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Analytical tools employed to determine pharmaceutical compounds in wastewaters after application of advanced oxidation processes

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Abstract Today, the presence of contaminants in the environment is a topic of interest for society in general and for the scientific community in particular. A very large amount of different chemical substances reaches the environment after passing through wastewater treatment plants without being eliminated. This is due to the inefficiency of conventional removal processes and the lack of government regulations. The list of compounds entering treatment plants is gradually becoming longer and more varied because most of these compounds come from pharmaceuticals, hormones or personal care products, which are increasingly used by modern society. As a result of this increase in compound variety, to address these emerging pollutants, the development of new and more efficient removal technologies is needed. Different advanced oxidation processes (AOPs), especially photochemical AOPs, have been proposed as supplements to traditional treatments for the elimination of pollutants, showing significant advantages over the use of conventional methods alone. This work aims to review the analytical methodologies employed for the analysis of pharmaceutical compounds from wastewater in studies in which advanced oxidation processes are applied. Due to the low concentrations of these substances in wastewater, mass spectrometry detectors are usually chosen to meet the low detection limits and identification power required. Specifically, time-of-flight detectors are required to analyse the by-products.

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Keywords Advanced oxidation processes · Pharmaceutical compounds · Wastewater · Sample preparation · Determination methods

Abbreviations

AC	Activated carbon
AOPs	Advanced oxidation processes
API	Atmospheric pressure ionisation
CNF	Carbon nanofiber
E1	Estrone
E2	17-beta-estradiol
EAOPs	Electrochemical AOPs
EDCs	Endocrine disruptor compounds
EE2	17-alpha-ethinylestradiol
ESI	Electrospray ionisation
GC	Gas chromatography
HS	Head space
LC	Liquid chromatography
LLE	Liquid-liquid extraction
LOD	Limit of detection
LOQ	Limit of quantification
MS	Mass spectrometry
MTBSTFA	*N*-(*t*-butyldimetylsilyl)-*N*-methyltrifluoroacetamid
NSAIDs	Non-steroidal anti-inflammatory drugs
DAD	Diode array detector
POPs	Persistent organic pollutants
PPCPs	Pharmaceutical and personal care products
SBSE	Stir-bar sorptive extraction
SPE	Solid-phase extraction
TAP	Thermally activated persulfate
TOF	Time-of-flight
UHPLC	Ultra-high performance LC
US	Ultrasonic

UV	Ultraviolet
UV-vis	UV-visible
WWTPs	Wastewater treatment plants

Introduction

The quality of the water supply is essential to maintaining the lifestyle of modern society. The increase in population, accumulation of people in large and industrialised cities and growing use of chemical substances in our ordinary life demand that we pay more attention to water purification and reuse. It is estimated that almost one billion people around the world do not have access to safe water resources and that 200 million people die every year because of infections caused by water (Amin et al. 2014). In addition to well-known persistent organic pollutants (POPs), over the last few decades, the scientific community has focused on so-called emerging contaminants. This group of compounds includes different families of analytes from sources such as pharmaceuticals, personal care products, hormones, detergents and flame retardants. These have not been studied in depth. Therefore, there is not enough information about their long-term consequences in the environment. Current wastewater treatment plants (WWTPs) are designed to control a wide range of substances, such as particulates, carbonaceous substances, nutrients and pathogens, but are not specifically designed to eliminate other pollutants. As a consequence, the emerging contaminants pass through the treatment processes without being eliminated and may end up in the aquatic environment via marine outfalls or sludge spreading on lands, threatening both wildlife and the drinking water industry (Bolong et al. 2009). The occurrence of emerging contaminants in the aquatic environment has frequently been associated with short-term and long-term toxicity, endocrine-disrupting effects, development of antibiotic resistance by micro-organisms (Fent et al. 2006), bioaccumulation and carcinogenicity (Trapido et al. 2014).

Specifically, the occurrence and fate of pharmaceutically active compounds in aquatic media have been recognised over the last decade as a serious environmental problem in most developed countries (Valavanidis et al. 2014). To date, there are no discharge guidelines, and only a few countries or regions have adopted regulations for a small number of compounds (Luo et al. 2014). The Directive 2013/39/EU promotes preventive action and the development of innovative treatment technologies and a watch list of substances has been established by the European Commission to be monitored according to the available information of matrices that should be investigated as well as the respective methods of analysis (Decision 2015/495, 20 March 2015). The watch list includes pharmaceutical compounds, such as the non-steroidal anti-inflammatory drug (NSAID) diclofenac, the synthetic hormone 17-alpha-ethinylestradiol (EE2), the natural hormones estrone (E1) and 17-beta-estradiol (E2) as well as and the macrolid antibiotics erythromycin, clarithromycin and azithromycin (Barbosa et al. 2016).

To improve the quality of wastewater before being discharged or reused, different purification methods have been applied. WWTPs generally employ a primary treatment (removal of suspended solids), a secondary treatment (removal of dissolved and suspended biological matter, typically performed by indigenous, water-borne micro-organisms in a managed habitat) (Ajobo and Abioye 2014) and an optional tertiary treatment, which are commonly used to produce higher quality discharged water for certain purposes, such as water reuse; however, these treatments are always associated with high cost (Luo et al. 2014). Secondary (activated sludge) or tertiary treatment processes (activated carbon, nanofiltration and reverse osmosis membrane) are often not effective at treating complex polluted waters containing pharmaceuticals, personal care products, surfactants or industrial additives (Amin et al. 2014) or at removing some recalcitrant compounds, such as the carcinogenic azo dyestuffs generated by the textile, paper, food, cosmetic and pharmaceutical industries (Thennarasu and Sivasamy 2015).

Because of these limitations, advanced treatment technologies have been proposed, with the most promising being membrane filtration and advanced oxidation processes, including several modifications with UV applications (H_2O_2/UV, ozone/UV, ozone/H_2O_2/UV, H_2O_2/Fe^{2+}/UV and TiO_2/UV). The membrane filtration process is very effective at solid-liquid separation and the removal of organic and inorganic materials. Its most important application is desalination by reverse osmosis, but microfiltration and ultrafiltration could be useful for the disinfection of resistant micro-organisms.

Advanced oxidation processes (AOPs) were defined in 1987 as water treatment technologies that are performed at room temperature and normal pressure and are based on the in situ generation of a powerful oxidising agent at a sufficient concentration to effectively decontaminate water (Glaze 1987). The ·OH radical is one of the strongest oxidising species, and it is able to accelerate the rates of contaminant oxidation. Usually, the combination of ozone (O_3), hydrogen peroxide (H_2O_2), titanium dioxide (TiO_2), UV radiation, ultrasound and/or high electron beam irradiation accelerates the generation of ·OH radicals. The main advantages of the implementation of AOPs over solo conventional treatment processes are as follows: (a) they have a higher effectiveness at removing resistant organic compounds, (b) they almost completely mineralise organic contaminants into carbon dioxide, (c) they only have a minor susceptibility to the presence of toxic chemicals, (d) they produce a minor amount of harmful by-products and (e) they have a better microbial disinfection (Zhou and Smith 2002).

Pharmaceuticals are commonly present at trace concentrations ranging from a few nanogrammes per litre to several

micrograms per litre, which makes their analysis difficult using conventional procedures and creates challenges for purification processes (Luo et al. 2014). The complexity of the matrix often implies the need to apply a previous treatment of the sample to purify and pre-concentrate it before analysis. To clean and pre-concentrate the sample, the most commonly used preparative technique is solid-phase extraction, while several mass spectrometry detectors with different ionisation sources are usually preferred for detection, taking into account the low concentration levels of the analytes. However, reviewing the literature of the analytical methodologies employed for the evaluation of AOPs is often difficult because authors typically pay more attention to the removal and clean-up technique, while they only briefly describe the analytical procedure.

In the last few years, different general reviews regarding AOPs applied to remove emerging pollutants have been published (Wols and Hofman-Caris 2012; Trapido et al. 2014; Oturan and Aaron 2014; Buthiyappan et al. 2015; Ribeiro et al. 2015; Sathishkumar et al. 2016). There have also been reviews devoted to describing AOP techniques applied to specific families of emerging compounds, such as gasoline additives (Levchuk et al. 2014), cytostatics (Zhang et al. 2013), alkylphenols (Priac et al. 2014), organic dyes (Martínez-Huitle and Brillas 2009; Brillas and Martínez-Huitle 2015) or pharmaceutical compounds (Feng et al. 2013; Rivera-Utrilla et al. 2013; Kanakaraju et al. 2014; Mohapatra et al. 2014).

Nevertheless, there are few publications that have focused on elimination procedures and not on the analytical methods used to evaluate them. For this reason, we review the recent analytical procedures, including determination and sample preparation, published between 2010 and 2015 that have been employed to test advanced oxidation processes for the removal of pharmaceutical compounds from wastewater samples.

Advanced oxidation processes

There are different categories and classifications of AOPs depending on the author. For example, we can distinguish between several processes based on the in situ formation of ·OH radicals by the means of chemical, photochemical, sonochemical or electrochemical reactions (Babuponnusami and Muthukumar 2014). In addition to the Fenton method, a chemical AOP in which a mixture of a soluble iron (II) salt and H_2O_2, known as Fenton's reagent, which is the oldest and most-used AOP, other photochemical, sonochemical and electrochemical processes are increasingly being developed because of their better performance (Oturan and Aaron 2014). Meanwhile, Fernández-Castro et al. (2015) grouped AOPs into the following categories: (i) Fenton processes that include conventional Fenton, Fenton-like and photo-Fenton processes; (ii) photolytic and photocatalytic systems; (iii) electrochemical technologies that take electro-oxidation, photo-electro-oxidation and photo-electrocatalytic processes, and electrical discharges into consideration; (iv) technologies based on ultrasound, such as sonolysis and sonocatalysis, and hydrodynamic cavitation; and (v) γ-radiolysis and heavy ions.

The most widely discussed AOPs for wastewater treatment are ultraviolet (UV), H_2O_2/UV, ozone/UV, ozone/H_2O_2, ozone/H_2O_2/UV, photocatalytic oxidation, Fenton and photo-Fenton reactions. It seems that the combination of the Fenton reaction with UV radiation results in better degradation of organic contaminants compared with the typical Fenton reaction (Buthiyappan et al. 2015). Adopting the classification of Babuponnusami and Muthukumar (2014), Fig. 1 shows the most representative AOPs, which will be described in the following sections.

Chemical AOPs

The Fenton method has been applied to the oxidation and degradation of organic pollutants as early as the mid-1960s. This oxidation in the presence of ferrous or ferric ions with hydrogen peroxide is a very simple and flexible method that produces hydroxyl radicals without any special reactants or apparatus. Iron is a non-toxic, relatively inexpensive and very abundant element, while hydrogen peroxide is easy to handle and environmentally safe (Mohapatra et al. 2014). Moreover, this procedure has no need for energy input, but has some disadvantages. Its efficiency depends on various factors (temperature, pH, H_2O_2 and catalyst concentrations), and the accumulation of iron sludge must be removed at the end of the treatment (Oturan and Aaron 2014).

Other types of chemical AOPs are ozonation and peroxonation. Ozonation is a widely employed and investigated technique because it is known to be highly effective. It is commonly used as a disinfecting agent in WWTPs. However, the combination of ozonation with hydrogen peroxide, known as peroxonation (O_3/H_2O_2), is especially convenient because it improves the degradation of many organic pollutants. Unlike H_2O_2, which reacts very slowly with the ozone molecule in aqueous solution, its conjugate base (HO_2^-) can rapidly react with molecular ozone to generate hydroxyl radicals (Klavarioti et al. 2009).

In general, this combined oxidation process usually has a higher reaction efficiency than an individual oxidation process because of the enhanced generation of hydroxyl radicals (Mohapatra et al. 2014).

Photochemical AOPs

Photochemical approaches appear to overcome some of the limitations of existing chemical AOPs, as they are generally

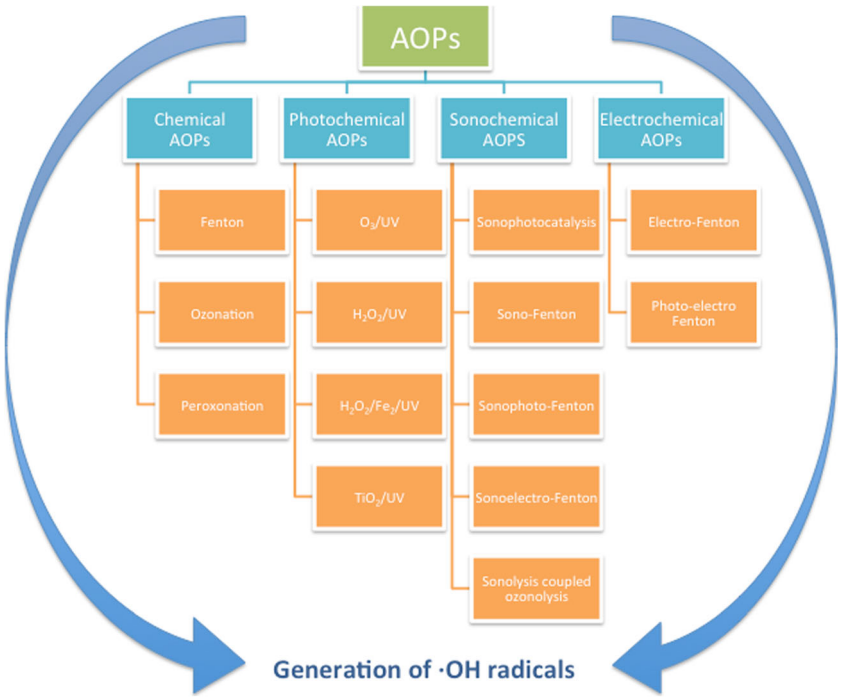

Fig. 1 Classification of the most commonly employed AOPs

simpler, cleaner, relatively cheaper (dependent upon the use of radiation) and are also more efficient because their combination with light irradiation enhances the generation of hydroxyl radicals (Huber et al. 2003). Moreover, photochemical approaches are an efficient and sustainable alternative for the degradation of recalcitrant contaminants compared with the use of UV alone (Buthiyappan et al., 2015). The most used photochemical AOPs are O_3 photolysis (O_3/UV), H_2O_2 photolysis (H_2O_2/UV), the photo-Fenton process (H_2O_2/Fe^{2+}/UV) and heterogeneous photocatalysis (TiO_2/UV). H_2O_2, unlike ozone, has low molar absorption in the wavelength range of 200 to 300 nm. The Fenton process can also be improved by irradiation at wavelengths greater than 300 nm, accelerating the degradation of organic pollutants. In addition, it has been recently demonstrated that the UV-vis/ferrioxalate/H_2O_2 combination is more efficient than the photo-Fenton reaction for the degradation of organic pollutants because the irradiation of ferrioxalate in acidic solution generates carbon dioxide and ferrous ions (Fe^{2+}), either free or combined with oxalate, which in combination with H_2O_2 provides a continuous source of Fenton's reagent (Oturan and Aaron 2014). Heterogeneous photocatalysis (most often, TiO_2/UV) is a promising technology. However, there are very few real applications for this technology, despite its effectiveness in the partial or full mineralisation of recalcitrant pollutants. Heterogeneous photocatalysis consists of the catalysis of photochemical reactions on the surface of a catalyst, usually a semiconductor and involves simultaneous oxidation and reduction reactions. These reactions occur through oxidation–reduction processes, generating HO· radicals by water dissociation (da Silva et al. 2015). Titanium dioxide (TiO_2) is the most frequently used photo-catalyst because it is inexpensive, non-toxic, and chemically resistant (Badawy et al. 2014).

Sonochemical AOPs

Sonolysis is considered to be a safe, clean and versatile technique (Nejumal et al. 2014). There are several combinations of AOPs that use the sonolysis technique, such as sonophotocatalysis, the sono-Fenton technique, the sonophoto-Fenton technique, the sonoelectro-Fenton technique or sonolysis coupled with ozonolysis (Sathishkumar et al. 2016). These techniques stand out from other AOPs that require intensive chemical and energy inputs for acceptable removal efficiencies. Moreover, ultrasound waves have the ability to be perfectly transmitted through opaque systems, unlike those of ultraviolet light (Ince et al. 2001). One drawback of ultrasonic systems is that they are extremely sensitive and vulnerable to operational parameters, which cannot be controlled without good knowledge and understanding of the physical and chemical phenomena involved (Ince et al. 2001).

Recently, the combination of ultrasound with the Fenton reaction has been developed, resulting in a very promising approach for decontamination purposes. However, for its application at the industrial level in real-time wastewater treatment plants, it is still necessary to demonstrate its economic and commercial feasibility because most experimental

workups until now have been performed at the laboratory scale using artificial systems (Oturan and Aaron 2014).

Electrochemical AOPs

Electrochemical technologies for the elimination of organic contaminants from wastewater show advantages, such as high energy efficiency, amenability to automation, ease of use (simple equipment), safety (mild conditions) and versatility. Among these, electrochemical advanced oxidation processes (EAOPs) have received great attention, and combined methods with fewer harmful effects (often referred to as process-integrated environmental protection) have been developed (Brillas and Martínez-Huitle 2015). This type of AOP generates ·OH radicals by applying a potential or current density to an electrochemical cell containing one or more pairs of electrodes instead of using chemical reagents (da Silva et al. 2015). Pollutants are adsorbed on the anode surface and are then destroyed through anodic electron exchange (direct oxidation) or are degraded in the bulk liquid with the mediation of the electroactive species, which act as intermediaries for the transfer of electrons between the electrode and organic compounds (indirect oxidation) (Homem and Santos 2011). The electro-Fenton process, which requires a lower Fe^{2+} concentration than the conventional Fenton process, is among the most eco-friendly electrochemical AOPs. Basically, it is an electrically assisted Fenton process. Moreover, the efficiency of the electro-Fenton process can be increased by applying UV radiation, and this particular process is called the photo-electro-Fenton process (Ribeiro et al. 2015).

Analytical methodologies

Over the last 6 years, there have been an increasing number of publications related to the removal of emerging pollutants, particularly pharmaceuticals, from wastewater samples using AOPs. Figure 2 shows the ratio of studies containing the keywords "pharmaceuticals," "advanced oxidation process (AOPs)" and "wastewater or sewage" in the title or abstract, as determined from the Scopus database. The reviews that have been published have generally focused on describing the varieties of techniques used to degrade these groups of compounds (Ikehata et al. 2006; Esplugas et al. 2007; Ikehata et al. 2008), and no attention has been paid to explaining the correct use of the analytical methodologies.

For this reason, in the following sections, we will describe the analytical procedures that have been employed by authors to probe the validity of their advanced oxidation processes applied to degrade pharmaceutical compounds in wastewater samples. Table 1 summarises the publications in the selected time period (2010–2015), which are classified by the type of AOP, target pharmaceutical compounds and different steps of

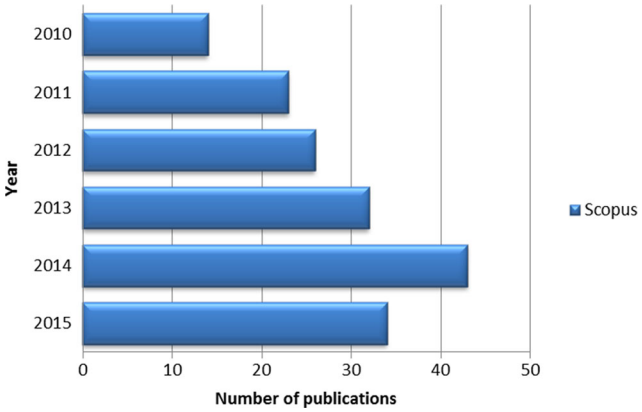

Fig. 2 Number of publications per year from 2010 to 2015 from the Scopus database

the analytical methodology. These methodologies include both sample preparation and determination procedures. The detection and quantification systems are used with a greater or lesser degree of sensitivity depending on the amount and concentration of contaminants as well as the type of sample that requires analysis. However, in many cases, sample preparation is necessary after applying AOPs and before the determination procedure, either because of the low concentration or to stop the oxidative activity.

Regarding the origin of the employed samples in these works, most do not use real water from WWTPs to validate their procedures; instead, they use artificially prepared samples. Generally, we found lab-scale experiments (Trovó et al. 2011; Razavi et al. 2011; Palo et al. 2012). Pilot-scale (Gerrity et al. 2010; Álvarez et al. 2011; Köhler et al. 2012) and full-scale experiments (Reungoat et al. 2010; Abdelmelek et al. 2011) are less frequently employed. For example, Badawy et al. (2014) employed a simulated hospital wastewater sample prepared by mixing five pharmaceutical compounds, while Espejo et al. took wastewater from the first sedimentation unit (primary effluent) of a WWTP that were then were spiked with nine selected pharmaceuticals (Espejo et al. 2014a, b). Hey et al. (2014) and Romero et al. (2014) used real water to validate their optimised methodologies, collecting samples from four municipal WWTPs in Sweden and the secondary clarifier of a wastewater treatment plant (WWTP) from Spain, respectively. Miralles-Cuevas et al. (2014a) dissolved the target compounds in effluent wastewater from the secondary biological treatment supplied at the municipal WWTP for their pilot-scale experiments. James et al. (2014) also carried out micropollutant removal experiments using a pilot plant that treated 600 m^3 day^{-1} of final effluent from a WWTP with a conventional activated sludge process. More complete studies provide results obtained by both pilot and full-scale experiments. For example, Gerrity et al. (2012) used eight wastewaters to evaluate the ability of pilot- and full-scale systems to oxidise 18 organic contaminants, mainly pharmaceutical compounds.

Table 1 The overview of AOPs and the analytical methodologies used for pharmaceutical compounds in aqueous samples from 2010 to 2015

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
Electrochemical: electro-Fenton	Caffeine	LLE, derivatisation	LC-DAD, GC-MS (by-products)		Ganzenko et al. (2015)
Chemical: ozonation Photochemical: photolysis, photolytic ozonation, photocatalysis, photocatalytic ozonation	Ibuprofen, naproxen, tramadol, azithromycin, clarithromycin, erythromycin, sulfamethoxazole, trimethoprim, fluticasone propionate, montelukast, warfarin, clopidogrel, metoprolol, propranolol, hydrochlorothiazide, atorvastatin, bezafibrate, simvastatin, carbamazepine, citalopram, fluoxetine, norfluoxetine, venlafaxine, diphenhydramine, E2, EE2, E1, clofibric acid	SPE	LC-DAD, UHPLC-MS/MS		Moreira et al. (2015)
Chemical: thermally activated persulfate (TAP)	Naproxen	SPE: recovery 98 %	LC-DAD-MS-ESI Ion trap LC-DAD-MS-ESI Ion trap or GC-MS Ion trap (by-products)		Ghauch et al. (2015)
Sono-electrochemical	Ibuprofen		Spectrophotometry, LC-MS/MS (by-products)		Tran et al. (2015)
Photochemical: gamma-irradiation/ozonation	Paracetamol	SPE, derivatisation	GC-MS Ion trap		Torun et al. (2015)
Photochemical: UV/H_2O_2 Chemical: ozonation	Naproxen, trimethoprim, ketoprofen, sulfamethoxazole, diclofenac, clarithromycin, gemfibrozil, carbamazepine, diazepam, lorazepam, atenolol	Catalase enzyme, SPE	LC-MS/MS-ESI	LOD: 5 ng L^{-1}	Justo et al. (2015)
Photochemical: UV/H_2O_2	Diclofenac, fluoxetine, iohexal, iopamidol, iopromide, simazine, sulfamethoxazole, ibuprofen, naproxen, atenolol, carbamazepine, gemfibrozil, primidone, trimethoprim, clofibric acid, ditiazem.	SPE: recovery, 61.2–145.1 %	LC-MS/MS	LOD, 0.1–13.1 ng L^{-1}	Yu et al. (2015)
Photochemical: photolysis, photocatalysis	Carbamazepine		Spectrophotometer, LC-MS/MS-ESI Ion Trap (by-products)	LOD, 0.2 μg L^{-1}	Carabin et (al. 2015)
Photochemical: UV/$TiSiO_4$ (titanium silicone oxide), UV/H_2O_2/O_2, UV/H_2O_2/$TiSiO_4$	Balsalazide		Spectrophotometer		Sikarwar and Jain (2015)
Chemical: ferrous ion-activated persulfate; peroxide-activated persulfate; base-activated persulfate	Levofloxacin		LC-DAD		Epold and Dulova (2015)
Photochemical: UV/H_2O_2	Atenolol, bezafibrate, carbamazepine, clofibric acid, cyclophosphamide, diatiazoic acid, diclofenac, erythromycin, fluoxetine, furosemide, gemfibrozil, ifosfamide, ketoprofen, metoprolol, metronidazole, naproxen, paroxentine, phenazone, prednisolone, propranolol, sotalol,	Filtered	UHPLC-MS/MS	LOD, 0.01–0.025 μg L^{-1}	Wols et al. (2015)

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
	sulfachloropyridine, sulfadiazine, sulfamethoxazole, sulfaquinoxolin, trimethoprim, venlafaxine				
Chemical: ozonation, O_3/H_2O_2 Photochemical: UV/O_3, UV/O_3/H_2O_2	Berberine hydrochloride		Spectrophotometer, CG-MS spectra (degradation process)		Qin et al. (2015)
Sonochemical: Fenton/US, sonolysis Chemical: Fenton	Amantadine	Filtered, SPE	GC-MS ion trap		Zeng et al. (2015)
Sonophotochemical: US/UV/H_2O_2	Salicylic acid, chloramphenicol, paracetamol, diclofenac		Spectrophotometer		Ghafoori et al. (2015)
Sonochemical: Fenton/US, sonolysis, US/Fenton/TiO_2, US/TiO_2, US/CCl_4 Chemical: Fenton	Acetaminophen, naproxen	Filtered	LC-DAD		Im et al. (2015)
Photochemical: UV/H_2O_2	Iopromide, iopamidol	Filtered	LC-MS-ESI-Q-TOF		Singh et al. (2015)
Electrochemical: anodic oxidation with a boron-doped diamond (BDD) anode	Sulfadiazone, hydrochlorothiazide, trimethoprim, ranitidine, ibuprofen, norfloxacin, lincomycin, sertraline, gemfibrozil, acetaminophen, roxithromycin, tramadol, metoprolol, citalopram, diatriazole, diclofenac, carbamazepine, phenytoin, caffeine, enrofloxacin, venlafaxine, iopromide	SPE	UHPLC-QTrap-MS-ESI	LOQ, 1.5–74.3 ng L^{-1}	Garcia-Segura et al. (2015)
Chemical: cobalt (II) activation of oxone	Caffeine		LC-DAD		Yunleiyu Guo et al. (2015)
Photochemical: heterogeneous photocatalysis (Ag/TiO_2)	Chloramphenicol, paracetamol, salycylic acid, sulfamethoxazole, diclofenac		LC		Badawy et al. (2014)
Photochemical: UV/H_2O_2, UV/H_2O_2/TiO_2	Metoprolol		LC-DAD, LC-ESI-MS, and LC-MS-TOF (by-products)		Romero et al. (2014)
Sonochemical: sonolysis	Atenolol		LC-DAD, LC-ESI-Q-TOF (by- products)		Nejumal et al. (2014)
Photochemical: nanofiltration + solar photo-Fenton	Carbamazepine, flumequine, ibuprofen, ofloxacin, sulfamethoxazole	SPE: recovery 80 %	UHPLC-DAD	LOD, 0.06–2 μg L^{-1}	Miralles-Cuevas et al. (2014b)
Photochemical: UV/H_2O_2	E1, E2, EE2		LC-MS/MS		James et al. (2014)
Chemical: ozonation (O_3/H_2O_2)	Clomipramine, sulfamethoxazole repaglinide, EE2, fexofenadine, codeine, naproxen, diltiazem, eprosartan, atracurium, carbamazepine, trimethoprim, rosuvastatin, hydroxyzine, orphenadrine, cilazapril, haloperidol, beclomethasone, diclofenac, citalopram, tramadol, irbesartan, risperidone, sertraline, bisoprolol, metoprolol, venlafaxine,	SPE: recovery 25.2–129 %	LC-MS/MS	LOQ, 0.1–10 ng L^{-1}	Hey et al. (2014)

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
	biperiden, maprotiline, amitriptyline, fluoxetine, bupropion, oxazepam, levonorgestrel, memantine, fluconazole, flutamide, ketoprofen, ibuprofen				
Photochemical: photocatalytic ozonation (Espejo et al. 2014b), O_3/UVA/Fe(III), O_3/UVA/Fe_3O_4 (Espejo et al. 2014a)	Acetaminophen, antipyrine, caffeine, carbamazepine, diclofenac, hidrochlorothiazole, ketorolac, metoprolol, sulfamethozaxole		LC-DAD	LOD, 2 μg L^{-1}	Espejo et al. (2014b) Espejo et al. (2014a)
Photochemical: TiO_2/UVA, TiO_2/UVC, H_2O_2/UVC	Acetaminophen, caffeine, carbamazepine, cimetidine, propranolol, sulfamethoxazole		LC-DAD		Choi et al. (2014)
Photochemical: UV/H_2O_2 (OH·), Rose Bengal (RB)/H_2O_2 (O_2)	Ranitidine, cimetidine		Spectrophotometry		Brame et al. (2014)
Photochemical: photo-initiated, photo-induced (UV/H_2O_2)	Sulfamethazine		LC, LC-MS-ESI-TOF (by-products)	LOD, 0.170 mg L^{-1}	Batista et al. (2014)
Chemical: induced cavitation/H_2O_2	Clofibric acid, ibuprofen, naproxen, ketoprofen, carbamazepine, diclofenac	Filtered; SPE: recovery 81–95 %; derivatisation	GC-MS	LOD, 0.4–3.7 ng L^{-1}	Zupanc et al. (2014)
Electrochemical: electro-Fenton, electro-Fenton/UV	Salicylic acid	LLE, derivatisation	GC-HS-MS		George et al. (2014)
Photochemical: solar photo-Fenton	Carbamazepine, flumequine, ibuprofen, ofloxacin, sulfamethoxazole	SPE: recovery 90 %	LC-DAD	LOD, 0.06–2 μg L^{-1}	Miralles-Cuevas et al. (2014a)
Sonophotochemical: US/UV/H_2O_2	Salicylic acid, chloramphenicol, paracetamol, diclofenac		Spectrophotometer		Mowla et al. (2014)
Chemical: ozonation, O_3/H_2O_2	Carbamazepine, clarithromycin, diclofenac, furosemide, lidocaine, meferamic acid, ranitidine, sotalol, sulfapyridine, sulfamethoxazole, atenolol, metoprolol, tramadol, venlafaxine, bezafibrate, gabapentin, oxazepam, primidone, valsartan, fluconazole, iopromide, levertiracetam	Filtered, SPE	LC-MS/MS	LOQ, 1–7000 ng L^{-1}	Lee et al. (2014)
Photochemical: photolysis, photo-Fenton, UV/H_2O_2, UV/H_2O_2/Fenton	Ibuprofen, sulfamethoxazole, diclofenac		LC-DAD		Trapido et al. (2014)
Chemical: ozonation Electrochemical: electrolysis, electro-peroxone	Ibuprofen	SPE	LC-DAD, UHPLC-ESI-MS/MS, and UHPLC-Q-TOF-MS (ESI) (by-products)		Li et al. (2014)
Chemical: ozonation Photochemical: UV/O_3	Ketoprofen		LC-DAD-MS (ESI)	LOD, $2.5 \cdot 10^{-8}$ mol d-m^{-3}	Illés et al. (2014)
Sonochemical: sonolysis	Diclofenac, carbamazepine, amoxicillin		Spectrophotometer, LC-MS/MS (ESI)	LOQ, 1 ng L^{-1}	Secondes et al. (2014)
Photochemical: UV/H_2O_2	Atenolol, bezafibrate, carbamazepine, clenbuterol , clindamycin, clofibric acid, cortisol, cortisone, cyclophosphamide, diatrizoic acid,		UHPLC-MS/MS	LOD, 0.01–0.025 μg L^{-1}	Wols et al. (2013)

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
	diclofenac, erythromycin, fluoxetine, furosemide, gemfibrozil, ifosfamide, ketoprofen, lincomycin, metformin, metoprolol, metronidazole, naproxen, niacin, paracetamol, paroxetine, penicillin, pentoxifylline, phenazone, pindolol, prednisolone, propranolol, salbutamol, sotalol, sulfachloropyridazine, sulfadiazine, sulfamethoxazole, sulfaquinoxalin, terbutaline, tramadol, trimethoprim, venlafaxine				
Photochemical: UV/H_2O_2	Naproxen, carbamazepine, diclofenac, gemfibrozil, ibuprofen, caffeine, 2,4-D, 2,4-DCP, mecoprop		LC-DAD		Shu et al. (2013)
Chemical: ozonation Sonochemical: O_3/US	Acetaminophen, 4-aminoantipyrine, atorvastatin, bezafibrate, ciprofloxacin, clarithromycin, clindamycin, diclofenac, enalapril, erythromycin, gemfibrozil, ibuprofen, ketoprofen, lincomycin, lorazepam, naproxen, ofloxacin, salicylic acid, sulfamethazine, sulfamethoxazole, venlafaxine, valsartan, irbesartan, furosemide, carbamazepine, gabapentin	SPE	UHPL-ESI-MS/MS	LOQ, 0.2–170 ng L^{-1}	Ibáñez et al., (2013)
Chemical: ozonation Photochemical: black-light /TiO_2, AC/TiO_2	Acetaminophen, norfloxacin, metoprolol, caffeine, antipyrine, sulfamethoxazole, ketorolac, hydroxybiphenyl, diclofenac		LC-DAD, LC-MS-ESI-TOF		Encinas et al. (2013)
Chemical: ozonation, ceramic honeycomb monoliths coated with carbon nanofibers (CNF)	Bezafibrate, erythromycin,		LC-DAD		Derrouiche et al. (2013)
Chemical: ozonation Photochemical: UV, UV/H_2O_2	Carbamazepine, ciprofloxacin, diclofenac, metoprolol, sulfamethoxazole	Filtered	LC-QTrap-MS		Eyser et al. (2013)
Photo-electrochemical: Ti/TiO_2	Carbamazepine		Spectrophotometer, LC-MS/MS ion trap (ESI; by-products)		Daghrir et al. (2013)
Photochemical: UV, UV/TiO_2	Ciprofloxacin		UPLC-MS/MS (ESI)		Vasquez et al. (2013)
Sonochemical	Acetaminophen, atenolol, atrazine, carbamazepine, diclofenac, metoprolol, caffeine, iopromide, erythromycin, fluoxetine, trimethoprim, propranolol, sulfamethoxazole, ibuprofen, naproxen, gemfibrozil, triclosan		Spectrophotometer, LC-QTrap-MS/MS (ESI)		Naddeo et al. (2013)
Chemical: ozonation	Fluoxetine, norfluoxetine, paraxantine, sertraline, citalopram, fluvoxamine, venlafaxine, amitriptyline, nortriptyline, carbamazepine	SPE	LC-MS/MS (ESI), LC-Q-TOF-MS/MS (ESI; by-products)		Lajeunesse et al. (2013)
Chemical: ozonation, O_3/H_2O_2	Acetylsalicylic acid, sulfadiazine, sulfamethoxazole, amoxicillin, atenolol, azithromycin, bendroflumethiazide, bezafibrate,	SPE	LC-MS/MS		Nielsen et al. (2013)

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
	bisoprolol, capecitabine, carbamazepine, cefuroxime, chloramphenicol, ciprofloxacin, citalopram, clarithromycin, clindamycin, clofribic acid, cyclophosphamide, diclofenac, erythromycin, erythromycin, fenofibrat, fenofibrinsaure, furosemide, gemcitabine, ibuprofen, ifosfamide, ketoprofen, megastrol, metoprolol, metronidazol, naproxen, ofloxacin, oxcarbazepine, paracetamol, phenanzon, propranolol, roxithromycin, simvastatin, sotalol, sulfadiazine, sulfametazine, sulfamethizole, sulfamethoxazole, tamoxifen, tramadol, trimethoprim, venlafaxin, E1, E2, EE2, amidotrizoeacid, iohexol, iomeprol, iopamidol, iopromide, ioversol.				
Photochemical: photolysis, UV/H_2O_2, photo-Fenton Chemical: Fenton/H_2O_2	Amitriptyline hydrochloride, methyl salicylate, 2-phenoxyethanol		LC-DAD		Real et al. (2012)
Chemical: Fenton/H_2O_2	Triclosan	SBSE	LC-DAD, GC-MS-TOF (by-products)	LOD, 0.05–0.001 mg L^{-1}	Munoz et al. (2012)
Chemical: O_3/H_2O_2 Photochemical: UV/H_2O_2	Equilenin, fenoterol, tetracycline, triclosan, E2, methicillin, metformin, sulfamethoxazole. Gemfibrozil, clofibric acid, iomeprol		LC-DAD	LOD, 0.007–0.16 μg L^{-1}	Jin et al. (2012)
Photochemical: UV photolysis, UV/H_2O_2	Mestranol, progesterone, estrone, estriol, E2, EE2		UHPLC-DAD-FD	LOD, 50–100 μg L^{-1}	Pereira et al. (2012)
Chemical: ozonation	Phenytoin, atenolol, meprobamate, atrazine, naproxen, carbamazepine, primidone, diclofenac, sulfamethoxazole, gemfibrozil, triclosan, ibuprofen, trimethoprim	SPE: recovery 88–118 %	LC-QTrap-MS	LOD, 10–25 ng L^{-1}	Gerrity et al. (2012)
Photochemical: UV photolysis, UV-H_2O_2	Acetyl-sulfamethoxazole, ciprofloxacin, clarithromycin, erythromycin, sulfamethoxazole, diclofenac, lidocaine, naproxen, carbamazepine, atenolol, cyclophosphamide, ifosfamide, iodixanol, iohexol	SPE	LC-MS/MS		Köhler et al. (2012)
Chemical: ozonation	Carbamazepine		LC-DAD		Palo et al. (2012)
Chemical: ozonation Sonochemical: sonolysis, US/O_3	Diclofenac		Spectrophotometer		Naddeo et al. (2012)
Chemical: O_3/H_2O_2, Fenton Photochemical: photolysis, UV/O_3, UV/O_3/H_2O_2, UV/H_2O_2	Ibuprofen, sulfamethoxazole		LC-DAD		Epold et al. (2012)
Photochemical: UV/H_2O_2	Carbamazepine		LC-QTrap-MS (by-products)		Keen et al. (2012)
Photochemical: UV/O_3/TiO_2	Diclofenac		LC-DAD (by-products)		Aguinaco et al.

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
					(2012)
Chemical: O_3, O_3/H_2O_2	Atenolol, trimethoprim, carbamazepine, atrazine, phenytoin, primidone, meprobamate	SPE: recovery 88–118 %	LC-QTrap-MS/MS	LOD, 10–25 ng L^{-1}	Pisarenko et al. (2012)
Chemical: O_3 Photochemical: UV/O_3/TiO_2	Diclofenac, sulfamethoxazole, caffeine		LC-DAD	LOD, 100 μg L^{-1}	Beltrán et al. (2012)
Photochemical: UV/chlorine, UV/HOCl, UV/ClO_2	Sulfamethoxazole, carbamazepine, diclofenac, benzotriazole, tolyltriazole, iopamidole, EE2	SPE	LC-MS/MS	LOD:1–10 ng L^{-1}	Sichel et al. (2011)
Photochemical: heterogeneous photocatalysis (TiO_2)	Metoprolol, propranolol	Filtered samples	LC-DAD, ESI-MS and LC-MS-TOF (by-products)		Romero et al. (2011)
Photochemical: solar photo-Fenton	Acetaminophen, antipyrine, atrazine, caffeine, carbamazepine, diclofenac, flumequine, ibuprofen, ketorolac, ofloxacin, progesterone, sulfamethoxazole, triclosan	SPE	UHPLC-DAD	LOD, 0.6–5.0 μg L^{-1}	Klamerth et al. (2010, 2011)
Chemical: sulphate radical oxidation	Carbamazepine	2 mL quenched with 100 μL of an aqueous solution of $NaNO_2$ (10 M)	LC-DAD-FD, LC-ESI-MS/MS ion trap (by-products)		Matta et al. (2011)
Chemical: ozonation	Sulfasimethoxine, sulfamethoxazole, erythromycin, lincomycin, ciprofloxacin, levofloxacin, doxycycline, tetracycline, trimethoprim, carbamazepine, primidone, iopromide, ibuprofen, acetaminophen, diclofenac, triclosan, EE2, caffeine	SPE: recovery 36–184 %, derivatisation	GC-MS, LC-MS/MS	LOD, 10–5000 ng L^{-1}	Yang et al. (2011)
Chemical: ozonation Photochemical: UV/TiO_2	Sulfamethoxypyridazine	Centrifugation	LC-DAD, LC-API-MS (by-products)		Chuang et al. (2011)
Photochemical: UV/O_3/H_2O_2	Ciprofloxacin, trimethoprim, cyclophosphamide	Lyophilisation	LC-DAD-MS (ESI)		Lester et al. (2011)
Photochemical: UV/Fenton Sonochemical: US	Penicillin		LC-DAD		Saghafinia et al. (2011)
Photochemical: photolysis, UV/H_2O_2	Sulfamethoxazole, sulfamethazine, sulfadiazine, trimethoprim, diclofenac	Catalase, filtered	LC-DAD		Baeza and Knappe (2011)
Chemical: ozonation, O_3/H_2O_2, AC/O_3 Photochemical: photolysis	Paracetamol, diclofenac, sulfamethoxazole, ketorolac, metoprolol		LC-DAD		Álvarez et al. (2011)
Photochemical: solar photo-Fenton	Diclofenac	Catalase	LC-DAD	LOD, 0.14 mg L^{-1}	Trovó and Nogueira (2011)
Chemical: O_3/H_2O_2	Caffeine, ciprofloxacin, clofibric acid, nicotine, sulfamethoxazole, azythromycin, cotnine, loratidine, salicilic acid	SPE	LC-QTrap-MS/MS		Rodríguez et al. (2011)
Photochemical: UV/H_2O_2 Electrochemical: electron pulse radiolysis	Gemfibrozil, naproxen, carbamazepine, ofloxacin, erythromycin, trimethoprim, venlafaxine, atenolol, metoprolol, caffeine, nalidixic acid, iohexol, sulfamethoxazole, atorvastatin,	Filtered, SPE	UHPLC-MS/MS (ESI)	LOD, 0.01–2.0 μg L^{-1}	Abdelmelek et al. (2011)

Table 1 (continued)

AOPs	Compounds	Sample preparation	Determination	LOD/LOQ	Ref.
	lavastatin, enrofloxacin, sulfamethazine, sulfamethizole, sulfamesazine, cimetidine, famotidine, ranitidine, iopamidol, iomeprol, iopromide				
Electrochemical: electron pulse radiolysis	Fluvastatin, lovastatin, pravastatin, simvastatin		LC-DAD, LC-MS (ESI) (by-products)		Razavi et al. (2011)
Chemical: O_3, O_3/H_2O_2	Acetaminophen, atenolol, caffeine, carbamazepine, diclofenac, iopromide, naproxen, cefaclor, sulfamethoxazole, dilantin, ibuprofen	SPE	LC-API-MS		Sarp et al. (2011)
Photochemical: UV/Fenton	Amoxicillin	Catalase, filtered	LC-TOF-MS (ESI)	LOD, 5 μg L^{-1}	Trovó et al. (2011)
Photochemical: UV/H_2O_2	Meprobamate, carbamazepine, dilantin, atenolol, primidone, trimethoprim		LC-MS	LOD, 10 ng L^{-1}	Rosario-Ortiz et al. (2010)
Chemical: O_3 Photochemical: UV/H_2O_2, UV/O_3	Carbamazepine, clofibric acid, diazepam, diclofenac	SPE	LC-QTrap-MS (ESI)	LOD, 0.001–0.002 ng L^{-1}	José et al. (2010)
Chemical: O_3 Photochemical: UV/H_2O_2, UV/O_3	Acetaminophen, antipyrine, diclofenac, ethenzamide, fenoprofen, indomethazine, isopropylantipyrine, ketoprofen, mefanomic acid, naproxen, atenolol, disopyramide, metoprolol, propranolol, bezafibrate, prenzepine, caffeine, diltrazem, dipyridamole, azithromycin, chloratetracycline, clarithromycin, erythromycin, levofloxacin, lincomycin, nalidixic acid, norfloxacin, sulfadimethoxine, sulfamethoxazole, tetracycline, trimethoprim, carbamazepine, primidone, cyclophosphamide, sulpiride, theophylline	Filtered, SPE	LC-MS/MS (ESI)	LOD, 0.02–6.18 μg L^{-1}	Kim and Tanaka (2010)
Chemical: TiO_2	Fluoroquinolone, norfloxacin, levofloxacin, lomefloxacin	Filtered	LC-ESI-MS/MS (by-products)		An et al. (2010)
Electrochemical: non-thermal plasma (NTP)	Meprobramate, dilantin, primidone, carbamazepine, atenolol, trimethoprim, atrazine	SPE	LC-MS/MS	LOD, 10–25 ng L^{-1}	Gerrity et al. (2010)

Determination

To optimise and check the validity of advanced oxidation technologies, the most frequently used determination systems have been both liquid and gas chromatography (LC and GC) coupled with different detectors (see the relative percentage in Fig. 3), which the scientific community employs to analyse emerging pollutants in aqueous samples, regardless of their origin (Wille et al. 2012). However, traditional optical methods, such as UV-vis spectroscopy, have also been used in a few studies. Regardless, the use of either system is not dependent on the choice of AOP, but rather on the types and amounts of the compounds. The matrix also has a role in the selection of the detection technique.

In general, spectrophotometry is applied to determine one or a few pollutants that have a relatively high concentration (higher than real samples). For example, Tran et al. (2015) used ibuprofen to develop a sono-electrochemical procedure that removes up to 90 % of the compounds from wastewater samples. Brame et al. (2014) optimised different photochemical AOPs to degrade two pharmaceutical compounds (ranitidine and cimetidine). The anti-inflammatory drug balsalazide was photodegraded after applying two processes in a study by Sikarwar and Jain (2015). Moreover, Mowla et al. (2014) and

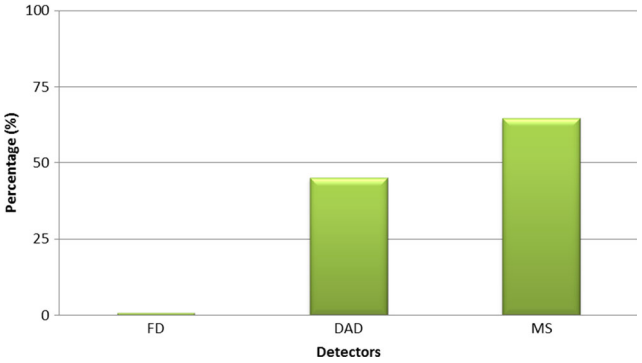

Fig. 3 Relative percentages of the reviewed works concerning the use of different detectors coupled to chromatographic systems

Ghafoori et al. (2015) used sonophotolysis to remove the same groups of drugs. All of the studies used spectrophotometry to follow the degradation of the target compounds, and it was necessary to use spiked samples in the micro- to milligrammes per litre range to calculate the degradation kinetics because of the high limit of detection of this method and the produced spectral interferences by transformation intermediates, which may absorb radiation in the same spectral region as the target compound. Despite this assumption, spectrophotometric methods provide a quick and indicative determination of degradation (Naddeo et al. 2013).

In contrast, chromatographic systems can be useful to simultaneously control a large number of compounds at lower concentration levels (in the range of ng L^{-1} to μg L^{-1}). LC or GC can be used, depending on the type of target compound and the characteristics of the required analysis. GC has been used to evaluate the performance of chemical, photochemical and electrochemical AOPs to degrade different pharmaceuticals and their by-products (Yang et al. 2011; Munoz et al. 2012; George et al. 2014; Zupanc et al. 2014; Ganzenko et al. 2015; Torun et al. 2015; Ghauch et al. 2015). However, in recent years, LC has been the most commonly applied methodology for removing pharmaceuticals because degradation is carried out in aqueous media. Thus, an important advantage of this technique is the possibility of directly injecting samples without any preparation of the sample.

Another important point under this heading is the use of different detectors coupled to chromatographic systems (see the relative percentage in Fig. 3). Optical detectors, such as diode array detectors (DADs), and different mass analysers have been used to verify the efficiencies of developed AOPs. Generally, the differences between the diverse types of detectors are in the limit of detection (LOD) and also in the ability to follow the parent compounds and by-products. In this way, Encinas et al. (2013) treated a water solution of pharmaceuticals by chemical (ozonation) and photochemical (activated carbon (AC)/TiO_2 or black-light/TiO_2) AOPs, merging the LC-DAD and LC-MS-ESI-TOF methods to determine the high and low concentrations, respectively. In addition, LC-DAD has been applied by different authors to determine the identity of parent compounds and, in the same studies, a LC-MS/MS ion trap, LC-MS-TOF, LC-MS-ESI-TOF or LC-API-MS was used to determine the by-products of the target pharmaceutical compounds after varying treatments. For example, UV/H_2O_2 was used to remove up to 73 % of total sulfamethazine (Batista et al. 2014), to perform complete mineralisation of carbamazepine by sulphate radical oxidation (Matta et al. 2011), and to sonochemically oxidise degrade atenolol between 90 and 100 % (Nejumal et al. 2014). Heterogeneous photocatalysis, UV/H_2O_2 and their combinations were used with a high efficiency in Milli-Q water (above 94 %), but with a very low efficiency in real water (Romero et al. 2011, 2014). The study of Li et al. (2014) carried out an electro-phenton process to degrade ibuprofen using three different pieces of analytical equipment: a LC-DAD to quantify the parent and phenolic intermediates as well as an UHPLC-Q-TOF-MS and UHPLC-ESI-MS/MS to identify the by-products and major aromatic intermediates, respectively.

Generally, in order to carry out a suitable determination of intermediates, only a restricted number of analytes is used. This can provide a better approximation of the degradation pathway of the target compound without potential interference. Mass detection is necessary for this type of determination, and the most commonly used detector is a MS-TOF or its variations (Munoz et al. 2012; Batista et al. 2014; Nejumal et al. 2014) because this method provides excellent automatic screening. In some studies, the identification of the provisional structure is compared with authentic standards (Tran et al. 2015), but this procedure is rarely executed. In addition, other determination procedures, such as ion-exclusion LC or ionic chromatography, are also employed to analyse carboxylic acids or different cations or anions produced during the degradation of the parent compound, with the objective of following the intermediates (Ganzenko et al. 2015).

Several authors have combined both traditional optical and chromatography methods in the same studies to monitor the target compounds. The purpose of this type of analytical procedure can be: (1) to quantify higher and lower levels of concentrations; for example, Secondes et al. (2014) used a spectrophotometer and LC-MS after a sonochemical AOP to determine pharmaceuticals in the milli- to nanogrammes per litre range, respectively; (2) to quantify the parent compound using a spectrophotometer as well as its products of degradation using MS detectors coupled with chromatography systems (LC or GC) (Daghrir et al. 2013; Qin et al. 2015; Carabin et al. 2015); and (3) to optimise a few compounds using spectrophotometric analysis and validate the optimal conditions of the AOP with a greater amount of pharmaceuticals by mass spectrometric determination. In this sense, Naddeo et al. (2013) used a spectrophotometer as an analytical method to quantify two compounds to develop a sonochemical treatment, which was used to remove 23

pharmaceutical compounds (diclofenac and carbamazepine) and was evaluated by LC-QTrap-ESI-MS/MS.

Regarding LODs, values on the order of microgrammes per litre have been achieved using LC-DAD by certain authors (Klamerth et al. 2010, 2011; Jin et al. 2012; Espejo et al. 2014a, b). However, better LODs on the order of ng L^{-1} were obtained by MS in other studies of pharmaceuticals after diverse photochemical AOPs (Rosario-Ortiz et al. 2010; Sichel et al. 2011; Hey et al. 2014). In particular, if we consider the effectiveness of the treatment, these results could emphasise that the authors who used optical detectors expressed the results in terms of complete degradation; however, it is still possible to assign a numerical value when the study was carried out using an MS detector. In this case, transformations can be achieved anywhere in the range of 0 to 100 %.

Because of analytical limitations, Pereira et al. (2012) spiked water with an initial concentration in the milligrammes per litre range. This is a higher concentration than is typically found in environmental samples and was necessary to follow the degradation of compounds using direct injection into an UHPLC-DAD (ultra-high performance liquid chromatography-DAD) after applying UV photolysis and UV/H_2O_2, which produced a high removal efficiency. This problem can be solved during sample preparation by using preconcentration techniques.

Encinas et al. (2013) and Tran et al. (2015) comment on the influence of matrix effects on the efficiency of AOPs when low initial concentrations of the emerging contaminants are used. In light of these effects, it is very important to use an analytical method that has a suitable performance to follow this type of pollutant at the same concentration level as the environmental samples and to ensure that these treatments are successful under real conditions. Regardless, publications generally focus on the details of data optimisation for advanced oxidation techniques and ignore the importance of analytical methodologies, such as the study of Badawy et al. (2014), which did not provide a sufficient number of parameters.

Sample preparation

Sample preparation is geared toward two main objectives, to stop any oxidation process that may affect the instrumentation and to improve the limit of detection by concentrating and cleaning the samples. Therefore, this important step improves the quality of the determination procedure, and in some cases, it is essential to perform the analysis.

If chemical catalysts suspended in the solution are used as oxidants, one should be especially careful with the use of direct injection, and the particles should be removed or inactivated before analysis. For this reason, Romero et al. (2011) filtered the samples with a 0.45-μm polyethersulphone membrane filter to remove the suspended TiO_2 catalyst before LC analysis, although a centrifugation step can also be used. In contrast, Matta et al. (2011) performed treatment using a sulphate radical and then quenched a 2-mL sample with 100 μL of an aqueous solution of $NaNO_2$ (10 M) before injecting it onto an LC column. A catalase solution is often employed to quench the reaction and guarantee the absence of hydrogen peroxide (catalase consumes residual H_2O_2) (Trovó et al. 2011; Trovó and Nogueira 2011; Baeza and Knappe 2011; Keen et al. 2012; Justo et al. 2015). In Gerrity et al. (2010), the residual oxidants in each sample were quenched with calcium thiosulfate.

The disadvantage of using gas chromatography to analyse pharmaceuticals is the necessity of an additional step for sample preparation. This procedure requires a chemical reaction, which increases the selectivity, namely, derivatisation (Olariu et al. 2010). For this, Torun et al. (2015) and Zupanc et al. (2014) used trimethylsilane and *N*-(*t*-butyldimetylsilyl)-*N*-methyltrifluoroacetamid (MTBSTFA), respectively, to derivatise before their respective determinations.

The pre-concentration and extraction techniques applied in this field range from more conventional techniques, such as liquid-liquid extraction (LLE), to the latest micro-extraction procedures. LLE coupled to GC-MS was used by George et al. (2014) and Ganzenko et al. (2015) to follow the degradation of salicylic acid and caffeine (with derivatisation), respectively, after electro-Fenton processing. In contrast, Munoz et al. (2012) analysed the by-products of triclosan using SBSE and GC-MS-TOF after a Fenton/H_2O_2 procedure with a LOD below 1 ng L^{-1}.

However, within the realm of conventional techniques, solid-phase extraction (SPE) is the most commonly used pre-treatment to clean and concentrate the sample to take advantage of the levels of detection that are capable of being measured by the instrumentation. This technique, coupled with a detection system, achieves LODs on the order of nanogrammes per litre or a few microgrammes per litre. In many publications in which the authors use SPE followed by LC (with different detectors) with spiked samples, chemical and photochemical AOPs were developed to remove EDCs and PPCPs (Klamerth et al. 2010, 2011; Sichel et al. 2011; Ibáñez et al. 2013; Hey et al. 2014; Miralles-Cuevas et al. 2014b). However, Moreira et al. (2015) used the same methodology to degrade different micro-pollutants in non-spiked urban wastewater using a large variety of AOPs. In all cases, nearly complete degradation was obtained.

It is necessary to have adequate knowledge of the possible matrix effects generated from the use of AOPs before applying them in a full-scale treatment. The use of a validated analytical methodology (in terms of both sample preparation and the determination procedure) also offers a closer approximation to the real removal rates of AOPs. These percentages can be confusing for methodologies with high detection limits. Non-identification of a compound may not correspond to

100 % removal. Therefore, it is advisable to describe the effectiveness of the AOP relative to the analytical technique used. This means proposing different scales, depending on the sensitivity of the method. One option is the use of either a qualitative scale (low, medium or high/complete degradation) for less sensitive methods or a quantitative scale (providing a numerical percentage) for more accurate methodologies.

Overall, there is little information regarding the analytical procedures used. Thus, this is an unresolved issue for future research.

Future trends

The inability of conventional wastewater treatments to completely degrade emerging pollutants is well known. Alternative treatments, such as different AOPs, have appeared as improvements to conventional procedures, but generally, they are limited because they require a large economic investment and have very few real applications. Therefore, the main advantage of AOPs, which cause the complete mineralisation of pollutants, can only be obtained with very long contact times, causing very high operative costs, and, in practice, AOP are almost never used. Consequently, there is an increasing need for alternative wastewater treatment processes that have high removal efficiencies and a reasonable cost (Zhang et al. 2014). Moreover, because the determination of pharmaceutical compounds and other emerging compounds in complex matrices, such as wastewater, may be difficult, the chemical additives employed in some AOPs may add further difficulty to the analysis. Thus, the development of advanced procedures without the requirement of using additives would facilitate the determination of pollutants using simple analytical methods. Additionally, the use of aquatic plant-based systems is gaining attention and has been recommended for wastewater purification for small communities (<2000 population equivalent) (Herrera-Melián et al. 2015). However, although advanced procedures have been studied to remove conventional pollutants, their application to emerging compounds is still scarce.

Regarding the preparation and determination procedures, to evaluate the efficiency of AOPs to remove pharmaceutical compounds, it is essential to apply the most sensitive and specific techniques because these pollutants are found at very low concentrations. Conventional extraction and preconcentration techniques are often not able to meet the purification and the detection limits required for these types of samples. The current trend in analytical chemistry is toward automatised techniques, such as on-line SPE coupled to LC, which avoids manual errors and allows complete injection of the sample, instead of a portion of a few millilitres, such as in conventional SPE. On the other hand, the availability of a very selective detector is imperative to follow the degradation of the pollutants and determine their by-products. In the future, all studies involving the degradation of pharmaceutical and other emerging compounds should include an analysis of these transformation products because the negative effects of these products could be more important that those generated by the original substance.

Conclusions

Different AOPs and their combinations have seen rapid development, resulting in a very promising approach for the treatment of different wastewaters. Nevertheless, the majority of assays have been carried out at the laboratory scale; thus, their applicability has not been sufficiently demonstrated in real urban wastewater treatment plants. Moreover, very few studies have been conducted to evaluate the economic feasibility of this novel technology.

In any study based on the use of AOPs, it is relevant to note that employing the proper analytical methodology is essential to obtain an idea of the effectiveness of the treatment. However, currently, the information provided by many authors regarding the analytical methodology is scarce. The accurate estimation of elimination rates is closely linked with a good understanding of the analytical limitations related to the particular characteristics of the compounds and also to the interferences that could affect the identification or quantification of the target analytes. Thus, efforts should be made to clarify and expand the chosen preparation and determination procedures.

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