysis as $8.61 (\pm 0.002) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$ [56], respectively.

4.3.4 Evolution of the degradation intermediates of naproxen

To investigate the detail of the reaction between naproxen and $\bullet\text{OH}$ by electro-Fenton process, the produced intermediates (i.e. aromatic intermediates and short-chain carboxylic acids) were identified and quantified. The experiments were performed at a lower current intensity of 50 mA with Pt as anode, which allows slow reactions to proceed and ease the monitoring the by-products produced during the degradation.

Figure 4.2.A shows that high molecular weight aromatic intermediates were almost degraded in less than 60 min and lower molecular weight aromatic intermediates such as benzoic acids were removed within 140 min electrolysis time. 5-dihydroxynaphthalene and 2-naphthol were produced firstly, and then disappeared quickly, followed by phenol, 1-naphthalenacetic and 3-hydroxybenzoic acids. The concentration of most of these intermediates was less than 0.017 mM. Other intermediates such as catechol, benzoic acid, phthalic acid, pyrogallol, phthalic anhydride and hydroquinone reach their highest concentration between 20 and 40 min electrolysis time, then decreased gradually within the electrolysis time till 140 min. However, these by-products were all formed in small quantities. All the detected intermediates except benzoic acid were completely removed before the total elimination of naproxen. Considering the fact that persistent intermediates were formed in Fenton-

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based reactions, containing polar functional moieties, such as hydroxyl and carboxyl groups, they are expected to be highly mobile in environmental systems, even if they are of high molecular weight. The low amount of the oxidant, which does not allow complete mineralization, should stimulate oxidation operated under economically and ecologically feasible conditions, aiming at reducing high operating costs.

The concentration of carboxylic acid produced were higher than that of aromatics (Fig. 4.2 B), indicating that short-chain carboxylic acids were quickly transformed from the oxidative breaking of the aryl moiety of aromatic in the electro-Fenton process [45]. Glycolic and malic acids were identified at the beginning electrolysis time and disappeared gradually. Formic acid got to its maximum peak concentration of 0.08 mM after 60 min electrolysis time and then decreased gradually. Glyoxylic acid constantly appeared in the electrolysis time below 0.004 mM. Acetic acid was formed as the largest amount with its highest amount of 0.076 mM formed after 120 min electrolysis time. Oxalic acid gradually increased to its maximum peak concentration of 0.197 mM at 120 min, meaning it can be produced from other carboxylic acids oxidized by $\bullet\text{OH}$ (Fig. 4.2.B). The glyoxylic acid may also come from the oxidation of aryl moieties and then converted to oxalic acid [50]. Oxalic and acetic acids were persistent as the ultimate intermediates during the whole processes.

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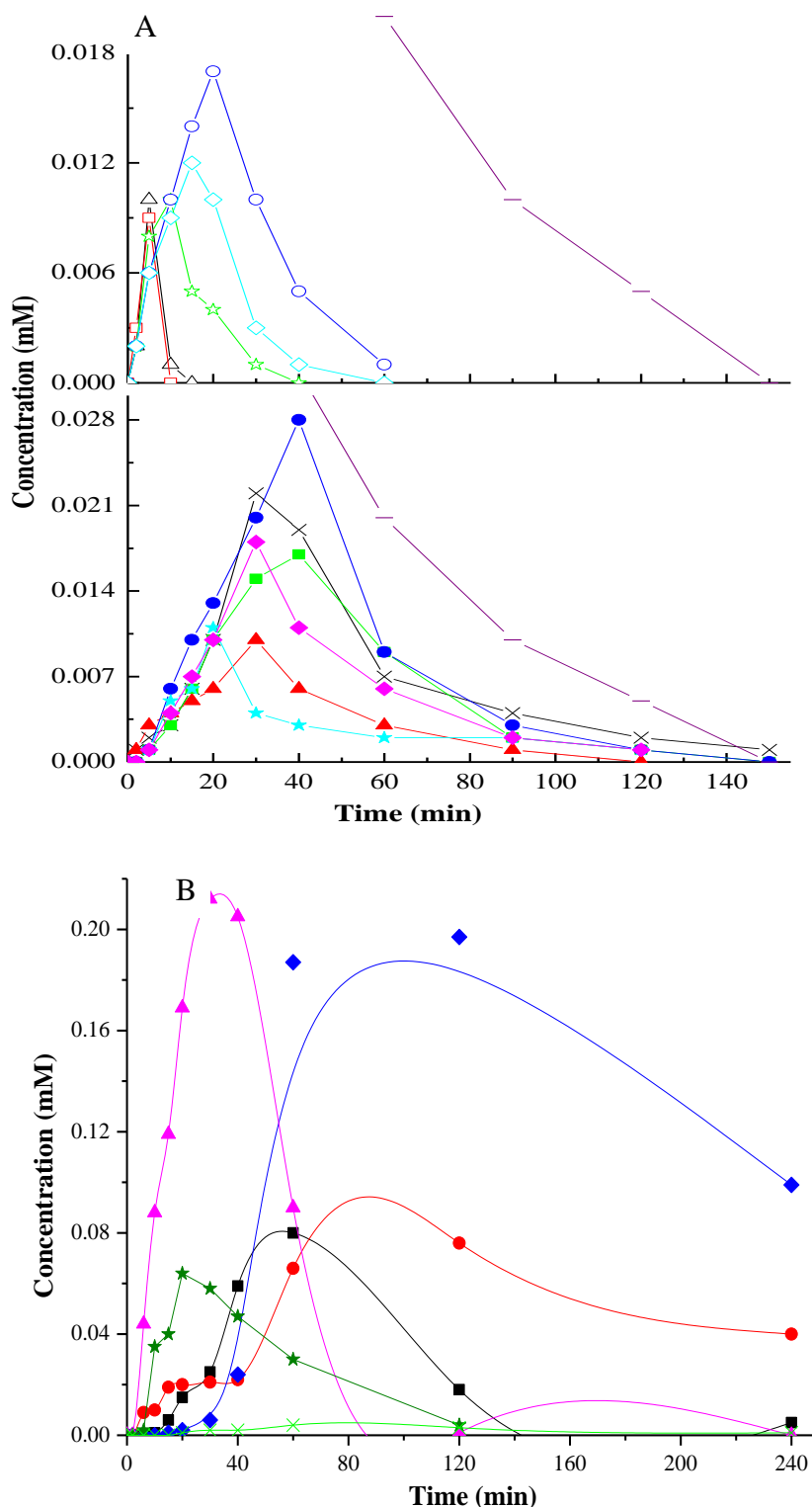


Fig. 4.2. Time course of the concentration of the main intermediates (A) and short chain carboxylic acids (B) accumulated during degradation of naproxen in tap water medium: electro-Fenton process with Pt as anode; A (aromatic derivatives): 3-hydroxybenzoic acid (○); 1-naphthalenetic (◇); phenol (☆); 1,5-dihydroxynaphthalene (△); 2-naphthol (□); catechol (●); benzoic acid (×); phthalic acid (■); pyrogallol (◆);

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phthalic anhydride (▲); hydroquinone (★); naproxen (-); B (carboxylic acids): acetic (●); oxalic (◆); formic (■); glycolic (▲); malic (★); glyoxylic (×) acids; $C_0 = 0.198$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; $[\text{Fe}^{2+}] = 1$ mM; pH = 3.0; current intensity = 50 mA.

4.3.5 Reaction pathway proposed for naproxen mineralized by $\bullet\text{OH}$

From the intermediates (aromatic and carboxylic acids) detected and other intermediates formed upon oxidation of naproxen on related literature published [18, 57], the degradation pathway of naproxen by EF process was proposed in Fig. 4.3. The reaction speculated happen as decarboxylation, yielding carbon dioxide and a benzyl radical, then further produced carboxylate group. Side chain on the C(β)-atom of polycyclic aromatic hydrocarbons was oxidized to form intermediates as numbered 1-4 in figure 4.3, 2-naphthol, 1,5-dihydroxynaphthalene, and 1-naphthalenacetic. In parallel reaction, hydroxylation led to rich hydroxylated polycyclic aromatic hydrocarbons. Further reaction with the cleavage of the aromatic ring in the electron-rich benzene formed hydroxylated benzenes as di/tri-hydroxybenzenes of corresponding as 3-hydroxybenzoic acid, phenol, catechol, benzoic acid, phthalic, pyrogallol, phthalic anhydride and hydroquinone. Finally, these intermediates were mineralized to carbon dioxide by further reactions with $\bullet\text{OH}$, such as acetic, oxalic, formic, glycolic, malic and succinic acids, which originate from the oxidative breaking of the benzenes' moiety of aromatic intermediates. In the end, the ultimate carboxylic acids were oxidized to carbon dioxide and water or oxalic acid and its hardly oxidizable iron complexes.

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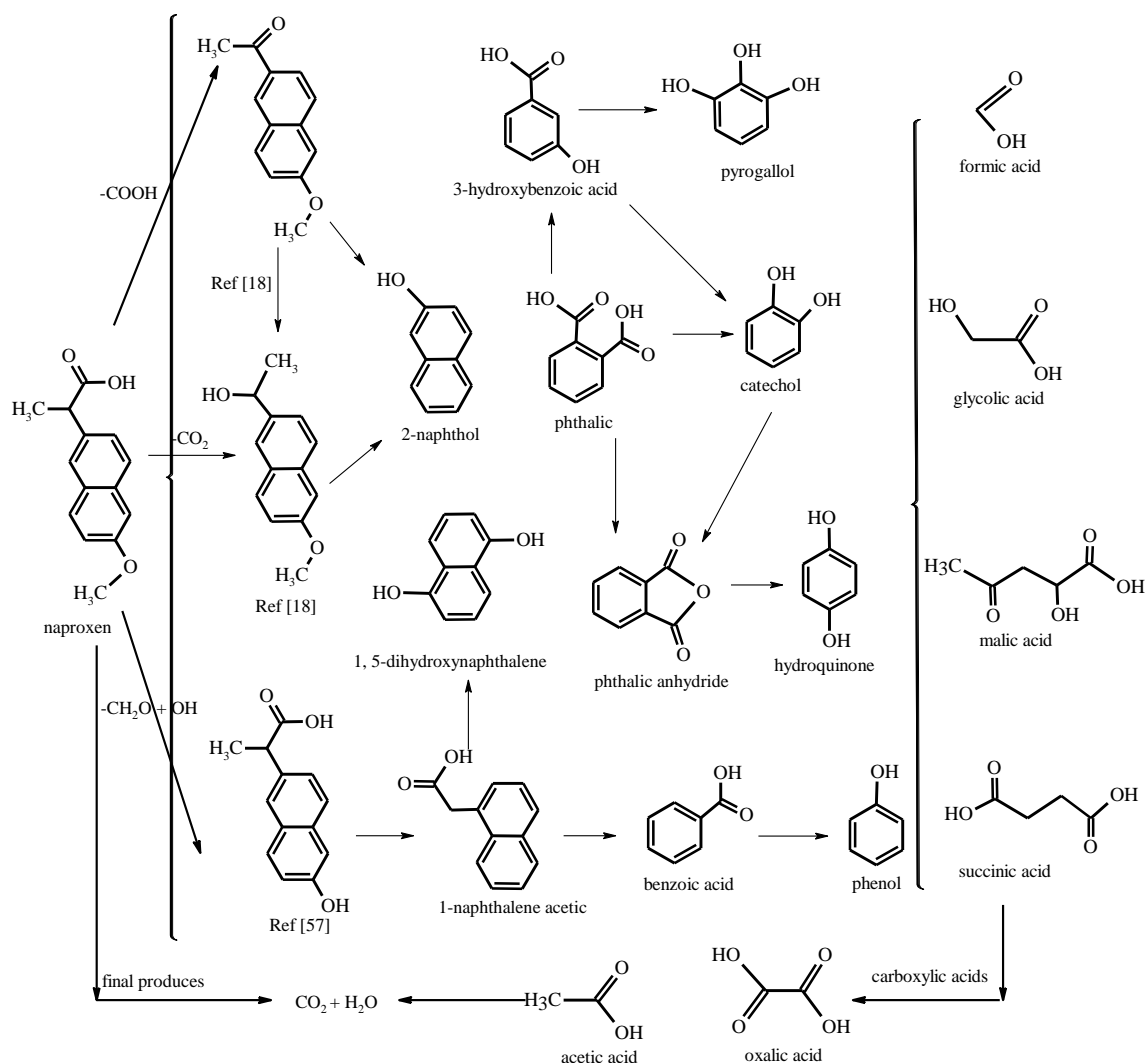


Fig. 4.3. General reaction sequence proposed for the mineralization of naproxen in aqueous medium by $\bullet\text{OH}$ (electro-Fenton with Pt anode). The compounds displayed in the pathway proposed had been detected as by-products from literature [18, 57].

4.3.6 Toxicity analysis

As mentioned earlier in the present paper, the intermediates produced from naproxen could have a higher toxicity than the parent molecule itself [18]. In parallel, it is of importance to understand naproxen's evolution of toxicity since EF processes have showed such high removal efficiency. For this test, the bioluminescence measurements were conducted under standard conditions after 15 min exposure of marine bacteria *V. fischeri* with solutions electrolyzed at two constant current intensities ($I = 100, 300 \text{ mA}$) with BDD and Pt anodes at different time over 120 min electrolysis (Fig. 4.4). The experiments conducted were in triplicate. It can be seen from the curves, that there were significant increase of luminescence inhibition peaks within 10 min of electrolysis time,

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which clearly showed that highly toxic intermediates were produced. After about 20 min treatment, compared to the initial condition, all the samples displayed a lower percentage of bacteria luminescence inhibition, indicating that toxic intermediates were eliminated during the treatment. Afterwards, the curves continuously decreased and there was no much difference between the curves of different anodes application. It may be due to the main products in the medium were short-chain carboxylic acids, as evolution curve of carboxylic acids showed (Fig. 4.2.B).

It was observed that luminescence inhibition was higher at lower current intensity value, compared with the one at higher current intensity value, the reason of which can be attributed to the lower rate of destruction of intermediates at low formation of the $\bullet\text{OH}$.

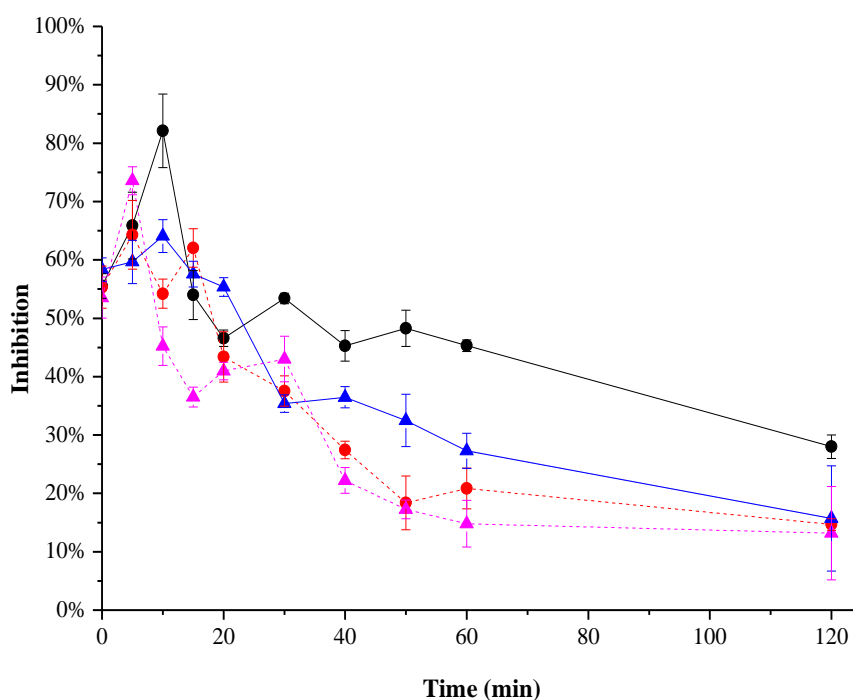


Fig. 4.4. Evolution of the inhibition of *Vibrio fisheri* luminescence (Microtox® test) during electro-Fenton processes; EF- Pt (●); EF-BDD (▲); 100 mA (line); 300 mA (dash line); $C_0 = 0.198$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; $[\text{Fe}^{2+}] = 0.1$ mM; pH = 3.0.

4.3.7 Energy cost

For the consideration of economic aspect of EF treatment, the energy cost for the tests was calculated by the equation (4.12) at 100, 300 and 1000 mA current density [43]:

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$$\text{Energy cost (kWh g}^{-1} \text{ TOC)} = \frac{VIt}{\Delta(\text{TOC})_{\text{exp}} V_s} \quad (4.12)$$

in which, V is the cell voltage, and all other parameters are the same with that of the Eq. (4.10).

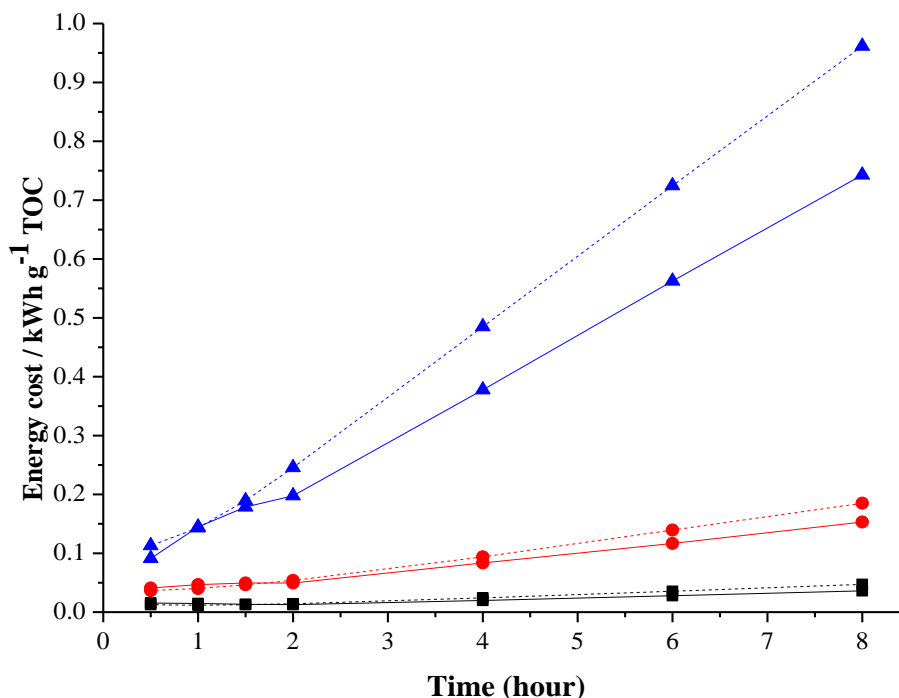


Fig. 4.5. Energy cost of electro-Fenton processes; EF- Pt (line); EF-BDD (dash line); 100 mA (■); 300 mA (●); 1000 mA (▲); $C_0 = 0.198$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; $[\text{Fe}^{2+}] = 0.1$ mM; pH = 3.0.

As expected, the energy cost increases with increasing current density. Application with BDD in EF process has a slightly higher consumption than that with Pt. The values were between 0.012 and 0.036, 0.012 and 0.047 kWh g⁻¹ TOC at 100 mA for EF-Pt and EF-BDD, respectively. However, at 1000 mA, the initial values were 0.09 and 0.11 kWh g⁻¹ TOC at 0.5 hour for EF-Pt and EF-BDD, respectively. It is clear that in the first 2 hours, the energy cost did not increase too much at 300 mA, even with a decrease at 100 mA in both EF processes. The results confirm that the fast mineralization of naproxen and intermediates (Fig. 4.1 B) at the beginning time would enhance the efficiency with a lower energy cost but later, the slower mineralization rate due to the persistent by-products formed during the processes could higher up the energy cost, which decrease cost efficiency of the treatments.

The results obtained as mineralization, evolution of the toxicity and energy cost

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proved that the removal of naproxen solution could be considered operated under lower current density (100 to 300 mA).

4.4 Conclusions

The electro-Fenton removal of naproxen in aqueous solution was carried out at lab-scale. It has been found out that 0.198 mM naproxen could be almost completely eliminated in 30 and 40 min at 300 mA by EF-Pt and EF-BDD processes, respectively. In addition, the TOC removal yield could reach 84.6% and 97.2% at 100 mA after 8 h treatment with EF-Pt and EF-BDD processes, respectively. The optimized ferrous ion concentration was determined as 0.1 mM. A high MCE value was obtained at low current density. The degradation curves of naproxen by hydroxyl radicals within electrolysis time followed pseudo-first-order reaction kinetics and the absolute rate constant of naproxen was determined as $(3.67 \pm 0.3) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$. Electro-Fenton with BDD anode showed higher removal ability than electro-Fenton with Pt anode because of generation of additional $\bullet\text{OH}$ and high oxidation/mineralization power of the former anode. From the intermediates identified during the treatment, a plausible oxidation pathway of naproxen by $\bullet\text{OH}$ was proposed. The formation of short-chain carboxylic acids (that are less reactive toward $\bullet\text{OH}$) produced from the cleavage of the aryl moiety explained the residual TOC remaining at the end of the treatment. From the evolution of toxicity of the treated solution, it can be noticed that some highly toxic products produced at the beginning of the electrolysis disappeared quickly with electrolysis time. It can be concluded that electro-Fenton process could eliminate naproxen rapidly and could be applied as an environmentally friendly technology to efficient elimination of this pharmaceuticals from water.

Acknowledgements

The authors would like to thank the European Commission for providing financial support through the Erasmus Mundus Joint Doctorate Programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA n°2010-0009.

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Chapter 5. Research Paper

Electrochemical oxidation of naproxen in aqueous medium by the application of a boron-doped diamond anode and a carbon felt cathode

Chapter 5: Electrochemical oxidation of naproxen in aqueous medium by the application of a boron-doped diamond anode and a carbon felt cathode

Abstract:

Oxidation of naproxen in aqueous medium by hydroxyl radicals generated in electrochemical advanced oxidation processes was studied. The electro-Fenton process and anodic oxidation process, with carbon felt cathode and boron-doped diamond anode were assessed based on their best naproxen removal efficiency. The electro-Fenton process was proved to be much more effective than anodic oxidation due to the extra hydroxyl radicals produced by Fenton's reaction. The degradation of naproxen followed a pseudo-first-order kinetics. The optimum condition of degradation and mineralization rate for both processes was lower pH and higher current density. The aromatic intermediates and short chain carboxylic acids were identified by using liquid chromatography analyses. The inhibition of luminescence of bacteria *Vibrio fischeri* was monitored to follow the evolution of toxicity of treated aqueous solutions that exhibited a lower inhibition value after treatments.

Keywords: Naproxen; Anodic Oxidation; Electro-Fenton; Boron-Doped Diamond Anode; Toxicity Assessment.

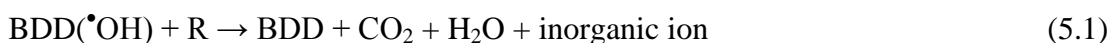
Chapter 5: Electrochemical oxidation of naproxen in aqueous medium by the application of a boron-doped diamond anode and a carbon felt cathode

5.1 Introduction

The electrochemical advanced oxidation processes (EAOPs), such as electro-Fenton (EF) and anodic oxidation (AO), have been gained great interests as outstanding effective technologies to remove toxic and biorefractory micropollutants [1-4]. The oxidation processes mainly depend on the formation of electrogenerated species such as hydroxyl radicals ($\bullet\text{OH}$) to oxidize the organic pollutants till the final products as water and carbon dioxide in a non-selected way [5].

Among the EAOPs, the EF process has been applied for the degradation of pesticides, pharmaceuticals and other pollutants [6-10], which is operated successfully on cathodically electrogenerated H_2O_2 by continuous supply of O_2 gas. The catalyst (i.e. Fe^{2+}) reacts with the H_2O_2 generated in acidic medium to produce $\bullet\text{OH}$ and Fe^{3+} via Fenton's reaction [11, 12]. More interesting, the reaction benefits by less input of catalyst as regeneration of Fe^{2+} from electrochemical reduction at the cathode of Fe^{3+} formed from Fenton's reaction [5]. Cathode materials, as graphite [13], carbon-PTFE O_2 diffusion [14, 15] and three-dimensional carbon felt [16], are proposed as suitable materials for the electrochemical oxidation application. Especially, lower H_2O_2 decomposition, fast O_2 reduction, large surface area, and lower cost make the 3D carbon felt as a favoring cathode in removal of pollutants with H_2O_2 electrogeneration [5, 16, 17].

In the AO process, $\bullet\text{OH}$ is mainly generated at the anode surface from water oxidation, whose production rate is determined by the character of the anode material [18, 19]. On the other hand, the high-efficiency electrodes of metal oxide (PbO_2) and conductive-diamond (boron-doped diamond (BDD)) anodes, with a promotion of higher mineralization rate of organics, have been widely applied to treat persistent pollutants [10, 20, 21]. BDD electrode, with a high O_2 over potential and lower adsorption ability, could generate others reactive oxygen species, as ozone and H_2O_2 [22, 23], is able to allow the total mineralization of organics as:



Naproxen, in the list of popular pharmaceutical consumed, known as non-steroidal anti-inflammatory analgesic drug, which has been used widely higher than several decades of tons per year for nearly 40 years. Due to its desired therapeutic effect, a stable polar structure and adsorption ability make it persistent against the biological

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degradation, which may be responsible for the incomplete removal in the conventional wastewater treatment plants [24]. The frequent detection of naproxen up to $\mu\text{g L}^{-1}$ level in effluent of wastewater confirmed once again the non-complete removal and therefore it is accepted that the pharmaceutical effluents play an important role as pollutant source. The by-products of naproxen degradation in water has been proved as toxicant [25], whereas, higher toxicity than that of naproxen was also confirmed by bioassay test [26]. There is a lack of information of the long-term ingestion of the mixtures of residual pharmaceuticals and other pollutants in aqueous system. As the lower efficiency of the traditional wastewater treatments is responsible for the presence of naproxen in aqueous system, high performance treatments such as EF and AO processes with BDD anode were applied in this study on the removal of naproxen in drinking water.

Therefore, in this work, the elimination of naproxen in drinking water was conducted by the highly efficient EAOPs. The experiments were designed to study the effect of pH, air bubbling condition, and current density on AO and EF processes, in which condition would benefit the higher production of $\bullet\text{OH}$ at carbon felt cathode and BDD anode surface. The aim was to find the optimum values for operating conditions. Monitoring of the by-products formation and evolution of the toxicity during the mineralization for the optimal operating conditions was studied. A detailed study of the oxidation process on naproxen by EAOPs was provided to assess the environmental impact of the treatments.

5.2 Materials and methods

5.2.1 Materials

Naproxen was obtained from Sigma-Aldrich, dissolved at a higher concentration as 45.6 mg L^{-1} (0.198 mM) in 250 mL drinking water without any other purification (45.6 mg L^{-1} , 0.198 mM). Sodium sulfate (anhydrous, 99%, Acros) and iron (II) sulfate heptahydrate (97%, Aldrich) were supplied as background electrolyte and catalyst, respectively. Reagent grade *p*-hydroxybenzoic acid from Acros Organics was used as the competition substrate in kinetic experiments. All other materials were purchased with purity higher than 99%. The initial pH of solutions was adjusted using analytical grade sulfuric acid or sodium hydroxide (Acros).

5.2.2 Procedures and equipment

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The experiments were performed at room temperature in an undivided cylindrical glass cell of 250 mL capacity, equipped with two electrodes. A 3D carbon-felt (18.0 cm × 6.0 cm × 0.6 cm, from Carbone-Lorraine) covering the total internal perimeter, and a 24 cm² BDD thin-film deposited on both sides of a niobium substrate, centered in the electrolytic cell. All the trials were controlled under constant current density by using a DC power supply (HAMEG Instruments, HM 8040-3). 0.05 M Na₂SO₄ was introduced to the cell as supporting electrolyte. Prior to electrolysis, compressed air at about 1 L min⁻¹ was bubbled for 5 min through the solution to saturate the aqueous solution and reaction medium was agitated continuously by a magnetic stirrer (800 rpm) to homogenize the solution and transfer of reagents towards/from electrodes. For the electro-Fenton experiment, the pH of the medium set to 3.0 by using 1.0 M H₂SO₄, and was measured with a CyberScan pH 1500 pH-meter from Eutech Instruments, and an adequate concentration of FeSO₄ 7H₂O was added to initial solutions as catalyst.

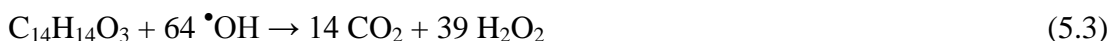
5.2.3 Total organic carbon (TOC)

The mineralization of naproxen solution was measured by the dissolved organic carbon decay, as total organic carbon (TOC). The analysis was determined on a Shimadzu VCSH TOC analyzer. The carrier gas was oxygen with a flow rate of 150 mL min⁻¹. A non-dispersive infrared detector, NDIR, was used in the TOC system. Calibration of the analyzer was attained with potassium hydrogen phthalate (99.5%, Merck) and sodium hydrogen carbonate (99.7%, Riedel-de-Haën) standards for total carbon (TC) and inorganic carbon (IC), respectively. Reproducible TOC values with ±1% accuracy were found using the non-purgeable organic carbon method. From the mineralization data, the Mineralization Current Efficiency (MCE in %) for each test at a given electrolysis time *t* (h) was estimated by using the following equation [27]:

$$\text{MCE} = \frac{n F V_s \Delta(\text{TOC})_{\text{exp}}}{4.32 \times 10^7 m I t} \times 100 \quad (5.2)$$

where *F* is the Faraday constant (96487 C mol⁻¹), *V_s* is the solution volume (L), Δ(TOC)_{exp} is the experimental TOC decay (mg L⁻¹), 4.32 × 10⁷ is a homogenization units (3600 sh⁻¹ × 12,000 mg mol⁻¹), *m* is the number of carbon atoms of naproxen (14, following Eq. (5.3)) and *I* is the applied total current (0.1-1A). *n* is the number of electrons consumed per molecule mineralized as 64, the total mineralization reaction of naproxen as:

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5.2.4 High performance liquid chromatography (HPLC)

The time course of the concentration decay of naproxen and *p*-HBA, as well as that of aromatic by-products, was monitored by reversed phase high performance liquid chromatography (HPLC) using a Merck Lachrom liquid chromatography equipped with a L-2310 pump, fitted with a reversed phase column Purospher RP-18, 5 μm , 25 cm \times 4.6 mm (i.d.) at 40° C and coupled with a L-2400 UV detector selected at optimum wavelengths of 240 nm. Mobile phase was consisted of a 69:29:2 (v/v/v) methanol/water/acetic acid mixtures at a flow rate of 0.2 mL min⁻¹. Carboxylic acid compounds produced during the electrolysis were identified and quantified by ion-exclusion HPLC using a Supelcogel H column (φ = 4.6 mm \times 25 cm), column at room temperature at λ = 210 nm. 1% H₃PO₄ solution at a flow rate of 0.2 mL min⁻¹ was performed as mobile phase solution. The identification and quantification of by-products were achieved by comparison of retention time and UV spectra with that of authentic substances.

In the analysis, all the injection volume was 20 μL and measurements were controlled through EZChrom Elite 3.1 software.

5.2.5 Toxicity test

For testing the potential toxicity of naproxen and of its reaction intermediates, the measurements were carried out with the bioluminescent marine bacteria *Vibrio fischeri* (Lumistox LCK 487), provided by Hach Lange France SAS, by means of the Microtox[®] method, according to the international standard process (OIN 11348-3). The two values of the inhibition of the luminescence (%) were measured after 5 and 15 min of exposition of bacteria to treated solutions at 15°C. The bioluminescence measurements were performed on solutions electrolyzed at constant current intensities of 100 and 300 mA, and on a blank ($C_{0(\text{Nap})} = 0 \text{ mg L}^{-1}$).

5.3 Results and discussion

5.3.1 Optimization of pH and air bubbling for anodic oxidation process by BDD

A series of experiments were performed by oxidizing naproxen (0.198 mM, 45.6 mg L⁻¹) solutions of 50 mM Na₂SO₄ in 250 mL solution. The effect of different pH

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conditions (from 3 to 10) at 300 mA current intensity on naproxen degradation and mineralization was evaluated. According to the degradation curves display on figure 5.1.A, higher naproxen removal rate was obtained at pH 3 than with other pH conditions (i.e. pH 7.5 and 10). However, the naproxen removal rates at pH 7.5 and 10 are close but significantly low compare to that of pH 3. A part from the effect of pH, the influence of air bubbling on the process efficiency was also monitored under the fastest and slowest degradation rate, respectively obtained at pH 3 and 10. Air bubbling flow rate was shown to have a significant impact on naproxen degradation rate at the better pH value of 3 (Fig. 5.1.A).

Figure 5.1.B shows that the mineralization rate has the same degradation features as naproxen at different pH. The quickest TOC removal rate was obtained at pH 3.0, yielding about 96% TOC removal after 4 hours electrolysis. Comparatively, it was only 77%, 68% at pH 7.5 and 10, respectively. TOC removal percentage was 92% and 75% without air bubbling at pH 3 and 10, respectively. The MCE results indicate that better efficiency can be reach in the early stage of electrolysis. Then, the MCE values decrease till to reach similar current efficiencies after about 4 hours treatment time for all experimental conditions.

Low pH favors the degradation and mineralization of naproxen in anodic oxidation process. This can be ascribed to that more H_2O_2 can be produced at cathode surface in acidic contaminated solution [5]:



Moreover, in the alkaline solution, the O_2 gas is reduced to the weaker oxidant as HO_2^- [5]:



Under the same current density application, with the help of production of $\bullet OH$ by anode, the oxidants produced by cathodic process can be highly promoted by adjusting pH in anodic oxidation process.

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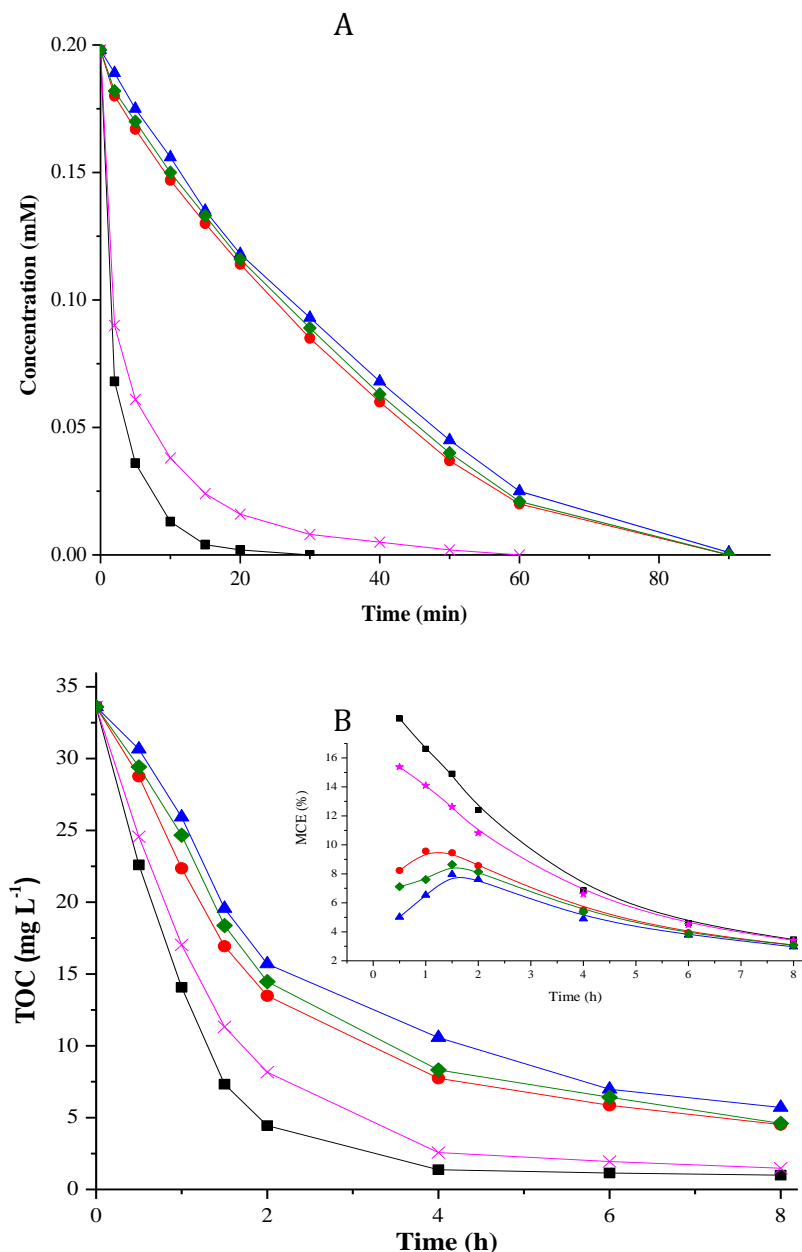


Fig. 5.1. Effect of pH and air bubbling on the degradation kinetics (A) and mineralization degree (B) of naproxen in tap water medium by AO at 300 mA: pH = 3 (■); pH = 3 without air bubbling (×); pH = 7.5 (●); pH = 10 (◆); pH = 10 without air bubbling (▲); dash line: MCE (%). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L.

5.3.2 Influence of current density on EAOPs of naproxen

The current density is an important parameter in EAOPs which could determine the oxidation efficiencies. The effect of current density on EF-BDD and AO-BDD was tested with naproxen (0.198 mM, 45.6 mg L⁻¹) solutions in 50 mM Na₂SO₄. For EF process, the optimum pH was set as 3.0 and catalyst (Fe²⁺) concentration at 0.1 mM (see

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chapter 4). Figure 5.2 shows that TOC removal rate increased with increasing current density for both EF-BDD and AO-BDD. In AO-BDD, this is due to higher amount of BDD(\bullet OH) formed at anode surface from water discharge when higher current density is applied [15]:



EF shows better TOC removal rate compared to AO process. . EF-BDD provided better results than AO-BDD. The TOC abatement of 4 h electrolysis reached to an almost total mineralization, with TOC reduction by 94.6, 96 and 97.3% for EF-BDD, whereas 68.8, 77 and 92.7% for AO-BDD, at 100, 300, and 1000 mA current density, respectively. The MCE curves showed an opposite tendency for TOC decay with current density, decreased as current density increased. Highest value of MCE was achieved as 42.6% and 24.9% for EF-BDD and AO-BDD within 1.5 h treatment at 100 mA current density, respectively. The lower MCE obtained at longer electrolysis time, as result of formation of short chain carboxylic acids (Fig. 5.2), hardly oxidizing by products or complex compounds accumulated in the solutions vs. electrolysis time, which wasted the \bullet OH and BDD(\bullet OH). Meanwhile, under the higher current density, deceleration of mineralization rate could be associated to the wasting reactions by oxidation of BDD(\bullet OH) to BDD and reaction of H_2O_2 giving weaker oxidant [28, 29]:



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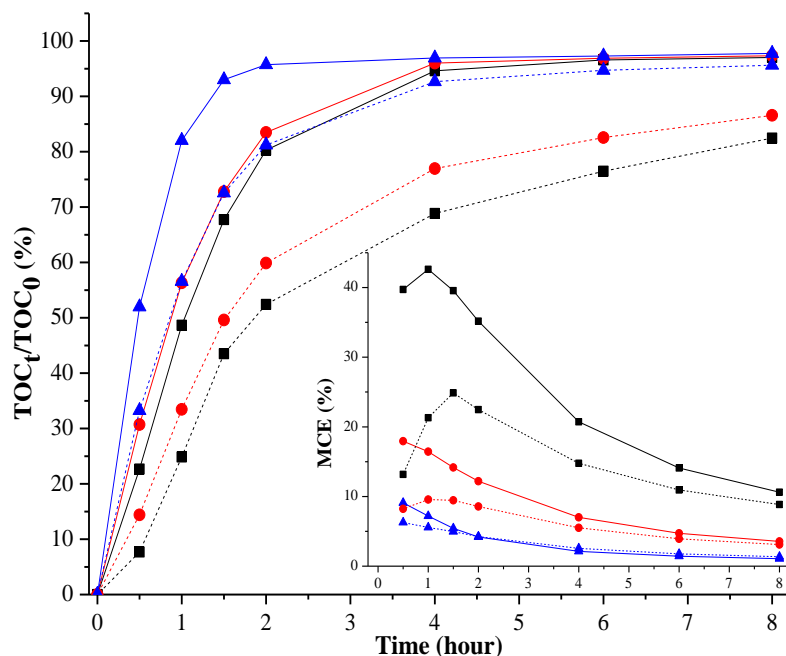


Fig. 5.2. Effect of applied current on the mineralization efficiency (in terms of TOC removal percentage) and MCE during treatment of 0.198 mM naproxen in tap water medium by EAOPs: 100 mA (■); 300 mA (●); 1000 mA (▲); EF-BDD: solid line; AO-BDD: dash line. $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. EF: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0. AO: pH: 7.5.

The degradation of naproxen under the same condition as TOC decay was conducted ranging from 100 to 2000 mA current density. The concentration of naproxen removal curves were well fitted a pseudo-first-order kinetics (k_{app}). The analysis of k_{app} showed in Table 5.1 illustrated an increasing k_{app} values from 100 to 2000 mA current density were obtained from 1.25×10^{-1} to $9.11 \times 10^{-1} \text{ min}^{-1}$ for EF-BDD and from 1.8×10^{-2} to $4.17 \times 10^{-1} \text{ min}^{-1}$ for AO-BDD, respectively. The value of k_{app} at 1000 mA current density of AO-BDD was similar with the one for EF-BDD at 300 mA current density. Meanwhile, the k_{app} of EF-BDD could be about 10 times higher than that of AO-BDD at same current density (100 to 300 mA). The higher k_{app} values were due to more $\bullet\text{OH}$ generated at higher current density at anode surface (Eq (5.6)), and in the bulk, high amount of Fe(II) is regenerated accelerating Fenton's reaction (Eqs. (5.4), (5.9) and (5.10)) [30]:



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Table 5.1. Apparent rate constants of degradation of naproxen at different currents intensities in tap water medium by electrochemical processes.

| mA | EF-BDD | AO-BDD |
|------|--|--|
| 100 | $k_{app} = 1.25 \times 10^{-1}$ ($R^2 = 0.928$) | $k_{app} = 1.8 \times 10^{-2}$ ($R^2 = 0.998$) |
| 300 | $k_{app} = 1.85 \times 10^{-1}$ ($R^2 = 0.981$) | $k_{app} = 2.9 \times 10^{-2}$ ($R^2 = 0.995$) |
| 500 | $k_{app} = 2.46 \times 10^{-1}$ ($R^2 = 0.928$) | $k_{app} = 9.3 \times 10^{-2}$ ($R^2 = 0.98$) |
| 750 | $k_{app} = 6.37 \times 10^{-1}$ ($R^2 = 0.986$) | $k_{app} = 1.31 \times 10^{-1}$ ($R^2 = 0.983$) |
| 1000 | $k_{app} = 7.79 \times 10^{-1}$ ($R^2 = 0.998$) | $k_{app} = 1.86 \times 10^{-1}$ ($R^2 = 0.988$) |
| 2000 | $k_{app} = 9.11 \times 10^{-1}$ ($R^2 = 0.999$) | $k_{app} = 4.17 \times 10^{-1}$ ($R^2 = 0.997$) |

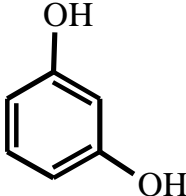
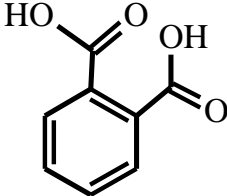

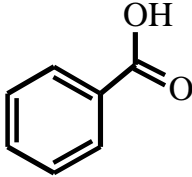
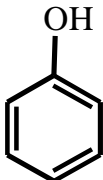
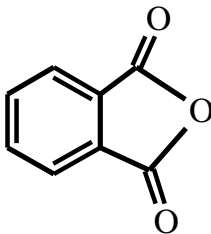
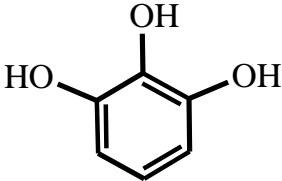
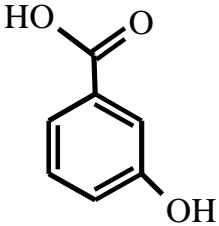
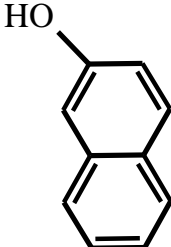
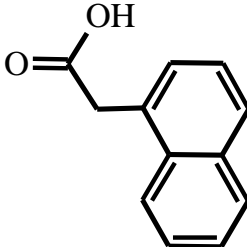
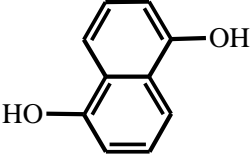
5.3.3 Detection and evolution of by-products of naproxen by EAOPs

The aromatic intermediates of oxidation of naproxen by $\bullet\text{OH}$ were identified by comparison of their retention time (t_R) with that of standards compounds under the same HPLC condition, during experiments performed at a low current density by EF-BDD at 50 mA. The intermediates identified were list in table 5.2. It was expected that the aromatic intermediates were formed at the early stage of the electrolysis in concomitance with the disappearance of the parent molecule. The attack of $\bullet\text{OH}$ on naproxen happened by addition of $\bullet\text{OH}$ on the benzenic ring (hydroxylation) or by H atom abstraction on side chain leading to its oxidation or mineralization (as 2-naphthol, 1,5-dihydroxynaphthalene and 1-naphthalenacetic). These intermediates were then oxidized to form polyhydroxylated products that underwent finally oxidative ring opening reactions (3-hydroxybenzoic acid, phthalic, phthalic anhydride), leading to the formation of catechol, hydroquinone and pyrogallol.

Table 5.2. General by-products of the mineralization of naproxen in aqueous medium by $\bullet\text{OH}$ (electro-Fenton with BDD anode)

| By-products tR (min) | Stucture | By-products tR (min) | Stucture |
|-------------------------|----------|-------------------------|----------|
| | | | |

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| | | | |
|----------------------------------|--|------------------------------|---|
| Catechol 4.2 |  | Phthalic acid 4.7 |  |
| Hydroquinone 5.1 |  | benzoic acid 5.9 |  |
| Phenol 6.4 |  | phthalic anhydride 7.4 |  |
| Pyrogallol 8.1 |  | 3-hydroxybenzoic acid 8.9 |  |
| 2-naphthol 9.8 |  | 1-naphthalenacetic 10.9 |  |
| 1,5-dihydroxynaphthalene 12.1 |  | | |

The short-chain carboxylic acids as the final products of the processes were detected during the mineralization of naproxen by EAOPs. The experiments were operated under the optimum conditions by EF-BDD and AO-BDD at 50 mA to capture the most intermediates. The predominant acids produced in the first stage were glycolic,

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succinic and malic acids, which could be transferred into acetic, oxalic and formic acids. Oxalic and formic acids persisted longer, being ultimate carboxylic acids that are directly converted into CO₂ [31, 32]. Figure 5.3 highlights that in EF, oxalic acid was accumulated up to 0.196 mM at 60 min, further being reduced to 0.039 mM at 360 min, since their Fe(III) complexes are slowly destroyed by BDD([•]OH). The glycolic acid was the most accumulated acid formed in EF reaching the maximum concentration up to 0.208 mM at 30 min, then quickly degraded. Other acids all reached to less than 0.08 mM and gradually disappeared. For AO, Figure 5.3 evidences a slower accumulation of oxalic acid, reaching 0.072 mM at 120 min, and practically disappearing at 480 min as a result of the combined oxidation of Fe(III)-oxalate and Fe(III)-oxamate complexes by BDD([•]OH). Acetic acid was mostly produced in AO, up to 0.108 mM around 60 min, and while others only reached lower to 0.04 mM during the whole process.

A lower acids concentration obtained by AO-BDD than EF-BD, but a higher TOC remaining, as well as later the higher micro-toxicity (mainly due to aromatic intermediates) showed for AO-BDD, indicates slower oxidation of naproxen solution by AO compared with EF process. There is smaller mass balance of the acids with TOC, value at the end of treatment that means there were undetected products formed, which are not removed by [•]OHs.

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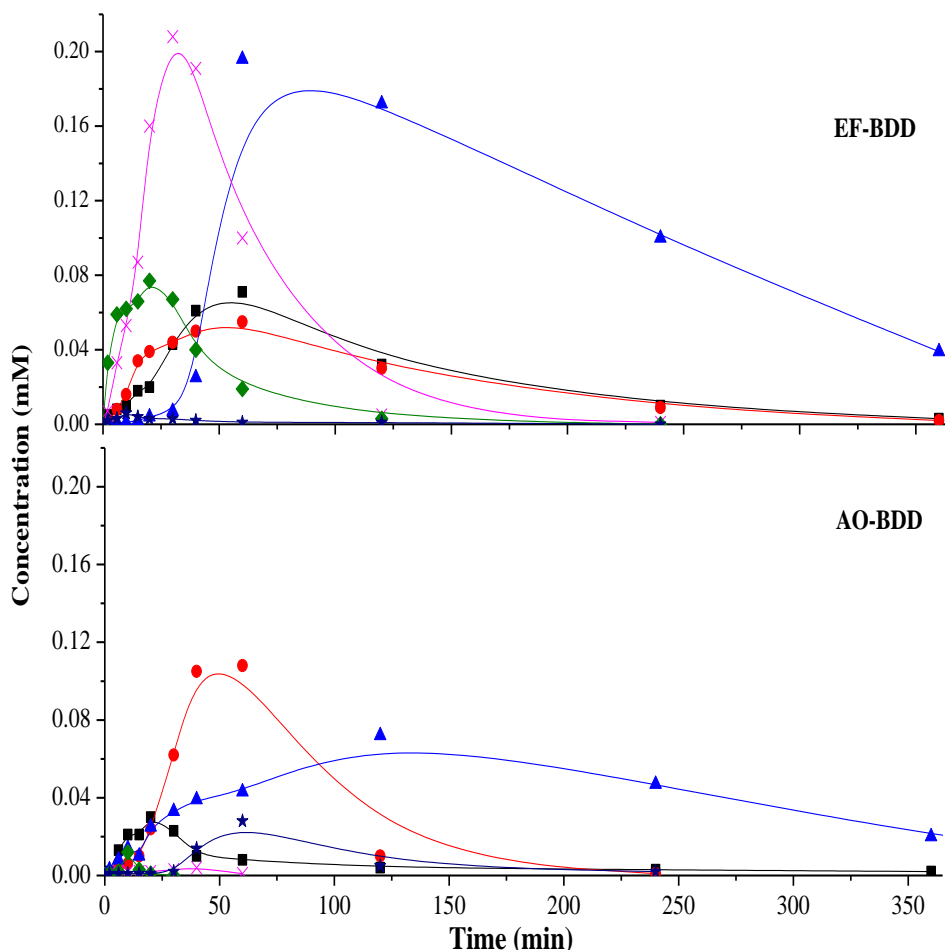


Fig. 5.3. Time course of the concentration of the main carboxylic acid intermediates accumulated during EAOPs treatment of naproxen in tap water medium; acetic (●); oxalic (▲); formic (■); glycolic (x); malic (◆); succinic (☆). Current density: 50 mA; C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. Electro-Fenton: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0; AO: pH: 7.5.

5.3.4 Toxicity test for naproxen under EAOPs treatment

In the last step of the experiments, the evolution of the toxicity of the solution electrolyzed at different constant current intensities ($I = 100, 300 \text{ mA}$) with EF-BDD and AO-BDD, and on a blank ($C_0 = 0 \text{ mg L}^{-1}$) over 120 min electrolysis treatment was studied. The measurements were conducted under standard conditions after 15 min exposure to marine bacteria *V. fischeri*, by the inhibition of the bioluminescence. Figure 5.4 shows that a significant increase of luminescence inhibition percentage (around 20%) occurred within the first 20 min for all the processes, indicating highly toxic intermediates were produced during this electrolysis time. Then, the inhibition curves decreased vs. electrolysis time that means the toxic intermediates were eliminated

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gradually during the treatments. The lower percentage of bacteria luminescence inhibition than the initial condition was achieved in all the samples.

As evolution of toxicity for EF-BDD and AO-BDD showed, lower applied current intensity produced a higher luminescence inhibition, which was attributed to the slower destruction of the naproxen and its oxidation products by smaller $\bullet\text{OH}$ amount produced under lower current density. At the same current intensity, AO treatment exhibits higher inhibition degree, due to the lower oxidation power of AO with the slower degradation of the organic matters in solutions, as indicated by lower TOC abatement. At the later stage, the value of the inhibition was similar for all the process, which related to formed short-chain carboxylic acids which are biodegradable. Isidori et al. [26] obtained similar results showing higher toxic intermediates produced than the naproxen by phototransformation. High efficiency on removal of naproxen and decreased toxicity of the treated naproxen solution make EF processes as a practicable wastewater treatment.

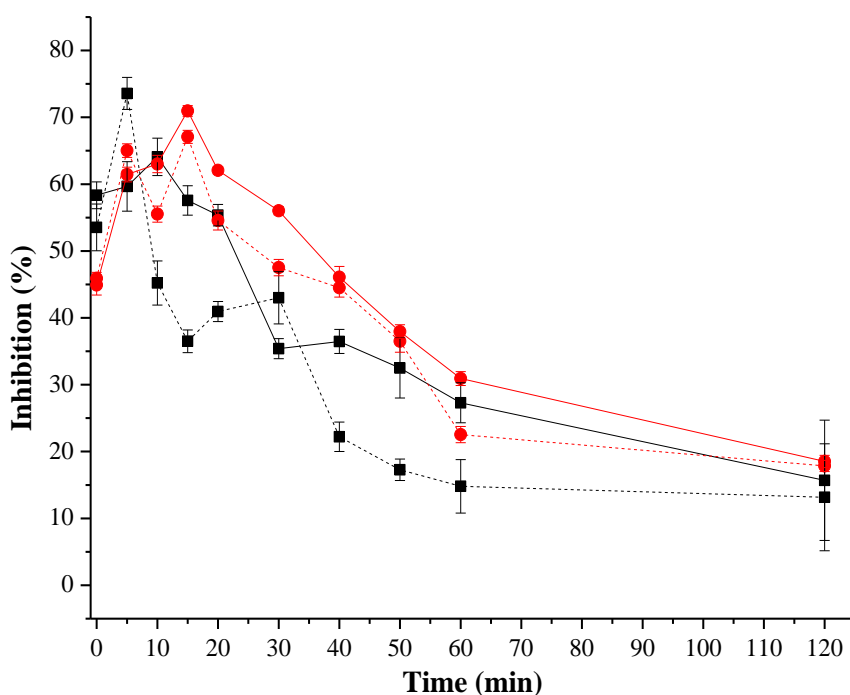


Fig. 5.4. Evolution of the solution toxicity during the treatment of naproxen aqueous solution by inhibition of marine bacteria, *Vibrio fisheri* luminescence (Microtox® test) during EAOPs in tap water medium: (■): EF-BDD (100 mA: line; 300 mA: dash line); (●): AO-BDD (100 mA: line; 300 mA: dash line). C_0 : 0.198 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. EF: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0; AO: pH: 7.5.

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5.4 Conclusion

It can be concluded that the electrochemical oxidation processes with BDD as anode and carbon-felt as cathode could be efficiently applied to remove naproxen in synthetic solution prepared with tap water. Electro-Fenton process showed a higher oxidation power than anodic oxidation process. In both EAOPs, the increasing current density accelerates the degradation and mineralization processes, but with a loss in mineralization current efficiency due to the side reaction and energy loss on the persistent byproducts produced. In both oxidation processes, the lower pH favors higher efficiency. The decay of naproxen followed a pseudo-first-order reaction. The aromatic intermediates were oxidized at the early stage by addition of $\cdot\text{OH}$ on the benzenic ring (hydroxylation) or by H atom abstraction from side chain, leading to increase of the inhibition of the luminescence of bacteria *Vibrio fischeri*. Then, the oxidative cleavage of polyhydroxylated aromatic derivatives conducts to the formation of short chain carboxylic acids (glycolic, malic, succinic, formic, oxalic, and acetic acids), causing the decrease of solution toxicity.

Acknowledgement

The authors would like to thank the European Commission for providing financial support through the Erasmus Mundus Joint Doctorate Programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA n°2010-0009.

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Chapter 6. Research Paper

*Removal of piroxicam from aqueous solution:
comparison of anodic oxidation and electro-Fenton
processes*

Chapter 6: Removal of piroxicam from aqueous solution: comparison of anodic oxidation and electro-Fenton processes performances

Abstract

Anodic oxidation and electro-Fenton processes were applied for the first time to remove piroxicam from tap water. The degradation of piroxicam, mineralization of its aqueous solution and evolution of toxicity during treatment of piroxicam (0.08 mM) aqueous solutions were carried out in an undivided electrochemical cell equipped with a 3D carbon felt cathode. The kinetics for piroxicam decay by hydroxyl radicals followed a pseudo-first-order reaction and its oxidation rate constant increased with increasing current intensity. A total organic carbon abatement could be achieved to 92% for piroxicam by BDD anode at 6 h treatment at 100 mA current intensity, while 76% of TOC abatement was achieved when using Pt anode. Lower mineralization current efficiency was obtained at higher current intensity in all processes. The absolute rate constant of the second order reaction kinetics between piroxicam and $\bullet\text{OH}$ was evaluated by competition kinetic method and its value was determined as $(2.19 \pm 0.01) \times 10^9 \text{ M}^{-1}\cdot\text{s}^{-1}$. Ten short-chain carboxylic acids, identified and quantified by ion-exclusion HPLC, were largely accumulated using Pt but rapidly eliminated under BDD anode, thus explaining the partial mineralization of piroxicam by electro-Fenton with the former anode. The release of inorganic ions such as NO_3^- , NH_4^+ and SO_4^{2-} was measured by ionic chromatography. The evolution of toxicity was monitored by the inhibition of luminescence of bacteria *Vibrio fischeri* by Microtox method during the mineralization, showing a decreasing toxicity of piroxicam solution after treatments. As results showed, electro-Fenton process with BDD anode was found efficient on the elimination of piroxicam as an ecologically optional operation.

Keywords: Piroxicam; Anodic Oxidation; Electro-Fenton; Hydroxy Radical; Toxicity Evolution; Rate Constant; Mineralization.

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6.1 Introduction

In the last decade, the presence of pharmaceutical ingredients in the aquatic environment has become a subject of growing concern worldwide [1-5]. This is mostly due to rather low removal efficiency of the traditional wastewater treatment plants, who plays an important role as releasing sources for pharmaceuticals [6-8]. One of the most consumed medications group corresponds to the pharmaceutical class “Non-Steroidal Anti-Inflammatory Drugs” (NSAIDs) that is considered as a new class of emerging environmental pollutants [9, 10], with a concentration from ng L^{-1} to $\mu\text{g L}^{-1}$ detected in effluents of wastewater treatment plants, surface water, groundwater and drinking water [11-14]. Great concern of their potential toxicological effect on humans and animals has been raised highlighted from the related researches revealed recently [15-17]. More effective technologies are needed in order to prevent significant release of such contaminants into natural environment [18-21].

Piroxicam belongs to the list of NSAIDs popular consumed medicines, and has been used in the management of chronic inflammatory diseases for almost 30 years [22]. It has a low solubility and high permeability in environment, with a reported of LD_{50} for barnacle nauplii of 2.26 mg L^{-1} [23]. The piroxicam concentration detected concentration in wastewater effluent could be in the range of $0.5\text{-}22 \text{ ng L}^{-1}$ [24].

Due to non-satisfaction in the removal of micro-pollutants by conventional biological wastewater treatment processes, advanced oxidation processes (AOPs) have been widely studied for removing biologically toxic or recalcitrant molecules such as aromatics, pesticides, dyes and volatile organic pollutants potentially present in wastewater [25-30]. In these processes, hydroxyl radical ($\bullet\text{OH}$) as main oxidant (known as the second strongest oxidizing agent ($E^0_{(\bullet\text{OH}/\text{H}_2\text{O})} = 2.80 \text{ V/SHE}$)), is generated *in situ* and can effectively reacts with a wide range of organic compounds in a non-selective oxidation way. Thus, electrochemical advanced oxidation processes (EAOPs) are based on the production of this highly oxidizing species from water oxidation on the anode surface (direct oxidation) or via electrochemically monitored Fenton's reaction in the bulk (indirect oxidation), which are regarded as powerful, environmental friendly technologies to remove pollutants at low concentration [31, 32].

Indirect electro-oxidation is achieved by continuous generation of H_2O_2 in the solution by the reduction of O_2 (Eq. (6.1)) at the cathodic compartment of the electrolytic cell.

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In such procedures, mostly used cathodes are carbon-felt (CF), graphite and O₂-diffusion ones [31, 33]. The most prevalent indirect oxidation process is electro-Fenton (EF), with •OH homogeneously produced by the reaction of iron catalyst (Fe²⁺ added initially and regenerated in the system) with the H₂O₂ in an acidic medium (Eq. (6.2)). At the same time, Fe³⁺ can be propagated by the cathodic reduction to Fe²⁺ as Eq. (6.3) showed [34-36] in order to catalyse Fenton's reaction (Eq. (6.2)):



The oxidation rate of pollutant to be treated mainly depends on H₂O₂ formation and iron electrogeneration rates, which could be highly accelerated by the usage of better performance cathode. As known, CF electrode has a large active surface and allows fast reaction of H₂O₂ formation and reduction of Fe³⁺ to Fe²⁺ to guarantee a high proportion of Fe²⁺ in the solution. In an undivided cell, high amount •OH can be formed due to high and quick regenerated Fe²⁺ in the solution that could lead to a nearly total mineralization of the micropollutants [37, 38].

Direct electrochemistry, well known as anodic oxidation (AO), involves the charge transfer at the anode (M) with the formation of adsorbed hydroxyl radical (M(•OH)), which from the oxidation of water [39, 40]. Especially mentioned, BDD, which has high O₂ overvoltage, is able to produce high amount of •OH from reaction (6.4), and shows a high efficiency on degradation of pollutants [41]



The oxidation of pollutants by EF process, not only happens via reaction of homogeneous •OH in the bulk solution but also the heterogeneous of M(•OH) at anode surface. While in an undivided electrochemical cell, other weaker oxidants like hydroperoxyl radical (HO₂•) is formed at the anode [42] contributing to overall oxidation process:



To the best of our knowledge, there is no study related to the removal efficiency of piroxicam from contaminated wastewater. Therefore we report in this study its comparative removal efficiency from water by two EAOPs, namely electro-Fenton (EF)

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and anodic oxidation (AO) processes in tap water for the first time. The optimization of the operating parameters as well as the impact of the electrode materials on piroxicam removal and mineralization efficiency was monitored. Meanwhile, the intermediates produced and their toxicological impacts were investigated during the mineralization procedure.

6.2 Materials and methods

6.2.1. Chemicals

Piroxicam (4-hydroxy-2-methyl-2H-1,2-benzothiazine-1-(N-(2-pyridinyl)carboxamide)-1,1-dioxide) ($C_{15}H_{13}N_3O_4S$, cas number: 9012-00-4), anhydrous sodium sulfate (99%, Na_2SO_4) and acetic acid ($C_2H_4O_2$) were supplied by Sigma-Aldrich. Sulfuric acid (98%, H_2SO_4), iron (II) sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$), *p*-Hydroxybenzoic acid (*p*-HBA, $C_7H_6O_3$), methanol (CH_3OH), carboxylic acids: acetic ($C_2H_4O_2$), glyoxylic ($C_2H_2O_3$), oxalic ($C_2H_2O_4$), formic (CH_2O_2), glycolic ($C_2H_4O_3$) acids, as well as ammonium nitrate, sodium nitrate, nitrite, and sulfate were purchased from Fluka, Merck, and Acros Organics in analytical grade. All other products were obtained with purity higher than 99%.

Piroxicam solution with the concentration of 0.08 mM (max solubility, 26.48 mg L^{-1}) was prepared in tap water, and all other stock solutions were prepared with ultra-pure water obtained from a Millipore Milli-Q-Simplicity 185 system (resistivity > 18 M Ω at 25°C). The pH of solutions was adjusted using analytical grade sulfuric acid or sodium hydroxide (Acros).

6.2.2 Electrolytic systems for the degradation of piroxicam

For all the EAOPs, the electrolysis was performed in an open, undivided and cylindrical electrochemical cell of 250 mL capacity. Two electrodes were used as anode: a 4.5 cm high Pt cylindrical grade or a 24 cm² boron-doped diamond (BDD, thin-film deposited on a niobium substrate (CONDIAS, Germany)). A tri-dimensional, large surface area carbon-felt (18.0 cm × 6.0 cm × 0.6 cm, Carbone-Lorraine, France) electrode was used as cathode.

In all the experiments, the anode was centered in the electrochemical cell and surrounded by the cathode (case of carbon-felt), which covered the inner wall of the cell. H_2O_2 was produced *in situ* from the reduction of dissolved O_2 in the solution. The

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concentration of O_2 in the solution was maintained by continuously bubbling compressed air through a frit at 1 L min^{-1} . A period of 10 min before electrolysis was sufficient to reach a stationary O_2 level. Solutions were vigorously stirred by a magnetic PTFE stirrer during the treatment to ensure the mass transport toward electrodes. All the experiments were conducted at room temperature with $0.05 \text{ M Na}_2\text{SO}_4$ introduced as supporting electrolyte. The current and the amount of charge passed through the solution were measured and displayed continuously throughout electrolysis by using a DC power supply (HAMEG Instruments, HM 8040-3).

Especially, for the EF experiments, pH of 3.0 was considered optimum for the process, which was adjusted by $\text{H}_2\text{SO}_4/\text{HCl}$ (for inorganic detection experiments) with a CyberScan pH 1500 pH-meter from Eutech Instruments, and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ was added to initial solutions as catalyst.

6.2.3 Analytical methods

The mineralization of initial and electrolyzed samples of piroxicam solution was measured by Shimadzu VCSH TOC analyzer in terms of total organic carbon (TOC). Reproducible TOC values with $\pm 2\%$ accuracy were found using the non-purgeable organic carbon method.

Piroxicam and *p*-HBA were determined by reversed-phase high performance liquid chromatography (HPLC, Merck Lachrom liquid chromatography) equipped with a Purospher RP-18: $5 \mu\text{m}$; $25 \text{ cm} \times 3.0 \text{ mm}$ (i.d.). The measurement was made under an optimum wavelength of 240 nm at $40 \text{ }^\circ\text{C}$ with a mobile phase of 40:60 (v/v) KH_2PO_4 (0.1 M)/methanol mixtures at flow rate of 0.6 mL min^{-1} . Under this condition, the corresponding retention time for piroxicam was 5.6 min.

Carboxylic acid compounds generated were identified and quantified by ion-exclusion HPLC with a Supelcogel H column ($9 \mu\text{m}$, $\phi = 4.6 \text{ mm} \times 25 \text{ cm}$ (i.d.)). Mobile phase solution was chosen as 1% H_2SO_4 solution. The condition of the analysis of the equipment was set at a flow rate of 0.2 mL min^{-1} , and under $\lambda = 210 \text{ nm}$ at room temperature.

Inorganic ions produced during the mineralization were determined by ion chromatography-Dionex ICS-1,000 Basic Ion Chromatography System. For the determination of anions/cations (NO_3^- , SO_4^{2-} and NH_4^+), the system was fitted with an IonPac AS4A-SC (anion-exchange) or IonPac CS12A (cation-exchange) column of 25

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cm \times 4 mm (i.d.). For ion detection, measurements were conducted with a 1.8 mM Na₂CO₃ + 1.7 mM NaHCO₃ aqueous solution as mobile phase. The mobile phase was circulated at 2.0 mL min⁻¹ at 35 °C. For cation determination, a 9.0 mM H₂SO₄ solution was applied as mobile phase, circulating at 1.0 mL min⁻¹ at 30 °C. The sensitivity of this detector was improved by electrolyte suppression in using an ASRS-ULTRA II or CRS-ULTRA II self-regenerating suppressor for anions and cations, respectively.

In the analysis, all the injection volume was 20 μ L and measurements were controlled through EZChrom Elite 3.1/Chromleon SE software. The identification and quantification of the intermediates were conducted by comparison of retention time with that of pure standard substances.

The monitoring of toxicity of the piroxicam solution and its electrolyzed intermediates were performed on the samples collected on regular time points during the electrolytic treatments. The measurements were performed under the international standard process (OIN 11348-3), based on the inhibition of luminescence of the bacteria *V. fischeri* (Lumistox LCK 487) after 15 min of exposition to these treated solutions at 15 °C. The measurements were conducted on samples electrolyzed at two constant current intensities ($I = 100$ and 300 mA) as well as on blank ($C_0 = 0$ mM) samples.

6.3. Results and discussion

6.3.1. Kinetic analysis of piroxicam degradation by the electrochemical treatments

The performance of EF process depends on catalyst concentration applied [43]. Therefore, the effect of iron concentration (0.05 to 1 mM) on the degradation kinetics was firstly monitored for electro-Fenton process with BDD anode. The degradation of piroxicam by \bullet OH exhibited an exponential behaviour indicating a pseudo-first-order kinetic equation. The apparent rate constants k_{app} was calculated from the pseudo first-order kinetic model (see from chapter 3.3) and inserted in figure 6.1 in table form. Figure 6.1 shows the degradation rate increasing with Fe²⁺ concentration from 0.05 to 0.2 mM then decreasing with increasing Fe²⁺ concentration from 0.2 to 1 mM. The highest decay kinetic was obtained with 0.2 mM of Fe²⁺ in the electro-Fenton process with $k_{app} = 0.24$ min⁻¹ ($R^2 = 0.994$), while the lowest at 1 mM of Fe²⁺ input with $k_{app} = 0.1$ min⁻¹ ($R^2 = 0.996$). The little difference of k_{app} for 0.05 (0.17 min⁻¹, $R^2 = 0.996$) and 0.1 mM (0.19 min⁻¹, $R^2 = 0.996$) iron concentration was evidenced in this study. As shown, in the electro-Fenton process, there is an optimal iron concentration to reach the

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maximum pollutant removal rate. The lower efficiency obtained with higher concentration of catalyst is ascribed to the enhancement of side $\cdot\text{OH}$ reaction with Fe^{2+} [44].

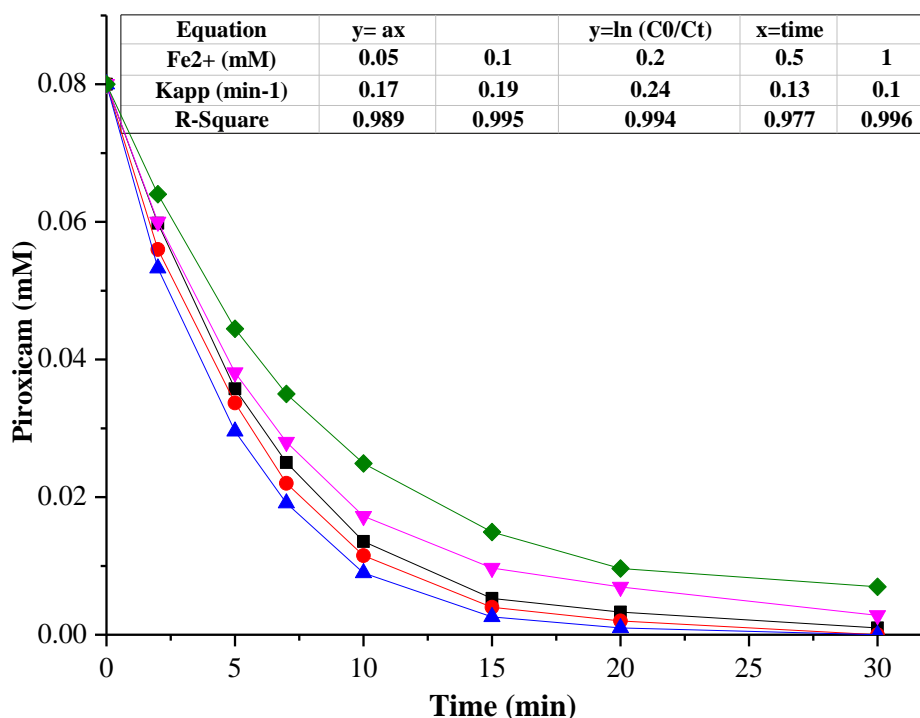


Fig. 6.1. Effect of catalyst (Fe^{2+}) concentration on the degradation and decay kinetics of piroxicam in tap water by electro-Fenton with BDD anode. 0.05 mM (■); 0.1 mM (●); 0.2 mM (▲); 0.5 mM (▼); 1 mM (◆); $C_0 = 0.08$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; current intensity = 100 mA; pH = 3.0.

The influence of pH as another parameter influencing anodic oxidation process was examined. The effect of pH (pH 3.0, 5.5 (natural pH) and 9.0) on the decay kinetics of piroxicam (0.08 mM) was studied at an applied current intensity of 300 mA in 50 mM Na_2SO_4 of 250 mL solution. Results show that pH significantly influenced the decay of piroxicam in AO process (Fig. 6.2). The decay kinetic at pH 3 was more than 5 times comparing of that of pH 9. This is an indication that AO treatment efficiency of pharmaceuticals selected in acidic condition was higher than that of alkaline condition (see chapter 3, 4 and 5). The reason may be more easily oxidizable products are formed during the oxidation in acidic solution, and at the same time, more BDD ($\cdot\text{OH}$) will be produced at low pH [45], and lower adsorption ability of anode in acidic condition [46,

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47]. Since air bubbling endures the O₂ saturation, the effect of introduced air on the decay kinetics of piroxicam degradation by AO was conducted at pH 3 (with the high degradation rate). It shows 20% reduction of decay kinetic rate without continuous air input (Fig. 6.2).

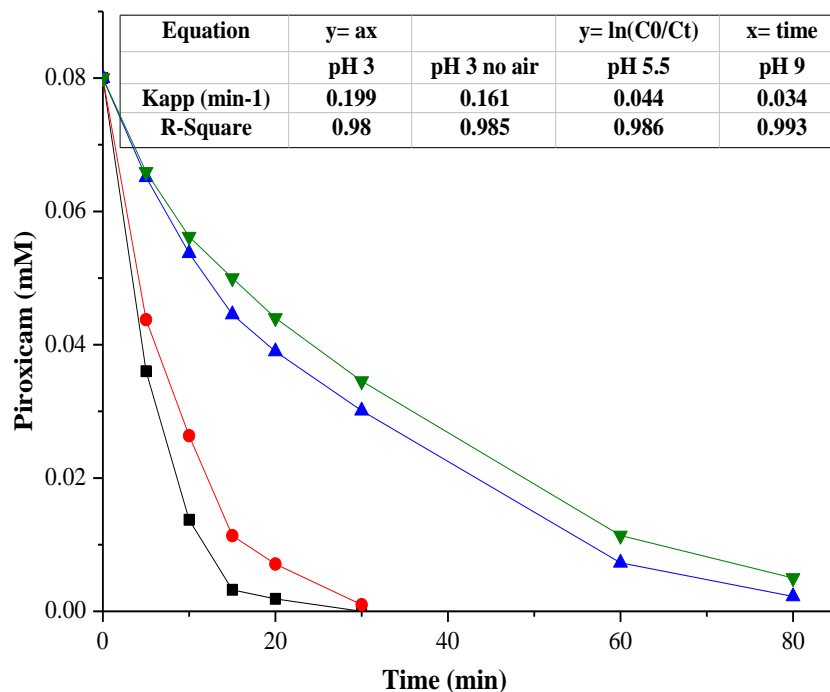


Fig. 6.2. Influence of pH on anodic oxidation processes with BDD anode of piroxicam in tap water. pH 3 (■); pH 3 with no air bubbled (●); pH 5.5 (natural solution value) (▲); pH 9 (▼); C₀ = 0.08 mM; [Na₂SO₄] = 50 mM; V = 0.25 L; current intensity = 100 mA.

For electrode reactions, electrogenerations of oxidants are affected by the current intensity supplied in the cell. Then oxidative degradation of piroxicam (0.08 mM) at different current intensities (ranging from 100 to 1000 mA) was investigated in 50 mM Na₂SO₄ by EF-Pt, EF-BDD and AO-BDD processes. As Figure 6.3 shows, a decreasing concentration of piroxicam was obtained for all the treatments and the apparent rate constants increased with increasing applied current. The time needed to reach a complete piroxicam removal by EF-BDD process was 10 min electrolysis time at 1000 mA, while 20 min were needed for AO-BDD process. As data shows, the removal efficiency of EF process was better than that of AO process. The apparent kinetic constant of EF-BDD at 100 mA was 7 times higher than that of AO-BDD, confirming

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that Fenton's reaction (Eq. (6.2) and (6.3)) highly improved the efficiency of the oxidation processes on piroxicam. The enhancement of oxidation ability with increasing current intensity is due to higher current intensity leading to the higher generation of $\bullet\text{OH}$ in the medium and at the anode surface. Increase of applied current intensity increases H_2O_2 concentration generated (Eq. (6.1)), and accelerate iron regeneration rate (Eq. (6.3)), which also lead to an increasing generation of $\bullet\text{OH}$ (Eq. (6.2)). Comparison of the kinetic constant of EF-BDD and EF-Pt at 100 mA current intensity shows that EF-BDD displays a constant which is more than 2 times than that of the EF-Pt process. The BDD($\bullet\text{OH}$) has a higher oxidative ability than that of Pt($\bullet\text{OH}$) that enhances the oxidation power of the process. As degradation curve shows, above 300 mA current applied in AO, the degradation rate remained constant, which mean there is an optimal current intensity for practical application to save the energy and also avoid adverse effect such as heat on equipment.

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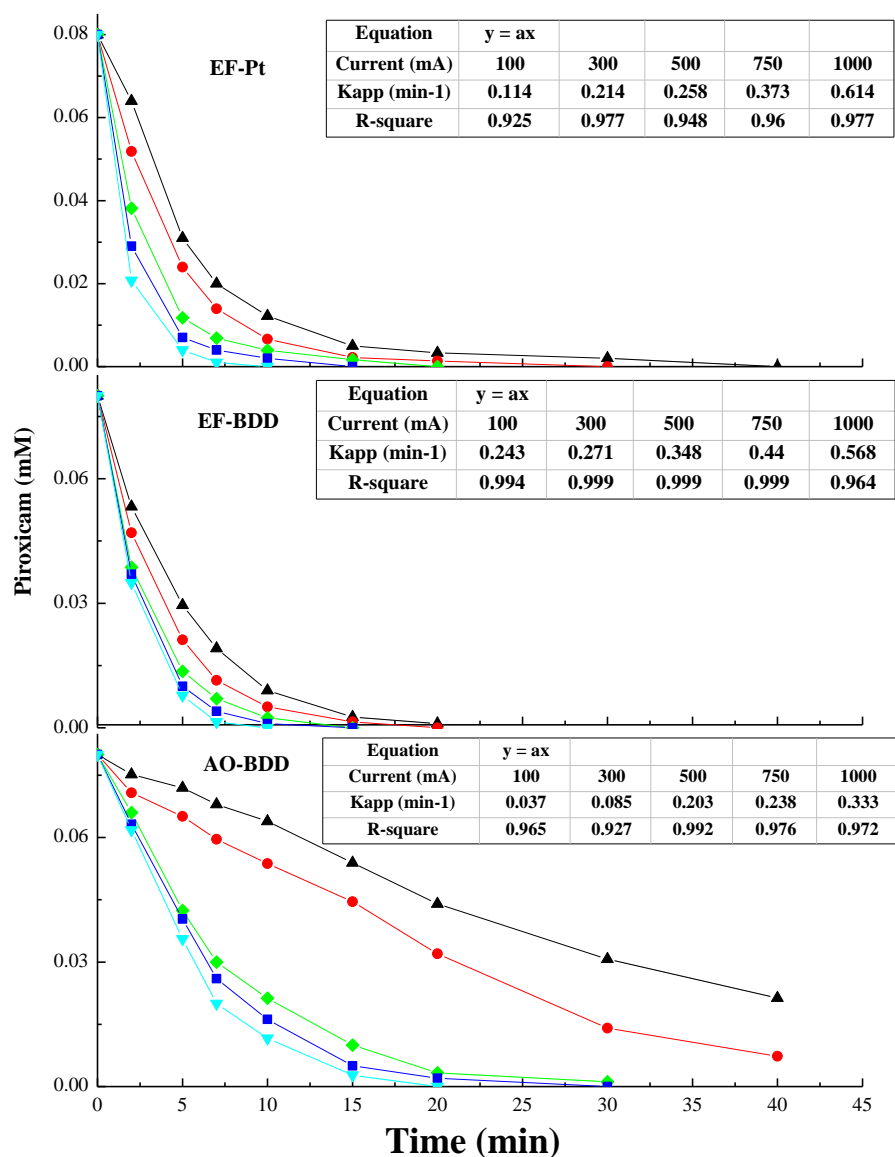


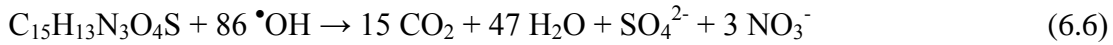
Fig. 6.3. Effect of current intensity on the degradation and decay kinetics for piroxicam in tap water by electro-Fenton/anodic oxidation process. Current intensity varied: 100 (\blacktriangle); 300 (\bullet); 500 (\blacklozenge); 750 (\blacksquare); 1000 (\blacktriangledown); the corresponding kinetic analyses assuming a pseudo-first-order decay for piroxicam in the insert panels. $C_0 = 0.08$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L. For electro-Fenton: pH = 3.0. For anodic oxidation: pH = 5.5.

6.3.2. Effect of operating parameters involved on piroxicam mineralization in electrochemical processes

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In order to investigate the effect of operating parameters on mineralization of electrochemical oxidation processes, similar experiments as degradation of piroxicam were performed by extending electrolysis time up to 360 min in all cases.

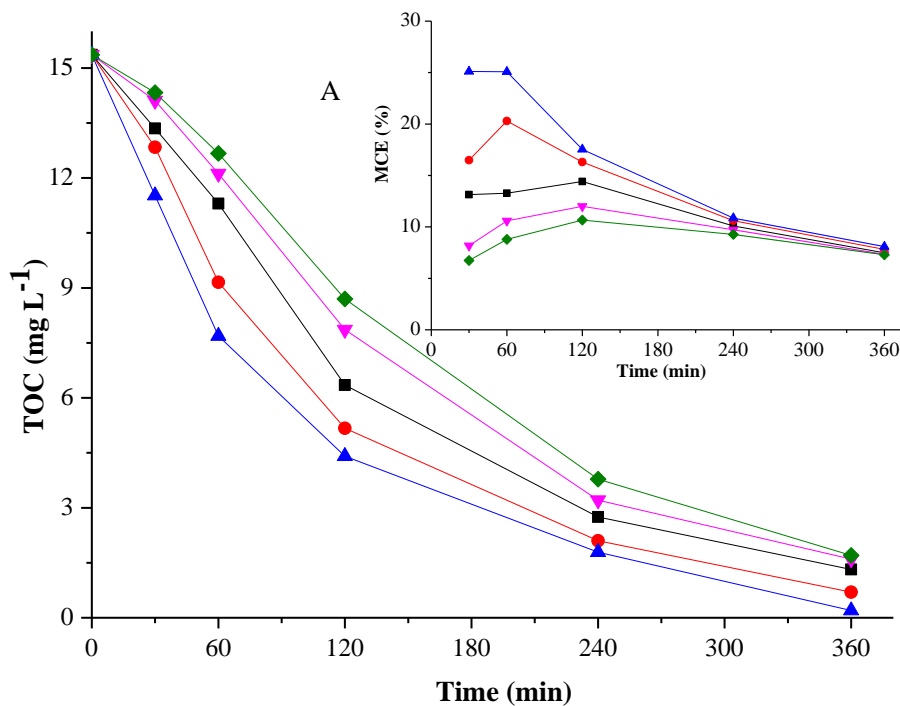
The mineralization reaction of piroxicam by $\bullet\text{OH}$ can be written as follows:



The mineralization current efficiency (MCE in %) at a given electrolysis time t (h) was calculated by the following equation (6.7) [48],

$$\text{MCE} = \frac{nFV_s\Delta(\text{TOC})_{\text{exp}}}{4.32 \times 10^7 \text{mlt}} \times 100 \quad (6.7)$$

where n is the number of electrons consumed per molecule mineralized (i.e. 86), F is the Faraday constant (96487 C mol^{-1}), V_s is the solution volume (L), $\Delta(\text{TOC})_{\text{exp}}$ is the experimental TOC decay (mg L^{-1}), 4.32×10^7 is a homogenization factor ($3600 \text{ sh}^{-1} \times 12,000 \text{ mg mol}^{-1}$), m is the number of carbon atoms of piroxicam (15) and I is the applied total current (0.1-1A).



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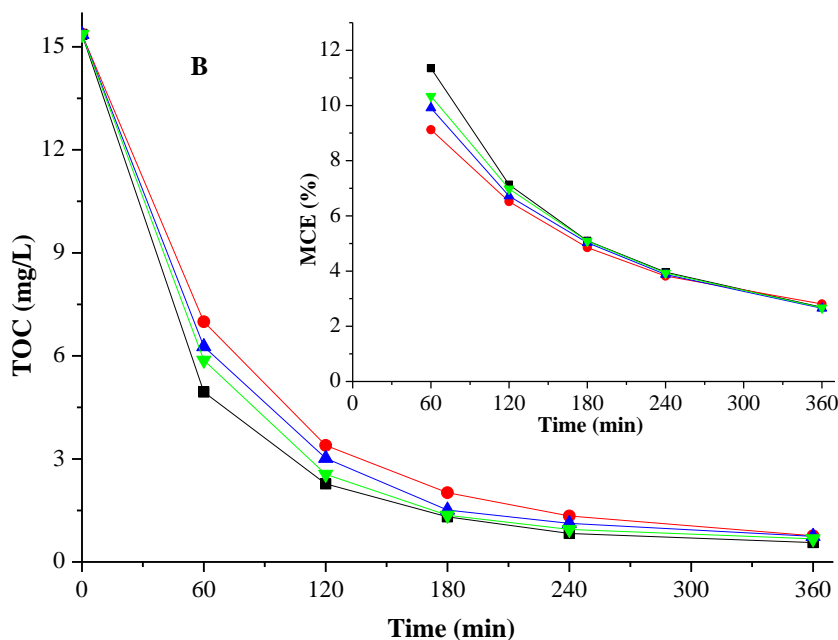


Fig. 6.4. Effect of iron concentration and pH on the mineralization and MCE for piroxicam in tap water by electro-Fenton/anodic oxidation with BDD anode. A: iron concentration varied in electro-Fenton process, 0.05 mM (■); 0.1 mM (●); 0.2 mM (▲); 0.5 mM (▼); 1 mM (◆); B: pH varied in anodic oxidation process, pH 3 (■); pH 3 with no air bubbled (●); pH 5.5 (▲); pH 9 (▼); insert figure indicates MCE. $C_0 = 0.08$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L; current intensity = 100 mA. For electro-Fenton: pH = 3.0. For anodic oxidation: pH = 5.5.

Figure 6.4 A shows the effect of iron concentration on the mineralization of 0.08 mM piroxicam (corresponding to 15.4 mg L^{-1} TOC) by EF with BDD anode with 50 mM Na_2SO_4 at pH 3.0 under a current intensity of 100 mA. Most piroxicam was mineralized during the first 2 h electrolysis and mineralization rate order was the same as the one for piroxicam degradation rate (Fig. 6.1). TOC removal with 0.2 mM Fe^{2+} in EF process reaches 98.7% after 6 h electrolysis time. A peak value was reached with 26.5% of MCE after 60 min electrolysis (Fig. 6.4A). MCE showed a high value at the beginning 2 h, and then decreased to a similar level afterwards for different iron concentration. According to the obtained results, 0.2 mM Fe^{2+} was chosen as the optimum catalyst concentration under these experimental conditions and was used in the rest of the study.

Meanwhile, the effect of pH on piroxicam mineralization in AO was also

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monitored (Fig. 6.4. B). It clearly shows that mineralization rate was better at pH 3 with air injection than at pH 3 without air bubbling, followed by the operating condition at pH 9.0 and 5.4. The removal rate indicates that the air bubbling influences greatly piroxicam mineralization, however, not as much as pH which significantly influences the degradation process in AO process. In the last stage of treatment (i.e. after 2 h electrolysis), there was no much difference in value of removal rate and MCE of mineralization of piroxicam at different adjustments in AO process.

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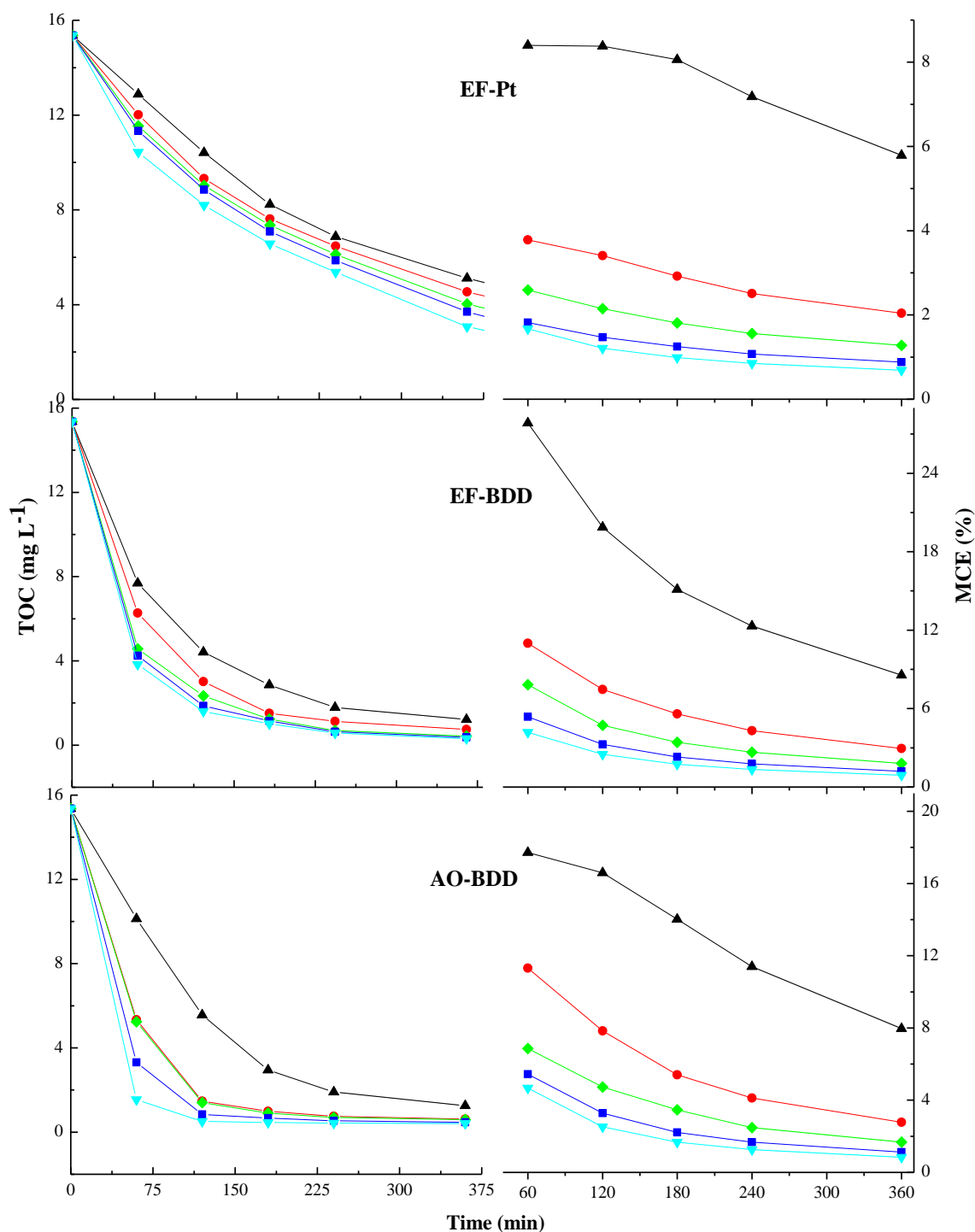


Fig. 6.5. Effect of current intensity on the mineralization and MCE for piroxicam in tap water by electro-Fenton/anodic oxidation. Current intensity varied: 100 (▲); 300 (●); 500 (◆); 750 (■); 1000 (▼); $C_0 = 0.08$ mM; $[\text{Na}_2\text{SO}_4] = 50$ mM; $V = 0.25$ L. For electro-Fenton: pH = 3.0. For anodic oxidation: pH = 5.5.

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The EF and AO treatments of 250 mL piroxicam solution (0.08 mM) were comparatively tested to clarify their relative oxidation power on mineralization. Figure 6.5 shows that, mineralization rate increased with increasing current intensity in all cases, due to high concentration of $\bullet\text{OH}$ produced accelerating the oxidation process (Eqs. (6.1), (6.2) and (6.4)). The evolution of MCE with electrolysis time decreased with current intensity increased, and with an obvious difference between current density of 100 and 300 mA, but not too much from 300 to 1000 mA. About 97% mineralization percentage was achieved in BDD anode applied system after 6 h electrolysis at 1000 mA in both EF and AO system. However, it was about 80% mineralization percentage for Pt anode in EF. Meanwhile, the maximum value of MCE in BDD ($\bullet\text{OH}$) system was about 30% but only 8% for Pt ($\bullet\text{OH}$), indicating a lower oxidative ability of Pt($\bullet\text{OH}$) compared to BDD($\bullet\text{OH}$) in mineralization of piroxicam. In BDD($\bullet\text{OH}$) application system, EF leads to a faster mineralization than that of AO [49, 50].

As showed in Fig. 6.5, mineralization process can be divided into two stages. In the early electrolysis time, piroxicam and its intermediates are mineralized into CO_2 , which was evidenced by a quick TOC decrease and a higher MCE achieved. In the later stage, the mineralization rate as well as MCE slow down and become similar in different processes. This could be ascribed to the formation of more hardly oxidizable by-products in the treated solution, such as carboxylic acids, ion-complexes and etc. Less oxidizing ability oxidants are produced when overload $\bullet\text{OH}$ produced in solution, as reaction listed below, which wastes the oxidative ability energy, lowers the efficiency vs. electrolysis time [51, 52],



6.3.3. Kinetic study of piroxicam oxidation with hydroxyl radicals

The determination of absolute rate constant (k_{pir}) of piroxicam oxidized by $\bullet\text{OH}$ was achieved by the method of competitive kinetics [53], which was performed in equal molar concentration (0.08 mM) of piroxicam and *p*-hydroxybenzoic acid (*p*-HBA) by EAOPs. The analysis was performed at the early time of the degradation to avoid the influence of intermediates produced during the process. The reaction of most organic

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molecules with $\bullet\text{OH}$ is assumed as a pseudo - first - order kinetic, that the absolute rate constant is calculated by [54]:

$$\frac{k_{pir}}{k_{pHBA}} = \frac{\text{Ln} \frac{[pir]_0}{[pir]_t}}{\text{Ln} \frac{[pHBA]_0}{[pHBA]_t}} \quad (6.10)$$

where k_{pHBA} is well known as $2.19 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [55], the subscripts 0 and t are the reagent concentrations at time $t = 0$ (initial concentration) and at any time t of the reaction.

$\text{Ln} [pir]_0/[pir]_t / \text{Ln} [pHBA]_0/[pHBA]_t$ provides a good linear relationship ($R^2 = 0.999$), with “b” as 1.002. The value of the rate constant k_{pir} was calculated as $2.19 (\pm 0.01) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, which is less than the data reported as $17 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ [56]

6.3.4. Evolution of the intermediates formed during the EAOPs

The final by-products of piroxicam generated by EAOPs are not only water, carbon dioxide, but also inorganic ions such as ammonium, nitrate, and sulfate ions, and some short chain carboxylic acids. Figure 6.6 presents the formation of inorganic ions, as NH_4^+ , NO_3^- , and SO_4^{2-} during the mineralization of piroxicam by the three oxidation processes at low current intensity (100 mA). As can be seen, the release of NH_4^+ and SO_4^{2-} was relatively slower than that of NO_3^- ions. About 70% of the content of nitrogen atoms in the parent molecules was transformed into NO_3^- ions, whereas only about 25% NH_4^+ ions were formed to a lesser extent. Meanwhile, about 95% of sulfur atoms initially present in the parent molecules were converted into SO_4^{2-} ions at the end of the electrolytic treatments. Results indicate that the order of releasing concentration of inorganic ions was EF-BDD > AO-BDD > EF-Pt, which was in good agreement with TOC abatement under the same operation condition. The mass balance of nitrogen (95% of mineralization) was slightly lower than the reaction stoichiometry, indicating loss of nitrogen by formation of volatile compounds such as NO_2 or gas N_2 [34, 57]. However, the release of inorganic ions into the treated solutions at very close concentration to the stoichiometric amounts can be considered as another evidence of the quasi-complete mineralization of the aqueous solutions by the EAOPs.

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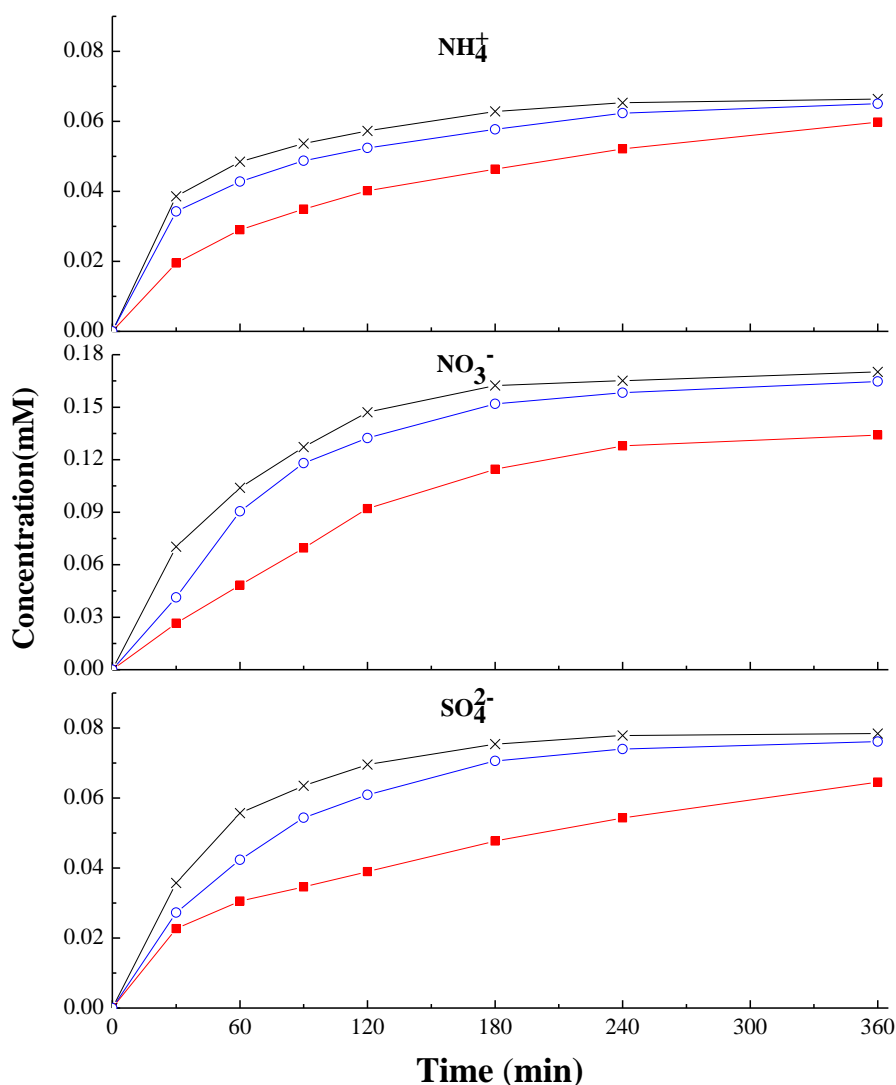


Fig. 6.6. Time-course of inorganic ions concentration during EAOPs of piroxicam in tap water: EF-BDD (×); EF-Pt (■); AO-BDD (O); C_0 : 0.08 mM; [KCl]: 50 mM; current intensity: 100 mA; V: 0.25 L. For electro-Fenton: [Fe²⁺]: 0.1 mM; pH: 3.0. For anodic oxidation: pH = 5.5.

Due to similarities of piroxicam mineralization rate and evolution of inorganic ions release for EF-BDD and AO-BDD processes, the identification and quantification of short chain carboxylic acids produced during piroxicam electrolysis were performed at the same current intensity for EF-Pt and EF-BDD processes. Figure 6.7 shows that, maleic, malonic, oxamic, glyoxylic acids appeared at early electrolysis time and reached their maximum concentration after about 50 min electrolysis time, while acetic and oxalic acids were persistent for both processes. It can be observed that the main

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carboxylic acids produced were largely accumulated using Pt but rapidly eliminated using BDD anode. All the organic acids formed during the process, except the persistent ones, were reduced to a non-detected level and finally the ultimate carboxylic acids were converted to carbon dioxide and water with an almost total mineralization. The highest amount of organic acids formed were glycolic (0.02 mM) and oxamic (0.015 mM) acids for EF-Pt, while maleic (0.019 mM) and oxalic acids (0.015 mM) for EF-BDD, respectively. At 6 h electrolysis time, oxalic acid contributed 0.078% and 0.03% to the TOC in EF-Pt and BDD processes, respectively. The persistence of oxalic acid in solution may be able to explain the remaining TOC observed for the treatments. The formation of stable complex of oxalic acid with Fe^{2+} or some other hardly oxidizable compounds may explain the non-complete removal of organic compounds [39, 57].

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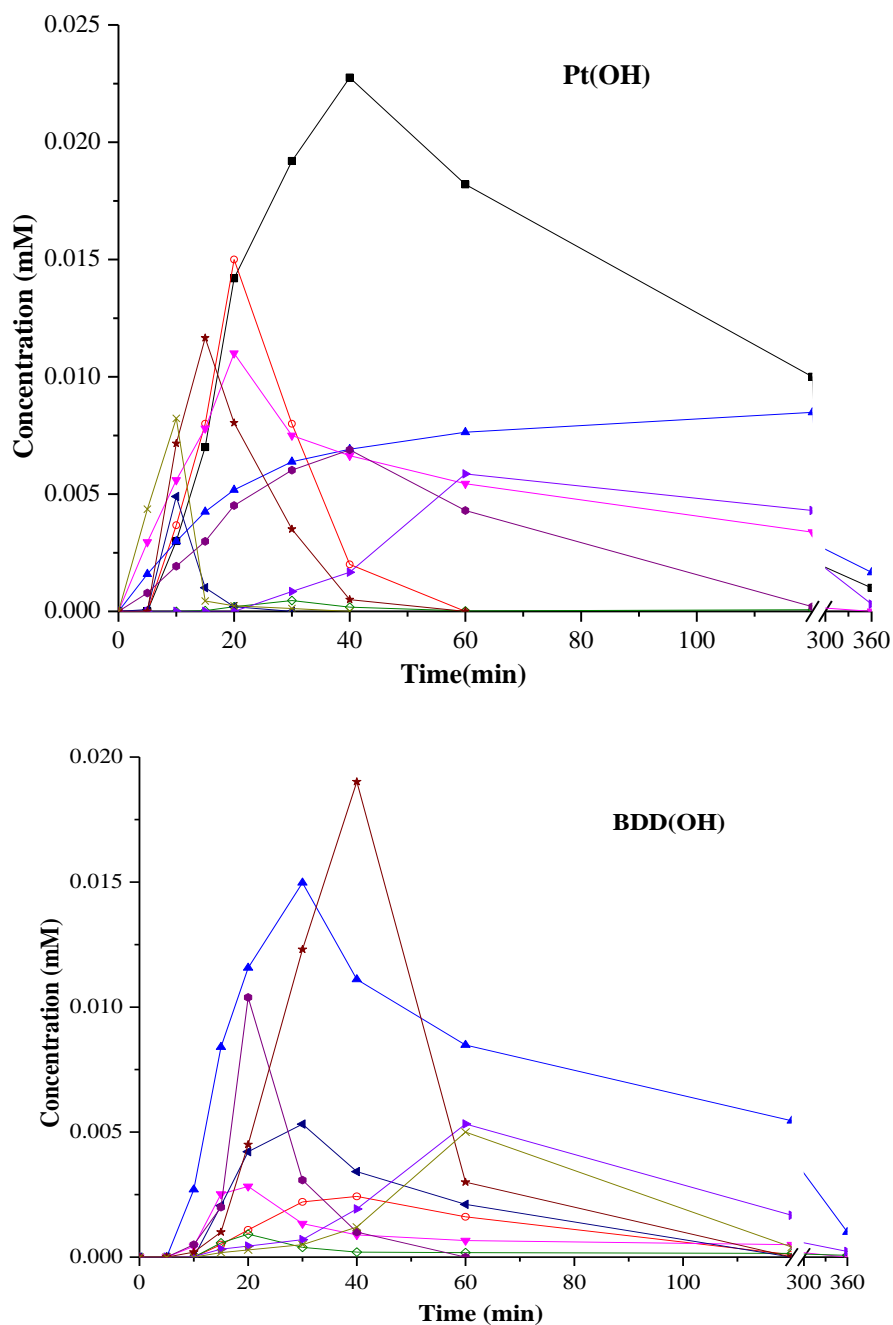


Fig. 6.7. Evolution of the concentration of intermediates generated during the EAOPs of piroxicam in tap water. Carboxylic acids: glycolic (■), oxamic (○), oxalic (▲), glyoxylic (▼), fumaric (◇), malonic (◀), acetic (▶), succinic (●), maleic (★), malic (x); C_0 : 0.08 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; current intensity: 100 mA; V: 0.25 L. For electro-Fenton: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0.

6.3.5. Evolution of toxicity during the EAOPs

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The general evolution of toxicity of piroxicam in tap water during the EAOPs were analysed comparatively in this research in triple. Figure 6.8 shows the inhibition percentage of luminescent bacteria *V. fischeri* after 15 min exposure as a function of electrolysis time (up to 120 min) in EF-Pt, EF-BDD and AO-BDD processes, at current intensities of 100 mA and 1 A. In all treatments, the luminescence inhibition increased to its highest peak within 15 min electrolysis treatment, indicating there were more toxic intermediates generated at the beginning of electrolysis. Then, the inhibition rate decreased gradually at 100 mA current intensity for all the EAOPs. For 1 A application, the rate decreased sharply and displayed a lower percentage of bacteria luminescence inhibition compared to the initial condition within 40 min treatment time, indicating that the highly toxic intermediates have been quickly degraded during the treatments.

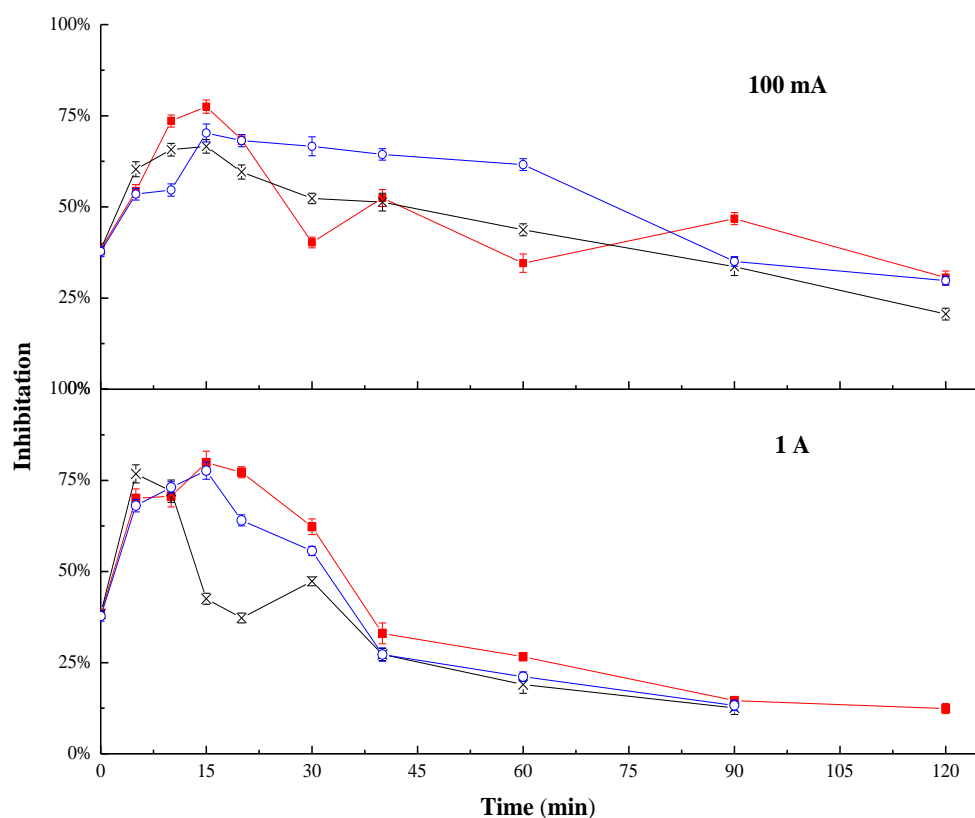


Fig. 6.8. Evolution of the inhibition of marine bacteria luminescence (*Vibrio fischeri*) (Microtox® test) during ECPs of piroxicam in tap water: EF-BDD (×); EF-Pt (■); AO-BDD (O); C_0 : 0.08 mM; $[\text{Na}_2\text{SO}_4]$: 50 mM; V: 0.25 L. For electro-Fenton: $[\text{Fe}^{2+}]$: 0.1 mM; pH: 3.0. For anodic oxidation: pH = 5.5.

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It is obvious that there was no clear difference between processes applied (EF-Pt, EFF-BDD or AO-BDD) on the evolution of toxicity of piroxicam treated samples. However, at 1 A, the toxicity was lower than the initial value after 40 min electrolysis. The presence of luminescence inhibition peaks is related to formation of toxic intermediates accumulated or degraded at different rate vs. electrolysis time. As the results show, later, the toxicity decreased enough low that indicated that EAOPs could be operated as effective and practicable treatments at wastewater treatment plants.

6.4 Conclusion

The electrochemical oxidation of piroxicam by electro-Fenton and anodic oxidation processes by using BDD or Pt anode at lab-scale have been studied to get insight on the applicability of this technology for the removal of piroxicam in tap water. The fastest degradation and mineralization rates of piroxicam were achieved upon addition of 0.2 mM Fe^{2+} in EF process. It was found that pH of solution influenced the degradation rate as well as air bubbling on mineralization efficiency of piroxicam in AO process. The higher current intensity applied, the higher removal rate was achieved, but with lower value of MCE obtained. The EF system provided higher degradation efficiency compared to AO process, while BDD ($\bullet\text{OH}$) showed a higher mineralization rate compared to Pt($\bullet\text{OH}$). The absolute rate constant of piroxicam with $\bullet\text{OH}$ was obtained as $(2.19 \pm 0.01) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ by competitive kinetics method. The evolution of short chain carboxylic acids and inorganic ions concentrations during piroxicam mineralization by EAOPs were monitored. The results were in good agreement with TOC abatement under the same operation condition. Finally, the toxicity of solution oxidized by EAOPs showed that current intensity influenced more on the toxicity removal than the kind of treatment applied. As showed by the results of degradation, mineralization, evolution of the intermediates and toxicity of piroxicam in tap water, EF-BDD could be an effective and environment friendly technology applied in wastewater treatment plants.

Acknowledgements

Ling Feng is a Doctoral research fellow of the Erasmus Mundus Joint Doctorate programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA no. 2010-0009.

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Chapter 7. Research Paper

Pharmaceuticals cytotoxicity evolution and removal with ozonation and biofiltration

The work was presented in the paper:

Feng, L, Michael J. W., Yeh, D., van Hullebusch, E. D., Esposito, G.
Removal of Pharmaceutical Cytotoxicity with Ozonation and BAC
Filtration. *Submitted to ozone: science and engineering*

Chapter 7: Pharmaceuticals cytotoxicity evolution and removal with ozonation and biofiltration

Abstract

Three non-steroidal anti-inflammatory drugs - ketoprofen, naproxen and piroxicam - in both organics-free and surface water (Tallahassee, FL), were exposed to varying ozone treatment regimes, including O₃/H₂O₂ advanced oxidation on the laboratory bench. Oxidation intermediates were identified with advanced analytical techniques, and a *Vibrio fischeri* bacterial toxicity test was applied to assess the predominant oxidation pathways and associated biological effects. Recently-spent, biofilm-supporting granular activated carbon (BAC) was sampled from a municipal drinking water treatment facility (Tampa, FL), and employed to determine the bio-availability of chemical intermediates formed in the ozonated waters. The removal rates of ketoprofen, naproxen, and piroxicam increased with increasing ozone dose, ratio of H₂O₂ to O₃, and empty bed contact time with BAC. Following ozonation with BAC filtration, also had the effect of lowering the initial ozone dose required to achieve > 90% removal of all 3 pharmaceuticals (when an initial ozone dose < 1 mg L⁻¹ was combined with empty bed contact time (EBCT) < 15 min). Considering the observed evolution of cytotoxicity (direct measurement of bioluminescence before and after 5 and 15 min exposures) in treated and untreated waters with either ketoprofen, naproxen, or piroxicam, ozone doses of 2 mg L⁻¹, with a ratio of H₂O₂ and O₃ of 0.5, followed by an 8 min EBCT with BAC were optimal for removing both the parent contaminant, and its associated deleterious effects on water quality.

Keywords: Ozone, Pharmaceuticals, Biofiltration, Activated Carbon, Toxicity

Chapter 7: Pharmaceuticals cytotoxicity evolution and removal with ozonation and biofiltration

7.1 Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used medication among pharmaceutical compounds for relieving mild and moderate pain with 70 million prescriptions each year in the U.S. (2011 Consumers Union of United States, Inc). With such consumption, a large part of the original drug and its metabolite are discarded to solid waste disposal sites or flushed (human body only metabolizes a small percentage of drug) into municipal sewers in excrement [1-3]. Meanwhile, NSAIDs have been detected in the order of ng L^{-1} or $\mu\text{g L}^{-1}$ in effluents of wastewater treatment plants, surface water, groundwater and drinking water [4-6]. Considering that in many areas, surface water is the main source for drinking water, the potential adverse impact of NSAIDs on water resources have gathered considerable attention [7-12]. In 2011, the World Health Organization (WHO) published a report on pharmaceuticals in drinking-water which reviewed the risks to human health associated with exposure to trace concentrations of pharmaceuticals in drinking-water, raising the fear that the continuous input of pharmaceuticals may pose a potential risk for organisms living in both terrestrial and aquatic environments [13-15].

Naproxen, ketoprofen and piroxicam, are frequently consumed NSAIDs [16-18], which have been detected in environmental samples, with up to $33.9 \mu\text{g L}^{-1}$ (naproxen) in the effluent of the secondary settler of a municipal waste water treatment plant [19-23]. Once in receiving waters, possible adverse effects such as reducing lipid peroxidation by bivalves were reported for naproxen [24, 25], and sometimes leading to the accumulation of intermediates more toxic than the parent compound [26, 27]. The co-toxicity of naproxen with other pharmaceuticals was also studied, that toxicity of mixture was considerable, even at concentrations for which the single substances showed no or only very slight effects [28]. Reported EC_{50} as low as $21.2 \mu\text{g L}^{-1}$ for the ToxAlert[®] 100 test and $35.6 \mu\text{g L}^{-1}$ for the Microtox[®] test was obtained for naproxen [23].

Considering the hazards of persistent pharmaceuticals in the environment, various technologies for removing them have been studied. Ozonation treatment, utilizing the high redox potential of O_3 ($E^\circ = 2.07 \text{ V/SHE}$) [29], can be effective against chlorine-resistant pathogens, and is applied as a useful tool for plant operations to help control taste and odor, color, and bacterial growth in filtration beds used in purification of drinking water and wastewater [30-34]. With wide-scale adoption of ozonation for water treatment in both North America and the E.U., the study of the removal of

Chapter 7: Pharmaceuticals cytotoxicity evolution and removal with ozonation and biofiltration

pharmaceuticals by ozonation has significant practical benefit. Anthropogenic organic contaminants, like NSAIDs, are often simultaneously directly-oxidized by aqueous O_3 , and indirectly-oxidized by $\bullet OH$. Conditions which favor the production of highly reactive species such as hydroxyl radicals ($\bullet OH$) include high pH (O_3/OH^-) and addition of hydrogen peroxide (O_3/H_2O_2) [35, 36].

The potential removal efficiency of NSAIDs with ozonation can be assessed by reported rate constants for both direct (k_{O_3}) and indirect (k_{OH}) oxidation. Benitez et al. studied the apparent rate constants of aqueous pharmaceuticals, and found that, for naproxen, the k_{O_3} value varies with pH (2.5-9), ranging between 2.62×10^4 and $2.97 \times 10^5 M^{-1} s^{-1}$, and k_{OH} as $8.4 \times 10^9 M^{-1} s^{-1}$ [37]. Huber et al. observed a k_{O_3} value of $2 \times 10^5 M^{-1} s^{-1}$, and k_{OH} of $9.6 \times 10^9 M^{-1} s^{-1}$ for naproxen [38]. The second-order rate constant for ketoprofen was determined by O_3 as $0.4 \pm 0.07 M^{-1} s^{-1}$, and k_{OH} (Fenton process) as $8.4 \pm 0.3 \times 10^9 M^{-1} s^{-1}$ [39]. The ozone oxidation kinetics of piroxicam are unknown

Ozone applied for water treatment can increase biodegradable organic carbon levels (BDOC), producing readily bio-degradable substrates for down-stream bacteria and biofilm growth [40]. To control post- O_3 BDOC, water treatment facilities have employed biologically-active filtration media. Granular activated carbon (GAC) is one popular support medium that has been shown to remove a wide-range of organic contaminants [41], and has ample surface area for biofilm attachment along with the ability to adsorb some of the influent biodegradable organic matter or organic materials released by microorganisms [42]. Both aqueous pollutants and ozonation by-products are adsorbed on the solid support medium and oxidized by supported microorganisms into environmentally acceptable metabolites such as carbon dioxide, water and additional biomass. As expected, most investigated pollutants so far have shown excellent removals by combination of ozone and GAC application [43, 44].

The objective of this study was to observe the oxidation kinetics for 3 emerging aquatic pollutants of concern (the NSAIDs: piroxicam, ketoprofen, and naproxen) under varying ozone treatment regimes, and to both quantitatively and qualitatively assess the pathways for intermediates formation. Finally, bench-scale biological filtration was employed to determine the bio-availability of chemical intermediates formed in ozonated surface water. Of particular interest, changes in bacterial cyto-toxicity (% luminescence inhibition) were measured both after ozonation, and sequential ozonation and simulated biofiltration. Both ozonation conditions and empty-bed contact times that

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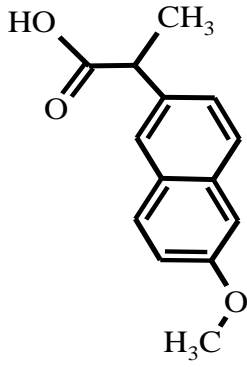
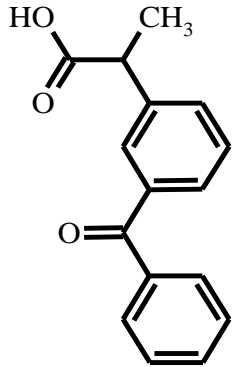
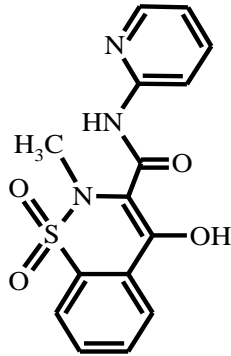
are favorable for mitigating toxic by-product formation in surface waters contaminated with NSAIDs are discussed.

7.2 Materials and Methods

7.2.1 Chemicals

Analytical grade reagents (purity $\geq 99\%$) of ketoprofen (2- [3- (benzoyl) phenyl] propanoic acid), naproxen (6-methoxy- α -methyl-2-naphthalene acetic acid), piroxicam (4-hydroxy-2-methyl-2H-1,2-benzothiazine-1-(N-(2-pyridinyl)carboxamide)-1,1-dioxide), bisphenol A (as competition substrate in kinetic experiments, 2,2-Bis(4-hydroxyphenyl) propane* 4,4'-isopropylidenediphenol, BPA, $C_{15}H_{16}O_2$), methanol (HPLC analysis grade, CH_3OH), sodium phosphate dibasic anhydrous (Na_2HPO_4), sodium phosphate monobasic (NaH_2PO_4), and hydrogen peroxide 30% solution (H_2O_2) were purchased from Sigma-Aldrich, or Macron Chemicals and used as received. NSAIDs solutions with the concentration of 2 mg L^{-1} were prepared in laboratory-grade Type II or surface water (SW), and all other stock solutions were prepared with Type II water. Achieving desired pH of test solutions required different ratios of NaH_2PO_4 and Na_2HPO_4 .

Table 7.1. Chemical identification and structures of selected NSAIDs.

| Structure | Naproxen | Ketoprofen | Piroxicam |
|---|---|---|-----------------------|
|  |  |  | |
| Formula | $C_{14}H_{14}O_3$ | $C_{16}H_{14}O_3$ | $C_{15}H_{13}N_3O_4S$ |
| Mass ($g\text{ mol}^{-1}$) | 230.3 | 254.3 | 331.4 |
| CAS No. | 22204-53-1 | 22071-15-4 | 36322-90-4 |
| Log Kow | 4.45 | 4.15 | 6.3 |

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| | | | |
|--|----|-----|----|
| Solubility (mg L ⁻¹ at 20 °C) | 51 | 144 | 23 |
|--|----|-----|----|

7.2.2 Surface Water Sampling

The surface water samples were collected from Lake Bradford, Tallahassee, FL, USA (Latitude 30.40 N and longitude -84.34 W). The physicochemical data were obtained from published reports, or measured according to *Standard Methods* [45]. The water sample was filtered through a 0.2 µm micropore membrane before using. The basic character of surface water is listed in Table 7.2.

Table 7.2. Physicochemical properties of Lake Bradford water.

| | | | |
|-------------------------------|-------------------|---|-----------------|
| Color (Pt-Co cu) | 127 ^b | pH | 6.7 |
| Total P (mg L ⁻¹) | 0.03 ^a | Alkalinity (mg L ⁻¹ as CaCO ₃) | 4.6 |
| Total N (mg L ⁻¹) | 0.61 ^a | Conductance (µS cm ⁻¹ at 25 °C) | 25 ^b |
| Cl (mg L ⁻¹) | 5.6 ^b | TOC | 3.8 mg/L |

^a from water quality report for selected lakes and streams, Leon County Public Works; ^b from Florida Lake Watch water chemistry summary.

7.2.3 Ozonation

Ozone stock solution (20-30 mg O₃ L⁻¹) was produced with a plasma-arc ozone generator (RMU16-04, Azcozon) utilizing compressed, purified oxygen (moisture removed through anhydrous CaSO₄). The temperature of the ozone stock solution was maintained at 6°C or less in an ice bath through a water-jacketed flask containing 10 mM phosphate buffered solution (pH 6). Ozone dosing was performed by injecting the ozone stock solution (0-4 mg L⁻¹) via a digital titrator (Titronic basic) into a 100 mL amber boston-round bottle, continuously stirred, and immediately capped to prevent ozone degassing. At specific reaction times, indigo solution was added to quench the residual O₃. For select samples H₂O₂ was added 30 seconds prior to the addition of ozone stock solution (1 mg L⁻¹), with continuous mixing.

Ozone concentration was determined according to the standard colorimetric method (4500-O₃) with indigo trisulfonate at $l = 600 \text{ nm}$ ($\epsilon = 20000 \text{ M}^{-1} \text{ cm}^{-1}$) [45]. All

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experiments were conducted in triplicate at an ambient temperature of $24\pm 1^\circ\text{C}$. Dilution factors were assessed when analyzing data.

7.2.4 BAC Bio-filtration

Biological activated carbon (BAC) testing, with GAC media sampled from an active bio-filtration facility (Tampa, FL), was conducted using rapid, small-scale column tests to predict its performance. The sampled filtration media was added to a 5 cm diameter transparent PVC column of a 30 cm bed at varying volumes (V_F) to simulate empty bed contact times (EBCT) of 2, 4, 8, 12, 20 min. GAC was acclimated for a period of at least one month with fresh Tampa surface water prior to filtration testing. Treated waters were continuously pumped at a controlled flow-rate (FH 100M Multichannel Pumps, Thermo Scientific) into the bottom of each filter column. Two different duplicate control samples were prepared. One control sample included “virgin” GAC without microorganisms while the second control sample contained spiked target compounds without GAC.

7.2.5 Analytical

7.2.5.1 High performance liquid chromatography (HPLC)

NSAID concentrations in solution, as well as BPA concentration were monitored by HPLC, using a ESA model 582 pump/solvent delivery system (Thermo Fisher), fitted with a C18 hypersil ODS-2 (Thermo Fisher; $5\ \mu\text{m}$, $100\ \text{mm} \times 4.6\ \text{mm}$ (i.d.) column) coupled with a ESA 528 UV-VIS detector (optimum $\lambda=230\ \text{nm}$). The mobile phase for all analyses was a methanol/water mixture (50:50, v/v) at a flow rate of $0.3\ \text{mL min}^{-1}$ with $100\ \mu\text{L}$ of sample injected. Lowest detected concentrations for the three NSAIDs were 0.018, 0.013, $0.01\ \text{mg L}^{-1}$ for naproxen, ketoprofen and piroxicam, respectively.

7.2.5.2 Total organic carbon (TOC)

Carbon mineralization in oxidized samples was monitored by total organic carbon content, as measured with a Teledyne Tekmar Phoenix 8000 UV persulfate TOC analyzer. A non-dispersive infrared detector (NDIR) was used to measure CO_2 . Calibration of the analyzer was attained by dilution of Teledyne Instruments-Tekmar certified standard solution (800 ppm), standards for total carbon (TC) and inorganic

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carbon (IC), respectively. Reproducible TOC values with $\pm 2\%$ accuracy were found using the non-purgeable organic carbon method.

7.2.5.3 Microbial toxicity

Cytotoxicity of the NSAIDs and their oxidized intermediates in treated solutions was assessed with a commercially-available bio-assay using bioluminescent marine bacteria *V. fischeri* (Microtox, Modern Water), according to manufacturer's specifications. The reduction in measured luminescence (RLU) is reported as inhibition (%) in cell viability after sample exposures of 5 and 15 min at 15°C. The bioluminescence measurements (GloMax 20/20 Luminometer, Promega) were realized in solutions oxidized with varying degrees of ozonation, and on a blank ($C_0 = 0 \text{ mg L}^{-1}$ of O_3).

7.2.5.4 Electrospray ionization mass spectrometry (ESI-MS)

The intermediates produced during the ozonation of NSAIDs were determined by an electro-spray-ionization-mass spectrometry (ESI-MS) system (AccuTOF JEOL; 90 eV). The needle voltage was 2000 V. The temperature of the orifice, de-solvation chamber and interface were 80, 250 and 300 °C. Samples were diluted 10 times in MeOH (0.1% formic acid), while 20 μL of this was injected in a stream of MeOH (0.1% formic acid, v/v), flowing at a rate of 200 $\mu\text{L min}^{-1}$.

7.3 Results and Discussion

7.3.1 Removal efficiency by ozonation/AOP ($\text{O}_3/\text{H}_2\text{O}_2$) of NSAIDs in surface water and Type II lab water

The treatment efficiency of ozonation highly depends on the chemical structure of the target compounds, as ozone is known to favor compounds with unsaturated double bonds or moieties with electron donation potential [46]. For instance, different removal efficiencies of pharmaceuticals were reported for the same compound in river water as compared to distilled water with ozonation [47, 48]. Advanced oxidation processes with the addition of hydrogen peroxide to promote hydroxyl radical reactions may help to improve contaminant elimination during ozonation, however like all unit processes, ozonation requires optimization before any treatment effect can be noticed.

For the optimization of ozonation/AOP for the target NSAIDs (initial concentration of 2 mg L^{-1}), the following parameters were varied: water matrix (Type II lab water, lake water), ozone dose (0, 0.5, 1, 1.5, 2, 3, 4 mg L^{-1}), and the mole ratios of

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H₂O₂ to O₃ (0, 0.3, 0.5, 1). Residual ozone was quenched immediately following the prescribed contact time.

To achieve sufficient reaction between pollutants and ozone, NSAIDs solutions were firstly sampled at different oxidized times after adding an initial 2 mg L⁻¹ O₃ dose. Results confirmed 2 min was adequate to ensure >90% oxidation of all 3 organic compounds in Type II lab water (Fig. 7.1).

As expected, increasing the initial ozone dose contributed to greater oxidation of selected NSAIDs (contact time = 2 min). The trend of increasing removal efficiency at increasing ozone dose for NSAIDs in surface water was similar to that of Type II lab water (Fig. 7.2). However, a lower removal rate was obtained, due to background oxidant scavengers in the surface water. At an ozone dose of 4 mg L⁻¹, the removal rate was 95%, 99% and 96% in Type II lab water (Fig. 7.2. A), while 84%, 90%, and 77% removal was observed in surface water for ketoprofen, naproxen and piroxicam (Fig. 7.2. B), respectively. In the range of ozone dose (from 0.5 mg L⁻¹ to 2 mg L⁻¹) applied in Type II lab water, the degradation rate increased more than 40%, while in the range of 2 mg L⁻¹ to 4 mg L⁻¹, the removal rate increased less than 6%. Based on the results, 2 mg L⁻¹ could be selected as the optimal oxidant dose for remaining ozone exposures to achieve >90% of the NSAIDs. The research of Huber et al. confirmed that ≥ 2 mg L⁻¹ ozone dose applied in wastewater effluent could oxidize more than 90% naproxen and other pharmaceuticals [38].

Figure 7.3 shows the effect of AOP (O₃/H₂O₂) on degradation of NSAIDs by different molar ratio of H₂O₂ and O₃, with the ozone dose fixed at 1 mg L⁻¹ (which applied alone at 1 mg L⁻¹ in ozonation showed in dash line). Theoretically, 1 mole O₃ yields 0.7 mole •OH, while 1 mole O₃/H₂O₂ produced 1 mole •OH. The results of the O₃/H₂O₂ bench-scale testing validated the theory that while the efficiency of O₃/H₂O₂ treatment is higher than in the sampled surface water, there are secondary reactions which contribute to observed contaminant oxidation. The degradation rates at a molar ratio of 1 were 96%, 98%, and 98% in Type II lab water, while 81%, 83%, and 76% was observed in surface water for ketoprofen, naproxen and piroxicam, respectively. It is obvious that addition of H₂O₂ highly improved the removal rate of NSAIDs compared with ozone application alone. For Type II lab water, there is no much difference among H₂O₂ and O₃ of 0.3 to 1 on the degradation rate, meanwhile, for surface water, the removal rate increased obviously with increasing ratio. It can be seen that in surface

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water, there may be other species competing with NSAIDs for the selective and non-selective oxidants, therefore requiring a higher oxidant dose to achieve the desired level of elimination.

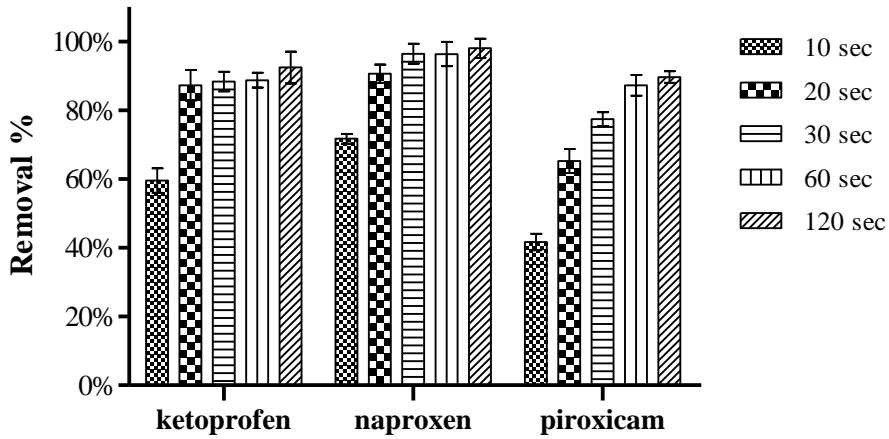
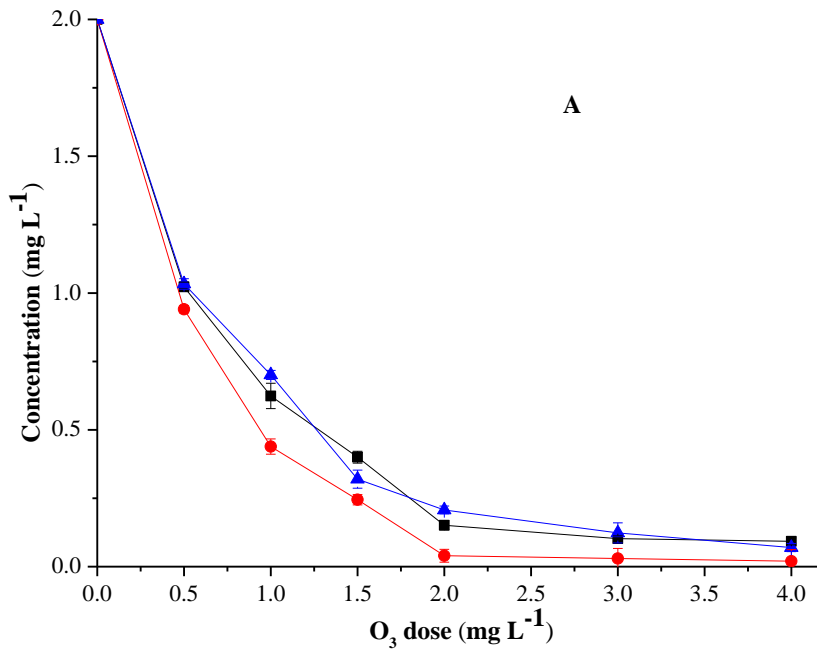


Fig. 7.1. Removal percentage of three drugs selected by ozonation at different ozone contact time in Type II lab water; $C_0=2 \text{ mg L}^{-1}$; O_3 dose: 2 mg L^{-1} ; V : 100 mL.



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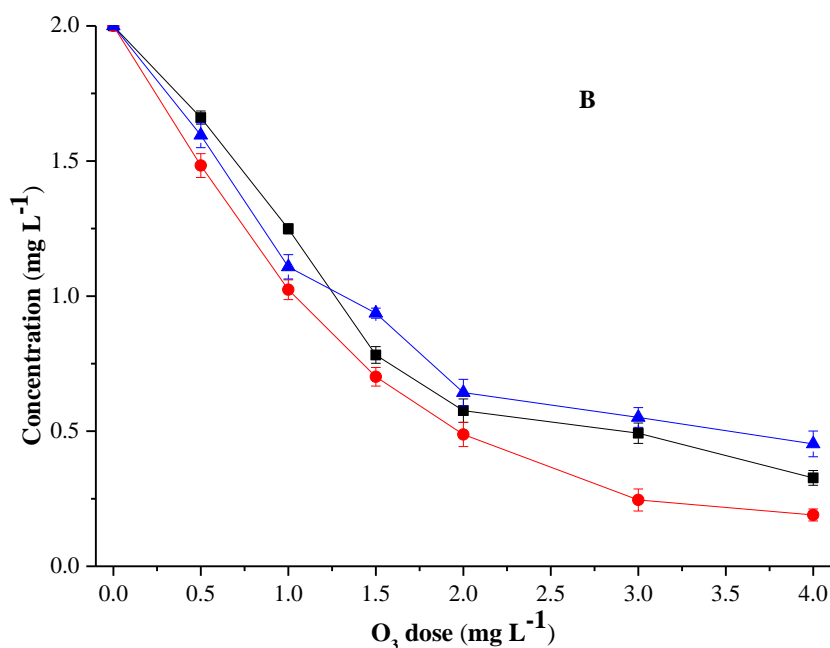


Fig. 7.2. Effect of O₃ dose on degradation of NSAIDs in Type II lab water (A) and surface water (B) by ozonation; ketoprofen (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; V: 100 mL; Ozone contact time: 2min

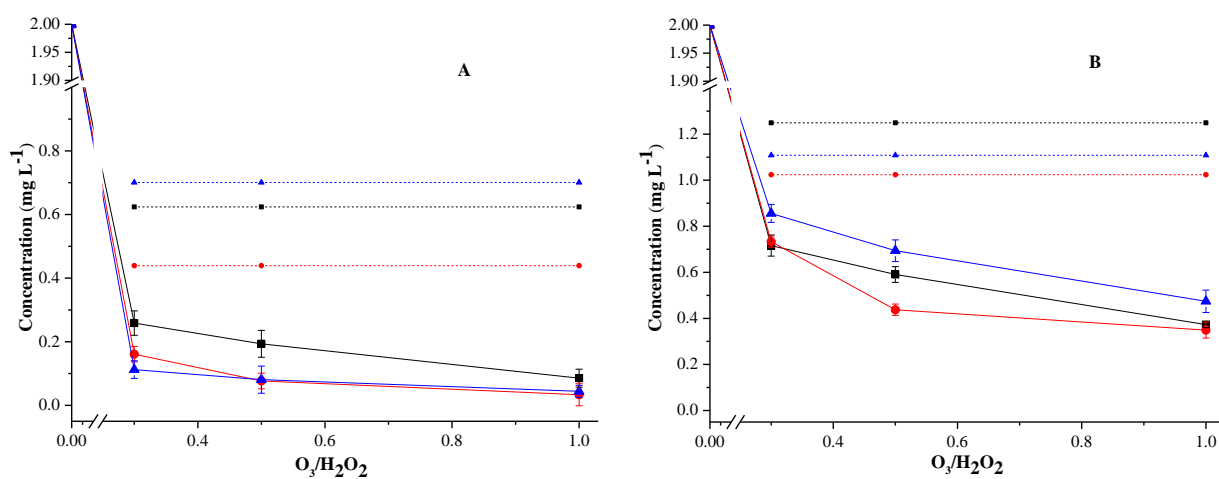
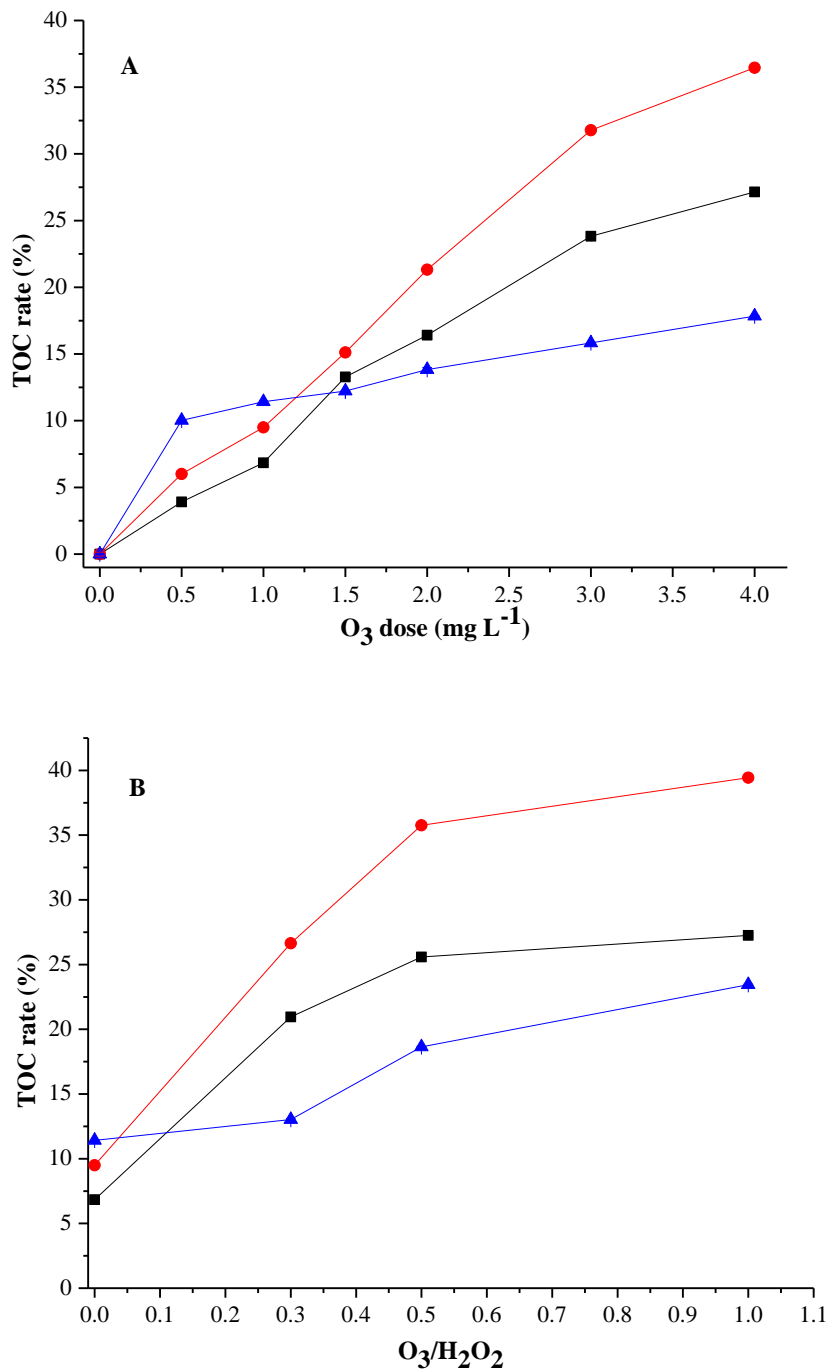


Fig. 7.3. Effect of molar ratio of H₂O₂ and O₃ on degradation of NSAIDs in Type II lab water (A) and surface water (B) by AOP; dash line indicates the removal of NSAIDs by O₃ alone (1 mg L⁻¹); ketoprofen (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; O₃ dose: 1 mg L⁻¹; V: 100 mL; Ozone contact time: 2 min.

TOC measurements were conducted after ozone and AOP (O₃/H₂O₂) treatment in sampled surface water to quantify the extent of organics mineralization. The mineralization rates after a 2 mg L⁻¹ O₃ dose were 16.4%, 21.3%, and 13.8%, with up to

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27.1%, 36.4%, and 17.8% TOC mineralization at an O_3 dose of 4 mg L^{-1} , for ketoprofen, naproxen and piroxicam, respectively (Fig. 7.4 A). The results indicate that the higher input of ozone could potentially reduce the impact of cytotoxic ozone by-products. The observed rates of mineralization increased with the production of $\bullet OH$, as 27.2%, 39.4%, and 23.4% at mole ratio of O_3/H_2O_2 at 1 for ketoprofen, naproxen, and piroxicam, respectively (Fig. 7.4 B). The reduction in TOC suggests that ozone did contribute to significant organics mineralization in the treated surface water.



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Fig. 7.4. Effect of O₃ doses (A) and H₂O₂ and O₃ ratio (B) on mineralization rate of NSAIDs in surface water by ozonation and AOP, respectively; ketoprofen (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; O₃ dose in AOP: 1 mg L⁻¹; V: 100 mL; Ozone contact time: 2min.

7.3.2 Kinetic of ozonation of piroxicam in Type II lab water

The absolute rate constant (k_{PIR,O_3}) of piroxicam degradation by O₃ was determined by accepted competition kinetics methods [49]. The reference compound, bisphenol A (BPA, k_{BPA} : $2.7 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$), was selected due to its known reaction rates with ozone under acidic condition, and with $\bullet\text{OH}$ [50]. The ozonation treatment was performed on both compounds in equal molar concentration (6 μM) and under the same operating conditions (ozone dose = 0, 0.25, 0.5, 0.75, 1, 1.5 mg L⁻¹, pH = 6.0, V = 150 mL), while mechanically stirring. At acidic pH, ozone decomposition to $\bullet\text{OH}$ becomes negligible [51]. Concentrations of both the reference and probe compounds remaining in solution were analyzed by HPLC. Under direct ozonation, the absolute rate constant was calculated by:

$$\frac{k_{PIR}}{k_{BPA}} = \ln \frac{[PIR]_n}{[PIR]_0} / \ln \frac{[BPA]_n}{[BPA]_0} \quad (7.1)$$

where the subscripts 0 and n are the ozone dose of the reaction.

The resulting linear relationship allows for the determination of the absolute rate constant for oxidation of piroxicam with ozone, by the slope of the integrated kinetic equation ($y_{PIR} = 1.22 \times k_{BPA}$, $R^2 = 0.98$). The value of k_{PIR,O_3} was determined to be $3.3 (\pm 0.1) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$.

7.3.3 Sequential ozonation and biofiltration

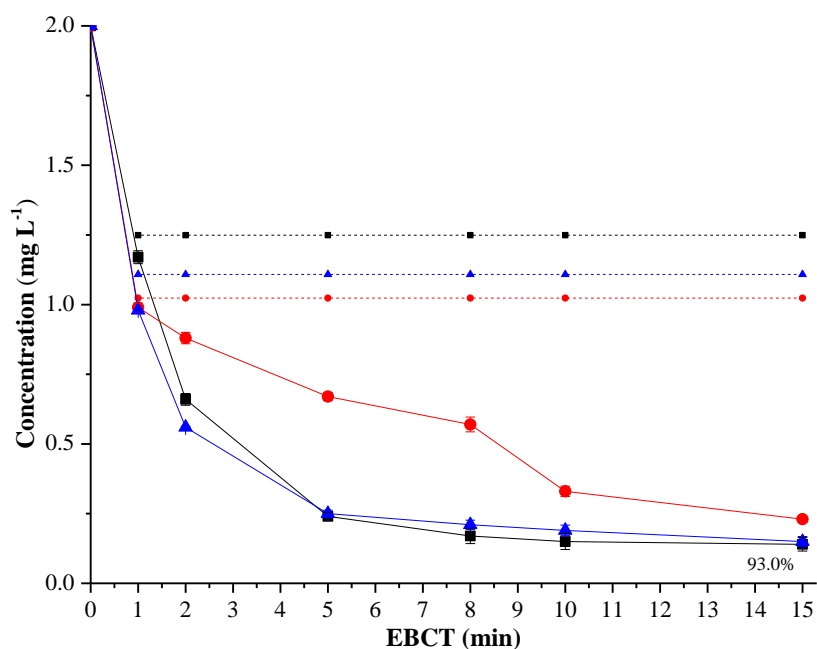
With an initial O₃ dose of 1 mg L⁻¹, the biofiltration was set up to treat the solution oxidized by ozonation at different EBCT while measuring both degradation of NSAIDs and associated toxicity. The EBCT presents the extent of solution contact with the biofilm-supporting GAC filtration bed. Biofiltration was able to improve NSAIDs removal rates following ozonation by 50%, 17%, and 43%, at 5 min of EBCT for ketoprofen, naproxen and piroxicam, respectively. The removal efficiency was better than that of the application of H₂O₂ and O₃ at ratio of 1, with the exception of naproxen solutions. At an EBCT of 15 min, the total removal rate of combined

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ozonation/biofiltration achieved 93%, 88% and 92% for ketoprofen, naproxen and piroxicam, respectively. As the results showed, an EBCT of 5 min is effective contact time for ketoprofen and piroxicam while 10 min was most effective for naproxen (Fig. 7.5). With the observed poor removal percentage at low EBCT, limitations on pollutant mass-transfer into the biofilm are evident. Increasing solution temperature helped to improve the removal efficiency of NSAIDs in ozonated surface water, as bacterial activity increased with increasing temperature. At a temperature of 35 degrees, ketoprofen, piroxicam, and naproxen had removal rates of 76%, 68% and 85%, respectively.

It appears that ketoprofen and piroxicam are biodegradable with similar removal rates obtained during biofiltration applications. It has been previously reported that, as low as 1.4 min of EBCT has been used to achieve efficient removal of aldehydes [52].

As described by Joss et al. [53], naproxen is considered bio-recalcitrant, with a low biodegradation constant rate ($1.0\text{-}1.9 \text{ L g}_{\text{SS}}^{-1} \text{ d}^{-1}$ for CAS, $0.4\text{-}0.8 \text{ L g}_{\text{SS}}^{-1} \text{ d}^{-1}$ for MBR) obtained by activated sludge from nutrient-removing municipal wastewater treatment plants. Comparing the observed bio-filtration and advanced oxidation rates of naproxen, it is clear that indirect oxidation via $\cdot\text{OH}$ provides an equivalent level of removal as an EBCT of 15 min, with a much shorter hydraulic retention time. Similar to previously reported results, observed adsorption of the selected NSAIDs was minimal (lower than 3% sorption with 24 hour contact time with biological GAC) [54].



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Fig. 7.5. Effect of EBCT on degradation of NSAIDs in Lake Bradford surface water by ozonation/BAC; dash line inserted as the removal at O₃ alone (1 mg L⁻¹) on NSAIDs; ketoprofen (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; O₃ dose: 1 mg L⁻¹; V: 100 mL; Ozone contact time: 2 min.

7.3.4 Degradation pathways of ozone/AOP on NSAIDs in Type II lab water

Intermediates derived from target compounds during ozonation/AOP processes were subjected to a close examination of chemical structure with ESI (+)/MS analysis. Mineralization pathways were proposed to provide a qualitative tool for toxicity assessment. As previously discussed, ozonation follows two basic reaction paths: 1) direct oxidation, which is rather slow and selective, and 2) auto decomposition to the hydroxyl radical. Since ozone and •OH are both present in the solution, ozone as well as •OH reactions with NSAIDs are considered [55].

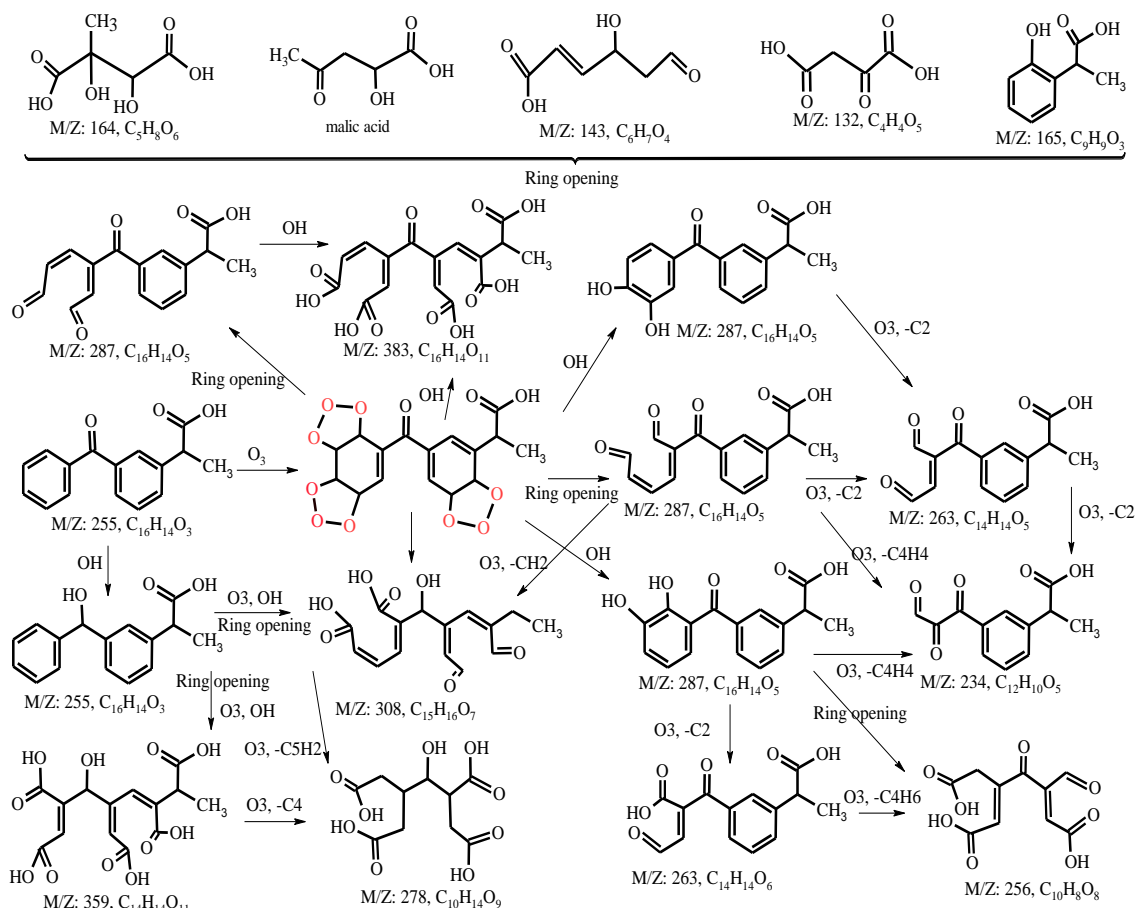
One abundant peak corresponding to the protonated ketoprofen ion [M-H⁺] was seen at *m/z* 255. At a 0.5 mg L⁻¹ O₃ dose, there was still a ketoprofen peak in the spectra, with *m/z* at 287, 255 and 359, as the by-products for early stage of ozonation/AOP. At 2 mg L⁻¹, ketoprofen was almost eliminated and other *m/z* peaks such as 278, 143, 165, and 132 were identified, mostly as organic acids. For AOP treatment of ketoprofen, the similar spectra peaks at a 0.5 mg L⁻¹ O₃ dose were obtained. The most intensive ions of naproxen in ESI were *m/z* 231 and *m/z* 187, of which the last one was due to the loss of CO₂ (*m/z*=44). At O₃ of 0.5 mg L⁻¹ for naproxen, the main peaks were *m/z* 265, 263, and a small peak at *m/z* 231. While at 2.5 mg L⁻¹ O₃ dose, the low *m/z* peak as 144, 165 and 131 were easily identified in the spectra. Similar peaks with advanced oxidation (1.0 mg L⁻¹ O₃ dose and 0.35 mg L⁻¹ of H₂O₂) treatment were also obtained in treated naproxen solutions. The identification of piroxicam was mainly by *m/z* peak at 332. After ozonation at 0.5 mg L⁻¹, main peaks appeared at *m/z* 332 and 381 and 243. At O₃ dose of 2 mg L⁻¹, *m/z* peak mainly were 144, 173, 132. While the molecular ion [M⁺] of 132 and 122 were mostly observed at AOP process for piroxicam.

The pathways proposed for ketoprofen, naproxen and piroxicam by direct and indirect oxidation are presented in figure 7.6. The proposals are based on the monitoring [M-H]⁺, reasonable assumptions for mechanism of the oxidation reaction and related literature published. It is well known that ozone attacks selectively on the structures containing C=C bonds, activated functional groups (eg. R-OH, R-CH₃, R-OCH₃), or

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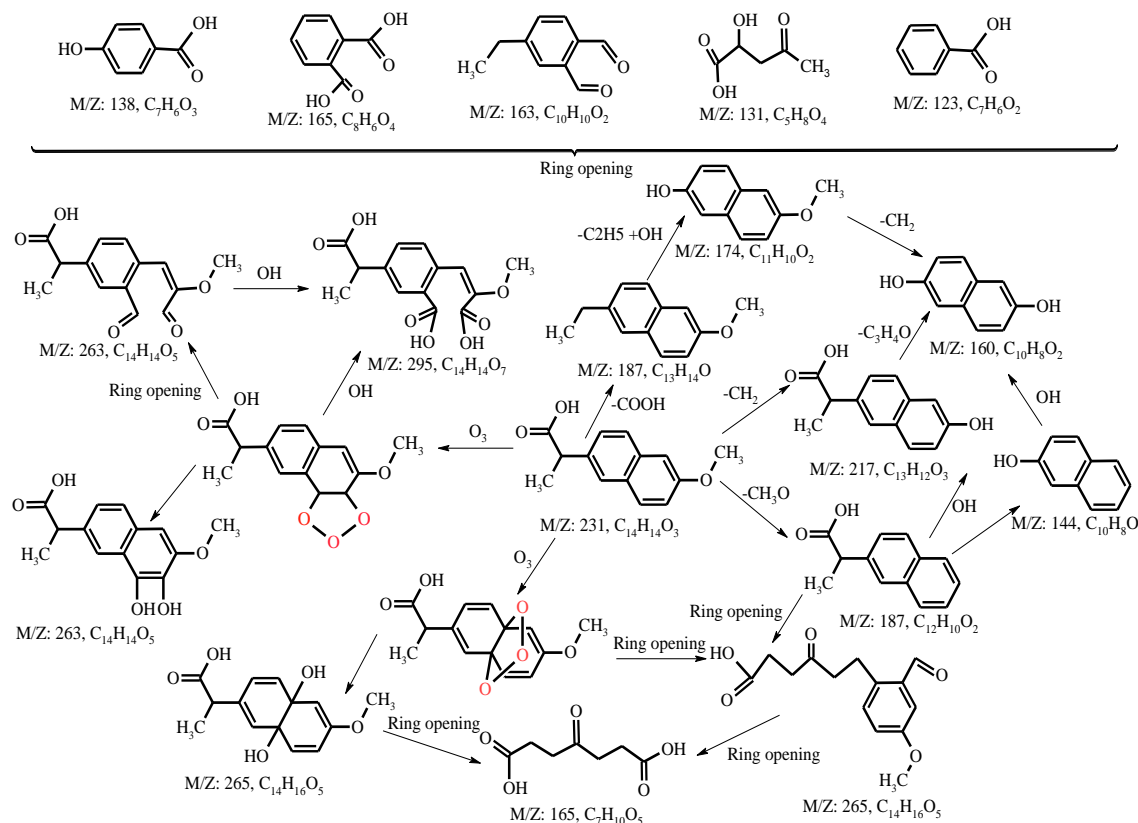
anions (eg. N, P, S, O) [56-58]. The reaction mainly happens by electrophilic substitution on an O-O-O (O_3) attack at the unsaturated electro-rich bonds as shown in red in figure 7.6, adding $\bullet OH$ or O on to the chain, increased m/z . Ozonation follows the Crigee mechanism, involving oxidative ring opening, leading to the formation of aldehyde moieties and carboxyl groups by cleavage. Furthermore, the $\bullet OH$ radicals and O-O-O continue to oxidize intermediates to form organic acids and keto acids by loss of a CH group, such as methyl group and saturated group.

The structures produced from ketoprofen have been identified by literatures of Salgado [59] via photodegradation, Kosjek also via phototransformation [60], and Quintana via biodegradation [61]. Naproxen's oxidative transformation pathways can be found in the literature of Hsu via the indirect photolysis of naproxen [62] with $\bullet OH$. With these published pathways as a guide, the following ozone transformation pathways are proposed.

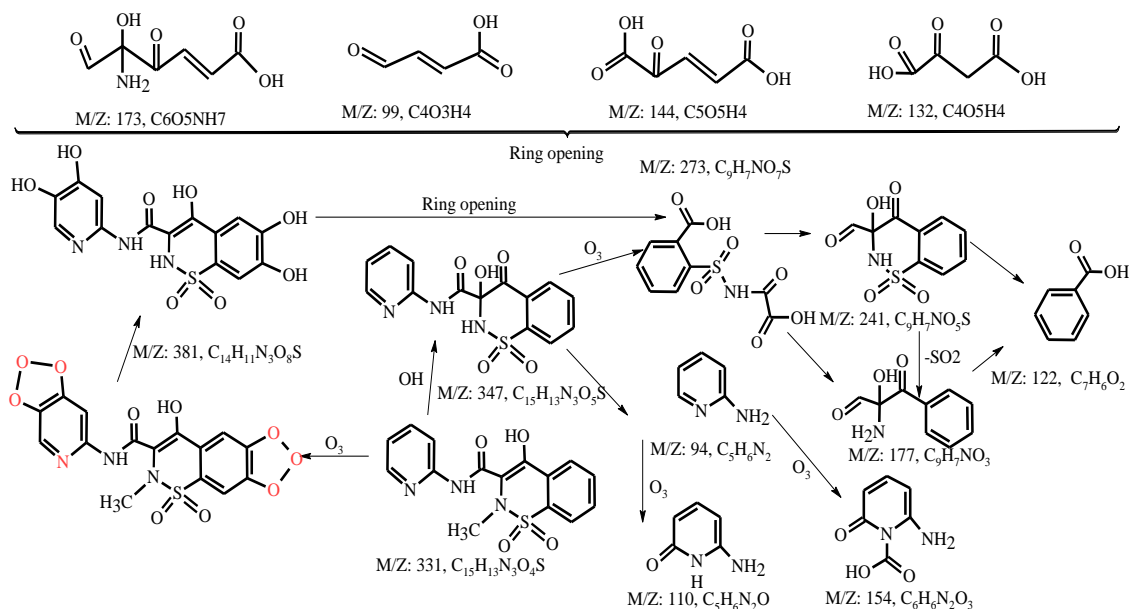


A: Ketoprofen.

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B: Naproxen.



C: Piroxicam.

Fig. 7.6. Pathway proposed for the oxidation of NSAIDs selected by ozonation/AOP.

Both direct and indirect oxidations happen simultaneously, and oxidants attack more than one position in one molecule, as Figure 7.6 shows. The hydroxylated

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derivatives formed are confirmed by the presence of compounds with an increased m/z of one more oxygen atoms or $\bullet\text{OH}$, which can come from direct reaction of ozone molecule or hydroxyl radical produced from the decomposition of ozone in aqueous media, or $\bullet\text{OH}$ produced during the AOP. In the last step, short chain carboxylic acids are formed as final mineralization produces and mainly contribute to TOC mineralization and biodegradability.

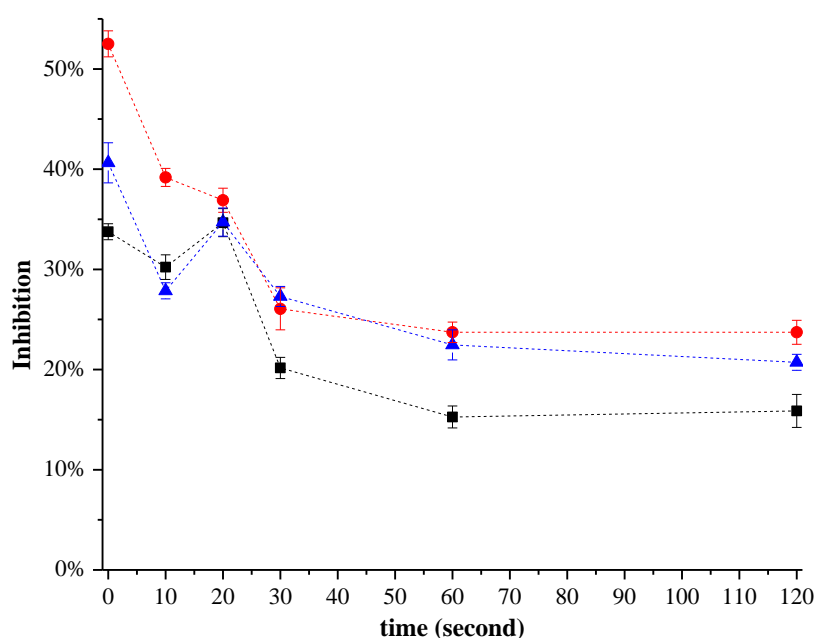
7.3.5 Toxicity Evaluation

Considering that in the array of intermediates formed during ozonation of NSAIDs in surface waters, some by-products will be more or less pharmaceutically-active than others. It is critical for water treatment plant operators to be able to assess formation of cytotoxic products with fluctuating influent and ozone oxidation conditions. In addition, for plants employing BAC filtration to quench residual toxicity and oxidants following ozone and AOPs, a rapid bioassay, like Microtox, can be used to assess multi-barrier treatment efficiency, and is known to indicate the toxic potency of a broad spectrum of compounds with different modes of action. After an initial ozone dose of 2 mg L^{-1} , Figure 7.7 depicts the evolution of cytotoxicity with increasing contact time. The trend of decreasing bioluminescence inhibition is evident, except at $t = 20 \text{ s}$ where there was an inhibition peak for all the three compounds. Evolution of toxicity of NSAIDs treated by ozonation at different ozone dosages is shown in Figure 7.8. The contact time for all ozone doses was 2 min before quenching. The toxicity decreased with the higher ozone doses applied in each water matrix containing NSAIDs. While at the ozone dose of 1 mg L^{-1} , an increase in toxicity for both piroxicam and ketoprofen occurred in both water matrices. At this dose, significant concentrations of toxic byproducts accumulated in the solution that were not eliminated, likely to be hydroxylated benzophenone, catechol, benzoic acid, and some alkyl groups [63]. The toxicity in Type II lab water decreased faster than in surface water, most likely due to the slower oxidation kinetics in surface water with increased oxidant scavenging by other dissolved solutes.

The effect of H_2O_2 and O_3 on inhibition of luminescence by *V. fischeri* bacteria in NSAIDs solutions was also studied. As shown in Figure 7.9, the inhibition curves for the compounds treated in Type II lab water decreased with the application of higher dose of H_2O_2 , whereas, naproxen's cytotoxicity dropped sharply from mole ratio of

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H_2O_2 to O_3 from 0.3 to 0.5. In all cases, luminescence inhibition was lower than with O_3 alone at a 1 mg L^{-1} dose. The application of AOP in surface water showed slightly lower inhibition than in Type II lab water at H_2O_2 to O_3 of 0.3 for all three compounds. While increased inhibitions was observed in naproxen solutions with a higher molar ratio of 0.3, which indicated that for naproxen in surface water, the ratio of H_2O_2 to O_3 of 0.3 could achieve better removal efficiency of NSAIDs, and leaving with lower residual toxicity. For piroxicam in surface water, there was peak inhibition at a ratio of 0.5 ($\text{O}_3/\text{H}_2\text{O}_2$), then the curve decreases. The toxic value was lower than that in Type II lab water at any ratio of $\text{O}_3/\text{H}_2\text{O}_2$ or ozone alone, which means the application of AOP, is most efficient for removal of piroxicam and its toxic intermediates. With the exception of $\text{O}_3/\text{H}_2\text{O}_2$ at a ratio of 1, the inhibition percentage of ketoprofen surface water solutions was lower than in Type II lab water with O_3 application. From the observed toxicity evolution for the three compounds selected, it was evident that naproxen exhibits higher toxicity to *V.fischeri* than the other selected NSAIDs, which can be explained by the potential for more aromatic by-products present in the solution (Fig. 7.5), raising solution toxicity. Meanwhile, the more organic acids produced by oxidation of ketoprofen and piroxicam favor further biological treatment in oxidized solutions. Following cytotoxicity evaluation, $\text{O}_3/\text{H}_2\text{O}_2$ at a ratio of 0.5, with an initial ozone dose of $2 \text{ mg L}^{-1} \text{ O}_3$ and a contact time of 2 min should be preferred for the treatment of NSAIDs in the tested water matrices.



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Fig. 7.7. Evolution of the inhibition of marine bacteria, *Vibrio fischeri* luminescence during ozonation in Type II lab water at increasing contact time with O₃; ketoprofen: (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; O₃ dose: 2 mg L⁻¹; V: 100 mL.

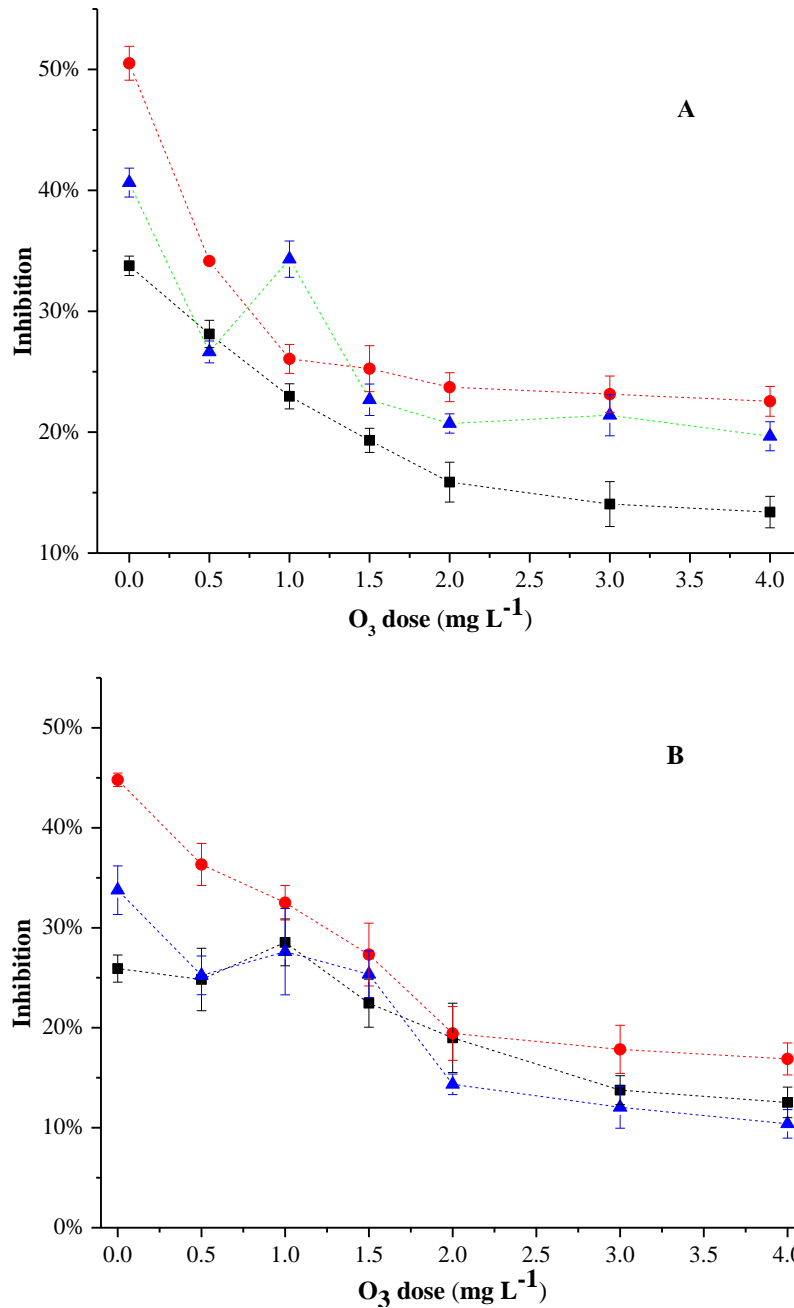


Fig. 7.8. Evolution of the inhibition of marine bacteria, *Vibrio fischeri* luminescence during ozonation in Type II Lab (A) and surface water (B) at different O₃ dose; ketoprofen: (■); naproxen (●); piroxicam (▲); C₀: 2 mg L⁻¹; V: 100 mL; Ozone contact time: 2 min.

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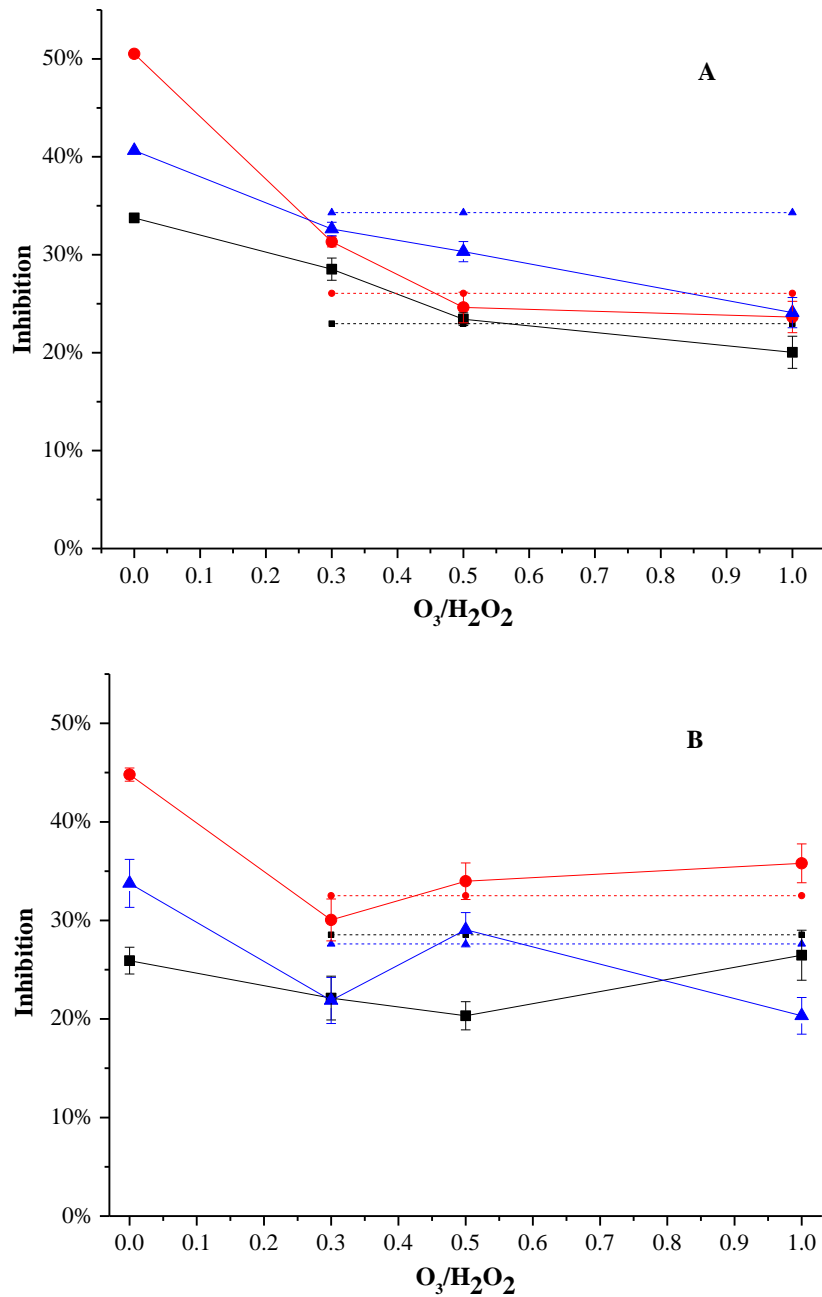


Fig. 7.9. Evolution of the inhibition of marine bacteria, *Vibrio fischeri* luminescence during AOP at different mole ratio of O_3/H_2O_2 in Type II Lab (A) and surface water (B); dash line indicates the inhibition (%) of ozone alone (1 mg L⁻¹) on NSAIDs; ketoprofen: (■); naproxen (●); piroxicam (▲); C_0 : 2 mg L⁻¹; O_3 dose: 1 mg L⁻¹; V: 100 mL; Ozone contact time: 2 min.

Figure 7.10 reveals a higher toxicity at this EBCT than when to piroxicam and naproxen solutions where treated with O_3 only. At this short contact time with bacteria

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in BAC, the initial metabolites can contribute to increased bioluminescence inhibition. However, solution toxicity was observed to decrease until an EBCT of 10 min, with another increase at 15 min of EBCT. The inhibitory effects of ketoprofen decreased up to 8 min EBCT, then increased; however, the observed level of inhibition was always lower than the value produced by O_3 alone. The increasing inhibition of bioluminescence at longer EBCT was also confirmed by Reungoat et.al [64], indicating that increasing the contact time during biofiltration would not improve the water quality further.

In combination with the efficiency of degradation at different EBCT, good removal rates and lower toxicity were achieved at 8 min for all three compounds. Due to the expected benefits to operating costs and observed rates of NSAID degradation and toxicity removal, ozonation followed by BAC treatment for polishing drinking water, can provide effective and efficient barriers to wastewater-derived, pharmaceutically-active organic contaminants in surface water.

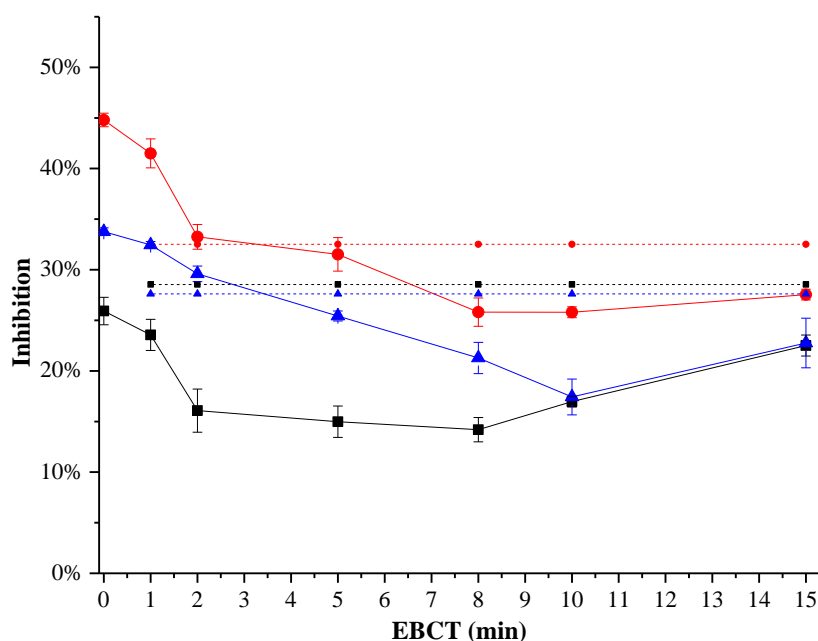


Fig. 7.10. Evolution of the inhibition of marine bacteria, *Vibrio fischeri* luminescence during ozonation/BAC at different EBCT; dash line indicates the inhibition (%) of ozone alone (1 mg L^{-1}) on NSAIDs; ketoprofen: (■); naproxen (●); piroxicam (▲); C_0 : 2 mg L^{-1} ; O_3 dose: 1 mg L^{-1} ; V: 100 mL; Ozone contact time: 2 min.

7.4 Conclusions

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The implications of this study were to investigate the removal efficiency and evolution of toxicity on *V. fischeri* on ketoprofen, naproxen and piroxicam by ozone/AOP/BAC treatments in Type II lab and SW water. Experiments were operated at O₃ dose, O₃/H₂O₂, EBCT and temperature for BAC. All 3 target pharmaceuticals were efficiently removed with an increasing rate v.s. increasing O₃ dose, O₃/H₂O₂, EBCT and temperature in ozone/AOP/BAC application, while with lower value in SW, compared with Type II lab water. Using competition kinetics, the rate of direct ozone oxidation of piroxicam was measured as $3.3 (\pm 0.1) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$. Their potentially toxic oxidation intermediates also were discussed in the context of background water quality, careful control of ozone dosing, and the importance of coupling ozonation with biological filtration. General, inhibition of bacterial luminescence dropped with higher O₃ dose, O₃/H₂O₂, longer EBCT, and temperature for all 3 oxidized pharmaceutical solutions. Best parameters could be obtained for ozonation/AOP/BAC under the consideration of removal rate and level of toxicity. From the results, it can be concluded it is useful and ecofriendly application of ozonation with biofilm treatment in conventional treatment for drinking water to remove NSAIDs.

Acknowledgments

Ling Feng is a Doctoral research fellow of the Erasmus Mundus Joint Doctorate programme ETeCoS³ (Environmental Technologies for Contaminated Solids, Soils and Sediments) under the grant agreement FPA no. 2010-0009.

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Chapter 8. General Discussion

8.1 Statements of the results

8.1.1 Optimization of the processes

8.1.1.1. Effect of experimental parameters on the electrochemical oxidation processes efficiency

The electrochemical oxidation of ketoprofen, naproxen at 0.198 mM and piroxicam at 0.08 mM has been conducted in tap water. 50 mM Na₂SO₄ was introduced to the cell as supporting electrolyte. For electro-Fenton (EF) processes, the experiments were operated at pH 3 using carbon felt as cathode and Pt or boron-doped diamond (BDD) as anode. In anodic oxidation (AO) process, the experiments were set-up with carbon felt as cathode and BDD as anode (Fig. 8.1).

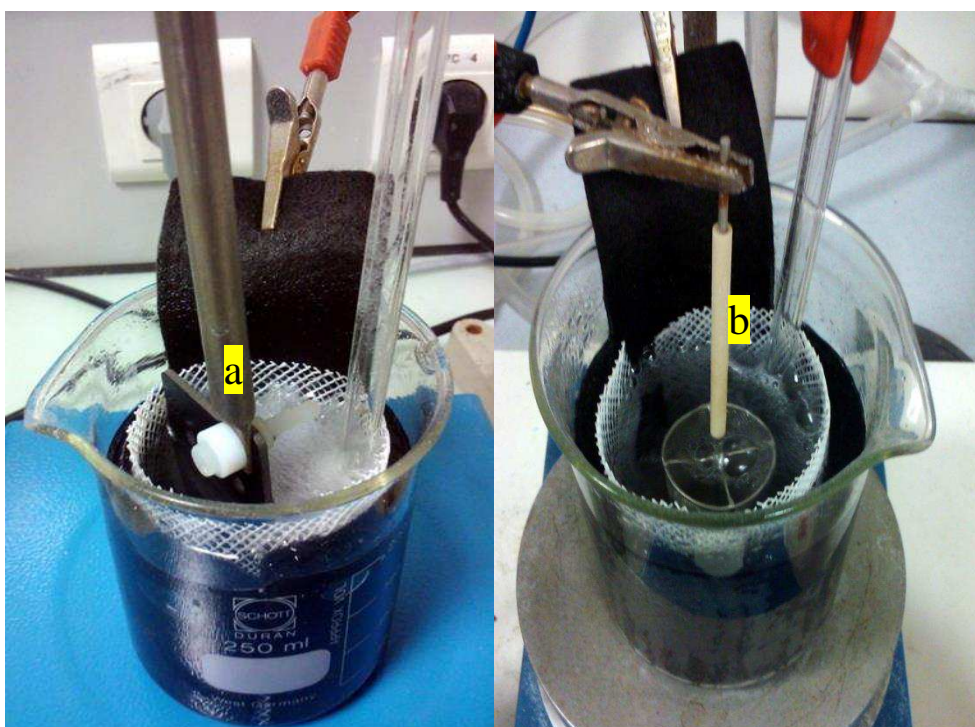


Fig. 8.1. Electrochemical oxidation processes with carbon felt as cathode and BDD (a) or Pt (b) as anodes.

As an important parameter influencing the process efficiency, a series of catalyst concentrations applied in EF was firstly operated at a low current intensity (i.e. 100 mA). The best removal rate was obtained with 0.1 mM Fe²⁺ for ketoprofen and naproxen, while 0.2 mM was needed for piroxicam. The degradation rate was significantly slowed

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down with 1.0 mM Fe²⁺; due to side reaction of iron with •OH (Eq. (8.1)) as wasting reaction:



With 0.1 mM Fe²⁺, 50 min were sufficient for the complete removal of both ketoprofen and naproxen. The time required for complete removal of 0.08 mM piroxicam was 30 min with 0.2 mM Fe²⁺. Accordingly, the optimized iron concentration for each compound was used in the rest of the experiments.

Due to the inconsistent removal values reported in the literature for AO process, the effects of pH and introduction of compressed air on the treatment efficiency were studied at an applied current intensity of 300 mA. Firstly, pH values of 3.0, 7.5 (natural pH) and 10.0 for ketoprofen and naproxen, while 3.0, 5.5 (natural pH) and 9.0 for piroxicam were tested in the oxidation processes. It was shown that, pH influenced significantly the nonsteroidal anti-inflammatory (NSAID) molecules degradation efficiency in AO process. The best degradation rate of ketoprofen and naproxen was achieved at pH 3.0, followed by pH 7.5, which was slightly better than pH 10. Similar results were obtained regarding the degradation of piroxicam. The removal rate followed the order of pH 3.0 > 5.5 > 9.0. It may due to at acidic condition, H₂O₂ is easily produced from (Eq. (8.2)):



In addition, O₂ gas can be reduced to the weaker oxidant as HO₂⁻ under alkaline condition (Eq. (8.3)):



In contrast when monitoring the mineralization rate for AO process, pH was not significantly influencing the NSAID molecules mineralization rate. Same mineralization removal trends were obtained for ketoprofen and naproxen. However, the mineralization rate was better at pH 3, followed by at pH 9.0 and 5.4 with no much difference for piroxicam.

Afterwards, effect of bubbling compressed air through the solution in AO process at pH of 3 (higher removal rate) was then performed. It showed that the air bubbling influenced efficiency, the removal rate was lower than pH of 3.0, but higher than other pH applied in this research.

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The applied current intensity is other main parameter for EAOPs oxidation, and the experiments were set-up with varying current intensity in the experiments. Oxidative degradation rate and mineralization of the solution increased by increasing applied current. The main reason is at higher current intensity, the enhancement of electrochemical reactions (Eqs. (8.3)-(8.6)) generating more heterogeneous $M(\bullet\text{OH})$ and at higher extent from Eq. (8.4), and high generation rate of H_2O_2 from Eq. (8.5).



Also, iron can be regenerated (Eq. (8.6)) with a higher rate to produce more $\bullet\text{OH}$ (Eq. (8.7)):



All the degradation kinetics well fitted to a pseudo–first order reaction.

The percentage of TOC removal can reach to above 90% at 2 hour electrolysis time of 1000 mA applied intensity. The trends of evolution of mineralization of current efficiency (MCE) with electrolysis time decreased with increasing current intensity. There was an obvious difference between current density of 100 and 300 mA, but not too much with the upper current values.

The EF process with BDD or Pt anode has better removal rate than AO with BDD anode in degradation as the results showed. While in the mineralization part, the EF-BDD has the best removal rate but followed by EF-Pt or AO-BDD for different pollutants treated.

8.1.1.2 Optimization of the ozonation/biofiltration treatments

The experiments using ketoprofen, naproxen and piroxicam of 2 mg L^{-1} in both lab (de-ionized) and surface water were operated for the optimization of the ozonation/biofiltration treatments.

The effect of contact time as well as efficient ozone doses requested to reach the best removal of three compounds in lab water was studied. The results showed that 2 min was enough to ensure >90% oxidation of all the three pharmaceutical compounds in lab water, and afterwards, 2 min was applied in all ozone experiments as contact time. The optimization of ozone dose was applied in both type II lab and surface water in the

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experiments. As expected, the increasing initial ozone dose contributed to greater oxidation in both lab water and surface water, but a lower removal rate in surface water, due to the presence of background oxidant scavengers (natural organic matters). In the range of ozone dose from 0.5 mg L^{-1} to 2 mg L^{-1} , the degradation rate increased more than 40%, while less than 6% in the range of 2 mg L^{-1} to 4 mg L^{-1} in type II lab water. Based on the results, 2 mg L^{-1} was selected as the optimal oxidant dose with >90% removal rate.

In sequential $\text{O}_3/\text{H}_2\text{O}_2$ part, different mole ratios of $\text{O}_3/\text{H}_2\text{O}_2$ molar ratios (ozone dose fixed at 1 mg L^{-1}) were applied in experiments. The efficiency of $\text{O}_3/\text{H}_2\text{O}_2$ in type II lab water was higher than in the surface water. It is obvious that addition of H_2O_2 highly improved the removal rate compared with ozone application alone. An improved value at $\text{O}_3/\text{H}_2\text{O}_2$ of 1 was obtained of 33%, 55% and 28% for ketoprofen, naproxen and piroxicam, respectively. Due to the secondary reactions with natural organic matters in surface water, the removal rate increased obviously with increasing ratio in surface water, but not much in type II lab water.

TOC values were measured for surface water after mineralized by ozone and $\text{O}_3/\text{H}_2\text{O}_2$. About 20% of the mineralization rate can be achieved at O_3 dose of 4 mg L^{-1} and more than 20% at mole ratio of $\text{O}_3/\text{H}_2\text{O}_2$ at 1. The results were higher than the data from other related literatures with a low TOC removal in the application of ozone/ O_3 and H_2O_2 .



Fig. 8.2. Saturated filter columns with varying volumes of sampled BAC media.

When ozone treatment is combined with biofiltration, oxidized surface water (O_3 dose at 1 mg L^{-1}) was injected through biofilm columns filled with biofilm-supporting granular activated from a municipal drinking water treatment facility (Fig. 8.2). The effect of the empty bed contact time (EBCT) and temperature on nonsteroidal anti-inflammatory molecules removal efficiency was evaluated. The removal efficiency of the three compounds by combination was better than that of the application of H_2O_2 and O_3 at ratio of 1 at 5 min for ketoprofen and piroxicam while 10 min for naproxen as EBCT. A removal rate of combined ozonation/biofiltration was achieved as 93%, 88% and 92% for ketoprofen, naproxen and piroxicam, respectively at an EBCT of 15 min. As the results showed, an EBCT of 5 min is an efficient contact time for ketoprofen and piroxicam while 10 min for naproxen, due to not much improvement of removal rate was obtained afterwards. Otherwise, the increasing solution temperature helped to improve the removal efficiency in ozonated surface water.

8.1.2. Kinetic study for the degradation

The absolute rate constant of the oxidation by electrochemically generated hydroxyl radicals was determined by using competition kinetics method. The p -

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hydroxybenzoic acid (*p*-HBA) was selected as standard competitor. The values were determined as $(2.8 \pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, $(3.67 \pm 0.03) \times 10^9 \text{ M}^{-1} \cdot \text{s}^{-1}$ and $(2.19 \pm 0.01) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for ketoprofen, naproxen and piroxicam, respectively. The absolute rate constant of piroxicam reacted with O_3 was determined as $(3.3 \pm 0.1) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$.

8.1.3 Pathway of the mineralization of the pharmaceuticals

For the investigation of electrochemical oxidation on the compounds selected, the identification of the intermediates formed during the mineralization was performed at a lower current intensity (i.e. 50 to 100 mA) with Pt as anode. It was observed that the aromatic intermediates were formed at the early stage of the electrolysis in concomitance with the disappearance of the parent molecule. For the evolution of main carboxylic acids, the similar trends were obtained but EF-BDD had a quicker removal rate than EF-Pt. Oxalic and acetic acids were persistent during the whole processes in all the compounds oxidized solutions.

For piroxicam, inorganic ions such as ammonium, nitrate, and sulfate ions were identified and quantified by ion chromatography during the mineralization. About 70% of the nitrogen atoms were transformed into NO_3^- ions, whereas only about 25% NH_4^+ ions were formed to a lesser extent. For sulfur atoms, about 95% converted into SO_4^{2-} ions at the end of the electrolytic treatments. Similarly, EF-BDD has a higher releasing inorganic ions concentration than EF-Pt.

Based on the identified aromatic intermediates and carboxylic acids as end-products before mineralization, plausible mineralization pathways were proposed. In total, the reaction happens by addition of $\bullet\text{OH}$ on the aromatic rings (hydroxylation) or by H atom abstraction reactions from the side chain propionic acid group. These intermediates were then oxidized to form polyhydroxylated products that underwent finally oxidative ring opening reactions, leading to the formation of aliphatic compounds. Mineralization of short-chain carboxylic acids constituted the last step of the process as showed by TOC removal data.

For the assessment of biological effect of the ozonation/biofiltration, intermediates derived from target compounds during ozone/AOP processes in type II lab were analyzed subject to a close examination of their chemical structures with ESI (+)/MS analysis. According the intermediates formed and mechanism, the oxidation

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mainly happens by electrophilic substitution on an O-O-O (O_3) attack at the unsaturated electro-rich bonds, involving oxidative ring opening and leading to the formation of aldehyde moieties and carboxyl groups by cleavage. Furthermore, the $\bullet OH$ radicals and O-O-O continue to oxidize intermediates to form organic acids and keto acids by loss of a CH group, such as methyl group and saturated group. Then short chain carboxylic acids were formed as final mineralization products. Oxidation pathways of the three compounds were proposed based on the intermediates formed. It well confirmed both direct and indirect oxidations happen simultaneously, and oxidants attack more than one position in one molecule.

8.1.4 Toxicity evolution of the solution treated

The evolution of effluent toxicity during AOPs treatments was monitored by Microtox[®] method with exposure of *Vibrio fischeri* luminescent bacteria to the oxidized solutions.

For EAOPs, experiments were conducted over 120 min electrolysis times at two current intensities. The toxicity (as % luminescence inhibition) increased quickly at the early treatment time, and then decreased below its initial percentage. This is due to the degradation of primary intermediates and formation to secondary/tertiary intermediates that can be more or less toxic than previous intermediates. Then toxic intermediates are removed by oxidation. It was observed no much inhibition difference between treatments, while luminescence inhibition lasted longer for smaller current intensities values, which was attributed to $\bullet OH$ formation rate as function of current intensity value.

When ozonation is combined with biofiltration system, the results indicated a decreasing bioluminescence inhibition for ozone contact time experiments for all the three compounds, except an inhibition peak at 20 seconds. The toxicity decreased with the higher ozone doses applied in each water matrix but an increasing value at the ozone dose of 1 mg L^{-1} for both piroxicam and ketoprofen was noticed. At this sampling solution oxidized, more toxic byproducts may be accumulated in the solution that were not eliminated, as hydroxylated benzophenone, catechol, benzoic acid, and some alkyl groups identified in intermediates part. The toxicity decreased faster in lab water than in surface water. This difference is likely due to the pollutants oxidation rate slowed down by other dissolved solutes (mainly natural organic matter).

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When ozonation is combined with H₂O₂ treatment, the luminescence inhibition of the combination application was significantly lower than with ozone applied alone.

At ozone/biofiltration treatments, the evolution of toxicity decreased till 10 min but with a slow increase afterwards, meaning that increasing the application time of biofiltration would not improve the water quality furthermore. With the increasing bacteria of high temperate, the toxicity decreased in the temperature from 0 to 35 degree.

In all the processes, the oxidized naproxen solution has higher inhibition value than other two as the toxicity evolution showed, which also can be concluded that more aromatic by-products present in the solution, which raises the toxicity.

8.2 Perspective for the future works

Beside the emphasis on the optimization of the AOPs, the elucidation of degradation pathway and the evolution of effluent toxicity, the improvements for AOPs to produce safe water for the future work have been summarized as follows.

1. As mentioned above (see chapter 2), most investigations are done at lab-scale. For a practical view and commercial uses, much more work is necessary to switch from batch work to a large scale to find out the efficiency and ecotoxicity of the processes.
2. Regarding most researches on model aqueous solutions or surface waters, more focus can be put in actual wastewaters from sewage treatment plants or effluents from pharmaceutical industrial units.
3. The rational combination of AOPs and other process can be a step towards the practical application in water treatments plants. The attention should be paid to the economical (biofiltration) and renewable energy (solar light), better removal efficiency, and lower ecotoxicity risk of complex pollutants during the oxidation.
4. More point of views, such as technical, socioeconomic and political one, can be applied for the assessment of AOPs. Also, these aspects are useful for the improvement of sustainability of the wastewater management.

8.3 Conclusion

The removal of the nonsteroidal anti-inflammatory drugs ketoprofen, naproxen and piroxicam from tap water was performed by EAOPs such as EF and AO. The effect of operating conditions on the process efficiency, such as catalyst (Fe²⁺) concentration,

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applied current intensity value; nature of anode material, bulk solution pH, and air bubbling was studied. The effectiveness of degradation by these AOPs was also studied by determining the intermediates generated and the toxicity of degradation products was evaluated. One can conclude that:

1. The fastest degradation rate of ketoprofen and naproxen by EF was reached with 0.1 mM of Fe^{2+} (catalyst) concentration, while 0.2 mM iron was requested for piroxicam. Further increase in catalyst concentration results in decrease of nonsteroidal anti-inflammatory drugs oxidation rate due to enhancement of the rate of the parasitic reaction between Fe^{2+} and $\bullet\text{OH}$.

2. The degradation curves by hydroxyl radicals within electrolysis time followed pseudo-first-order reaction kinetics. Increasing current density accelerated the degradation processes. The oxidation power and the removal ability was found to follow the sequence AO-BDD < EF-Pt < EF-BDD, indicating higher oxidation power of BDD anode compared to Pt anode.

3. Solution pH in AO affects greatly the oxidation efficiency of the process for all the three compounds. The value of pH 3 allows reaching the highest nonsteroidal anti-inflammatory drugs degradation rate.

4. The absolute (second order) rate constant of the oxidation reaction by $\bullet\text{OH}$ was determined as $(2.8 \pm 0.1) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, $(3.67 \pm 0.03) \times 10^9 \text{ M}^{-1} \cdot \text{s}^{-1}$, and $(2.19 \pm 0.01) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ by using competition kinetic method for ketoprofen, naproxen and piroxicam, respectively.

5. High TOC removal (mineralization degree) values were obtained using high current intensity, and the highest mineralization rate was obtained by EF-BDD set-up. The mineralization current efficiency (MCE) decreased with increasing current intensity, due to the side reaction and energy loss on the persistent byproducts produced, such as oxalic and acetic acids.

6. Intermediates identified showed aromatic intermediates were oxidized at the early stage, followed by the formation of short chain carboxylic acids from the cleavage of the aryl moiety. The remaining TOC observed can be explained by the residual TOC related to persistent oxalic and acetic acids present already in solution at trace level even in the end of treatments.

7. A plausible oxidation pathway for each compound by hydroxyl radicals was proposed based on the identification by HPLC.

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8. The evolution of the toxicity of treated solutions highlighted the formation of more toxic intermediates at early treatment time, while it was removed progressively by the mineralization of aromatic intermediates. The evolution of the toxicity was in agreement of the intermediates produced during the mineralization for the pollutants by EAOPs.

Finally the obtained results of degradation, mineralization, evolution of the intermediates and solution toxicity show that the EAOPs, in particular electro-Fenton process with BDD anode and carbon felt cathode, are able to achieve a quick elimination of the pharmaceuticals from water, could be applied as an environmentally friendly technology.

The removal efficiency, intermediates formed and evolution of toxicity toward *V. fischeri* for ketoprofen, naproxen and piroxicam after ozone/O₃/H₂O₂/BAC treatments in lab and lake water was monitored for ketoprofen, naproxen and piroxicam. Results showed:

1. 2 min is an efficient contact time for ozone reaction with the pollutants. The removal rates increase with increasing O₃ dose, O₃/H₂O₂, and EBCT in ozone/AOP/BAC application, albeit a lower oxidation rates obtained in the sampled surface water than in organics-free lab water.

2. The intermediates produced during the oxidation were identified and pathways for the mineralization were proposed. Inhibition of bacterial luminescence percentages declined with higher O₃ dose, O₃/H₂O₂, and limited longer EBCT, for all 3 oxidized pharmaceutical solutions.

3. The best management practice could be obtained for ozone/AOP/BAC under the consideration of removal rate and level of residual cytotoxicity, as ozone doses at 2 mg L⁻¹, a O₃/H₂O₂ of 0.5 and 8 min empty bed contact time with flow-up filtration.

The discussed results were in agreement with previous studies showing enhanced removal of advanced oxidation by-products by following O₃ treatment with BAC filtration.

Of the EAOPs and ozonation/biofiltration system, all the process could achieve >90% removal under the optimized condition. Under the best conditions, however, almost 100% removal achieved. The best treatment results were obtained with

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the EF process, which under the optimal pH equal to 3 and catalyst (Fe^{2+}) concentration around 0.1 mM for three compounds. For higher current intensity the removal efficiencies were less time dependent and essentially it was not worth increasing the current over 300 mA, as the benefit increase not significantly with a contact time of up to 40 min (degradation) and 4 h (mineralization) electrolysis time.

Regarding ozonation, this process gave excellent results of the removal of pharmaceuticals leading to >90% in 2 min at the ozone dose of 2 mg L^{-1} . At less dose of 1 mg L^{-1} of ozone, coupling with H_2O_2 addition or biofiltration application, the removal was also sufficient to reach more than 90%. In any case the necessity of coupling treatment by biofiltration would imply an additional step in the global treatment scheme.

On the basis of the results of the present study it is hypothesized that the performance of electrochemical oxidation is better than ozonation/biofiltration system with regard to the TOC abatement, detection of intermediates and evolution of solution toxicity (except $4 \text{ mg L}^{-1} \text{ O}_3$ achieved similar toxic value). During oxidation they accumulate in the solution and oxidize further, simultaneously removal of a primarily present pollutant.

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Areas of Specialization

- Advanced Oxidation Processes
- Bacteria DNA extraction from sample of environment and amplify technology
- Detection of Pollutants of Wastewater, Surface Water, Drinking Water, Soil, Sediments

Education

Ph. D. in Environmental Engineering, University of Paris-Est, Laboratoire Géomatériaux et Environnement (LGE), 2010-2013 (on processing)

Thesis title: Advanced Oxidation Processes for the Removal of Pharmaceuticals from Urban Water Cycle.

M.S. in Environmental Science, Environmental Science and Engineering, Nankai University, Tianjin, China, 2007-2010

Thesis title: Method of Extracting Different Forms of DNA and Detection of the Existing Forms of Antibiotic Resistance Genes in Environment.

B.S. in Environmental Science, Resource and Environment, Northwest Agriculture and Forest University, Shannxi, China, 2003-2007

Thesis title: The Composition of Soluble Cations and Their Relation to Mg^{2+} in Soils of Sunlight Greenhouse.

Research Experience

Florida State University, Civil & Environmental Engineering, Laboratory working, Ozonation and Biofiltration on Pharmaceuticals from Drinking Water, September 2012-February 2013

University of Cassino and Southern Lazio, Department of Mechanics Structures and Environmental Engineering, Office working, Modelling on Anodic Oxidation of Phenol, April 2013-July 2013

Conferences

18th International Conference on Advanced Oxidation Technologies for Treatment of Water, Air and Soil (AOTs-18) (11-15 November, 2012, Jacksonville, USA: Removal of Ketoprofen from Water by Electrochemical Advanced Oxidation Processes)
2013 World Congress & Exhibition International Ozone Association & International Ultraviolet Association (22-26 September, 2013, Las Vegas, USA, presented by Dr. Watts: Removal of Pharmaceutical Cytotoxicity with Ozone and BAC)

Summer Schools Attended

Summer School on Biological and Thermal Treatment of Municipal Solid Waste
(2-6 May 2011 - Naples, Italy)
Summer School on Contaminated Soils: from Characterization to Remediation
(18-22 June 2012 – Paris, France)
Summer School on Contaminated Sediments: Characterization and Remediation
(17-21 June 2013 –Delft, Netherlands)

List of Publications

Feng, L., van Hullebusch, E.D., Rodrigo, M.A., Esposito, G. and Oturan, M.A. (2013) Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced oxidation processes. A review. *Chemical Engineering Journal* 228, 944-964.

Feng L., Luo, Y. (2010) Methods of extraction different gene types of sediments and water for PCR amplification. *Asian Journal of Ecotoxicology* 5(2), 280-286 (paper related to master thesis).

Feng, L., Oturan, N., van Hullebusch, E.D., Esposito, G. and Oturan, M.A. Degradation of anti-inflammatory drug ketoprofen by electro-oxidation: comparison of electro-Fenton and anodic oxidation processes. *Accepted in Current Organic Chemistry*.

Feng, L., Michael J. W., Yeh, D., van Hullebusch, E. D., Esposito, G. Removal of Pharmaceutical Cytotoxicity with Ozonation and BAC Filtration. *Submitted to ozone: science and engineering*.

Mao, D.Q., Luo, Y., Mathieu, J., Wang, Q., Feng, L., Mu, Q.H., Feng, C.Y., Alvarez, P. Persistence of extracellular DNA in river sediment facilitates antibiotic resistance gene propagation. *Submitted to Environmental Science & Technology* (paper related to master thesis).

In preparation

Feng, L., Oturan, N., van Hullebusch, E.D., Esposito, G. and Oturan, M.A. Electrochemical oxidation of naproxen in aqueous medium by the application of a carbon felt cathode and a boron-doped diamond/Pt anode.

Feng, L., Oturan, N., van Hullebusch, E.D., Esposito, G. and Oturan, M.A. Electrochemical oxidation of naproxen in aqueous medium by the application of a boron-doped diamond anode and a carbon felt cathode.

Feng, L., Oturan, N., van Hullebusch, E.D., Esposito, G. and Oturan, M.A. Removal of piroxicam from aqueous solution: comparison of anodic oxidation and electro-Fenton processes.