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Review article

Removal of residual pharmaceuticals from aqueous systems by advanced oxidation processes

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ABSTRACT

Over the past few years, pharmaceuticals are considered as an emerging environmental problem due to their continuous input and persistence to the aquatic ecosystem even at low concentrations. Advanced oxidation processes (AOPs) are technologies based on the intermediacy of hydroxyl and other radicals to oxidize recalcitrant, toxic and non-biodegradable compounds to various by-products and eventually to inert end-products. The environmental applications of AOPs are numerous, including water and wastewater treatment (i.e. removal of organic and inorganic pollutants and pathogens), air pollution abatement and soil remediation. AOPs are applied for the abatement of pollution caused by the presence of residual pharmaceuticals in waters for the last decade. In this light, this paper reviews and assesses the effectiveness of various AOPs for pharmaceutical removal from aqueous systems.

Contents

1. Introduction . . . 402
2. Advanced oxidation processes . . . 404
3. Overview of AOPs for pharmaceutical removal . . . 404
4. Assessment of AOPs performance for pharmaceutical removal . . . 404
   4.1. Photolysis . . . 404
   4.2. Ozonation . . . 411
   4.3. Fenton oxidation . . . 412
   4.4. Heterogeneous photocatalysis . . . 412
   4.5. Electrochemical oxidation . . . 413
   4.6. Ultrasound irradiation . . . 413
   4.7. Sub-critical wet air oxidation (WAO) . . . 414
   4.8. Oxidative treatment of EDCs . . . 414
   4.9. Coupling AOPs with other treatment processes . . . 414
5. Conclusions . . . 415
References . . . 415

1. Introduction

Pharmaceuticals constitute a large group of human and veterinary medicinal compounds which have long been used throughout the world. Although the amount of these pharmaceuticals in the aquatic environment is low, its continuous input may constitute in the long-term a potential risk for aquatic and terrestrial organisms. Therefore, over the past few years they are considered to be an emerging environmental problem. Table 1 classifies, according to their therapeutic activity, groups of pharmaceuticals that are more commonly found in the environment; in each group, the most frequently detected pharmaceuticals are shown in bold.

In recent years and especially after the application of advanced measurement technologies (Fatta et al., 2007) many pharmaceuticals have been identified and detected at ng/L levels (trace concentrations)

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Nomenclature

AOP	advanced oxidation process
AOX	adsorbable organic halogen
BOD_5	biochemical oxygen demand—5 days
COD	chemical oxygen demand
DOC	dissolved organic carbon
DO	dissolved oxygen
EDC	endocrine disrupting compound
IC	inorganic carbon
IU	international units
LP	low pressure
MP	medium pressure
NSAID	nonsteroidal anti-inflammatory pharmaceutical
PhAC	pharmaceutically active compound
PPCP	pharmaceuticals and personal care products
SSNRI	selective serotonin and norepinephrine reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor
STP	sewage treatment plant
TOC	total organic carbon
WWTP	wastewater treatment plant

worldwide in the aquatic environment (Hua et al., 2006; Fatta et al., 2007). It is notable that several recent publications have been devoted to monitoring pharmaceuticals in various aqueous matrices (i.e. water and/or wastewater). These have been reported in a recent review article of ours and they are also summarized in Fig. 1 (Fatta et al., 2007). Pharmaceuticals end up in soil, surface waters and eventually in ground and drinking water after their excretion (in unmetabolized form or as active metabolites) from humans or animals via urine or faeces, through the sewage system and into the influent of wastewater treatment plants (Darlymple et al., 2007). In addition to metabolic excretion, disposal of pharmaceuticals which are being used in agriculture, industry, medical treatment and common households, also contributes to the entry of pharmaceuticals into fresh bodies. Veterinary pharmaceuticals on the other hand contaminate directly soil via manure and surface and ground waters by runoff from fields (Khetan and Collins, 2007).

Pharmaceuticals are designed to have a physiological effect on humans and animals in trace concentrations. Persistence against biological degradation and their biological activity are key properties of these pollutants. They retain their chemical structure long enough to do their therapeutic work and because of their continuous input they could remain in the environment for a long time and their presence there is considered dangerous in both low and high concentrations (Chatzitakis et al., 2008; Mendez-Arriaga et al., 2008). Their active ingredients are selected or designed because of their activity against organisms. Thus, it is expected that they will be effective against bacteria, fungi and possibly non target higher organisms. For many compounds their potential effects on humans and aquatic ecosystems are not completely understood, especially if it is considered that they co-exist in mixtures with other chemicals forming the so-called chemical "cocktails" (Halling-Sorensen et al., 1998; Chatzitakis et al., 2008).

The possible fates of pharmaceuticals, as all other xenobiotics once they enter the aquatic environment are mainly three: (a) the compound is ultimately mineralized to carbon dioxide and water, (b) the compound does not degrade readily because it is lipophilic and is partially retained in the sedimentation sludge and (c) the compound metabolizes to a more hydrophilic molecule, passes through the wastewater treatment plant and ends up in the receiving waters (which are surface waters, mainly rivers). These compounds exhibit the highest persistence in the environment.

Pharmaceuticals have been detected in ground and surface water (Andreozzi et al., 2003a,b; Perez-Estrada et al., 2005a), drinking water (Ternes et al., 2002; Buffle et al., 2006), tap water (Halling-Sorensen et al., 1998; Doll and Frimmel, 2003), ocean water, sediments and soil (Halling-Sorensen et al., 1998).

Pharmaceuticals released in the environment may impose toxicity (the extent of which depends on the specific compound in question) virtually on any level of the biological hierarchy, i.e. cells, organs, organisms, population, ecosystems, or the ecosphere. In addition to toxic effects, certain classes of pharmaceuticals like antibiotics may cause long-term and irreversible change to the micro-organisms genome, making them resistant in their presence, even at low concentrations. More importantly though, the presence of the so-called endocrine disrupting compounds (EDCs) in aquatic systems has caused considerable concern as these compounds are known to disrupt the human endocrine system (Bredhult et al., 2007).

From the aforementioned observations, it is inferred that the presence of residual pharmaceuticals in the environment and in aquatic systems in particular constitutes a serious environmental problem as these compounds (a) are extremely resistant to biological degradation processes and usually escape intact from conventional treatment plants, (b) may impose serious toxic and other effects to humans and other living organisms, and (c) are present at minute concentrations, thus requiring more sophisticated and laborious analytical tools for their accurate determination. Therefore, it is not surprising that research has recently been directed towards the application of non-biological processes for the destruction of pharmaceuticals in waters with emphasis on AOPs.

The aim of this study is to review and assess the effectiveness of advanced oxidation processes (AOPs) for the removal of pharmaceuticals from various aqueous systems.

Table 1
Most frequently detected pharmaceuticals in wastewaters and their concentrations (Data taken from Al-Rifai et al., 2007; Gómez et al., 2007; Santos et al., 2007; Vieno et al., 2007)

Therapeutic Use		Type and Name of Pharmaceutical
Antibiotics		Sulfonamides: sulfamethoxazole (0.02–0.58 (μg/L) fluoroquinolones: ofloxacin (6–52 ng/L), ciprofloxacin (6–60 ng/L) bacteriostatic: trimethoprim (0.11–0.37 μg/L) Penicillin group: penicillin G (<0.025 μg/L)
Analgesic/Antipyretics	Analgesic, antipyretic	Acetaminophen (10–23.33 μg/L)
	Nonsteroidal anti-inflammatory drugs (NSAIDs)	Diclofenac (0.01–510 μg/L), naproxen (0.5–7.84 μg/L), ibuprofen 0.49–990 μg/L), ketoprofen (0.13–3 μg/L) Carbamazepine (0.1–1.68 μg/L)
CNS (Central nervous system) drugs	Antiepileptics	
	CNS stimulant	Caffeine (3.2–11.44 μg/L)
Cardiovascular drugs	Beta blockers	Propranolol (0.05 μg/L), atenolol (10–730 ng/L), metoprolol (10–390 ng/L)
	Cholesterol and Triglyceride reducers	clofibric acid (0.47–170 μg/L), gemfibrozil (0.3–3 μg/L), fezafibrate (0.1–7.60 μg/L)
Endocrinology treatments	Steroid hormones	17α-ethinylestradiol (1 ng/L), estrone, 17β-estradiol, estriol (usually <10 ng/L)
Diagnostic aid-adsorbable organic halogen compounds	Iodinated X-ray contrast media	Iopromide (0.026–7.5 μg/L), iomeprol (1.6 μg/L)

2. Advanced oxidation processes

AOPs can be broadly defined as aqueous phase oxidation methods based on the intermediacy of highly reactive species such as (primarily but not exclusively) hydroxyl radicals in the mechanisms leading to the destruction of the target pollutant. Over the past 30 years, research and development concerning AOPs has been immense particularly for two reasons, namely (a) the diversity of technologies involved and (b) the areas of potential application. Key AOPs include heterogeneous and homogeneous photocatalysis based on near ultraviolet (UV) or solar visible irradiation, electrolysis, ozonation, the Fenton's reagent, ultrasound and wet air oxidation, while less conventional but evolving processes include ionizing radiation, microwaves, pulsed plasma and the ferrate reagent. Although water and wastewater treatment is by far the most common area for research and development, AOPs have also found applications as diverse as groundwater treatment, soil remediation, municipal wastewater sludge conditioning, production of ultrapure water and volatile organic compounds treatment and odor control.

Depending on the properties of the waste stream to be treated and the treatment objective itself, AOPs can be employed either alone or coupled with other physicochemical and biological processes. Process coupling is conceptually beneficial usually leading to improved treatment efficiencies. For instance, AOPs may be employed as a pre-treatment stage to convert initially biorecalcitrant compounds to more readily biodegradable intermediates followed by biological post-treatment. On the other hand and for effluents containing biodegradable fractions, biological pre-treatment followed by chemical post-treatment may be favorable as biodegradable compounds can be easily removed first, and so subsequently do not compete for the chemical oxidant. Recent reviews on the applications of AOPs for water and wastewater treatment can be found elsewhere (Mantzavinos and Psillakis, 2004; Comninellis et al., 2008).

3. Overview of AOPs for pharmaceutical removal

Table 2 gives an overview of the recent work undertaken in this field describing which commonly used pharmaceuticals have been treated so far by AOPs. There is an increasing interest on the use of AOPs for the removal of pharmaceuticals from water and this is reflected in the increasing number of journal articles published in recent years (Fig. 2). From the data of Table 2 several observations can be made as follows:

(1) Regarding treatment efficiency, AOPs are generally capable of completely destroying the specific pharmaceutical in question but this is not necessarily accompanied by total mineralization. In several cases, degradation by-products are more biodegradable and less toxic than the original substrate, thus implying that a biological post-treatment may be feasible.
(2) Regarding the type of AOPs employed heterogeneous photocatalysis with semiconductors, ozonation and Fenton and alike reactions are the most popular ones, while other processes involve wet air oxidation, electrolysis and sonolysis, as seen in Fig. 3.
(3) Regarding the water matrix, most studies deal with model aqueous solutions and surface waters (i.e. from rivers or lakes), while actual wastewaters from sewage treatment plants or effluents from pharmaceutical industrial units have received less attention.
(4) Finally, the most common pharmaceuticals tested are diclofenac, carbamazepine, sulfamethoxazole, clofibric acid and 17β-estradiol. Table 3 summarizes representative literature on the top 5 pharmaceuticals that have been treated by AOPs.

4. Assessment of AOPs performance for pharmaceutical removal

4.1. Photolysis

It involves the interaction of artificial or natural light with the target molecule and the induction of photochemical reactions which can lead to its direct degradation to intermediate products whose further decomposition eventually yields mineral end-products (Doll and Frimmel, 2003; Saritha et al., 2007). UV treatment (and in particular UVC irradiation) has traditionally been employed for the disinfection of drinking water with the advantage, compared to chlorination, of minimizing the formation of any regulated disinfection by-products (Pereira et al., 2007b). However, recent studies (Andreozzi et al., 2003c; Bartels and Tumpling, 2007; Canonica et al., 2008) have been undertaken in order to understand the aquatic photochemistry of pharmaceutical compounds which still remains a largely unexplored field.

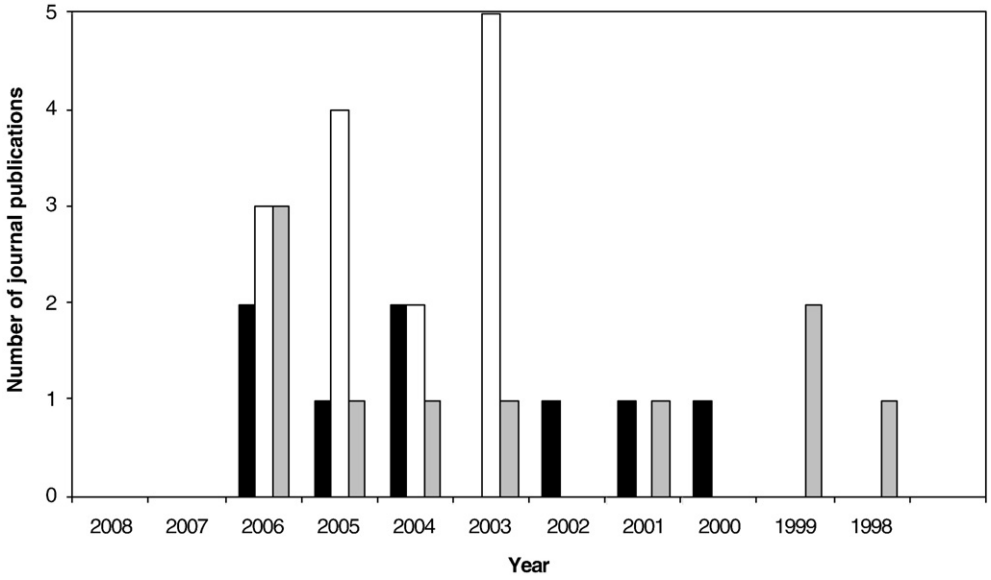

Fig. 1. Number of journal publications on the development of analytical techniques for pharmaceutical monitoring over the past decade. Black bars: water matrix; White bars: wastewater matrix; Grey bar: both water and wastewater matrices. Data taken from Fatta et al., 2007.

Table 2
Treatment of pharmaceuticals in waters by AOPs

Reference	Target drug/Initial concentration	Matrix	AOP features	Scale	Measure of degradability	Summary of results
UV/H_2O_2						
Hofl et al. (1997)	2 samples of unspecified composition COD=670–2700 mg/L AOX=3–5 mg/L	Pharmaceutical effluent	LP UV at 254 nm	Bench	COD, AOX	Quantitative AOX removal in 240 min. Comparison with other processes, i.e. O_3, UV, UV/O_3, Fe^{2+}/ H_2O_2
Andreozzi et al. (2003a)	Clofibric acid 5 10^{-8}–1.5 10^{-3} M	Distilled water	LP UV at 254 nm at pH=5	Bench	Specific drug, TOC	95% drug removal and 10% mineralization respectively after 60 min. Proliferation and validation of kinetic model
Andreozzi et al. (2003b)	Paracetamol 10^{-5} M	Distilled water	LP UV at 254 nm at pH=5	Bench	Specific drug, TOC	Complete drug removal and 40% mineralization in 1 and 4 min respectively. Identification of reaction by-products
Arslan-Alaton and Dogruel (2004)	Penicillin COD=1555 mg/L	Formulation effluent	LP UV at 254 nm at pH=7	Bench	COD, TOC, BOD5	10–20% COD removal after 60 min. Poor improvement in biodegradability
Vogna et al. (2004a)	Carbamazepine 0.02 mM	Distilled water with or without humic acid (HA)	LP UV at 254 nm at pH=5	Bench	Specific drug, TOC	Complete drug and 35% TOC removal in 4 min. Insignificant degradation with direct photolysis. HA acts as scavenger. Intermediates more toxic than carbamazepine
Vogna et al. (2004b)	Diclofenac 10^{-3} M	Distilled water	LP UV at 254 nm at pH=5–6	Bench	Specific drug, TOC	95% drug removal and 40% mineralization respectively after 90 min. Elucidation of reaction by-products and pathways
Shemer et al. (2006)	Metronidazole 1 mg/L	Deionized water	LP UV at 254 nm and MP UV at 200–400 nm at pH=6	Bench	Specific drug	Degradation follows first-order kinetics and rate increases with increasing H_2O_2 concentration. MP irradiation more effective than LP
Linden et al. (2007)	17β-Ethinylestradiol 10^{-5} mM	Laboratory grade water, surface water of low and high alkalinity	LP UV and MP UV	Bench	Yeast estrogen screen	Reduction in estrogenic activity occurs faster in laboratory water than in surface water indicating scavenging effects and also depends on water alkalinity. In most cases, complete removal occurs at ≤600 mJ/cm^2 fluence
Pereira et al. (2007a)	Naproxen, iohexol, carbamazepine, clofibric acid 1–3 μM	Laboratory grade water, surface water	MP UV at 200–300 nm at pH=7	Bench	Absorbance at 200–400 nm	Moderate degradation at 100 mJ cm^{-2} fluence and >99% at 600–1700 mJ cm^{-2} depending on the drug. Lower degradation with direct photolysis. Rates decrease in surface water compared to laboratory water
Pereira et al. (2007b)	Naproxen, ketoprofen, carbamazepine, clofibric acid, ciprofloxacin, iohexol 1–3 μM	Laboratory grade water, surface water	LP UV at 254 nm at pH=7	Bench	Absorbance at 200–400 nm	Complete degradation at 1700 mJ cm^{-2} fluence for all drugs. Lower degradation with direct photolysis. Rates decrease in surface water compared to laboratory water
Rosenfeldt et al. (2007)	17α-Ethinylestradiol, 17β-estradiol 5 μM	Deionized water, natural water	LP UV and MP UV at pH=7–8	Bench	Specific substrate, yeast estrogen screen	Substrate degradation and estrogenic activity removal follow comparable first-order kinetics. Development of kinetic model for estrogenic activity removal. Water matrix affects rates.
Ozonation						
Zwiener and Frimmel (2000)	Clofibric acid, diclofenac, ibuprofen 2 μg/L	Distilled water and natural river water	1–5 mg/L O_3 alone or O_3/H_2O_2 at pH=7	Bench	Specific drug	Reactivity order: diclofenac>ibuprofen>clofibric acid. Rates decrease in river water compared to distilled water. H_2O_2 enhances performance
Adams et al. (2002)	Sulfachlorpyridazine, sulfadimethoxine, sulfamerazine, Sulfamethazine, sulfathiazole, trimethoprim, carbadox	Deionized water and surface river water both spiked with 50 μg/L of each compound	7.1 mg/L O_3 at pH=7.5	Bench	Specific drug	>95% Degradation in 1.3 min in river water and even faster in distilled water. Comparison between ozonation and other techniques, i.e. UV irradiation, coagulation, PAC adsorption, ion exchange, reverse osmosis and chlorination
Andreozzi et al. (2002)	Carbamazepine 0.5 mM	Distilled water, surface river water	1 mg/L O3 at pH=5.5	Bench	Titrimetric quantification of CO_2, specific drug, bioassays	Complete degradation after 4 min and 30% mineralization after 60 min. The resulting stream is not toxic to algae
Ternes et al. (2002)	Bezafibrate, clofibric acid, carbamazepine, diclofenac, primidone 1 μg/L	Flocculated waterworks water	0.5–3 mg/L O_3 at pH=7.8	Bench	Specific drug	Reactivity order: carbamazepine–diclofenac>primidone>bezafibrate>clofibric acid
Andreozzi et al. (2003a)	Clofibric acid 5 10^{-8}–1.5 10^{-3} M	Distilled water	10^{-5} M O_3 at pH=5	Bench	Specific drug, TOC	Complete drug removal and 50% mineralization after 20 and 60 min respectively. Proliferation and validation of kinetic model
Andreozzi et al. (2003b)	Paracetamol 5 10^{-3} M	Distilled water	10^{-5} M O_3 at pH=2–7	Bench	Specific drug, TOC	Complete drug removal and 30% mineralization in 20 and 120 min respectively regardless solution pH. Identification of reaction by-products and pathways
Balcioglu and Otker (2003)	Human and veterinary antibiotics COD=250–1400 mg/L	Synthetic wastewater	2.96 g/(L h) O_3 alone or O_3/H_2O_2 at pH=3–10.6	Bench	COD, TOC, BOD5, absorbance at 254 nm	Degradation increases with increasing pH and decreasing initial organic load. H_2O_2 enhances performance. BOD_5/COD ratio increases consistently upon ozonation up to 60 min

(continued on next page)

Table 2 *(continued)*

Reference	Target drug/Initial concentration	Matrix	AOP features	Scale	Measure of degradability	Summary of results
Ozonation						
Huber et al. (2003)	Sulfamethoxazole carbamazepine, diclofenac, 17a-ethinylestradiol, roxithromycin, ibuprofen, iopromide, bezafibrate, diazepam 0.5 μM	Lake water, river water, well water	0.1–2 mg/L O_3 alone or O_3/H_2O2 at pH=8	Bench	Specific drug	Degradation follows second-order kinetics. First 5 drugs far more reactive than the rest. Water matrix affects ozone stability, radicals formation and scavenging. Both direct and indirect oxidation responsible for degradation. Bromate is a major ozonation by-product
Ternes et al. (2003)	17 Pharmaceuticals and estrone 0.015–2.1 μg/L each	Municipal WWTP effluent	5–15 mg/L O_3 at pH=7.2	Pilot plant	Specific substrate	Degradation below quantification limit for each compound within 18 min
Arslan-Alaton and Dogruel (2004)	Penicillin COD=1555 mg/L	Formulation effluent	2.8 g/(L.h) O_3 at pH=3–11.5	Bench	COD, TOC, BOD_5	COD removal increases with increasing pH and becomes 80% after 60 min at pH=11.5. Poor improvement in biodegradability
Arslan-Alaton et al. (2004)	Penicillin COD=840 mg/L	Formulation effluent	2.5 g/(L h) O_3 alone or O_3/H_2O_2 at pH=2.5–12	Bench	COD, BOD_5, absorbance at 274 and 344 nm	Degradation increases with increasing pH and in the presence of H_2O_2 up to 20–30 mM. BOD5/COD ratio increases 6 or 23 times upon ozonation or perozonation respectively for 20 min
Alum et al. (2004)	17α-Ethinylestradiol, 17 μ-estradiol, 100 nM	Deionized water	1.5 mg/L O_3 at pH=7.5	Bench	Specific substrate, e-screen (estrogenicity) assay	>99% Degradation in 1 min. Residual estrogenic behavior still present due to by-products. Ozonation is more efficient than chlorination
Cokgor et al. (2004)	Penicillin COD=710 mg/L	Formulation effluent	2.75 g/(L.h) O_3 at pH=3–11	Bench	COD, BOD5, TOC, respirometric measurements	Degradation increases with increasing pH. BOD_5/COD ratio increases substantially upon ozonation for 40 min. Biological oxidation tests in activated sludge systems
Huber et al. (2004)	17α-Ethinylestradiol 1 and 10 μM	Distilled water	5–100 μM O_3 at pH=5–9	Bench	Yeast estrogen screen, specific substrate	Reduction of estrogenic behavior by a factor of at least 200. Determination of reaction by-products. 17α-Ethinylestradiol partly reappears following ozonation
Qiang et al. (2004)	Lincomycin, spectinomycin 1 mM	Distilled water	0.06–0.1 mM O_3 at pH=2–9	Bench	Absorbance at 260 nm	Second-order reaction rates increase with increasing pH. Fast degradation of both antibiotics around neutral pH within ms
Tunay et al. (2004)	2 samples of containing unspecified antibiotics COD=1015–1060 mg/L	Synthetic wash-waters from antibiotics packaging	1.8 g/h O_3 at pH=2.5–7.7 with or without $MnSO_4$	Bench	COD, BOD5,	30% COD removal after 90 min of ozonation. Catalytic ozonation only slightly enhances performance
Vogna et al. (2004b)	Diclofenac 10^{-3} M	Distilled water	10^{-4} M O_3 at pH=5–7	Bench	Specific drug, TOC	Complete drug removal and 30% mineralization after 10 and 90 min respectively. Elucidation of reaction by-products and pathways. Proliferation and validation of kinetic model
Andreozzi et al. (2005)	Amoxicillin 5 10^{-4} M	Deionized water	1.6 10^{-4} M O_3 at pH=2–7	Bench	Specific drug, TOC	90% drug removal and 18% mineralization after 4 and 20 min respectively. Proliferation of kinetic model
Arslan-Alaton and Caglayan (2005)	Penicillin COD=200–600 mg/L	Synthetic formulation effluent	0.6–2.6 g/h O_3 at pH=3–12	Bench	Specific drug, TOC, COD	COD removal increases with increasing pH and applied O_3 dose and decreasing initial COD following first-order kinetics. Hydroxyl radical reactions play important role
Huber et al. (2005)	Macrolide and sulfonamide antibiotics, estrogens, diclofenac, naproxen, indomethacin 0.5–5 μg/L	Effluents from activated sludge and membrane bioreactor spiked with pharmaceuticals/estro gens	0.5–5 mg/L O_3 at pH=7	Pilot plant	Specific substrate	90–99% Degradation for O_3>2 mg/L. Water matrix in terms of suspended solids has minor effect on efficiency. More important is the effect of dissolved organic matter.
Irmak et al. (2005)	17β-Estradiol, 0.4 mM	Acetonitrile:water 30:70, distilled water	30–63 μM/min O_3 alone or O_3/LP UV at pH=5.3–6.3	Bench	Specific substrate	Degradation increases with increasing O_3 dose. UV irradiation enhances degradation compared to ozonation alone. Elucidation of reaction by-products.
Arslan-Alaton and Caglayan (2006)	Penicillin COD=600 mg/L	Synthetic formulation effluent	1.8 g/(L.h) O_3 with or without 10 mM H_2O_2 at pH=7–12	Bench	COD, BOD5, respirometric measurements, toxicity to *D. magna*	COD removal increases with increasing pH and in the presence of H_2O_2. Perozonation for 60 min at pH=7 improves aerobic biodegradability and reduces ecotoxicity but increases inhibition to activated sludge.
Buffle et al. (2006)	Carbamazepine 0.5–2 μM	Effluents from municipal WWTPs, drinking water from household tap and raw lake water	1.2–2.4 mg/L O_3 at pH=8	Bench	Specific substrate	Development of a continuous quench-flow system to model the very early stages (i.e. up to 20 s) of ozonation reactions
Hua et al. (2006)	Carbamazepine 0.3–3.8 ng/L, caffeine 2.3–24.0 ng/L, cotinine 0.1–1.6 ng/L	Raw intake water from river	1.5–2 mg/L O_3 at pH=7.5 as part of conventional treatment (coagulation/ flocculation/sedimentation/ filtration)	Pilot plant	Specific drug	66–100% Degradation after 20 min of ozonation. Conventional treatment alone fails to remove drugs
Lange et al. (2006)	Clarithromycin 10^{-4} M	Distilled water	10^{-5} M O^3 at pH=3.2–4.4	Bench	Specific drug, inhibition to *P. putida*	Second-order reaction rates increase with increasing pH. Elucidation of ozonation by-products which are less inhibitory than the drug

Skoumal et al. (2006)	Paracetamol 0.078–1 g/L	Distilled water	O_3 alone or O_s/UV at 300–420 nm, pH=2–6 with and without Fe^{2+} or Cu^{2+}	Bench	Specific drug, TOC	Catalysts and/or irradiation improve both drug degradation and mineralization by ozone. Conversion decreases with increasing drug concentration and decreasing metal loading and is pH insensitive in the range 2–4. Iron is more active than copper. Elucidation of by-products and reaction pathways
Dantas et al. (2007)	Bezafibrate 0.5 mm	Distilled water	O_3 at pH=6–8	Bench	Specific drug, TOC, COD, BOD5, toxicity to *V. fischeri*	Complete drug degradation is followed by low mineralization, enhanced biodegradability and increased ecotoxicity after 10 min. Performance increases with increasing pH. Determination of reaction by-products
Lei and Snyder (2007)	Several compounds including human hormone steroids and PPCPs 10–250 ng/L	Surface water from 3 rivers spiked with target compounds and tertiary municipal wastewater effluent	O_3 at ambient pH	Both bench and pilot plant	Specific substrate	Development of a structure-property relationship model to predict degradation. Comparison with chlorination
Nakada et al. (2007)	24 PhACs in the order of several ng/L	Municipal WWTP effluent	3 mg/L O_3 preceded by sand filtration	Full plant	Specific substrate	>80% Removal following filtration and 27 min ozonation
Oh et al. (2007)	Ibuprofen 10 μM	Distilled water	0.4 mg/(L min) O_3 at pH=5–7	Bench	Specific drug, DOC	Complete degradation after 15 min at pH=7 but <20% at pH=5. Mineralization is insignificant
Vieno et al. (2007)	Acebutolol, atenolol, metoprolol, sotalol, carbamazepine, bezafibrate, diclofenac, ibuprofen, ketoprofen, naproxen, ciprofloxacin, norfloxacin, ofloxacin in the order of few ng/L	Surface river water	1–1.3 mg/L O_3 at pH=7.5	Pilot plant	Specific substrate	Concentration profiles are followed at various stages of drinking water plant, i.e. coagulation, sedimentation, sand filtration, ozonation, adsorption and disinfection. Ozonation for 10–20 min removes most of the compounds below quantification limit
Dantas et al. (2008)	Sulfamethoxazole 200 mg/L	Distilled water	O_s at pH=3–11	Bench	Specific drug, TOC, COD, BOD5, absorbance at 254 nm, toxicity to *V. fischeri*	Complete drug degradation is followed by low mineralization and increased biodegradability after 60 min. Performance increases with increasing pH. Ecotoxicity remains unchanged. Determination of reaction by-products
Fenton and photo-Fenton						
Barek et al. (1998)	Amsacrine 150 mg/L, azathioprine 2 g/L, asparaginase 200 IU, thiotepa 60 mg/L	Deionized water	Fe^{2+}/H_2O_2 in the presence of 2N HCl	Bench	Specific drug, mutation assays	Over 98% drug degradation after 60 min. Elimination of mutagenicity is achieved. Comparison with sodium hypochlorite oxidation and hydrogen peroxide alone
Ravina et al. (2002)	Diclofenac TOC=20 mg/L	Distilled water	Fe^{3+}/H_2O_2/ LP UV-254 nm at pH=2.8	Bench	Specific drug, TOC, COD	Fast drug disappearance within few min is accompanied by slower mineralization (i.e. after 50 min). Mineralization increases with increasing light intensity and decreasing drug concentration
San Sebastian Martinez et al. (2003)	Mixture of biguanides, guanidines, triamines COD=362 g/L	Industrial wastewater of pharmaceutical origin	Fe^{2+}/H_2O_2 at pH=4	Bench	COD, BOD	A factorial design approach is implemented to optimize treatment regarding H_2O_2 and iron concentration and reaction temperature. 55% COD removal after 10 min at 3 M H_2O_2, 0.3 M Fe^{2+}, 40 °C
Arslan-Alaton and Dogruel (2004)	Penicillin COD=1555 mg/L	Formulation effluent	Fe^{2+}/H_2O_2 with or without LP UV-254 nm at pH=3	Bench	COD, TOC, BOD5	About 60% COD removal after 60 min for both dark and photo-reactions. Poor improvement in biodegradability. Comparison between Fe^{2+} and Fe^{3+} activity
Perez-Estrada et al. (2005a)	Diclofenac 50 mg/L	Distilled water	Fe^{2+}/H_2O_2/Sunlight at pH=6.5	Solar pilot plant	Specific drug, DOC	Fast drug degradation is accompanied by slower mineralization. Determination of 18 by-products and elucidation of reaction pathwaysss
Perez-Estrada et al. (2005b)	Diclofenac 50 mg/L	Synthetic fresh water	Fe^{2+}/H_2O_2/Sunlight at pH=7.2	Solar pilot plant	Specific drug, DOC	Drug degradation follows first-order kinetics and is faster than mineralization which follows zero-order kinetics. Iron concentration affects mineralization but not drug removal. Comparison with TiO_2 photocatalysis which is slower than photo-Fenton oxidation
Kajitvichyanukul and Suntronvipart (2006)	Mixed stream comprising wastes from hospital analysis room and labs COD=1350 mg/L	Hospital wastewater	Fe^{2+}/H_2O_2/UV-254 nm at pH=1–6	Bench	COD, BOD5, TOC, toxicity to *V. fischeri*	Increase of aerobic biodegradability and decrease of ecotoxicity at COD:H_2O_2:Fe^{2+} ratio 1:4:0.1 and pH=3. The pre-treated effluent becomes suitable for activated sludge post-treatment
Munoz et al. (2006)	α-Methyl-phenylglycine 500 mg/L	Distilled water	Fe^{2+}/H_2O_2/Sunlight at pH=2.8	Pilot plant	Specific drug, DOC, COD	Complete drug and 60% COD removal after 70 min. Life cycle assessment is implemented to assess environmental impact
Shemer et al. (2006)	Metronidazole 1 mg/L	Deionized water	Fe^{2+}/H_2O_2 with or without MP UV-(200–400 nm) at pH=3.5	Bench	Specific drug	Degradation follows second-order kinetics and rate increases with increasing Fe^{2+} concentration. Photo-Fenton reaction is faster than dark Fenton
Tekin et al. (2006)	Nine pharmaceutical chemicals in the COD range 1.8–14 or 9–70 or 18–140 mg/L each	Synthetic wash-waters from medium scale, drug manufacturing plant	Fe^{2+}/H_2O_2 at pH=3–4.5 coupled with coagulation at pH=7–9	Both bench and full plant	COD, BOD5	Treatment efficiency depends on COD:H_2O_2:Fe^{2+} ratio as well as effluent pH for oxidation and coagulation. Full-scale application for combined Fenton-aerobic oxidation

(continued on next page)

Table 2 (*continued*)

Reference	Target drug/Initial concentration	Matrix	AOP features	Scale	Measure of degradability	Summary of results
Fenton and photo-Fenton						
Xing et al. (2006)	Mixture of metabolites of lincomycin hydrochloride aerobic/anaerobic degradation COD=992 mg/L	Biologically pre-treated pharmaceutical wastewater	Fe^{2+}/H_2O_2 at pH=2–5 coupled with coagulation at pH=5	Bench	Specific substrate, COD, color	94% color and 73% COD removal after 30 min oxidation at pH=3, H_2O_2:Fe^{2+} ratio 3:1, COD:H_2O_2 ratio 1:0.27 and coagulation at pH=5
Gonzalez et al. (2007)	Sulfamethoxazole, 200 mg/L	Distilled water	Fe^{2+}/H_2O_2/UV-365 nm at pH=2.8	Bench	Specific drug, COD, BOD5, TOC, toxicity to *V.fischeri*, oxygen uptake	Increase of aerobic biodegradability at drug:H_2O_2:Fe^{2+} ratio 1:(1.5–5):0.05. Drug degradation and mineralization increase with increasing H_2O_2 concentration. Neither the original drug nor its metabolites are ecotoxic or inhibitory
Kulik et al. (2008)	Mixtures of spent chemicals from ointment production already treated by adsorption, flocculation and filtration COD=4–13.1 g/L	Actual wash-waters from ointment manufacturing plant	Fe^{2+}/H_2O_2 followed by lime or NaOH coagulation	Bench	COD, BOD7	87–96% COD removal and biodegradability increase after 120 min oxidation at H_2O_2:Fe^{2+} molar ratio 10:1, COD:H_2O_2 weight ratio 1:2 and 0.5 g/L lime coagulation
Semiconductor photocatalysis						
Coleman et al. (2000)	17β-Estradiol 0.05–3 μM	Acetonitrile/water	Immobilized TiO_2/UV-(300–400 nm) at pH=1–12	Bench	Specific substrate, TOC	98% Degradation after 210 min following Langmuir–Hinshelwood kinetics
Ohko et al. (2002)	17β-Estradiol 1 μM	Deionized water	Suspended Degussa TiO_2/UV-365 nm	Bench	Specific substrate, CO_2 evolution, yeast-based estrogenicity assay	Complete estrogen removal after 30 min with first-order kinetics. Complete mineralization after 180 min. Determination of by-products. Estrogenic activity is lost upon estrogen removal
Tanizaki et al. (2002)	Several compounds including 10 endocrine disruptors, 17β-estradiol, estrone, ethinylestradiol 0.1 mg/L	Deionized water	Immobilized nanostructured TiO_2/UVA	Bench	Specific substrate, TOC	First-order kinetics for all substrates. Rate depends on the specific compound and, in general, takes values between 10^{-1}–10^{-2} 1/min
Nakashima et al. (2003)	17β-Estradiol, estrone 250 μg/L	Deionized water and treated effluent from a sewage treatment plant	Immobilized TiO_2/UV-black fluorescent lamp	Bench	Specific substrate	Fast degradation of both estrogens following first-order kinetics. Rate increases with increasing catalyst surface area and temperature
Calza et al. (2004)	Buspirone 15 mg/L	Distilled water	Suspended Degussa TiO_2/Artificial sunlight	Bench	Specific drug	Complete drug removal after 30 min with first-order kinetics. Determination of by-products and pathways
Coleman et al. (2004)	17β-Estradiol, estrone, 17α-ethylestradiol 10 μg/L	Distilled water	Immobilized TiO_2/UVA	Bench	Yeast-based estrogenicity assay	50% and complete removal of estrogenic activity for all three steroids after 10 and 60 min respectively with first-order kinetics. Photolysis is 2.4–9 times slower than photocatalysis
Doll and Frimmel (2004)	Clofibric acid, carbamazepine, iomeprol, iopromide 0.5–10 mg/L	Distilled water	Suspended Degussa or Hombikat TiO_2/Artificial sunlight at pH=3.4–6.5	Bench	Specific substrate, DOC	First-order kinetic rates increase with increasing catalyst loading and decreasing initial concentration. Degussa is generally more active than Hombikat. Determination of by-products and pathways
Mitamura et al. (2004)	Unconjugated and conjugated estrone and estradiol 1 mM	Distilled water	Immobilized TiO_2/UVA	Bench	Specific substrate	Conjugated estrogens degrade much slower (by about an order of magnitude) than their unconjugated counterparts with first-order kinetics
Augugliaro et al. (2005)	Lincomycin 10–75 μM	Distilled water	Suspended Degussa TiO_2/Sunlight coupled with nanofiltration	Pilot plant	Specific drug, TOC	Fast first-order drug degradation. Filtration separates catalyst particles and reaction by-products from the permeate
Coleman et al. (2005a,b)	17α-Ethinylestradiol, 17β-estradiol, estriol 0.1–3 μM	Acetonitrile/water	Immobilized Degussa TiO_2/UVA & B at pH=4 and 3 respectively	Bench	Specific substrate	First-order estrogen degradation in the order: 17α-ethinylestradiol>17β-estradiol>estriol. Photolysis is slower than photocatalysis. Rate decreases with decreasing light intensity and initial concentration. TiO_2 doping with Pt or Ag has no effect on catalyst activity
Doll and Frimmel (2005a)	Iomeprol, clofibric acid, carbamazepine ~2 mg/L	Deionized water	Suspended Degussa or Hombikat TiO_2/UV-254 nm coupled with microfiltration at pH=6.8	Pilot plant	Specific substrate, DOC	Assessment of long-term stability/activity of catalysts following membrane separation and reuse. Hombikat is more active than Degussa
Doll and Frimmel (2005b,c)	Carbamazepine, clofibric acid, iomeprol 0.5–5.2 mg/L	Spiked lake water	Suspended Degussa or Hombikat TiO_2/Artificial sunlight at pH=6.5	Bench	Specific substrate	First-order rates decrease with increasing concentration of NOM and other xenobiotics. Degussa is more active than Hombikat for carbamazepine and clofibric acid but less for iomeprol. Rate increases with increasing catalyst loading. Determination of by-products and pathways
Kaniou et al. (2005)	Sulfamethazine 10–70 mg/L	Distilled water	Suspended Degussa TiO_2 or ZnO/UV-(350–400 nm) at pH=4.8	Bench	Absorbance at 260 nm, TOC	First-order rate increases with increasing catalyst loading and is enhanced in the presence of H_2O_2. ZnO is more activethan TiO_2 for both drug removal and mineralization

Malygina et al. (2005)	B-Estradiol 0.5 mg/L	Distilled water	Suspended TiO_2/UV-366 nm at pH=3–11	Bench	Specific substrate	Both dark adsorption and degradation increase considerable with increasing pH in the range 5–11
Baran et al. (2006)	Sulfacetamide, sulfathiazole, sulfamethoxazole, sulfadiazine 0.1 mM	Distilled water	Suspended TiO_2/UV-365 nm	Bench	Specific drug, BOD_5, toxicity to *C. vulgaris*	Complete degradation of all drugs within 180–300 min with first-order kinetics. Sulfamethoxazole is far more reactive than the rest. Intermediates are more biodegradable and less toxic than the parent compounds
Calza et al. (2006)	Diclofenac 0.76–15 mg/L	Distilled water	Suspended Degussa TiO_2/ Artificial sunlight at ambient pH	Bench	Specific drug, TOC, toxicity to *V. fischeri*	A factorial design approach is implemented to optimize conversion regarding catalyst loading and drug concentration. Determination of by-products and pathways. Toxicity increases during early stages and decreases thereafter
Molinari et al. (2006)	Furosemide, ranitidine, ofloxacin, phenazone, naproxen, carbamazepine, clofibric acid 5–10 mg/L	Distilled water and surface river water	Suspended Degussa TiO_2/MP UV coupled with nanofiltration at pH=2–12	Bench	Absorbance at 230–280 nm	First-order rate depends on solution pH in the range 3-11. Filtration separates catalyst particles but not reaction by-products from the permeate. Comparison of various membranes
Munoz et al. (2006)	α-Methyl-phenylglycine 500 mg/L	Distilled water	Suspended Degussa TiO_2/Sunlight	Pilot plant	Specific drug, DOC, COD	Complete drug and 85% COD removal after 1500 min. Life cycle assessment is implemented to assess environmental impact
Reyes et al. (2006)	Tetracycline 40 mg/L	Deionized water	Suspended Degussa TiO_2/UV >254 nm or solarium device (300–400 nm) or UV-365 nm	Bench	Specific drug, BOD, TOC, COD, microbiological assay with *S. aureus*	First-order rate depends on the light source in the order: UV (>254 nm)>solarium>UV(365 nm). Partial mineralization is accompanied by complete loss of antibacterial activity and increase of biodegradability after 55 min with solarium.
Rafqah et al. (2006)	Triclosan 15–37 μM	Distilled water and surface river water	Suspended Degussa or anatase TiO_2/UV-(300–450 nm) at pH=5	Bench	Specific drug, TOC	Degussa is far more active than pure anatase. Degradation increases with increasing catalyst concentration except at excessive loadings. Mineralization is much slower than drug degradation. Oxidation in river water is slower than in distilled water due to water matrix. Determination of by-products and pathways
Yu et al. (2006)	Triclosan 9 mg/L	Distilled water	Suspended Degussa TiO_2/UV-365 nm	Bench	Specific drug, TOC	Mineralization takes 3–4 times longer than drug degradation. Both improve with the addition of H_2O_2. Determination of by-products and pathways
Abellan et al. (2007)	Sulfamethoxazole 25–200 mg/L	Distilled water	Suspended Degussa TiO_2/ Artificial sunlight at pH=2–11	Bench	Specific drug, TOC, COD BOD_5	Drug removal and mineralization depend on catalyst loading and pH. Comparison of various kinetic models. Determination of by-products and mechanisms. Slight increase in biodegradability is achieved
Coleman et al. (2007)	17α-Ethinylestradiol, 17β-estradiol, estriol 0.8 mg/L	Distilled water	Immobilized Degussa TiO_2/ Artificial sunlight or UV-350 nm	Bench	Specific substrate	Degradation follows first-order kinetics for all three estrogens at comparable rates. UVA is more efficient than solar irradiation. Method of catalyst immobilization affects performance
Hu et al. (2007)	Sulfamethhoxazole 5–500 μM	Deionized water spiked with NOM and bicarbonates	Suspended Degussa or anatase or rutile TiO_2/UV-(324–400 nm) at pH=3–11	Bench	Specific drug, DOC	Degussa is more active than pure anatase or rutile. Rate depends on catalyst loading, initial drug concentration, solution pH and the water matrix (presence of NOM, bicarbonates, dissolved gases). Determination of by-products and pathways
Sakkas et al. (2007)	Salbutamol 15 mg/L	Distilled water	Suspended Degussa TiO_2/ Artificial sunlight at pH=2.5–9.5	Bench	Specific drug, TOC, toxicity to *V. fischeri*	A factorial design approach is implemented to optimize conversion regarding catalyst loading and pH. Mineralization takes 6 times longer than drug removal. Determination of by-products and pathways. Toxicity increases during early stages and decreases thereafter
Yurdakal et al. (2007)	Gemfibrozil, tamoxifen 2.5–47 mg/L	Deionized water	Suspended Degussa or anatase TiO_2/UV-360 nm at pH=10	Bench	Specific drug, TOC	Gemfibrozil undergoes only photocatalytic degradation but not photolytic. Tamoxifen undergoes direct photolysis but its metabolites undergo photocatalytic degradation. Degussa is more active than anatase. Mineralization takes much longer than drug removal
Zhang et al. (2007)	Estrone, 17β-estradiol 0.1–1 μg/L	Deionized water	Suspended Degussa TiO_2/UV-253 nm or UV-(238–579 nm) at pH=2–10	Bench	Specific substrate	Estrogens are equally reactive following first-order kinetics. Reaction at 253 nm is 3 times faster than at 238–579 nm. Degradation increases with increasing catalyst loading and adding H_2O_2 and also depends on pH. Humic substances facilitate degradation due to photosensitization
Calza et al., in press	Imipramine 15 mg/L	Deionized water	Suspended Degussa TiO_2/ Artificial sunlight combined with Fenton	Bench	Specific substrate, TOC, toxicity to *V. fischeri*	A factorial design approach is implemented to assess the effect of TiO_2, H_2O_2 and Fe^{2+} concentrations on conversion. Determination of by-products and pathways. By-products are as toxic as imipramine and resistant to mineralization
Chatzitakis et al. (2008)	Chloramphenicol 10–80 mg/L	Deionized water	Suspended Degussa or anatase TiO_2 or ZnO/UV-(320–400 nm) at pH=5	Bench	Absorbance at 276.5 nm, TOC, antimicrobial activity to *E.coli*	First-order rate increases with increasing drug concentration and catalyst loading and adding H_2O_2. Degussa TiO_2 and ZnO are equally active. Complete elimination of drug activity after 90 min corresponding to 70% mineralization
Mendez-Arriaga et al. (2008)	Diclofenac, naproxen, ibuprofen 25–200 mg/L	Deionized water	Suspended Degussa TiO_2/ Artificial sunlight	Bench	Specific drug, TOC, BOD5, COD, toxicity to *V. fischeri*	Diclofenac and naproxen are susceptible to photolysis but not ibuprofen. By-products of low biodegradability accompany diclofenac and naproxen degradation.

(continued on next page)

Table 2 (*continued*)

Reference	Target drug/Initial concentration	Matrix	AOP features	Scale	Measure of degradability	Summary of results
Semiconductor photocatalysis						
Yang et al. 2008	Paracetamol 2–10 mM	Deionized water	Suspended Degussa TiO_2/ UV-254 nm or UV-365 at pH=3.5–11	Bench	Specific drug, TOC	First-order rate under UVC irradiation is much faster than under UVA. Several factors such as initial drug, catalyst and oxygen concentrations, pH and light intensity are tested concerning drug degradation. Identification of by-products
Electrolysis						
Oturan et al. (1999)	Riluzole 1–5 mM	Distilled water	Glassy carbon and 1 mM Fe_2C_{13} at pH=2	Bench	Specific drug	Identification of by-products and elucidation of pathways
Rajkumar and Palanivelu (2004)	Phenolic compounds COD=8880 mg/L	Effluent from Bulk drug manufacturing	Ti/TiO_2 -RuO_2-IrO_2 as anode, graphite as Cathode, Cl -as electrolyte, pH=10.7	Bench	COD, TOC	95% COD removal at 44 Ah/L charge with first-order kinetics. Energy consumption is 17 kWh/kg COD
Hirose et al. (2005)	Epirubicin hydrochloride 200 mg/L, mixture of 12 antineoplastics 11.8 g/L	Distilled water	Pair of Pt/Ir electrodes, NaCl as electrolyte	Bench	Specific drug, microbiological assay with *S. aureus,* cytotoxicity and mutagenicity assays	Complete removal of drug, cytotoxicity, mutagenicity and microbiological activity after 360 min at 0.1 A. Similar results for the mixture
Pauwels et al. (2006)	17α-Ehinylestradiol 0.01–1 mg/L	Spiked drinking water, outlet of membrane bioreactor treating hospital wastewater	TiO_2 electrodes, NaCl as electrolyte, pH=7.5–8	Bench	Specific substrate	Estrogen removal increases with increasing applied current and electrolyte concentration. Water matrix in hospital effluent affects removal adversely compared to tap water. Electrolysis also provides disinfection for hospital effluent
Torriero et al. (2006)	Piroxicam 0.8 10^{-5}-2 10^{-4} M	Acetonitrile/water	Glassy carbon and Pt as working and counter electrodes	Bench	Specific drug	Identification of by-products and elucidation of pathways
Murugananthan et al. (2007)	17!-Estradiol 250–750 μg/L	Distilled water	Boron-doped diamond or Pt or glassy carbon as anode, NaCl or $NaNO_3$ or Na_2SO_4 as electrolyte, pH=2–10	Bench	Specific substrate, TOC	Degradation increases with increasing current and pH and decreasing initial concentration. Anode efficiency changes in the order: boron-doped>Pt>carbon. Electrolyte efficiency changes in the order: NaCl>Na_2SO_4>$NaNO_3$. Mineralization is at least 10 times slower than estrogen removal
Sires et al. (2007a,b)	Clofibric acid 179 mg/L	Distilled water	Pt or boron-doped dimond as anode, carbon/PTFE as cathode, Fe^{2+} as catalyst, with or without Na_2SO_4 as electrolyte, pH=3	Bench	Specific drug, TOC	Fe^{2+} enhances degradation inducing a Fenton-like reaction due to the electrogeneration of H_2O_2. Simultaneous UV-360 nm irradiation further increases performance. Degradation follows first-order kinetics. Determination of by-products and pathways. Boron-doped diamond is more effective than Pt for anodic mineralization but the opposite occurs for drug degradation
Sonolysis						
Emery et al. (2005)	Triphenylphosphine oxide 10–350 mg/L	Deionized water	Horn-type sonication at 20 kHz, 125–250 W, pH=7	Bench	Specific drug, TOC, toxicity to *V. fischeri*	First-order rate increases with increasing power and decreasing volume. Conversion decreases at increased initial concentrations and temperatures. Water matrix (H_2O_2, butanol, Fe^{2+}) affects performance. By-products are more toxic than the drug
Hartmann et al. (2008)	Diclofenac 50–100 mg/L	Distilled water	Sonication at 216, 617 and 850 kHz, 90 W with TiO_2, SiO_2, SnO_2 TiO_2/SiO_2	Bench	Specific drug, TOC	90% Degradation after 60 min at 216 or 617 kHz and 20% at 850 kHz without particles. Particles enhance degradation. Determination of by-products and pathways
Memarian and Farhadi, 2008	Ten dihydropyrimidinones 0.23 mM	Acetonitrile/water	Horn-type sonication at 24 kHz, 460 W/cm2	Bench	Specific substrate	Complete conversion at 70 °C in the presence of K2 S2O8 within 5–27 min depending on the substrate.
Sanchez-Prado et al. (2008)	Triclosan 5 μg/L	Deionized water, 3.5% NaCl in water, seawater, urban runoff, municipal wastewater before secondary treatment	Horn-type sonication at 80 kHz, 135 W, pH=7–8	Bench	Specific drug	First-order rate is affected strongly by the water matrix in the order: seawater>3.5% NaCl in water>urban runoff>deionised water>wastewater. In all samples but wastewater, complete removal after 120 min
Wet air oxidation						
Gotvajn et al. (2007)	Blood pressure DOC=800 mg/L	Diluted formulation effluent	240–280 °C, 3.3–9.8 MPa oxygen pressure, pH=7	Bench	DOC, COD, respirometric measurements, toxicity to *V. fischeri and D. magna*	First-order rate increases with increasing temperature. 80% removal after 120 min at 280 °C. Biodegradability increases and toxicity to *V. fischeri* decreases

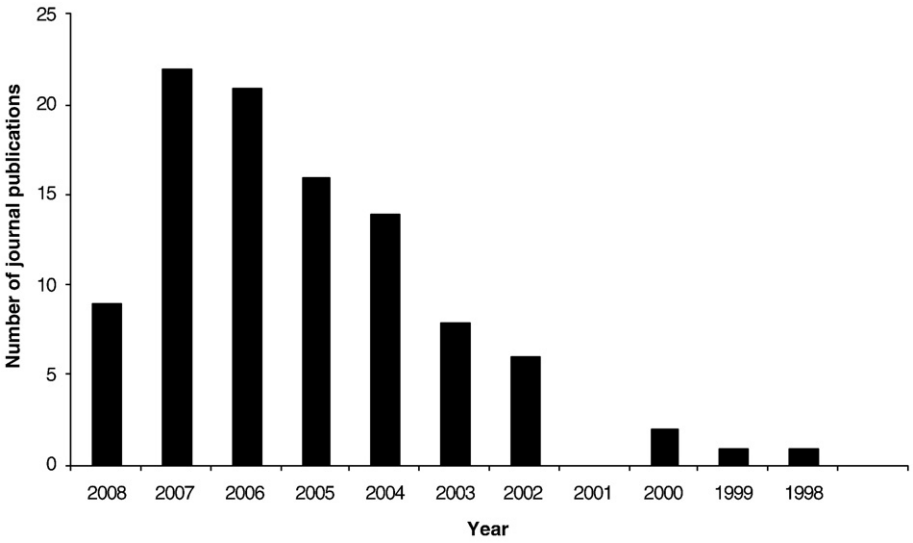

Fig. 2. Number of journal publications on pharmaceutical degradation by AOPs over the past decade. Publications as in Table 2.

The efficiency of direct photolysis is usually enhanced when irradiation is combined with hydrogen peroxide, a strong oxidant whose photolytic dissociation yields hydroxyl radicals, thus facilitating the degradation process. The beneficial role of hydrogen peroxide-promoted photolysis (also referred to as indirect photolysis) has been demonstrated in recent studies (Andreozzi et al., 2003a and 2003b; Arslan-Alaton and Dogruel, 2004; Rosenfeldt and Linden, 2004; Vogna et al., 2004a,b; Shemer et al., 2006; Pereira et al., 2007a,b) where bench scale experiments with artificial light were performed. The efficiency of photolytic degradation depends on several factors such as the absorbance spectrum of the pharmaceutical, the quantum yield of photolysis, the concentration of hydrogen peroxide employed and the water matrix. The latter appears to play an important role as the presence of natural organic matter (NOM) in waters may induce radicals scavenging, thus decreasing degradation (Vogna et al., 2004a; Pereira et al., 2007a,b). Nonetheless, it has been reported (Doll and Frimmel, 2003) that NOM acts as a precursor of reactive species (i.e. superoxide anion, hydroxyl radicals etc) and so its presence leads to a faster degradation due to the production of photochemically induced reactive species.

4.2. Ozonation

Ozone is a strong oxidant that either decomposes in water to form hydroxyl radicals which are stronger oxidizing agents than ozone itself, thus inducing the so-called indirect oxidation or attacks selectively certain functional groups of organic molecules through an electrophilic mechanism (Mantzavinos and Psillakis, 2004; Dantas et al., 2007, 2008). Depending on the type of the substrate and the operating conditions in question, ozone oxidation is usually favored at increased pH values due to the increased production of hydroxyl radicals. Moreover, treatment performance is enhanced if ozone is combined with light irradiation (Irmak et al., 2005), hydrogen peroxide (Zwiener and Frimmel, 2000, Balcioglu and Otker, 2003; Huber et al., 2003; Arslan-Alaton et al., 2004; Arslan-Alaton and Caglayan, 2006) or with iron or copper complexes that act as catalysts (Skoumal et al., 2006).

Ozonation has been traditionally employed in drinking water treatment for odor and taste control and disinfection, as well as (in some cases) for wastewater disinfection. Therefore, it is not surprising that several studies have been carried out onsite in drinking water plants (Ternes et al., 2002; Hua et al., 2006; Jasim et al., 2006; Vieno

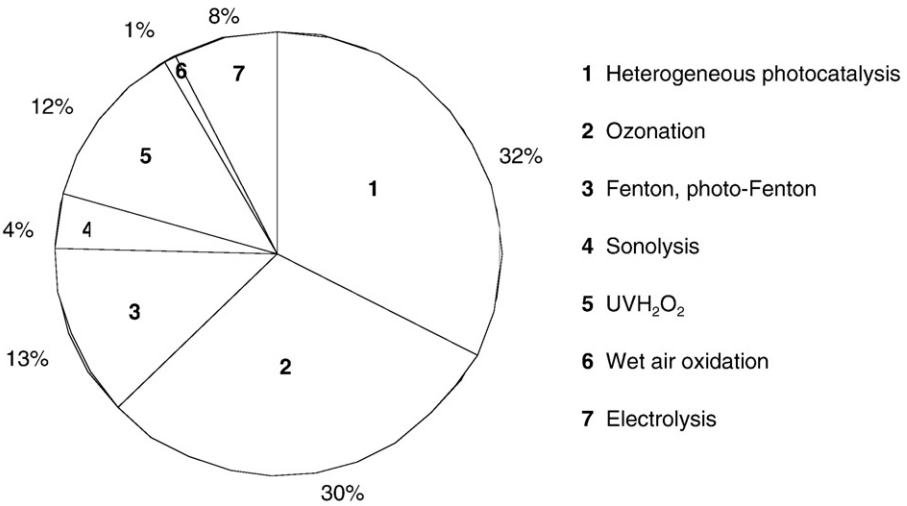

Fig. 3. Distribution of AOPs tested for pharmaceutical degradation. Publications as in Table 2.

Table 3
Representative studies dealing with the top 5 pharmaceuticals most commonly treated by AOPs. na: not available

Reference	Initial concentration	Water matrix	AOP	% Removal
Diclofenac ($C_{14}H_{10}Cl_2NO_2$, log k_{OW}=4.51, pKa=4.14, P_v=6.14 10–8 mmHg, Solubility>9 g/L)				
Perez-Estrada et al. (2005b)	50 mg/L	Fresh water	Photo-Fenton in solar pilot plant	Complete in 100 min
Calza et al. (2006)	15 mg/L	Distilled water	200 mg/L TiO_2/Artificial sunlight at 750 W/m^2	Complete in 60 min
Hartmann et al. (2008)	50 mg/L	Distilled water	Sonolysis at 617 kHz, 90 W in the presence of 100 mg/L TiO_2	85 in 30 min
Carbamazepine ($C_{15}H_{12}N_2O$, log k_{OW}=2.47, pKa=7, P_v=1.84 10^{-7} mmHg, Solubility=very low)				
Doll and Frimmel (2005b)	4.2 mg/L	Lake water with 0.5 mg/L NOM	100 mg/L TiO_2/Artificial sunlight	75 in 9 min
Hua et al. (2006)	0.3–3.8 ng/L	Raw river water	1.5–2 mg/L Ozone as part of conventional drinking water treatment plant	Complete in 20 min
Pereira et al. (2007a)	240–710 μg/L	Surface water	10 mg/L H_2O_2/UV(200–300 nm)	90 at 853 mJ/cm^2
Sulfamethoxazole ($C_{10}H_{11}N_3O_3S$, log k_{OW}=0.89, pKa=6, P_v=6.93 10^{-8} mmHg, Solubility=0.5 g/L				
Abellan et al. (2007)	100 mg/L	Distilled water	100 mg/L TiO_2/Artificial sunlight	88 in 360 min
Gonzalez et al. (2007)	200 mg/L	Distilled water	Photo-Fenton at 300 mg/L H_2O_2, 10 mg/L Fe^{2+}, 365 nm	Complete at 5 Einstein/m^3
Dantas et al. (2008)	200 mg/L	Distilled water	0.4 g/L Ozone	99 in 60 min
Clofibric acid ($C_{10}H_{11}O_3Cl$, log k_{OW}=na, pKa=na, Pv=na, Solubility=na)				
Andreozzi et al. (2003a)	215–320 mg/L	Distilled water	1 M H_2O_2/UVC (17 W)	90 in 60 min
			0.01 mM Ozone	Complete in 20 min
Molinari et al. (2006)	10 mg/L	Distilled water	1 g/L TiO_2/UV (125 W)	Complete in 20 min
Sires et al. (2007b)	179 mg/L	Distilled water	Electrolysis over boron-doped diamond at 100 mA/cm^2 and 1 mM Fe^{2+}	Complete in 7 min
17β-estradiol ($C_{16}H_{14}O_3$, log k_{OW}=4.01, pKa=10.3, P_v=1.26 10^{-8} mmHg, Solubility=3.6 mg/mL)				
Alum et al. (2004)	27 μg/L	Deionized water	1.5 mg/L Ozone	99 in 1 min
Coleman et al. (2005a)	0.8 mg/L	Acetonitrile/water	TiO_2 film/UV (125 W)	50 in 2 min
Murugananthan et al. (2007)	0.5 mg/L	Distilled water	Electrolysis over boron-doped diamond at 25 mA/cm^2, pH=10 and Na_2SO_4	Complete in 8 min

et al., 2007) and WWTPs (Ternes et al., 2003; Huber et al., 2005; Nakada et al., 2007). Special attention is given on WWTPs since pharmaceuticals usually exit secondary treatment unaffected and, therefore, they need to be treated in subsequent stages. Moreover, they may partly be adsorbed on primary and secondary sludge although data regarding their concentration in sludge is scarce due to inherent analytical difficulties associated with such samples. Interestingly, Carballa et al. (2007) have recently studied sludge preconditioning by ozonation with emphasis on the fate of adsorbed pharmaceuticals.

4.3. Fenton oxidation

Homogeneous oxidation with the Fenton reagent occurs in the presence of ferrous or ferric ions with hydrogen peroxide via a free radical chain reaction which produces hydroxyl radicals. It is considered to be a metal-catalyzed oxidation reaction, in which iron acts as the catalyst (Tekin et al., 2006; Saritha et al., 2007). Process efficiency is closely related to the solution pH whose optimal values are between 2 and 4 as well as the COD:H_2O_2:catalyst ratio in the feed. Moreover, efficiency may be enhanced in the presence of UV irradiation as more hydroxyl radicals are produced in the so-called photo-Fenton reaction compared to dark Fenton (Ravina et al., 2002; Perez-Estrada et al., 2005a; Shemer et al., 2006). Optimization of the catalyst and oxidant concentrations relative to the effluent's polluting load renders the process suitable to treat strongly polluted hospital effluents or effluents from pharmaceuticals manufacturing. In most cases, Fenton oxidation is capable of mineralizing a substantial fraction of the polluting load yielding effluents that are less toxic and more readily amenable to biological post-treatment (San Sebastian Martinez et al., 2003; Kajitvichyanukul and Suntronvipart, 2006; Tekin et al., 2006; Kulik et al., 2008).

Fenton systems are easy to handle and operate; adjusting working conditions accordingly, Fenton reactions may conveniently be employed to treat micro-pollution caused by residual pharmaceuticals in e.g. surface waters as well as industrial effluents (e.g. hazardous hospital wastes or from drug manufacturing) with increased organic loading. It should be noticed though that all previous studies regarding the application of Fenton and photo-Fenton processes for pharmaceuticals treatment deal with homogeneous reaction systems. Use of ferrous or ferric salts usually suffers two major drawbacks associated with (a) the narrow pH range of operation to avoid the formation and subsequent precipitation of iron oxyhydroxides and (b) the need to recover dissolved ions from the treated solution, thus requiring an additional treatment stage. In this respect, the immobilization of Fenton catalyst on a heterogeneous matrix would enable its use under non-controlled pH conditions as well as its easy recovery from the treated effluent; this is perhaps a step to the direct direction for future investigations.

4.4. Heterogeneous photocatalysis

Heterogeneous semiconductor photocatalysis using TiO_2 as the photocatalyst is an emerging technology with key advantages including operation at ambient conditions as well as the fact that the catalyst itself is inexpensive, commercially available at various crystalline forms and particle characteristics, non-toxic and photochemically stable (Doll and Frimmel, 2004). From a mechanistic point of view, illumination of an aqueous TiO_2 suspension with irradiation with energy greater than the band gap energy of the semiconductor generates valence band holes and conduction band electrons. Holes and electrons may either undesirably recombine liberating heat or make their separate ways to the surface of TiO_2, where they can react with species adsorbed on the catalyst surface. Valence band holes can react with water and the hydroxide ion (i.e. under alkaline conditions) to generate hydroxyl radicals, while electrons can react with adsorbed molecular oxygen reducing it to superoxide radical anion which, in

turn, reacts with protons to form peroxide radicals (Andreozzi et al., 1999; Abellan et al., 2007; Saritha et al., 2007).

The catalyst employed for almost all the pharmaceuticals photocatalytic treatment studies as clearly seen in Table 2 is TiO_2. Although available at various crystalline forms, a commercially available product containing 80:20 anatase:rutile (Degussa P25) shows exceptional activity and its superiority against other grades of TiO_2 is attributed to the morphology of its crystallites (Chatzitakis et al., 2008). This morphology allows an easy electron transfer from rutile to anatase, thus stabilizing charge separation and, therefore, lowering the recombination of photogenerated carriers. Besides TiO_2, ZnO and CdS have also been employed as photocatalysts in water treatment. In the context of pharmaceuticals treatment, Kaniou et al. (2005) and Chatzitakis et al. (2008) compared the catalytic activity of ZnO and Degussa TiO_2 for the degradation of sulfamethazine and chloramphenicol respectively and reported that ZnO was slightly more effective than TiO_2.

Photocatalytic reactions typically involve TiO_2 suspensions with the catalyst concentration being an important parameter that affects performance. Other parameters are the light wavelength and intensity, the solution pH which dictates the ionization state of the catalyst surface and consequently affects the extent of organics adsorption and degradation, the addition of H_2O_2 as an extra oxidant to promote reactions, and the water matrix (i.e. the presence of humic substances, bicarbonates or dissolved gases). Photocatalytic reactions usually obey to Langmuir–Hinshelwood kinetic model which is reduced to pseudo-first or -zero-order kinetics depending on the operating conditions.

From an engineering point of view, the use of catalyst in slurry form requires an additional treatment step to remove it from the treated effluent. In this view, Augugliaro et al. (2005) and Molinari et al. (2006) suggested a combined process comprising photocatalysis and membrane separation. The role of the membrane was to retain the used catalyst, the unreacted pharmaceuticals and their by-products, which could then be recycled to the photoreactor. Alternatively, the catalyst may be immobilized on suitable support matrices, thus eliminating the need for post-treatment removal as has been demonstrated in several studies (Coleman et al., 2000, 2004, 2005a,b, Nakashima et al., 2003). However, it should be pointed out that catalyst immobilization unavoidably leads to a decrease of the surface area available for reactions compared to suspended systems.

From an economic point of view, heterogeneous (as well as homogeneous) photocatalysis is likely to benefit from the use of renewable energy sources to power the process. In this direction, solar photocatalysis has gained considerable attention and several studies report the use of natural (Doll and Frimmel, 2003; Augugliaro et al., 2005; Munoz et al., 2006; Coleman et al., 2007) or simulated (Calza et al., 2004, 2006; Doll and Frimmel, 2004, 2005b,c; Reyes et al., 2006; Abellan et al., 2007; Sakkas et al., 2007; Mendez-Arriaga et al., 2008) sunlight irradiation for pharmaceuticals treatment. A solar photocatalytic system comprising 100 m^2 of compound parabolic collectors has recently been developed to treat effluents at flowrates up to 250 L/h (Malato et al., 2007). This industrial-scale unit, whose application has been demonstrated for the treatment of α-methyl-phenylglycine solutions, is designed to treat various types of effluents through a combination of solar photo-Fenton pre-treatment and immobilized biomass post-treatment. Furthermore, its environmental impact was evaluated by means of life cycle analysis and compared to that of a similar system comprising TiO_2 photocatalysis instead of photo-Fenton pre-treatment (Munoz et al., 2006). It was concluded that homogeneous photocatalysis involved a substantially lower environmental impact than the respective heterogeneous process.

4.5. Electrochemical oxidation

Electrochemical oxidation over anodes made of graphite, Pt, TiO_2, IrO_2, PbO_2, several Ti-based alloys and, more recently, boron-doped diamond (BDD) electrodes in the presence of a suitable electrolyte (typically NaCl) has been employed for the decontamination of various organic-containing effluents, including very recently pharmaceuticals. Two mechanisms are responsible for organic matter electrochemical degradation, namely: (a) direct anodic oxidation where the pollutants are adsorbed on the anode surface and destroyed by the anodic electron transfer reaction and (b) indirect oxidation in the liquid bulk which is mediated by the oxidants that are formed electrochemically; such oxidants include chlorine, hypochlorite, hydroxyl radicals, ozone and hydrogen peroxide.

Critical operating parameters dictating performance are the working electrode, the type of supporting electrolyte and the applied current. Other factors include the effluent pH and the starting organic concentration. In recent years, BDD anodes have received growing attention for pollutants oxidation since they exhibit significant chemical and electrochemical stability, good conductivity as well as they achieve increased rates of mineralization with very high current efficiencies (Comninellis et al., 2008). This has been demonstrated in the work of Sires et al. (2007a,b) who reported that although clofibric acid electrooxidation over Pt was three times faster than over BDD, the latter was far more effective for complete mineralization to carbon dioxide and water. Moreover, the superiority of BDD over Pt and glassy carbon anodes to oxidize 17β-estradiol has been reported (Murugananthan et al., 2007). NaCl is commonly employed as the supporting electrolyte whose role is twofold: (a) to increase effluent conductivity and (b) to provide chlorine and secondary oxidants for the indirect, bulk oxidation of contaminants; in this respect, NaCl is more effective than other electrolytes such as Na_2SO_4 or $NaNO_3$ (Murugananthan et al., 2007). Nonetheless, the use of NaCl raises concern as toxic organochlorinated compounds may be formed as reaction by-products (Giannis et al., 2007). In light of this, Pauwels et al. (2006) who studied the electrochemical degradation of 17α-ethinylestradiol in spiked drinking water and biologically pre-treated hospital effluents over a TiO_2 anode, reported the possibility of forming chlorinated estrogens in the presence of NaCl. Such by-products may include 4-chloroethinylestradiol and 2,4-dichloroethinylestradiol with the former being as estrogenic as the parent compound and the latter only partially estrogenic (Moriyama et al., 2004).

Interestingly, the efficiency of electrooxidation may be enhanced by the synergistic action of dissolved iron which catalyzes the degradation of electrogenerated H_2O_2 to hydroxyl radicals, thus mimicking a Fenton reaction. This has been demonstrated by Sires et al. (2007a,b) who reported increased efficiencies for the electro-Fenton oxidation of clofibric acid compared to electrolysis alone. Alternative to external addition of Fe^{2+} in the reaction mixture is the use of sacrificial iron electrodes that progressively leach, thus serving as both the Fenton catalyst and coagulant.

4.6. Ultrasound irradiation

Ultrasound irradiation or sonolysis is a relatively new process in water treatment and, therefore, has unsurprisingly received less attention than other AOPs. This is also reflected to the small number of publications concerning pharmaceuticals treatment. Sonochemical reactions are induced upon high-intensity acoustic irradiation of liquids at frequencies that produce cavitation (typically in the range 20–1000 kHz). Thus, cavitation serves as a means of concentrating the diffused energy of ultrasound into micro-reactors with the simultaneous release of reactive radicals with each reactor serving as a hot spot. There are three potential sites for sonochemical reactions, namely: the cavitation bubble itself, the interfacial region between the bubble and the surrounding liquid and the solution bulk. Pyrolytic reactions inside or near the bubble as well as solution radical chemistry are the two major pathways of sonochemical degradation (Emery et al., 2005). Organics of low solubility and/or high volatility are likely to undergo fast sonochemical degradation as they tend to accumulate inside or around the gas–liquid interface; in this respect, the process may be well suited to tackle pharmaceutical micro-pollutants.

Several factors may affect process efficiency in a complex way; the most important ones are the frequency and intensity of ultrasound, reactor geometry, type and nature of contaminant, bulk temperature and the water matrix. The latter is of outmost importance, i.e. the presence of dissolved gases or solids usually improves performance as they serve as extra nucleation centers. This has been demonstrated in a recent study (Sanchez-Prado et al., 2008) dealing with the degradation of triclosan at 80 kHz in various matrices, i.e. seawater, urban runoff, inlet of municipal WWTP, pure water and saline water. The authors reported that the first-order kinetic constant of triclosan degradation decreased by about two orders of magnitude from seawater to influent domestic wastewater. Moreover, water sonolysis yields H_2O_2 (Hartmann et al., 2008) and the presence of iron ions usually enhances degradation, thus mimicking a (sono)Fenton reaction (Emery et al., 2005).

4.7. Sub-critical wet air oxidation (WAO)

WAO belongs to the family of AOPs and is a thermochemical process where hydroxyl radicals and other active oxygen species are formed at elevated temperatures (i.e. 200–320 °C) and pressures (i.e. 2–20 MPa) (Levec and Pintar, 2007). The process has great potential for the treatment of wastewaters with moderate to high organic content (i.e. 10–100 g/L COD) converting dissolved organic pollutants into highly oxidized intermediates and eventually to carbon dioxide and water. At temperatures and pressures above the critical point of water (374 °C, 22 MPa), the process is referred to as supercritical water oxidation (SCWO) with its main feature being that gas and liquid phases form a homogeneous single phase. In this respect, organics and oxygen become completely miscible, thus eliminating mass transfer limitations which, in conjunction with increased reaction temperatures, lead to very high reaction rates.

In light of this, treatment of micro-pollutants by WAO is not an economically viable option as it would result in excessive specific energy consumption (i.e. energy per unit mass of pollutant destroyed). Nonetheless, WAO may be well suited to treat partially or completely effluents from drug manufacturing (Gotvajn et al., 2007) or hospital wastes but this has yet to be proven.

4.8. Oxidative treatment of EDCs

The oxidation of endocrine disrupting compounds has received considerable attention as they constitute an emerging group of contaminants that are known to cause adverse effects on humans and the wildlife via interactions with the endocrine system. Pesticides, polycyclic aromatic hydrocarbons, phthalates, polychlorinated biphenyls, alkylphenols and synthetic steroids are all known to behave as endocrine disruptors (Benachour et al., 2007; Heudorf et al., 2007). Particular emphasis has been given on the estrogenic activity related to the presence of natural estrogens (17β-estradiol, estriol, estrone), synthetic estrogens (17α-ethinylestradiol), as well as their oxidation metabolites in waters. In a classical approach, sensitive analytical techniques have been employed to identify major reaction intermediates. Huber et al. (2004) and Irmak et al. (2005) who studied the ozonation of 17α-ethinylestradiol and 17β-estradiol respectively identified several by-products and proposed reaction pathways based on them. The TiO_2-induced photocatalytic degradation of 17β-estradiol was investigated by Ohko et al. (2002) who found the formation of testosterone-like intermediates and suggested degradation mechanisms. 17β-Estradiol degradation was also investigated by means of BDD electrolysis (Murugananthan et al., 2007) yielding quinone-type intermediates and dicarboxylic acids.

A more attractive approach involves the use of rapid *in vitro* and *in vivo* assays to monitor estrogenicity. Yeast estrogen screen (YES) is the more commonly employed *in vitro* assay based on the interactions between the human estrogen receptor (expressed by the recombinant yeast strain) and estrogenic compounds (Ohko et al., 2002; Alum et al., 2004; Coleman et al., 2004; Huber et al., 2004). Rosenfeldt et al. (2007) reported that the rates of 17α-ethinylestradiol and 17β-estradiol degradation by UV/H_2O_2 were equal to the respective rates of estrogenic activity reduction as evaluated by the YES assay. This implies that the need to identify specific reaction intermediates through laborious and sophisticated protocols is eliminated as the emphasis is on the determination of residual estrogenic activity rather than on certain compounds. In this view, Rosenfeldt et al. (2007) have also proposed a kinetic model for estrogenicity removal.

4.9. Coupling AOPs with other treatment processes

As clearly seen in Table 2, the majority of published work deals with the removal of trace quantities of specific compounds from surface waters or municipal WWTPs; nonetheless, some researchers have also concentrated their efforts on the treatment of effluents from pharmaceuticals manufacturing or hospital operation. Unlike surface and ground waters and WWTP effluents, this type of waste is highly contaminated (in the order of several g/L COD) and, therefore, should be treated as industrial effluent. In light of this, process integration may be required to maximize treatment performance. Kulik et al. (2008) reported that effluents from ointment manufacturing that had partly been pre-treated by an adsorption/flocculation/filtration process could subsequently be subject to Fenton oxidation/lime coagulation, thus yielding a final effluent suitable for disposal. A Fenton oxidation/alum coagulation process was also proposed by Xing et al. (2006) to treat pharmaceutical effluents that had already pre-treated in upflow anaerobic sludge bed and sequencing batch reactors; the resulting stream complied with local discharge standards for industrial effluents.

The concept of coupling AOPs as a pre-treatment stage to enhance biodegradability and reduce toxicity with biological post-treatment has gained a lot of attention over the past several years (Comninellis et al., 2008). This approach is relatively straightforward and based on the facts that (i) biological treatment is perhaps less costly and more environmentally friendly than any other destructive treatment, and (ii) complete mineralization by AOPs induces excessive treatment costs since the highly oxidized end-products that are formed during chemical oxidation tend to be refractory to total oxidation by chemical means. These end-products which are typically represented by short carboxylic acids can, however, be degraded easily biologically. The beneficial effect of pre-oxidation on biological properties was demonstrated by Gotvajn et al. (2007) and Kajitvichyanukul and Suntronvipart (2006) who studied respectively the treatment of effluent from blood pressure regulators manufacturing by WAO and hospital waste by photo-Fenton.

Treatment of effluents from antibiotic production has received considerable attention and several studies dealing with actual (Arslan-Alaton et al., 2004; Arslan-Alaton and Dogruel, 2004; Cokgor et al., 2004) or synthetic (Balcioglu and Otker, 2003; Tunay et al., 2004; Arslan-Alaton and Caglayan, 2005, 2006) formulation effluents exist in the literature. In these studies, the concept of coupling ozonation pre-treatment with biological post-treatment was evaluated measuring changes in aerobic biodegradability (as assessed by the BOD_5/COD) ratio and ecotoxicity before and after chemical oxidation; moreover, respirometric measurements and inhibition tests of unoxidized and oxidized effluents to activated sludge were also conducted. Arslan-Alaton and Caglayan (2006) recently demonstrated that 60 min perozonation pre-treatment of a synthetic formulation effluent at neutral conditions, although capable of rising the BOD_5/COD ratio and eliminating acute ecotoxicity to *D. magna*, inhibited the performance of activated sludge that had already been acclimated to the oxidized effluent. Their findings highlight (i) the need for process optimization should ozonation (or other AOPs indeed) be employed as a pre-conditioning stage and (ii) the fact that, although biodegradability and toxicity assays provide some useful information with respect to the

effect of chemical pre-treatment, trials integrating chemical and biological degradation experiments are often needed to obtain an additional, more realistic assessment of the combined process.

5. Conclusions

The occurrence and fate of pharmaceuticals in the environment, and in aquatic media in particular, have received considerable attention by the scientific community during the last two decades. Pharmaceuticals, which are designed to be biologically active substances, are usually lipophilic and resistant to biodegradation, thus having the potential for accumulation and persistence in the environment. Although they appear at relatively low concentrations ranging between ng/L and μg/L levels, they may impose serious effects on the environment. Searching for suitable technologies to destroy this type of xenobiotics, AOPs have recently been assessed for their treatment efficiency at several different matrices:

(i) The removal to below the limit of detection of pharmaceuticals from ground and surface waters destined for drinking water production is obviously imperative. Since conventional drinking water treatments (i.e. coagulation/flocculation, sedimentation, filtration) have failed to remove these compounds, it is not surprising that ozone oxidation has become part of the treatment battery in several water production plants (Ternes et al., 2002; Hua et al., 2006; Jasim et al., 2006).

(ii) The presence of pharmaceuticals in the discharge streams of municipal WWTPs has also been reported as these compounds usually go through secondary treatment unaffected and may partially be adsorbed to the activated sludge. So far, the need for the removal of pharmaceuticals has not been recognized as the effluent is most commonly disposed of in natural receivers and, occasionally, used for irrigation. However, the growing problem of water shortage in arid and semi-arid areas unavoidably leads to more efficient management schemes for the water resources, part of which is the production of "clean" water for WWTPs. In this view, the so-called "effluent organic matter (EOM)" which consists of humic-type substances has to be treated and this will, most likely, be achieved by a combination of physicochemical and oxidative processes. Moreover, the use of AOPs for EOM treatment will also bring about secondary benefits, i.e. water disinfection.

(iii) Pharmaceuticals are also found in hospital wastes as well as in drug manufacturing effluents. Unlike in WWTPs and drinking water plants, concentrations are relatively high in the order of several hundred mg/L or even g/L. In this case, the water matrix has to be considered as an industrial effluent and the most suitable treatment technique be identified.

Treatment of pharmaceuticals in aqueous media by AOPs is likely to be an expensive venture. This is so because (i) extremely high conversions are needed (ideally below detection limit) as these compounds retain their adverse properties even at minute concentrations and (ii) initial concentrations are very low, thus making the treatment cost per unit mass excessive. A step in this direction is the use of renewable energy sources to power the processes as exemplified in the case of solar photocatalysis. Although it is still common perception that the sustainability of AOPs, or indeed any other technology, to treat waters and wastewaters is eventually dictated by process economics, the water industry and policy makers may have to reconsider given the growing problem of high quality water shortage, which is expected to worsen due to global climate changes.

From a practical point of view, treatment-at-source may be a realistic option in (i) drinking water plants where ground and surface waters can be chemically oxidized to achieve destruction of pharmaceuticals micropollution as well as disinfection and (ii) pharmaceuticals manufacturing plants where formulation effluents are generated. Given the relatively high concentration of organics in such effluents, a process train comprising chemical and biological oxidation may be technically and economically feasible. Conversely, pharmaceuticals found in the outlet of municipal WWTPs may not require immediate attention regarding pharmaceuticals removal since these streams are typically disposed of in watercourses and the sea. Nevertheless, treatment-at-source may still be a plausible option replacing conventional chlorination by an AOP-induced disinfection/oxidation technique.

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