Application of Liquid Chromatography-Mass Spectrometry for the Analysis of Endocrine Disrupting Chemical Transformation Products in Advanced Oxidation Processes and Their Reaction Mechanisms

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Jin-Chung Sin, Sze-Mun Lam, and Abdul Rahman Mohamed

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Abstract

Advanced oxidation processes (AOPs) have gained a great deal of attention as they held great promise for the treatment of wastewater contaminated with noneasily removable organic pollutants. The assessment of transformation products allowed the overall efficiency of AOPs to be better understood since some transformation products possessed higher toxicity than the mother compounds. Liquid chromatography coupled to mass spectrometry has been heavily used as

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J.-C. Sin (✉)
Department of Petrochemical Engineering, Faculty of Engineering and Green Technology, Universiti Tunku Abdul Rahman, Kampar, Perak, Malaysia
e-mail: sinjc@utar.edu.my

S.-M. Lam
Department of Environmental Engineering, Faculty of Engineering and Green Technology, Universiti Tunku Abdul Rahman, Kampar, Perak, Malaysia

A. R. Mohamed
School of Chemical Engineering, Universiti Sains Malayisia, Engineering Campus, Nibong Tebal, Pulau Pinang, Malaysia

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an analytical tool in the environmental field as it allowed the best performance in assigning the identity of the transformation products detected. This chapter reviews liquid chromatography-mass spectrometry for the identification of endocrine disrupting chemical (EDC) transformation products formed from several AOPs such as photolysis, photocatalysis, sonolysis, and Fenton treatment. EDCs are a group of special interest due to their ability to exert hormonal imbalance activity and consequently caused adverse health effects in an organism or its progeny. Data concerning to the mechanism of AOP-mediated reactions on the EDCs degradation are also discussed in this chapter. Finally, the future prospects of AOPs on EDCs degradation are summarized and discussed.

Keywords
Advanced oxidation process · Endocrine disrupting chemical · Degradation intermediate · Liquid chromstography coupled to mass spectrometry

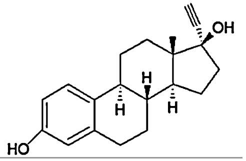
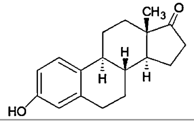
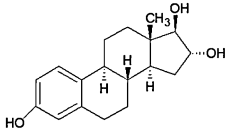
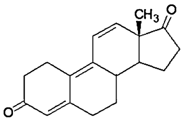
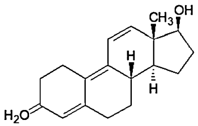
Introduction

Endocrine disrupting chemicals (EDCs) are defined as exogenous substances that can alter the functions of the endocrine system and consequently led to adverse health effects in an organism or its progeny or subpopulations (Avasarala et al. 2011; Sin et al. 2012). A plethora of the EDC substances can be classified into two categories: (1) natural hormones that are naturally present in the environment and (2) hormones that are fabricated. Their general nomenclature and representative examples are shown in Table 1. The classification of EDC substances is depended on mode of their endocrine actions including (1) mimicking the action of endogenous hormones, (2) antagonizing hormone receptors, (3) disrupting the hormones synthesis, metabolism, transport, and excretion, and (4) altering natural hormone production pathways. In addition, some EDCs have demonstrated multiple modes of action, which can lead to deleterious effects on the earth ecosystems (Eertmans et al. 2003). Myriad examples of reproductive and developmental abnormalities related to EDCs exposure have been revealed over the years in a broad spectrum of wildlife including mollusks, fish, reptiles, birds, and mammals (Esplugas et al. 2007; Skinner et al. 2011; Mennigen et al. 2017).

According to Caliman and Gavrilescu (2009), the total number of compounds suspected of interacting with the endocrine system was approximately 38,000. Nevertheless, there were more than 80,000 chemicals required to analyze and investigate their endocrine actions. The EDCs are typically detected in the environment at trace concentrations (ppm to ppb), which are still extremely toxic to aquatic biota (Sin et al. 2012). Sources by which the EDCs entered the environment mainly from sewage treatment plant (STP) effluents although other sources such as direct discharge, leakage from septic tanks, and run-off from agricultural lands (Laganà et al. 2004; Liu et al. 2009; Burkhardt-Holm 2010).

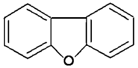
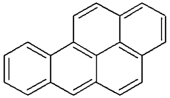
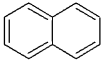
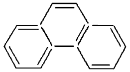
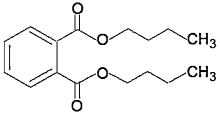
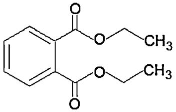
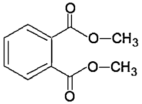
Wastewater treatment plants operated with technologies such as nanofiltration, reverse osmosis, lagoon or pond stabilization, biological treatment with chlorination,

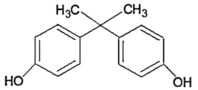
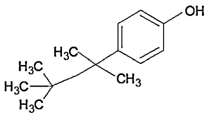
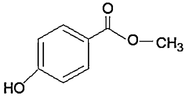
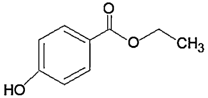
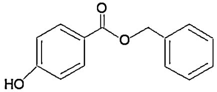
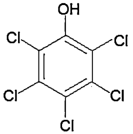
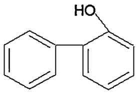
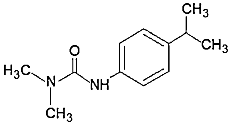
Table 1 Classification of various EDC compounds with representative examples

Class	Representative EDC	Empirical formula	Molecular weight (g/mol)	Chemical structure
Steroids and natural hormones	Estrone	$C_{18}H_{24}O_2$	270.37	
	17α-Ethinylestradiol	$C_{20}H_{24}O_2$	272.38	
	Estriol	$C_{18}H_{24}O_3$	288.38	
	Trendione	$C_{18}H_{20}O_2$	268.35	
	17α-Trenbolone	$C_{18}H_{22}O_2$	270.37	

(*continued*)

Table 1 (continued)

Class	Representative EDC	Empirical formula	Molecular weight (g/mol)	Chemical structure
Polycyclic aromatic hydrocarbon (PAHs)	Dibenzofuran	$C_{12}H_8O$	168.19	
	Benzopyrene	$C_{20}H_{12}$	252.31	
	Naphthalene	$C_{10}H_8$	128.17	
	Phenanthrene	$C_{14}H_{10}$	178.23	
Phthalates	Dimethyl phthalate	$C_{10}H_{10}O_4$	194.18	
	Diethyl phthalate	$C_{10}H_{10}O_4$	194.18	
	Di-n-butyl phthalate	$C_{16}H_{22}O_4$	278.34	

Alkylphenols and Bisphenol A	Bisphenol A	$C_{15}H_{16}O_2$	228.29	
	4-Tert-octylphenol	$C_{14}H_{22}O$	206.32	
Parabens	Methylparaben	$C_8H_8O_3$	152.15	
	Eythlparaben	$C_9H_{10}O_3$	166.17	
	Benzylparaben	$C_{14}H_{12}O_3$	228.24	
Pesticides	Pentachlorophenol	C_6Cl_5OH	266.34	
	o-phenylphenol	$C_{12}H_{10}O$	170.21	
	Isoproturon	$C_{12}H_{18}N_2O$	206.28	

oxidation by permanganate (VII), combined ozone, and filtration in sewage treatment plants currently are used on the elimination of EDCs (Acero et al. 2010; Al-Rifai et al. 2011; Stalter et al. 2011; Qiang et al. 2013; Zhang et al. 2013). However, most reported studies have shown that application of advanced oxidation processes (AOPs) provided a high degree of EDCs degradation in a short period of reaction time (Lau et al. 2007; Lam et al. 2013; Zhang and Li 2014; Simsek 2017). Most importantly, AOP methods can convert the EDCs into low molecular weight intermediate products and eventually led to mineralization to CO_2 and H_2O. Furthermore, there is no tendency to produce secondary pollution in AOP methods. Examples of AOPs applied to the oxidation of organic pollutants are photolysis, photocatalysis, sonolysis, photo-Fenton, and Fenton oxidation.

However, many intermediate products formed during the EDCs degradation could be more toxic than the parent compound been treated. Identifying the intermediate products generated in the course of the AOPs degradation of pollutants in water is thus gaining attention to understand the degradation pathways and the degradability of the intermediates produced. Recently, liquid chromatography coupled with mass spectrometry (LC-MS) has become a highly appropriated technique for by-products identification. Time-of-flight MS (TOF-MS) and hybrid quadrupole TOF (QTOF)-MS/MS systems in combination with ultra-high performance LC (UPLC) have also received preference in separating, monitoring, and identifying of intermediate products generated in wastewater treatment (Gu et al. 2011; Souissi et al. 2012; Zhu et al. 2012; Sirtori et al. 2014). Hitherto, characterization and identification of degradation products are still challenging tasks for researchers working in this area.

On the basis of the above consideration, this chapter provided a comprehensible review dealing with the use of LC-MS techniques in analyzing the different degradation products generated during the AOP-mediated EDCs degradation and to reveal their possible degradation pathways.

Chromatography Coupled with Mass Spectrometry for Intermediate Products Detection

During the EDCs degradation process, several degradation intermediates were formed and needed identification using a proper analytical method. Identification of these intermediates could give a further insight into the mechanism of EDCs degradation and can assist to obtain a total picture of the degradation pathway with their final mineralization products. The desired final mineralization products for a complete degradation process are CO_2 and H_2O.

The most commonly used analytical method is the chromatography coupled with MS (Souissi et al. 2012; Khataee et al. 2016). Gas chromatography-mass spectrometry (GC-MS) has been well recognized as the “gold standard” for both identification and quantification of nonpolar and volatile pollutants due to its high selectivity and sensitivity (Khataee et al. 2016; Ba-Abbad et al. 2017; Huang et al. 2017). However, its application was limited to some important problems such as the loss of analytes during the time-consuming derivatization process and its incompatibility with polar, thermally unstable and nonvolatile compounds. In recent years, LC-MS has therefore become analytical method of choice for identifying of degradation intermediates in aqueous solution. The LC-MS spectra can give information about the mass of the molecule through the quasi-molecular ion (MH^+). Therefore, the direct coupling of LC and MS has developed into a powerful method to analyze the evolution and breakdown of intermediate products in a degradation process. This coupling method was also beneficial to separate and detect polar compounds without a derivatization step (Medana et al. 2005). The development of ultra-high performance LC (UPLC) equipped with sub-2-μm-particle-size reversed-phase column also provided faster analysis duration, better resolution, reduction of matrix effects, and increase of sensitivity. The LC and UPLC have performed with the use of mobile phase mixtures of water-organic solvent (acetonitrile or methanol) and infrequently acidified to enhance the ionization efficiencies of the compounds (Sin et al. 2014; Al-Hamdi et al. 2016).

Advanced Oxidation Processes for EDCs Degradation

The AOPs has appeared as a promising method in wastewater treatment due to the fact that they offered different possible processes for strong oxidizing hydroxyl (•OH) radicals generation to react with organic pollutants and caused the ring cleavage. Unlike many other radicals, •OH radicals are nonselective and therefore readily to transform a large variety of organic pollutants into nontoxic molecules to eliminate the environmental pollution (Peller et al. 2001; Patil et al. 2010; Sin et al. 2013; Liu et al. 2016; Shen et al. 2017). With adequate reaction time and optimum operating experimental conditions, the AOPs can mineralize the hazardous organic pollutants to CO_2, which was the most stable final product for chemical oxidation. The common AOPs developed for destroying EDCs are photolysis, photocatalysis, sonolysis, and Fenton oxidation. Below is an overview on different AOPs for EDCs degradation with respect to the use of LC-MS for intermediate products analysis.

Photolysis for EDCs Degradation

Photolytical process is dependent on the ability of the pollutant to absorb the emitted radiation from artificial or natural light. In this method, the EDCs can react photochemically by reaching an excited state via the direct absorption of radiant energy or by •OH radicals generated from dissociation of water molecules (Vallejo et al. 2015). Weidauer et al. (2016) investigated the photodegradation of benzotriazoles (BTs) under sunlight irradiation (290–800 nm) at neutral pH in aqueous solution for 24 h. With the identification of degradation intermediates via LC-QTOF-MS, a proposed pathway of the photolysis of BTs is shown in Fig. 1. The results in their investigation showed that the aniline (TP 1) and aminophenol (TP 2) were the initial intermediate

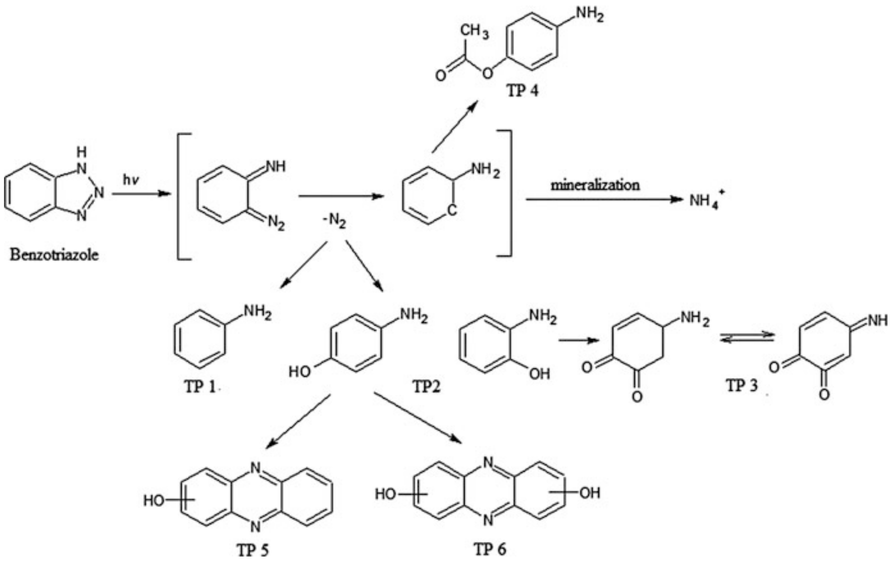


Fig. 1 Sunlight photolysis degradation of benzotriazoles (Adapted from Weidauer et al. 2016)

products based on the photolytic elimination of molecular N_2. A slight amount of NH_4^+ was also reported to form due to the mineralization of BTs. An acetate conjugate (TP 4) was also formed after the denitrogenation by a reaction with the acetate buffer. Finally, the aminophenol isomers were reported to convert into dihydroxyphenazine (TP 5), 1,6-phenazinediol (TP 6) and aminoquinone (TP 3).

The formation of intermediate products was also found from the direct photolysis of bisphenol A (BPA) under a UV-C lamp (Kondrakov et al. 2014). Their study demonstrated two catechol derivatives (BPA catechol and 4-(2-hydroxypropan-2-yl)-catechol were detected using LC-MS-TOF approach. They went further to describe the detected catechol derivatives have weaker estrogenic activity compared to BPA. Souissi et al. (2012) identified the degradation intermediates generated upon photolysis of estrone (E1) under simulated UV irradiation. Nine main degradation products for E1 were observed by LC-Q-TOF, which revealed one to three additional hydroxylation preferentially located on the aromatic ring of E1. In addition, they also observed that the phenolic structure of the photolysis by-products still maintained, which needed a further investigation to evaluate the estrogenic risk in the environment.

Jiao et al. (2008) investigated the photolytic degradation of tetracycline (TC) under a 500 W medium mercury lamp ($\lambda = 365$ nm, light intensity $= 0.53$ mW/cm^2). The degradation of TC improved at low initial TC concentration and high solution pH. The intermediate products from TC photolysis were identified using LC-ESI (electrospray ionization)-MS and a degradation pathway was proposed (Fig. 2). The degradation mechanism of TC was explained via the loss of N-methyl, amino, and hydroxyl groups. Only 15% decrease in the total organic carbon (TOC) of the degraded solution was also reported, revealing a majority of TC

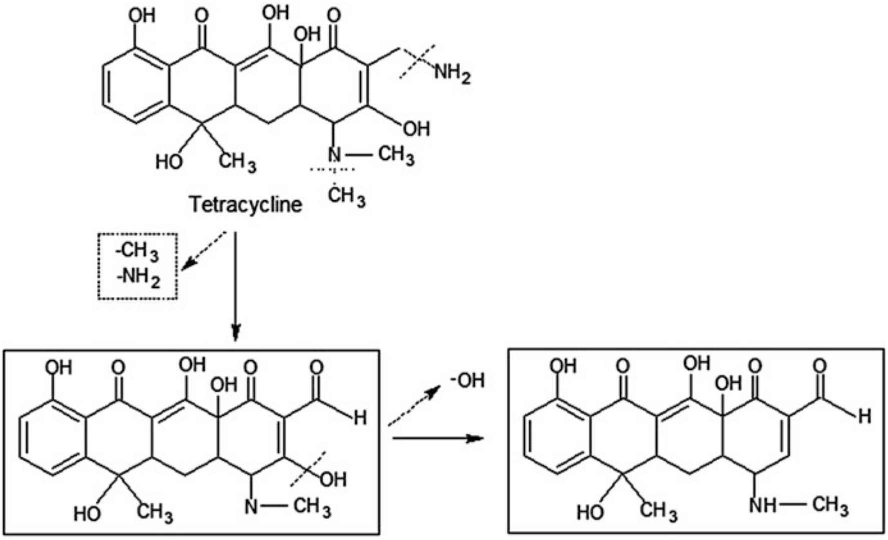


Fig. 2 Photolysis of tetracycline under UV-A irradiation (Adapted from Jiao et al. 2008)

converted into intermediate products without complete mineralization. More recently, the degradation of microcystin-LR (MC-LR) under UV-B photolysis has also been examined (Moon et al. 2017). Their results showed that high UVB light intensity benefited the degradation of MC-LR. The degradation rate constants were found to be 0.0020, 0.0043, and 0.0061 min^{-1} for 0.47, 0.58, and 1.57 mW/cm^2. Based on LC-MS/MS analysis, the degradation mechanism of MC-LR was determined and proceeded via two processes: (1) bond cleavage and (2) intramolecular electron arrangement by electron pair in the nitrogen atom.

Photocatalysis for EDCs Degradation

The photocatalysis process for the degradation of organic pollutants involved the use of semiconducting materials as photocatalysts to generate active species such as positive hole (h^+), superoxide anion ($O_2^{\bullet -}$) and •OH radicals. The active species were produced based on the generation of electron (e^-) in the conduction band and h^+ in the valence band when the photocatalysts subjected to light irradiation. The e^- can then reduce the adsorbed O_2 to $O_2^{\bullet -}$ radicals, whereas the h^+ can oxidize either the organic pollutants directly or adsorbed H_2O molecules to •OH radicals and hydrogen cation (H^+) (Weber et al. 2012; Sin et al. 2014; Chen et al. 2015; Lam et al. 2016). Therefore, enhancing the e^-–h^+ separation is an important consideration in photocatalysis to generate large amount of active species for organic pollutants degradation.

Norfloxacin (NOR) was subjected to $BiOBr/Fe_2O_3$ photocatalysis and the degradation by-products were analyzed using LC-(+ESI)-MS (Guo et al. 2017). It was postulated that the overall photocatalytic degradation process of the organic compounds was most likely to have been initiated by •OH radicals. Their studies proposed several pathways of the NOR degradation and indicated eleven intermediate compounds produced during the course of reaction (Fig. 3). Three different tentative pathways were postulated for the degradation of the NOR (piperazine ring transformation, decarboxylation, and defluorination). The report also showed that the NOR degradation started by cleavage of the piperazine ring. The primary reaction intermediates were further decarbonylated to give some of the amide group-bearing phenyl ring products with the loss of CO_2 gas. Further defluorination of the compounds was the possible reason that led to simpler molecules with *m/z* 278 and 192.

López-Muñoz et al. (2013) carried out the degradation of aqueous isoproturon using the TiO_2 (Degussa P25) as photocatalysts. Structural information of the main products formed during the photocatalytic reaction has been identified using LC-ESI-TOF-MS. A detailed mechanism for the different by-products formation has been suggested (Fig. 4). The processes partook are: (1) •OH radicals attacked on the isopropyl chain, dimethylamine group, and the aromatic ring, generating mono-hydroxylation (*m/z* 223), di-hydroxylation (*m/z* 239), and their oxidized products (*m/z* 221 and *m/z* 237), (2) N-demethylation and/or demethylation on the alkyl chain (*m/z* 193, 191, 165, 163, 151, 149, and 94), and (3) substitution or oxidation of NH_2 groups linked to the aromatic ring (*m/z* 121, 95, and 124). The chromatography-mass spectrometry was successfully employed in their study to identify intermediates that could not be detected by other techniques.

The photocatalytic degradation and biotoxicity reduction of tetracycline (TC) was investigated in the presence of TiO_2-supported on MCM-41 as a catalyst (Zhou et al. 2017). The intermediates and the final products of degradation were tentatively identified by the LC-(–ESI)-MS/MS technique. The results of LC-MS/MS demonstrated 10 major intermediates, which were in a tendency to increase first and subsequently declined with the degradation of the TC molecules. Several mass spectra of by-products with their *m/z* values were reported in their paper; however, no reaction mechanism towards the formation of various by-products was studied.

Indomethacin (IDM) was subjected to visible light in the presence of N-doped carbon dots/g-C_3N_4 photocatalysts, and the degradation products were tested using LC-MS/MS (Wang et al. 2017). It was suggested that the overall photodegradation of the IDM was initiated by •OH radicals. LC-MS/MS studies proposed possible pathways of IDM degradation, and inferred numerous of by-products were produced during the photocatalytic reaction (Fig. 5). Four different mechanistic pathways were suggested for the degradation of the IDM (cleavage of the amide bond, decarboxylation of the acetic chain, addition reaction of the C2–C3 double bond, and hydroxylation reaction of the chloro benzene ring). Furthermore, frontier electron densities (FEDs) data of the IDM molecules were calculated to predict the reaction sites for the radicals attack. The C19, C17, and C20 positions indicated higher $FED^2_{HOMO} + FED^2_{LUMO}$ values, which demonstrated the high possibility of •OH radicals substituted reactions took place at the chloro aromatic rings. The C17, C12, C5, C22, C16, and C2 atoms of IDM showed more positive point charge than others,

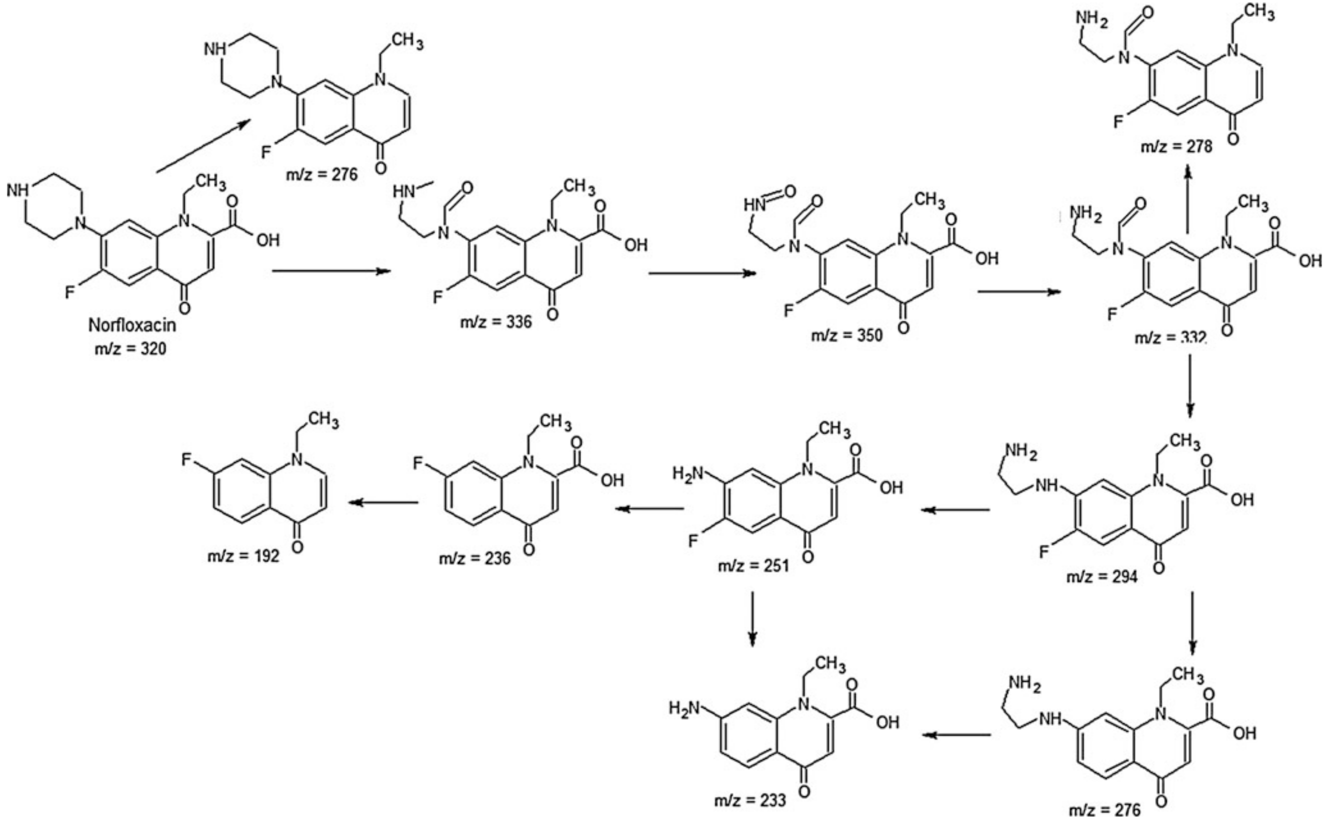


Fig. 3 Photocatalytic degradation of norfloxacin using BiOBr/Fe_2O_3 under visible light irradiation (Adapted from Guo et al. 2017)

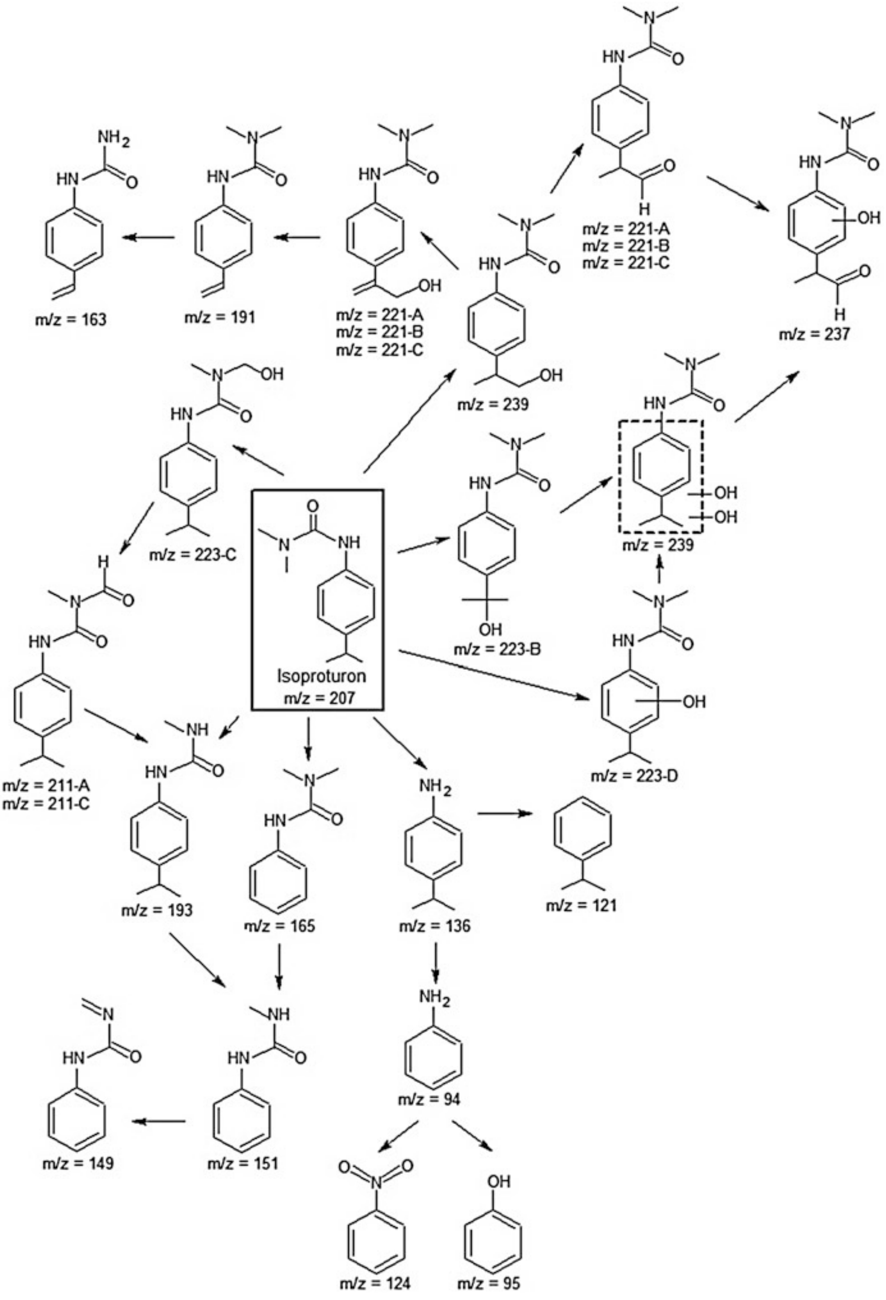


Fig. 4 Photocatalytic degradation of isoproturon over TiO_2-Degussa P25 under a 150 W medium pressure mercury lamp (Adapted from López-Muñoz et al. 2013)

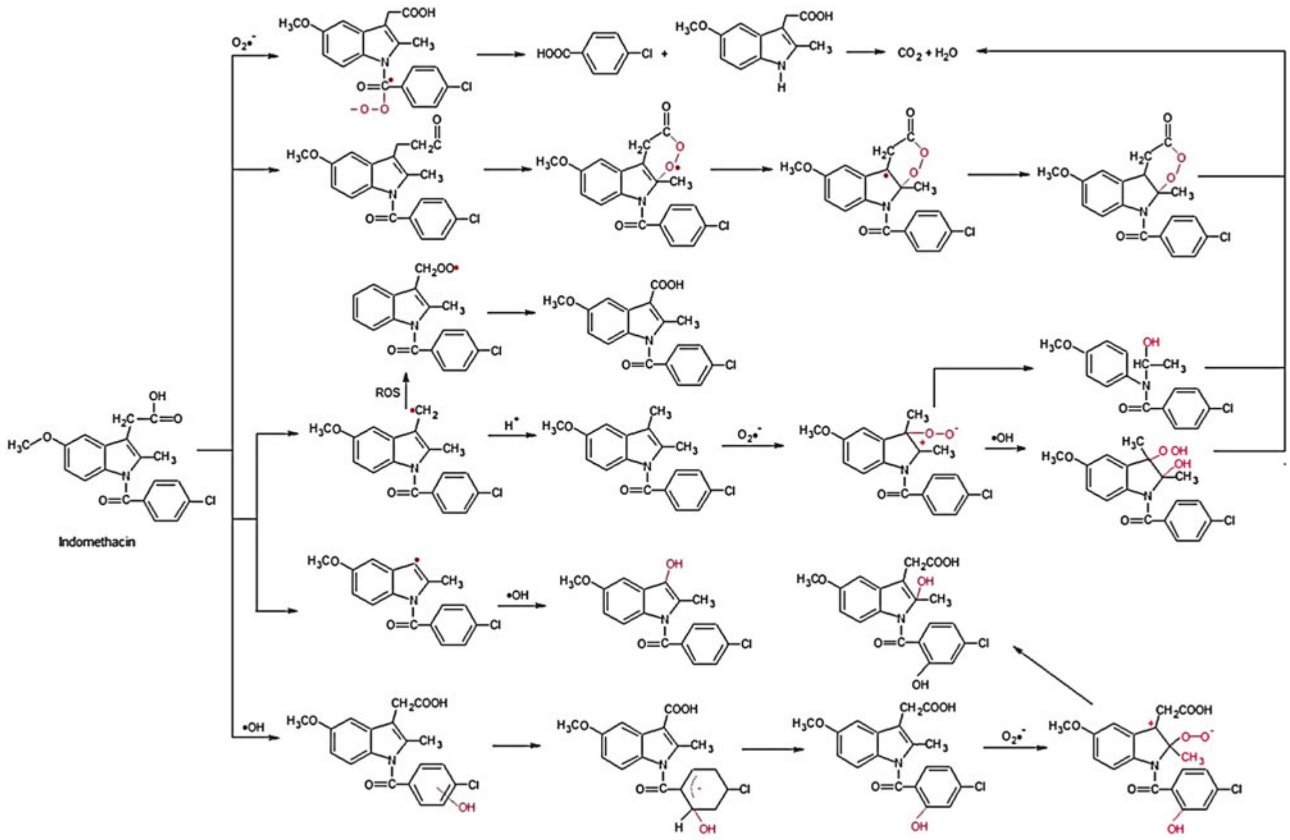


Fig. 5 Visible light photocatalytic degradation of indomethacin in the presence of N-doped carbon dots/g-C_3N_4 (Adapted from Wang et al. 2017)

which implied that C17, C12, C5, C22, C16, and C2 were attacked by $O_2\bullet^-$ via nucleophilic addition reactions. The prediction of potential attack positions by reactive species based on theoretical calculations was in accordance with their LC-MS/MS findings.

Mena et al. (2017) investigated the visible light photocatalytic ozonation to degrade N,N-diethyl-meta-toluamide (DEET) using WO_3 catalysts. The molecular structures of the by-products were deduced by analyzing the samples with LC-(-ESI)-QTOF-MS analysis. The parent molecule DEET showed a clear mass signal corresponding to *m/z* 206. The degradation mechanism encountered steps of mono- and poly-hydroxylation and/or oxidation, de-alkylation, and subsequently rupturing of the benzene ring to lead the production of short-chain aliphatic organic acids and eventually mineralized to CO_2. Their mineralization efficiencies were further confirmed by total organic carbon (TOC) removal.

Salma et al. (2016) reported an investigation on the identification of the degradation intermediates generated by UV-C photolytic and TiO_2 photodegradation in aqueous ciprofloxacin (CIP) at different pH values (pH 3, 5, 7 and 9). An UPLC-MS/MS method was used in their study together with high-resolution QTOF-MSA (Duo-Spray Ion Source working in negative ion mode). The results showed that there were (1) fluorine atom photo-substitution by an OH^- group at neutral and moderately basic conditions, (2) defluorination at neutral conditions, and (3) fluorine conservation at strongly acidic medium. They also added that high photon energy produced by UV-C irradiation significantly improved the photodegradation of CIP in the presence of TiO_2.

Investigation on the photodegradation mechanism of phenol and the efficiency of photocatalysis by commercial TiO_2 has also been carried out (Dang et al. 2016). A complete degradation of phenol aqueous solution was observed after 24 h of UV-C irradiation. The intermediate products from the phenol degradation were identified using LC-MS. Two different mechanistic pathways were proposed for the phenol degradation (Fig. 6). Their first degradation pathway suggested that phenol was degraded via hydroxylation reaction to form catechol, benzoquinone, hydroxyhydroquinone, and hydroxybenzoquinone. With a further attack of the •OH radicals, an oxidative aromatic ring-opening reaction occurred and rendered the formation of simple hydrocarbons, followed by oxidation to CO_2 and H_2O. They also suggested that 2-phenoxylcyclohexa-2,5-dienone, [1,1′-biphenyl]-4-ol, and tectoquinone were formed by combination of two phenoxide ions in the second degradation pathway.

Sonolysis for EDCs Degradation

During the sonochemical process, •OH radicals were generated over acoustic cavitation that induced the hemolytic scission of H_2O molecules. The acoustic cavitation was comprised of the formation, growth, and collapse of microbubbles in water. The microbubbles formed via the acoustic cavitation can tend to increase and decrease its size continuously until the resonance size reached prior to its violent collapse. The collapse of these microbubbles can generate extremely high

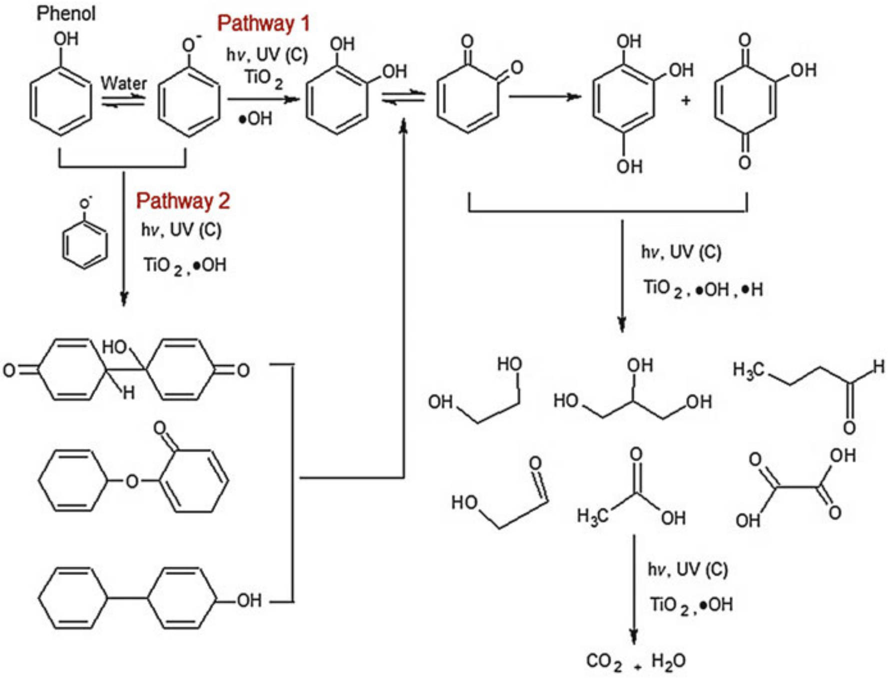


Fig. 6 Photocatalytic degradation of phenol in the presence of commercial TiO_2 under UV-C light irradiation (Adapted from Dang et al. 2016)

temperature (> 5000 °C) and pressure (> 1000 atm) inside the bubbles. Therefore, the EDC molecules can react with •OH radicals or be degraded by pyrolysis (Torres et al. 2007; Chowdhury and Viraraghavan 2009; Ayoub et al. 2010). Papadopoulos et al. (2016) identified the intermediates and degradation pathway of ethylparaben (EP) through LC-TOF-MS analysis. A proposed sonochemical degradation pathway of EP is shown in Fig. 7. The LC-TOF-MS analysis of EP at 8 h reaction time showed the formation of four degradation intermediates methylparaben (MP), 3,4-dihydroxybenzoic acid (3,4-DHB), 2,4-dihydroxybenzoic acid (2,4-DHB), and 4-hydroxybenzoic acid (4-HB) appearing at 6.9 min, 1.4 min, 1.6 min, and 2.5 min, respectively. All the above aromatic intermediates were proposed to further oxidize through ring rupturing reactions into aliphatic intermediates via the continuous attack of •OH and $SO_4^{\bullet-}$ radicals.

In another study of the paraben, Sasi et al. (2015) studied the •OH radicals-mediated sonolytic degradation of methylparaben (MPB). The detected degradation intermediates from the LC-QTOF-MS analysis showed that the MPB degradation occurred via three major steps: (1) aromatic hydroxylation, (2) hydroxylation at the ester chain, and (3) hydrolysis reaction. It was also reported from this study that the aromatic intermediates were further oxidized through ring cleavage reactions into lower aliphatic acids, which finally decomposed into CO_2 and H_2O as evidenced by their chemical oxygen demand measurement.

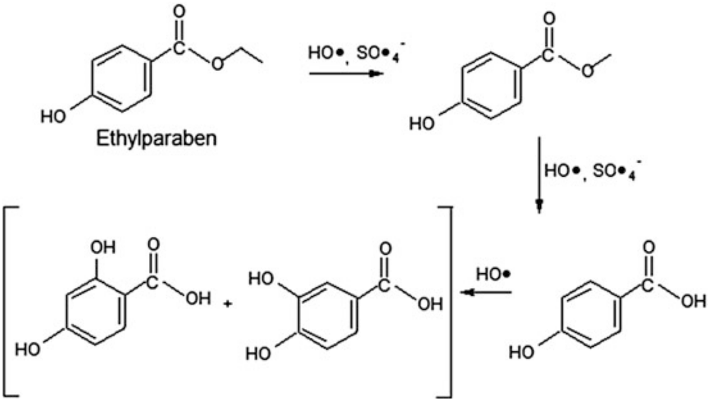


Fig. 7 Sonochemical degradation of ethylparaben (Adapted from Papadopoulos et al. 2016)

Sonolysis of persistent pharmaceutical carbamazepine (CBZ) was also performed, and LC-MS/MS was used in the structural characterization of the degradation intermediates (Tran et al. 2013). The analysis of degradation intermediates showed that the attack of •OH radicals on CBZ led to two different degradation pathways by the formation of 10,11-epoxy CBZ and 10,11-dihyroxy CBZ. In the first degradation pathway, 10,11-epoxy CBZ was further attacked by •OH radicals and then formed acridine via a deamination process. In the second pathway, 10,11-dihyroxy CBZ was also attacked by •OH radicals and produced anthranilic acid and salicylic acid. Then, the acidic intermediates were reported to convert into aniline and benzoic acid. It was proposed that these organic compounds were finally mineralized into CO_2 and H_2O.

Other EDCs such as 17β-estradiol (Ifelebuegu et al. 2014), 17α-ethinylestradiol (Ifelebuegu et al. 2014), phenol (Entezari et al. 2003; Lesko et al. 2006), 2,4,6-trichlorophenol (Park et al. 2011), pentachlorophenol (Park et al. 2011), tetracycline (Eslami et al. 2016), bisphenol A (Torres et al. 2007, 2008), alachlor (Bagal and Gogate 2012), and dichlorvos (Golash and Gogate 2012) have also been successfully degraded by sonochemical treatment. The results showed that this method can be served as an effective tertiary treatment option in wastewater applications.

Iron Catalyzed H_2O_2 Production for EDCs Degradation

Among transition metals, iron has been known to be a very effective catalyst for •OH radicals generation via Fenton process. The generally accepted mechanism of the Fenton process suggested that the generation of •OH radicals is based on the electron transfer between H_2O_2 and a homogeneous catalyst (iron) (Eq. 1). The iron can subsequently be reacted with H_2O_2 to produce hydroperoxyl (HOO•) radicals (Eq. 2). The generated •OH radicals have higher oxidation potential than the

HOO• radicals; thus, the degradation process was mainly due to the former (Wongniramaikul et al. 2007; Tay et al. 2011; Sirtori et al. 2014).

$$H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + \bullet OH + OH^- \quad (1)$$

$$H_2O_2 + Fe^{3+} \rightarrow Fe^{2+} + HOO\bullet + H^+ \quad (2)$$

Marković et al. (2015) investigated the degradation of ibuprofen (IBP) in aqueous solution by Fe^{2+}/H_2O_2 treatment. Under the experimental conditions (Fe^{2+}, H_2O_2, and IBP concentrations = 25.2, 306, and 60 mg/L, respectively), a significant decrease of IBP concentration was observed within 1 min and reached 78% degradation efficiency. The LC-MS-TOF analysis of degradation products showed that the Fenton reaction gave four aromatic products ($C_9H_{10}O_2$, $C_{13}H_{18}O_4$, $C_{10}H_{12}O_2$ and $C_{13}H_{18}O_3$) and two aliphatic products ($C_4H_6O_4$ and $C_7H_{12}O_2$) due to the powerful oxidizing •OH radicals.

The effect of Fenton reaction on the degradation of bisphenol A (BPA) in a novel electrical discharge plasma reactor was also reported (Dai et al. 2016). The structures of degradation intermediates and final products were identified using LC-QTOF-MS. Various degradation products such as bisphenol-o-quinone (BPA12QN), 5-hydroxybisphenol A (BPA2OH), 4-hydroxyacetophenone (BPAP2), 4-[2-(4-hydroxyphenyl)propan-2-yl]-2-nitrophenol ($BPA2NO_2$), 4,4′-propane-2,2-diylbis(2-nitrophenol) ($BPA210NO_2$), 5-[2-(4-hydroxy-3-nitrophenyl)propan-2-yl]-3-nitrobenzene-1,2-diol ($BPA210NO_26OH$), 4-[2-(4-hydroxy-3-nitrophenyl)propan-2-yl] benzene-1,2-diol ($BPA2NO_210OH$), and 5-[2-(4-hydroxy-3,5-dinitrophenyl)propan-2-yl]benzene-1,2,3-triol ($BPA26NO_21014OH$) were detected. Based on these degradation intermediates, a possible degradation pathway of BPA was proposed in Fig. 8. They concluded that the attack of •OH radicals on BPA hydroxyl group was the primary pathway for the by-products formation. They also added that all the identified degradation products have lower estrogenic activity than BPA and ultimately degraded into CO_2 as well as H_2O.

Sirtori et al. (2014) identified the thiabendazole fungicide (TBZ) degradation products in water over the Fenton treatment by LC-QTOF-MS. In their investigation, twelve degradation products were identified and most of them can be eliminated after 15 min of reaction time. They suggested possible transformation pathway of TBZ degradation and revealed numerous hydroxylation reaction occurred in both benzimidazole and thiazole rings by the •OH radicals attack (Fig. 9).

The effect of iron species has also been studied by analyzing the degradation of amoxicillin (AMX) aqueous solution under a solar simulator (Trovó et al. 2011). It was found that the degradation of AMX was favored over potassium ferrioxalate complex (FeOx) compared to $FeSO_4$. A complete oxidation of the solution over FeOx was obtained after 5 min, while 15 min of reaction time was necessary in the presence of $FeSO_4$. The intermediates generated during the treatment were also identified using LC-ESI-TOF-MS analysis, which allowed to suggest the degradation mechanism proceeded via the opening of the four-membered β-lactamic ring and further oxidized the methyl group to aldehyde and/or hydroxylation of benzoic

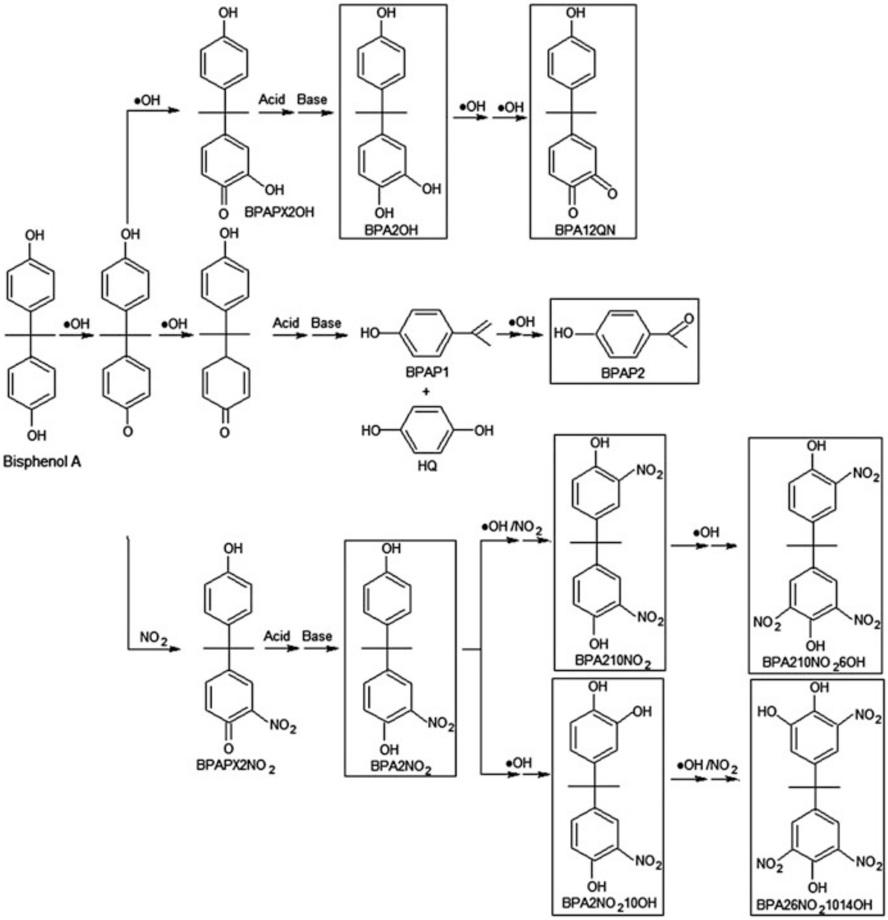


Fig. 8 Degradation pathway of bisphenol A by the Fenton treatment (Adapted from Dai et al. 2016)

ring, producing intermediate products after bound cleavage between different atoms and further oxidized to low molecular weight aliphatic compounds.

Using metoprolol (MET) as endocrine disrupting chemical, the efficiency of photo-Fenton treatment was studied under different irradiation sources: (1) UV-C ($\lambda = 254$ nm), (2) black blue lamps ($\lambda = 365$ nm), and (3) simulated sunlight (Romero et al. 2016). Their results showed that the photo-Fenton using black blue lamps gave the best degradation and mineralization efficiencies. Complete degradation of MET was obtained after 7 min of reaction time, and the corresponding total organic carbon (TOC) removal was reported to be 81.2% after 90 min of reaction time under the determined experimental conditions ($Fe^{2+} = 10$ mg/L and $H_2O_2 = 150$ mg/L). Using the intermediate products detected via the ESI-MS and a LC-MSD-TOF, their proposed degradation pathway of MET was presented where

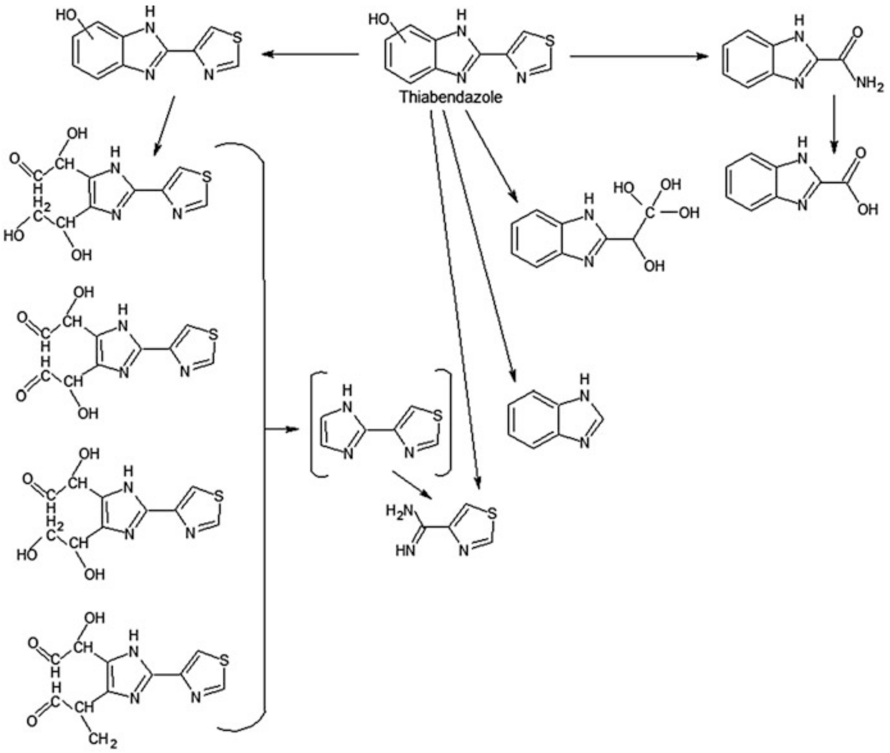


Fig. 9 Thiabendazole degradation pathway for the Fenton treatment (Adapted from Sirtori et al. 2014)

the essential degradation was possible owing to the attack of •OH radicals (Fig. 10). An overall toxicity reduction of treated MET solution was also observed in their photo-Fenton process.

Conclusion and Future Trends

The increasing usage of EDCs worldwide has garnered great public concern because of the vulnerability of humans and wildlife to numerous initiations of hormone-like activities even in trace concentrations in surface waters. Researches have shown that AOPs are potential technologies that widely studied and applied for degradation of organic pollutants including EDCs. The most typically investigated AOP method for destructing EDCs in water was semiconductor photocatalysis compared to photolysis, sonolysis, and Fenton treatments. Some of research works were also found in particularly with hybrid processes of AOPs to obtain advantages of synergistic effects as viable solution to treat these organic compounds in aqueous solution. Although a wide range of AOP processes have been applied, •OH radical generation

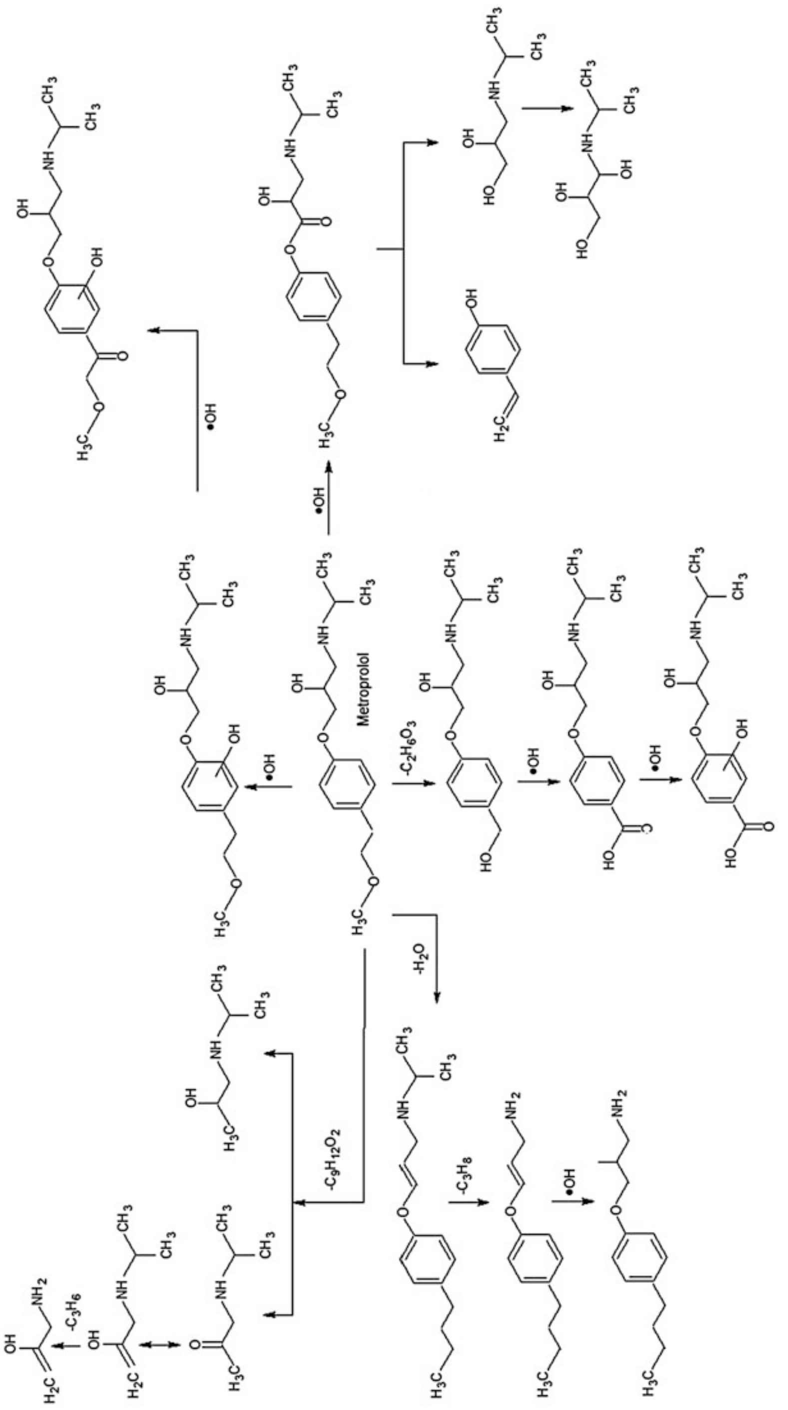


Fig. 10 Degradation pathway of metoprolol by the Fenton treatment (Adapted from Romero et al. 2016)

has been recognized as a main active species for EDCs degradation. At the same time, along with the EDCs degradation, it was crucial to develop a comprehensive database for a myriad of intermediates and by-products formed since they can possibly be more toxic and persistent than the parent compounds. LC-MS has shown attractiveness as a technique used for the determination of intermediate products of EDCs degradation owing to minimal sample preparation, ease of separation, relatively low operating cost, and compatibility of the LC-MS system with aqueous samples. In addition, the ionization techniques employed in the MS can deliver data related to the mass of the parent compound and intermediate products under analysis. Selected compounds can be further investigated using MS/MS fragmentation for structural indications.

Despite substantial progress has been accomplished, there are several technical points that required to be further examined. A great number of the technical papers involved investigating the behavior of an individual component tested in much higher concentrations than identified in the aqueous environment, while the real EDCs occurred in mixtures of multicomponents rather than as an individual component. In addition to target chemical analysis, research works should take account to carry out the toxicity screening in extending the understanding of AOPs effectiveness for EDCs degradation as toxicity bioassays are able to test the toxicity of either target or unknown contaminants. For the toxicity of the degradation intermediates, the Microtox method using bacteria *Vibrio fischeri* as toxicity indicator and the inhibition of *Escherichia coli* respiration can be used. At this point, the significance of degradation intermediates in point of ecotoxicological should consider in future AOPs studies. As a final remark, it should also be noticed that recent development and validation of suitable analytical protocols seem to be key in reliably assuring the transformation products of EDCs that can deliver good support to the examination of the overall performance of the treatment processes.

Cross-References

▶ Advanced Treatment Technologies

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