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Review Paper

Treatment options for wastewater effluents from pharmaceutical companies

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ABSTRACT: In recent years, concerns about the occurrence and fate of active pharmaceutical ingredients, solvents, intermediates and raw materials that could be present in water and wastewater including pharmaceutical industry wastewater has gained increasing attention. Traditional wastewater treatment methods, such as activated sludge, are not sufficient for the complete removal of active pharmaceutical ingredients and other wastewater constituents from these waters. As a result, complementary treatment methods such as membrane filtration, reverse osmosis and activated carbon are often used in conjunction with the traditional methods for treatment of industrial wastewater. Most of the literature published to date has been on the treatment of municipal wastewater. However, there is a growing body of research that looks at the presence of active pharmaceutical ingredients in industrial wastewater, the treatment of these wastewaters and the removal rates. This article, reviews these treatment methods and includes both traditional methods and advanced oxidation processes. The paper concludes by showing that the problem of pharmaceuticals in wastewaters cannot be solved merely by adopting end of pipe measures. At source measures, such as replacement of critical chemicals, reduction in raw material consumption should continue to be pursued as the top priority.

Keywords: *Advanced oxidation; Industrial wastewater; Pharmaticeutical effluent; Personal care products*

INTRODUCTION

The presence of Pharmaceuticals and personal care products (PPCPs) was first identified in surface and wastewaters in the United States and Europe in 1960s (Stumm-Zollinger and Fair, 1965). Concerns about their potential risk was raised in 1999 (Daughton and Ternes, 1999) with the issue attracting considerable interest after the presence of pharmaceuticals in river water was linked to feminisation of fish living downstream of Wastewater treatment plant (WWTP) outfalls (Larsson *et al*., 1999). Furthermore, a link between a non-steroidal anti-inflammatory drug, diclofenac and the renal failure of vultures contributing to the > 95 % decline in its population in the Indian subcontinent since the 1990's has been reported (Oaks *et al*., 2004). Public awareness were raised after a study showed that organic wastewater contaminants, including PPCPs, were present in 80 % of 139 U.S. streams (Kolpin *et al*., 2002). Although the concentration levels of PPCPs found in the environment are at trace concentrations, their chemical persistence, microbial resistance and synergistic effects are still unknown (Ankley *et al*., 2007; Madukasi *et al*., 2010), which is a cause for concern. Moreover, low concentrations can elicit adverse effects on aquatic life (Miege *et al*., 2008; 2009).

Pharmaceuticals enter the environment from a myriad of scattered points. The main sources of contamination include pharmaceutical production plants, WWTPs, hospitals, landfills and even graveyards (Khetan and Collins, 2007; Lillenberg *et al*.,

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2010). The most investigated route of entry of pharmaceuticals into the environment is that from municipal WWTPs. Human excretion of unchanged or slightly transformed Active pharmaceutical ingredients (APIs) conjugated to polar molecules such as glucoronide enters the WWTP where these conjugates may then be cleaved, releasing the original API into the environment (Heberer, 2002). Activated sludge WWTPs have received particular attention (Jones *et al*., 2007; Watkinson *et al*., 2007). A limited number of studies also found pharmaceuticals in drinking water (Webb *et al*., 2003) and hospital wastewater (Suarez *et al*., 2009). Monitoring of APIs being released from pharmaceutical production facilities is not routine and the importance of such releases has not yet been established (Larsson and Fick, 2009). Furthermore, pharmaceutical industry wastewaters may contain organic solvents, catalysts, additants, reactants, intermediates, raw materials and APIs (Sreekanth *et al*., 2009), which makes them difficult to treat. The presence of toxic or recalcitrant substances in such wastewater results in lower Chemical oxygen demand (COD) removal efficiencies (Chelliapan *et al*., 2006). It has been estimated that up to half of the pharmaceutical wastewater produced worldwide is released without any treatment (Enick and Moore, 2007). While some attention has been focused on Endocrine disrupting chemicals (EDCs) the removal of other specific APIs is largely ignored. Biological treatment of wastewater is the most common and economical wastewater treatment method (Kulik *et al*., 2008). However, biological methods have shown to be insufficient for the removal of all potentially hazardous constituents of the wastewater (Clara *et al*., 2005; Joss *et al*., 2005; Suman Raj and Anjaneyulu, 2005; Giri *et al*, 2008; 2010). Recently, Membrane bioreactor (MBR) technology, ozonation and advanced oxidation processes (AOPs) have shown varying degrees of efficiency for the treatment of pharmaceutical wastewaters (Andreozzi *et al*., 2005; Doll and Frimmel, 2005a, Perez-Estrada *et al*., 2005a; Andreozzi *et al*., 2006; Helmig *et al*., 2007). As the awareness of the inefficiencies of the individual treatment technologies for the removal of hazardous substances in pharmaceutical wastewater is increasing, the integration and combination of treatment technologies may provide a more effective, albeit expensive solution in the future. This review aims to provide an overview of the current knowledge regarding the range of treatment methods available for PPCP removal from industrial wastewaters in order to get baseline knowledge of the effectiveness of the various treatment options. This knowledge could help pharmaceutical production facilities to be prepared to take preventative measures before required to do so by legislation. This literature review was carried out at Dublin City University in 2010.

Conventional treatment methods

Biological treatment methods have traditionally been used for the management of pharmaceutical wastewater (Suman Raj and Anjaneyulu, 2005). They may be subdivided into aerobic and anaerobic processes. Aerobic applications include activated sludge, membrane batch reactors and sequence batch reactors (LaPara *et al*., 2002; Suman Raj and Anjaneyulu, 2005; Noble, 2006; Chang *et al*., 2008 and Chen *et al*., 2008). Anaerobic methods include anaerobic sludge reactors, anaerobic film reactors and anaerobic filters (Gangagni *et al*., 2005; Enright *et al*., 2005; Chelliapan *et al*., 2006; Oktem *et al*., 2007; Sreekanth *et al*., 2009). The wastewater characteristics play a key role in the selection of biological treatments. Solvents, APIs, intermediates and raw materials represent biologically recalcitrant substances which affect the efficiency of biological treatment systems (Oz *et al*., 2004; Helmig *et al*., 2007). Activated sludge (AS) treatment is unsuitable for the treatment of wastewater where the COD levels are greater than 4000 mg/L (Suman Raj and Anjaneyulu, 2005).

Conventional activated sludge with a long hydraulic retention time (HRT) has historically been the method of choice for the treatment of pharmaceutical industry wastewater (El Gohary and Abou-Elea, 1995; Oz *et al*., 2004). It has a lower capital cost than more advanced treatment methods and a limited operational requirement; it is generally more environmentally friendly than chlorination. However, high energy consumption, the production of large amounts of sludge (Sreekanth *et al*., 2009) and operational problems including colour, foaming and bulking in secondary clarifiers are associated with activated sludge plants (Oz *et al*., 2004). Factors which affect the efficiency of activated sludge facilities for the treatment of pharmaceutical wastewater include HRT, temperature, pH, dissolved oxygen (DO), organic load, microbial community, presence of toxic or recalcitrant substances and the

batch operation of pharmaceutical production facilities (LaPara *et al*., 2001a; LaPara *et al*., 2002; Suman Raj and Anjaneyulu, 2005). These variables require modification for adaptation to pharmaceutical industry wastewater.

Temperature is a key factor in the efficiency of activated sludge facilities. It has an important role in selecting individual microbial species and overall microbial diversity in the activated sludge. This is where industrial wastewater can be very different from municipal wastewater. COD removal and examination of 16s rRNA of the bacterial community in aerobic biological systems at 5 °C intervals between 30 and 70 °C showed that high temperatures were limiting factors to COD removal (LaPara *et al*., 2001b). The number of bacterial species decline with temperature between 30-60 °C, with the activated sludge process failing at temperatures above 60-65 °C (LaPara *et al*., 2001a). A two stage operation at 55 °C followed by 30 °C produced a lower quality effluent than operation at 30 °C alone. Therefore, water from high temperature processes must be cooled prior to treatment by AS, which increases the time and cost of treatment.

The impact of pharmaceuticals on the AS process appears to be negligible under normal operating conditions (Stamatelatou *et al*., 2003). However at higher concentrations, which may be expected in the wastewater of pharmaceutical manufacturing facilities, they may become inhibitory. While there are a number of limited studies on the removal efficiency of APIs from pharmaceutical manufacturing facilities, it is known that removal efficiency of municipal facilities is dependent on the APIs present in the wastewater (Urase *et al*., 2005). AS is an efficient method for the removal of some APIs, but not all from municipal facilities (Zwiener and Frimmel, 2003; Castiglioni *et al*., 2006; Watkinson *et al*., 2007). β-Lactam and quinlone drugs in particular appear to be susceptible to aerobic oxidation. In a WWTP in Brisbane Australia, β-Lactam antibiotics showed high biodegradability due to hydrolic cleavage of the β-lactam ring. Lincomycin and sulphonamides were the least affected by AS treatment (Joss *et al*., 2005). Similar studies have also found that the efficiency of the process is dependent on the compound under investigation (Joss *et al*., 2005). Ibuprofen, naproxen, bezafibrate and estrogens (estrone, estradiol and ethinylestradiol) showed a high degree of removal while sulfamethoxazole, carbamezapine and diclofenac showed limited removal (Clara *et al*., 2005; Joss *et al*., 2005; Xu *et al*., 2008). Removal efficiencies are likely to decrease due to the development of more resistant APIs (Khetan and Collins, 2007). A number of pilot scale studies were conducted using Sequence batch reactors (SBRs) and Membrane bioreactors (MBRs) in an attempt to improve the effectiveness of AS treatment (Clara *et al*. 2005; Radjenovic *et al*. 2007). SBR is an activated sludge method of treatment in which separate tanks for aeration and sedimentation are not required and there is no sludge return. This type of process is ideal for use in small systems or when land is limited (Ileri *et al*., 2003). In one study, removal rates of 82 % Biochemical oxygen demand (BOD), 88 % COD, 96 % NH_3 and 98 % Suspended solids (SS) from domestic and pharmaceutical wastewater were achieved with a SBR operated for a 4 h aeration and a 60 min sedimentation period (Ileri *et al*., 2003). In another study, slightly lower removal efficiencies at between 63-69 % of COD levels were achieved using SBR technology (Aguado *et al*., 2008).

MBRs are known to be effective for the removal of bulk organics and can replace traditional methods or operate in combination with conventional AS systems or as hybrid systems (Noble, 2006). The main advantages of MBRs over AS is that they require less space for operation (Yang *et al*., 2006), and can also treat variable wastewater compositions (Chang *et al*., 2008). High COD and BOD removal have been demonstrated in pharmaceutical production facilities (De Wever *et al*., 2007). For example, a 10 m^3 per day capacity MBR operated at a pharmaceutical facility in Taiwan, removed 95 % of COD and 99 % of BOD (Chang *et al*., 2008). However, complete removal of all APIs is rare (Helmig *et al*., 2007). While the MBR removed 17-α-estradiol, 17-β-estradiol, 17-α-dihydroequilin, trimegestone, estriol, medrogestone, norgestrel, and estradiol valerate to near and below the detection limits, estrone, ethinyl estradiol, and venlafaxine, a selective serotonin reuptake inhibitor (SSRI), were shown to be more resistant to the MBR treatment (Helmig *et al*., 2007). One explanation for this is that pharmaceutical compounds are generally smaller than the membrane pores and so only substances sorbed on particles are retained (Radjenovic *et al*., 2007). In order to remove the smaller compounds, membranes such as those used in reverse osmosis or nanofiltration are used, however these are expensive, which has limited their widespread use (Clara *et al*., 2005).

The advantages of anaerobic treatment over aerobic processes is its ability to deal with high strength wastewater, with lower energy inputs, sludge yield, nutrient requirements, operating cost, space requirement and improved biogas recovery. However, because a wide range of natural and xenobiotic organic chemicals in pharmaceutical wastewaters are recalcitrant and non-biodegradable to the microbial mass within the conventional treatment system, anaerobic processes are not always effective in removing these substances.

One way around this is to use anaerobic microorganisms such as methanogenic archaea, which can adapt to levels many times those that inhibit unadapted methanogens (Fountoulakis *et al*., 2008) as well as incorporating different configurations including biomembrane reactors, stirred tank reactors, up-flow anaerobic filters and fluidised bed reactors (Gangagni Rao *et al*., 2005; Chelliapan *et al*., 2006; Oktem *et al*., 2007). Up-flow anaerobic stage reactors (UASRs) used as a pre-treatment to activated sludge for industrial effluent have been shown to be efficient for the removal of pharmaceuticals even at high concentrations (Chelliapan *et al*., 2006; Oktem *et al*., 2007). A UASR fed with real pharmaceutical wastewater containing the antibiotics tylosin and avilamycin showed a high degree of COD and drug removal (Chelliapan *et al*., 2006). For a Hydraulic retention time (HRT) of 4 d, Organic loading rate (OLR) of 1.86 kg COD m^{-3}/d, COD reduction was 70-75 %, with an average of 95 % tylosin reduction; however, COD removal decreased with an increase in tylosin (Chelliapan *et al*., 2006). A hybrid Up-flow anaerobic sludge blanket reactor (USABR) which combines a UASR and anaerobic filter technology showed significant removal of COD at a much higher OLR from pharmaceutical wastewater (Oktem *et al*., 2007). For a HRT of 2 days and an OLR of 8 kg COD m^{-3}/d maximum rate of removal was found to be 5.2 kg COD m^{-3}/d (Oktem *et al*., 2007). A UASR operating in thermophillic mode (55 °C) showed a high COD (65-75 %) and BOD removal (80-94 %) even at high OLR of 9 kg COD m^{-3}/d (Sreekanth *et al*., 2009). Carbamazapine, however, was not degraded using a UASR.

Physio-chemical treatment options

As seen in oxidation reactionssection, conventional wastewater treatment systems can be effective in removing some, but not all pharmaceuticals from wastewater. Therefore, other treatment technologies have been explored with the intention of finding suitable polishing techniques to further reduce pharmaceuticals concentrations. These technologies include membrane separation, chemical removal, activated carbon, chlorination, ultraviolet irradiation and other novel approaches. The efficiency of these methods for the treatment of pharmaceutical wastewater varies significantly and is described below.

Membrane processes

Several membrane types and applications were evaluated for the removal of APIs at pilot and full-scale, including microfiltration, ultra filtration, nanofiltration, reverse osmosis, electro dialysis reversal, membrane bioreactors and combinations of membranes in series (Bellona and Drewes, 2007; Snyder *et al*., 2007). Microfiltration and ultra filtration are generally not fully effective in removing organic contaminants as pore sizes vary from 100-1000 times larger than the micro pollutants which can slip through the membranes.

The pressure-driven membrane processes Nanofiltration (NF) and Reverse osmosis (RO) have been the focus of attention of many researchers for the treatment of drinking water (Watkinson *et al*., 2007). However, the studies on the use of RO/NF for pharmaceutical removal is limited and most of the studies employed NF and RO membranes for tertiary treatment in wastewater recycling plant or for treating saline groundwater. (Nghiem *et al*., 2005; Yoon *et al*., 2006; Snyder *et al*., 2007). RO in different configurations showed efficient removal of thirty-six personal care products and endocrine disrupting chemicals including antibiotics, lipid regulators, hormones and oral contraceptives, antiepileptics and analgesics (Snyder *et al*., 2007; Watkinson *et al*., 2007).

RO membranes removed the majority of compounds investigated to levels below the limit of detection. However, pentoxifylline, iodopromide, dimethyltoluamide (DEET), meprobamate, phosphanetriyltripropanoic acid (TCEP), gemfibrozil, musk ketone and oxybenzone were detected in the permeate of a variety of the configurations (Snyder *et al*., 2007). A possible reason for this is short circuiting of the membrane or the failure of membrane support media. (Bellona *et al*., 2004). Radjenovic *et al*. (2007) investigated the removal of a range of pharmaceuticals including hydrochlorothiazide,

ketoprofen, diclofenac, propyphenazone and carbamazepine using NF and RO technologies for a full-scale drinking water treatment plant, with high rejection percentages (>85 %) for all the pharmaceuticals reported. Pharmaceuticals can be rejected on NF and RO membranes by one or a combination of three basic mechanisms: size exclusion (sieving, steric effect), charge exclusion (electrical) and physico-chemical interactions between solute, solvent and membrane. In laboratory-scale cross-flow tests with NF-90 membranes rejections of ketoprofen and diclofenac were reported to be greater than 90% (Amy *et al*., 2005; Xu *et al*., 2005). In another study with RO membranes the retention of negatively charged diclofenac was 95 % (Kimura *et al*., 2003). Some studies reported higher removal efficiencies of polar and charged compounds in NF/RO processes due to interactions with membrane surfaces (Ozaki and Li, 2002; Bellona *et al*., 2004; Amy *et al*., 2005; Braeken *et al*., 2005). Though both NF and RO treatment shows potential as an efficient method for removing pharmaceuticals from the wastewater, the disposal of the sludge which could contain the pollutant in a more concentrated form remains.

Activated carbon (AC)

AC is a recognised conventional technology for the removal of both natural and synthetic organic contaminants (Hrubec *et al*., 1983; Annesini *et al*., 1987). It is most commonly applied as a powdered feed or in granular form in packed bed filters. Granular activated carbon (GAC) can be used as a replacement for anthracite media in conventional filters, providing both adsorption and filtration. It can be applied following conventional AS treatment as an adsorption bed. However, carbon regeneration and disposal are environmental considerations (Snyder *et al*., 2007).

In general, sorption is described using Freundlich isotherms, with sorption behaviour quantified as the specific sorption coefficient, K_D (L/mg) (Nagaoka *et al*., 2002; Li *et al*., 2005). This coefficient is the ratio of equilibrium concentrations of a dissolved compound in a system containing a sorbent (AC or sludge or solids) and an aqueous phase and expressed as:

$$K_D = \frac{C_s^{ads}(eq)}{C_{aw}^{ads}(eq)} \quad (1)$$

Where $C_s^{ads}(eq)$ is the amount of the compound sorbed on the sorbent at sorption equilibrium (mg/g), and $C_{aw}^{ads}(eq)$ is the concentration of the compound in the aqueous phase at sorption equilibrium (mg/L). Sorption is negligible for substances with log K_D values less than 2, but is large when the log K_D value is greater than 4 (Clara *et al*., 2005). The reported Log K_D values of estrogens like Estrone, 17β-Estradiol and 17 α-Ethinylestradiol ranged from 2.2 to 2.8 (Carballa *et al*., 2008) and 2.0 to 2.84 (Ternes *et al*., 2004), respectively. Since these log K_D values are between 2 and 4, sorption can be suitable as a removal mechanism. Dutta *et al*. (1997) studied the adsorption and desorption of 6-aminopenicillanic acid (6-APA) in aqueous solution using activated carbon. They found that the adsorption process was highly reversible, the extent of reversibly adsorbed 6-APA was around 93 %.

Snyder *et al*. (2007) found that both powdered activated carbon (PAC) (5mg/L) and GAC removed greater than 90 % of estrogens (100–200 ng/L initial concentrations). However, dissolved organic compounds, surfactants and humic acids compete with binding sites and can block pores within the AC structure (Zhang and Zhou, 2005; Snyder *et al*., 2007). PAC, which was used at pilot scale, achieved greater than 90% removal for 19 of 26 APIs tested including trimethoprim, carbamezapine and acetaminophen. Poor results were seen where regular regeneration was not provided. The filtration step prior to the treatment of micro pollutants by PAC is important (Hartig *et al*., 2001). The general difficulty with PAC treatment lies in separating the carbon from the water. Various options are available: it can be done either via sedimentation, which necessitates the use of precipitants, or via (membrane) filtration, which requires additional energy. PAC performance can also be improved by increasing the retention time (Westerhoff *et al*., 2005; Yoon *et al*., 2005). The filtration step reduces the carbon demand of the wastewater due to reduced blocking of the micropores by high molecular weight compounds. Consequently PAC is only suitable for the treatment of pre-treated wastewaters or wastewaters with a low organic loading.

Chlorination

Chlorination has been shown to be effective for the removal of pharmaceuticals including 17α-ethinylestradiol and 17 β-estradiol (Alum *et al*., 2004) and sulfonamides (Qiang *et al*., 2006). Chlorine dioxide

is also effective for the removal of sulfamethoxazole, roxithromycin, 17α-ethinylestradiol and diclofenac (Khetan and Collins, 2007). Chlorination and ozonation when compared for the removal of bisphenol A, 17β-estradiol, and 17α-ethinylestradiol and byproduct estrogenicity from distilled water showed comparable results with ozonation resulting in 75-99 % removal (Alum *et al*., 2004). Residual chlorine and ozone was found to be low with > 99 % loss of the parent compound (Gharbani *et al*., 2010).

Lee and Von Gunten (2009) achieved 90 % conversion of estrogen, 17α-Ethinylestradiol with chlorine and increased the rate of 17β-Ethinylestradiol transformation by a factor of 3 with the addition of 0.25 mM Br^-. The accelerating effect of Br^- diminishes in the presence of dissolved organic matter as it consumes bromine faster than estrogens (Flores and Hill, 2008). Acetaminophen, diclofenac, sulfamethoxazole and fluoroquinlone all become oxidised during chlorination. By-products of acetaminophen include the toxic by-products *N*-acetyl-*p*-benzoquinine imine and 1,4-benzoquinone. Both metoprolol and sulfamethoxazole form carcinogens such as chloramines as one of their oxidation products and this may be due to the fact that ammonia chlorination was about one thousand times faster than phenol chlorination (Pinkston and Sedlak, 2004).

Oxidation reactions

The biological and physiochemical treatment methods described previously have shown limited success for the treatment of pharmaceutical wastewater. However, the development of oxidation processes is showing higher removal rates. Oxidation reactions have primarily been used to supplement rather than replace conventional systems and to enhance the treatment of refractory organic pollutants (Balcioglu and Otker, 2003). This technology has been successfully applied to the treatment of pharmaceuticals (Khetan and Collins, 2007). A chemical agent such as hydrogen peroxide, ozone, transition metals and metal oxides are required for AOPs. In addition, an energy source such as ultraviolet-visible radiation, electric current, gamma-radiation and ultrasound is required (Ikehata *et al*., 2006). AOPs are based on the production of free radicals, in particular the hydroxyl radical and facilitate the conversion of pollutants to less harmful and more biodegradable compounds (Ikehata *et al*., 2006). AOPs frequently include ozonation coupled with hydrogen peroxide and Ultraviolet (UV) irradiation. Fenton and TiO_2 photocatalysis are also employed. Heterogeneous mixtures of ozone, hydrogen peroxide, Fenton and titanium dioxide in light and dark have revealed a range of suitable treatment methods depending on the properties of the phammaceuticals and economic considerations.

The ultimate aim of AOPs is the mineralisation of pollutants, with conversion to carbon dioxide, water, nitrogen and other minerals. Various studies have confirmed the potential of AOPs for removing pharmaceuticals (Ternes *et al*., 2002; Huber *et al*., 2003). AOPs may change a compound's polarity and the number of functional groups which affect the functionality of the pharmaceutical in the body. Original medicinal modes of action should then disappear e.g. antibiotics which have been hydroxylated should not promote the formation of resistant strains (Ternes *et al*., 2003). However, degradation compounds must be identified and monitored as they may be more toxic that the parent compounds (Vogna *et al*., 2002). Photocatalytic degradation studies using the analgesic anxiolytic drug, buspirone, have revealed that the intermediates produced reflect those found in biotransformation in animal models (Calza *et al*., 2004). Methods that produce fewer intermediates must to allow for effective modelling and application are being developed (Gaya and Abdullah, 2008).

Photo initiated AOPs may be coupled with other biological, physical and chemical methods for mineralisation. Pre-treatments such as micro or ultra filtration, reverse osmosis followed by an AOP have proved effective for the treatment of industrial wastewater (Ollis, 2003). AOPs may enhance biodegradability as a pre-treatment method to biological treatment (Oller *et al*., 2007) or as a tertiary treatment. AOPs also handle fluctuating flow rates and compositions with less difficulty than microbes, as the same level of adaptation to the wastewater is not necessary (Ikehata *et al*., 2006). Cost of both the chemical agent and the energy source can be a major block to implementation of AOPs on an industrial scale (Legrini *et al*., 1993). However, by using solar irradiation the capital cost of AOPs may be substantially reduced (Trovo *et al*., 2008). Natural compounds as well as carbonate, bicarbonate and chloride ions may lead to a reduction in treatment efficiency as these compounds may act as antioxidants (Ikehata *et al*., 2006).

Ozonation

Ozone has been applied to the treatment of waters primarily due to its strong disinfection and sterilisation properties (Araña *et al*., 2002). Its application for the treatment of waters containing pharmaceutical residues is now a broad area of research (Balcioglu and Okter, 2003; Ternes *et al*., 2003; Andreozzi *et al*., 2005; Huber *et al*., 2005; Andreozzi *et al*., 2006; Nakada *et al*., 2007; Dantes *et al*., 2008). The main mode of action in the ozonation process is the formation of OH^- radicals due to ozone decay in the water, but there are also ozone molecules present for chemical attack. This increases the oxidation capacity (Ternes *et al*. 2003). Ozonation has been implemented as the principle treatment method or to enhance the biodegradability and efficiency of subsequent treatment (Cokgor *et al*., 2004). Ozone production is an energy intensive process, making it costly to implement. An ozone treatment system may increase the energy demand over a conventional wastewater treatment plant by 40-50 % (Larsen *et al*., 2004). The use of ozone as a means of breaking down pharmaceuticals in water has been the subject of numerous studies over the last ten years including (Andreozzi *et al*., 2003a; b; Vogna *et al*., 2004a; b). A significant contribution to this work has been in the area of antibiotic removal (Balcioglu and Okter, 2003; Ternes *et al*., 2003; Andreozzi *et al*., 2005; Andreozzi *et al*., 2006; Dantes *et al*., 2008), where removal rates >90 % have been reported. However, the reported removal rate for lipid regulators is less at about 50 % and about 60-80 % for β-blockers and below 50 % for some Antiphlogistics (Ternes *et al*., 2003).

Although the degree of removal and mineralisation of pharmaceuticals in water or synthetic industrial effluent has been reported, little or no literature exists on the ozonation of pharmaceuticals in actual pharmaceutical wastewater (Cokgor *et al*., 2004). Furthermore details of process optimisation and kinetics for the elimination of pharmaceuticals using ozone are limited (Arslan-Alaton and Caglayan, 2005). Also, disagreement exists for the ozone dose necessary for pharmaceutical removal. Ternes *et al*. (2003) reports almost complete removal of pharmaceuticals except for iopromide in a study using an ozone dose of 10 to 15 mg for every litre wastewater (contact time 18 min) treated in a municipal WWTP. On the other hand, Huber *et al*., (2003) pointed out, that only about 2 mg/L of ozone was needed to oxidise a range of pharmaceuticals (among them diclofenac and sulfamethoxazole) to a removal rate of 90 to 99 %. In general, both studies demonstrated that the increased pharmaceutical oxidation increased with ozone levels. The amount of ozone required depends on various parameters, such as the level of background dissolved organic matter and wastewater pH and alkalinity, as well as the desired elimination performance (Huber *et al*., 2005). The results of the various studies indicate that ozonation of pharmaceuticals depends on their chemical structure. While compounds with a C=C bond or aromatic structures seem to be susceptible to ozonation, compounds with amide structures are resistant to it (Nakada *et al*., 2007).

Recent kinetic studies on pharmaceuticals including amoxicillin, lincomycin, clofibric acid, acetaminophen, bisphenol A, 17-estradiol, and 17-ethinylestradiol have shown ozone to attack aromatic rings and amino groups (Andreozzi *et al*., 2003a; b; 2005; Arslan-Alaton and Caglayan, 2005; Andreozzi *et al*., 2006). A kinetic study of the effect of such an ozone attack on the antibiotic amoxicillin showed direct attack on the phenolic ring leading to the formation of hydroxyl derivative intermediates, with no evidence of oxidation of the sulphur atom (Andreozzi *et al*., 2005). Another kinetic analysis of the effect of 5-10 mg O_3/L on four beta blockers, (acebutolol, atenolol, metoprolol and propranolol) from reverse osmosis permeate also showed that ozone can attack aromatic rings and amine groups (Benner *et al*., 2008). The reaction of the aromatic structure is independent of solution pH. However amine groups do not react directly with ozone and so the reactivity of amines strongly depends on the pKa of the amine and the pH of the solution. As with all oxidation processes, the degradation products must be analysed as they may be more toxic than the parent compound (Andreozzi *et al*., 2006; Ikehata *et al*., 2006). It also must be considered that other compounds in the waste stream other than the target pharmaceutical may produce more harmful by-products as a consequence of the ozonation process. The main disadvantage of ozonation is that in general the target compounds are not fully mineralised, but merely transformed, and so even more harmful substances can be produced as a result. For example, Microtox analysis showed a slight increase in acute toxicity in the first stage of ozonation of sulfamethoxazole (Dantes *et al*., 2008). Therefore, an additional treatment such as sand filtration is required after ozonation to break down reactive oxidation products. However, as well as

removing micro pollutants, ozone reduces not only the microbial count but also odour, colour and foam. At the same time, it is associated with higher energy costs as described above (Larsen *et al*., 2004).

Perozonation

Perozonation, a combination of hydrogen peroxide and ozone, has been successfully used to degrade penicillin formulation effluent (Balcioglu and Okter, 2003; Arslan-Alaton *et al*., 2004; Cokgor *et al*., 2004). The conjugate base of H_2O_2 at low concentrations increases the rate of decomposition of O_3 into hydroxyl radicals (Balcioglu and Okter, 2003). 30 % removal of COD in penicillin formulation effluent was accomplished using ozonation alone (Arslan-Alaton *et al*., 2004). Removal efficiency was enhanced through the addition of H_2O_2, to a maximum of 76 % in the presence of 2mM of H_2O_2. However, it was found that a certain fraction of the resulting COD was non-biodegradable in the subsequent biotreatment. This inert fraction of the waste remained in the effluent. Only overall COD loading was monitored and not actual penicillin levels or breakdown compounds (Arslan-Alaton *et al*., 2004). Thus, the true treatment efficiency of the method in terms of the penicillin removal was unclear. Cokgor *et al*. (2006) investigated the pretreatment of synthetic penicillin formulation effluent containing procain penicillin G (PPG) with the O_3/H_2O_2 process (applied ozone dose = 1440 mg/h treatment time = 60 min; pH 7; H_2O_2 = 10 mM). The effect of chemical pretreatment was assessed on the basis of acute toxicity and biodegradability with activated sludge using water flea *Daphnia magna* toxicity. The pretreatment resulted in more than 70 % COD removal and a 50 % decrease in the acute toxicity towards *Daphnia magna*.

Other studies involving penicillin showed COD and aromaticity results increased from 69 % and 29 % for ozone alone to 95 % and 90 % in the presence of 20mM hydrogen peroxide (Balcioglu and Okter, 2003). The presence of UV increased the COD removal in penicillin formulation wastewater to almost 100%. For synthetic formulation effluents containing the antibiotics like ceftriaxone and enrofloxacin, only slight increases in efficiency were noted following the addition of hydrogen peroxide (Cokgor *et al*., 2006).

Combined UV, O_3 and H_2O_2 treatment was applied to a municipal wastewater treatment plant effluent containing seventeen pharmaceuticals including antibiotics, β-blockers, antiepileptics, antiphlogistics and lipid lowering agents at a German Municipal WWTP (Ternes *et al*., 2003). Removal of all target analytes below detection limits was noted following 18 min contact time at an ozone dose of 10-15 mg /L, with the exception of the iodinated X-ray contrast media, diatrizoate, iopamidol, iopromide and iomeprol which showed removal efficiencies of not higher than 14 %. Diatrizoate was removed by only 25 % following 10 mg/L O_3. The addition of H_2O_2 only slightly increased removal efficiency. The removal rates for a variety of pharmaceuticals using hydrogen peroxide show efficiencies ranging from 40 % for Acetominophen (Andreozzi *et al*., 2003b) to >95 % removal for some hormones when combined with UV (Rosenfeldt and Linden, 2004).

Fenton reactions

Fenton chemistry involves reactions of hydrogen peroxide in the presence of iron to generate hydroxyl radicals (Carey, 1992). Ultraviolet light enhances this generation by the photo reduction of Fe (III) to Fe (II). Since iron is abundant and non-toxic, Fenton reactions are a viable option for wastewater treatment. Photo-Fenton reactions have been used for the degradation of diclofenac (Ravina *et al*., 2002; Perez-Estrada *et al*., 2005b). Complete mineralisation of diclofenac and its intermediates via photo-Fenton reactions in a concentric photo reactor took approximately 50 min (Ravina *et al*., 2002). Compound parabolic collectors have also been used to mineralise diclofenac in approximately 60 min. Another advantage of Fenton reactions is that mineralisation is possible in sunlight avoiding the use of UV light (Pérez-Estrada *et al*., 2005a). Fenton (Fe^{2+}/H_2O_2) and Fenton-like (Fe^{3+}/H_2O_2) reactions were compared for both dark and photo-assisted reactions (Arslan-Alaton and Dogruel, 2004). Penicillin was completely removed after 40 min of advanced oxidation with Fe^{2+}/H_2O_2 at pH 3. Higher COD and Total organic carbon (TOC) removals were obtained with dark Fe^{2+}/H_2O_2 at pH 3 compared with dark Fenton-like Fe^{3+}/H_2O_2 (Arslan-Alaton and Dogruel, 2004). Photo-assisted reactions using UV-C provided only slightly higher removal efficiencies. TOC removal was higher with photo-Fenton reaction and COD removal was slightly higher with photo-Fenton-like reactions.

Since Fenton reactions operate at room temperature normal pressure and without the highly complicated apparatus, there should be a smooth transition from laboratory scale to large scale (Kavitha and Palanivelu, 2004). On the other hand, the strong dependence on

the aqueous solution pH (optimum pH 2-4 for the production of OH. radicals) and on the concentrations of hydrogen peroxide and ferric / ferrous ions and the disposal of the iron sludge are factors which need to be taken into consideration (Shemer *et al*., 2006). One possibility is the partial use of Fenton reactions to produce a non-toxic and biodegradable intermediate which could then be treated in an inexpensive biological step to achieve complete mineralisation (Munoz *et al*., 2006).

Direct photolysis

Direct photolysis occurs due to the breakdown of a compound by the absorption of light. Indirect photolysis is caused when photosensitisers, such as nitrate and dissolved organic matter, absorb light and generate reactive oxygenated radicals that subsequently degrade other compounds (Legrini *et al*., 1993). Many pharmaceuticals are readily susceptible to photolytic transformation. APIs that do not absorb light above 290 nm are more resistant to direct photolysis with natural light (Khetan and Collins, 2007). Lamps employed in the removal of micropollutants focus mainly on low and medium pressure mercury lamps. Low pressure mercury lamps characteristically generate light at 254 nm while medium pressure lamps emit their energy at multiple wavelengths (Takashi *et al*., 2007). Using a 110W, 254 nm UV lamp at 313K and 0.5 g/L, a 70 % conversion of 0.25 L of 2-chloropyridine (typically found in effluent of pharmaceutical processing) was achieved in 20 min (Stapleton *et al*., 2006). Mefenamic acid was observed to undergo direct photolysis with a half-life of 33 h under direct noon sunlight in mid-October at 45° latitude (Werner *et al*., 2005). Carbamazepine and clofibric acid have photodegradation half-life times of 100 d in winter at 50°N. Conversely sulfamethoxazole, diclofenac, ofloxacin and propranolol undergo faster degradation with half-lives of 2.4, 5.0, 10.6 and 16.8 days, respectively. In a different set of experiments, clofibric acid, diclofenac, fenoprofen, isopropylantipyrine, ketoprofen, phenytoin and triclosan were removed in a laboratory situation (> 96 %) by ultraviolet photolysis alone (Giri *et al*., 2011). A fundamental parameter that determines the rate of degradation for photolysis is the decadic molar absorption coefficient. The decadic molar extinction coefficient is a measure of the capacity of a compound to absorb light. Ibuprofen, diphenhydramine, phenazone, and phenytoin have decadic molar extinction coefficients of 256/M/cm, 388/M/cm, 8906/M/cm and phenytoin 1260/M/cm, respectively. As indicated by the decadic molar extinction coefficients, 27.4 % removal of 5 µm initial concentration of ibuprofen, 26.34 % of diphenhydramine, 95.78 % and 87.75 % degradation for phenazone and phenytoin, respectively, was observed (Yuan *et al*., 2009). The experiment was carried out using a 11W low pressure lamp producing monochromatic UV light at 254 nm in a 500 mL quartz reactor. The antibiotic metronidazole achieved only 6 % removal with a low-pressure and 12 % with a medium pressure mercury lamp after 5 min exposure. Metronidazole has a crucial absorption centered at about 310 nm, which can be readily excited by a medium pressure lamp. In contrast, low pressure lamps only emit light at 254 nm and as a result, the important absorption at 310 nm is missed. The adsorption-lamp emission mismatch consequently explains the low removal with UVC light (Yuan *et al*., 2009). As such, direct photolysis on its own is not an effective for removing pharmaceuticals from wastewater. Alternatively, photolysis coupled with Fe (III) and H_2O_2 or TiO_2 can remove over 98 % of pharmaceuticals including estrogens (Feng *et al*., 2005; Benotti *et al*., 2009).

TiO_2 photocatalysis

Photocatalysis is the acceleration of a photochemical transformation by the action of a catalyst such as TiO_2 or Fenton's reagent (Chatterjee and Dasgupta, 2005; Herrmann, 2005; Dalrymple *et al*., 2007). Most photocatalysts are semiconductor metal oxides which characteristically possess a narrow band gap. Radicals formed degrade impurities in the water relatively unselectively, reacting with impurities in the wastewater as well as the target pharmaceuticals (Lhomme *et al*., 2008). Since the degradation of chlorobipenyls and biphenyls from aqueous media using TiO_2 photocatalysis was first reported (Carey *et al*., 1976) the number of publications on the removal of micropollutants from aqueous media using TiO_2 has grown considerably (Doll and Frimmel, 2005a, b, c; Pérez-Estrada *et al*., 2005a). Titania is the most widely investigated of the heterogeneous photocatalyst due to its cost effectiveness, inert nature and photostability (Gaya and Abdullah, 2008). Investigations into the removal of the pharmaceuticals using TiO_2, include but are not limited to work on

antibiotics, lipid regulators, x-ray contrast media, antiepileptics and antiphlogistics (Doll and Frimmel, 2005a, b and c; Perez-Estrada *et al*., 2005a). Removal rates have been reported at 98 % for antibiotics when used in combination with UV (Addamo *et al*., 2005). However, removal rates for carbamazepine are under 10 % (Doll and Frimmel, 2005a). TiO_2 is available at a relatively modest price and would be recyclable in an industrial application when fixed on films or beads, reducing the quantities of TiO_2 required (Legrini *et al*., 1993). Furthermore, solar studies have proved effective for a wide range of pharmaceuticals replacing the expense of generating UV light. There are difficulties in implementation on a commercial scale due to the number of operating parameters e.g. type and geometry of reactor, the photocatalyst, optimum energy use and wavelength of radiation. Moreover, it is difficult to assess the true success of the photocatalytic process in the absence of identified intermediate compounds and end products.

Photocatalytic reactors and reaction kinetics

In the development of photocatalytic reactors, many factors need to be considered including mass transfer, reaction kinetics, mixer, catalyst installation and catalyst illumination. Based on the arrangement of the light source, reactor configurations can be categorised as: 1) immersion type where lamps are inserted into the reactor, and 2) external type where lamps are put outside the reactor (Ray, 1998). One of the major impediments to the commercialisation of photocatalytic water treatment is the high cost of generating artificial radiation. Therefore, solar photocatalytic reactors have received considerable interest. To ensure efficient conversion of the incident solar radiation to charge carriers, the design of the solar reactor is extremely important. There are four frequently used reactor configurations: Parabolic trough reactor (PTR), Thin film fixed bed reactor (TFFBR), Compound parabolic collector (CPC) and Double skin sheet reactor (DSSR) (Bahnemann, 2004). PTRs concentrate sunlight into a focal line using parabolic mirrors. A TFFBR consists of a sloping plate coated with the photocatalyst and rinsed with the polluted water in a very thin film. The DSSR is a flat and transparent structured PLEXIGLAS® box. The polluted water and the photocatalyst can be pumped through channels in the box. A CPC is a combination of parabolic concentrators and flat static systems. Reactors can also be classified into concentrating and non-concentrating. These two types of reactors are compared in Table 1. CPCs are low concentration collectors which are a good option for solar photocatalysis since they combine the better features of concentrating and non-concentrating collectors and none of the disadvantages. The photoreactor is tubular so that water can be pumped easily. CPCs use direct and diffuse solar radiation efficiently without solar tracking. The water does not heat up and there is no evaporation of volatile compounds (Malato *et al*., 2007).

Table 1: Comparison of reactor types (Bockelmann *et al*., 1995; Malato *et al*., 2007)

	Concentrating	Non-concentrating
Example	PTR	TFFBR, DSSR and CPC
Advantages	Turbulent flow conditions which favour mass transfer and avoid catalyst sedimentation problems	Total global irradiation is usable
	Two axis sun tracking system	High optical efficiency
	Nearly closed reactor-no vaporisation of volatile contaminants	Low manufacturing costs due to its simple construction
	Smaller reactor tube area which is able to support higher pressures and a large amount of area per unit volume	No additional H_2O_2 necessary since there is effective transfer of air into the water film.
		High quantum efficiency
		No heating needed
Disadvantages	Only direct irradiation can be used	The volatile reactants can vaporise
	Low optical efficiency	The catalyst is not protected from pollution
	Since sun-tracking is needed there are high investment costs	A large catalyst area is needed when purifying large volumes of wastewater
	The TiO_2 needs to be separated from the purified water	There is low mass transfer due to the laminar flow conditions
	Water over-heating can lead to leaks and corrosion	Requires significantly more photoreactor area
	Additional H_2O_2 may be needed	

The DSSR and the CPC were compared for their treatment of dichloroacetic acid as a model pollutant. Using 5 g/L Hombikat UV 100 as the photocatalyst, the TOC decreased from 51.1 to 16.8 mg/L in the DSSR and from 51.6 to 18.4 mg/L for the CPC within 150 min. The ratio of the kinetic parameters, $k_{3\,cpc}/k_{3\,dssr}$ values indicate that the DSSR was slightly more efficient than the CPC. This ratio (smaller than 1 in almost all cases) reflects the different ability of the photo reactors to utilise the available light (Dillert *et al*., 1999).

Four different reactors -PTR, CPC, Tubular collector (TC) and V shaped trough collector (VC)- were compared for their ability to degrade oxalic acid in an aqueous suspension of TiO_2 (Bandala *et al*., 2004). The performance of the four detectors is quite similar in terms of energy accumulated however the TC produced the least degradation.

CPCs have also been used to compare heterogeneous solar photocatalysis and solar photo-Fenton reactions for the degradation of methyl-phenylglycine (MPG) contaminated wastewaters (Munoz *et al*., 2006). A Life cycle assessment (LCA) was done whereby the environmental impact was assessed by identifying and quantifying energy and materials usage and waste discharge impacts and evaluation of opportunities for environmental improvements over the whole life cycle. While both processes degraded the MPG from 500 to 0 mg/L, the environmental performance of solar photo-Fenton coupled to biological treatment was 80-90 % better than that of coupled heterogeneous photocatalysis to biological treatment. This was mainly due to the large CPC field (2150 m^2) and the electricity consumption of the TiO_2 microfiltration required in the photocatalysis experiments. Despite the success of the photocatalytic reactors in removing pollutants, there are a number of problems associated with them. TiO_2 is mostly applied in powder form and either has to be separated at the end (which is time-consuming and costly) or immobilised on a rigid support as a thin film (which limits the contact between the reactants and catalyst and thus the reaction rate). A potential solution to this problem is to use a Carberry type photoreactor which combines the advantages of slurry and immobilised photocatalytic systems. It was used to degrade 4- chlorophenol as a model organic compound. Its photocatalytic activity was 3.8 times higher than a configuration of two TiO_2 slides (which served as an approximation of a TFFBR) (Cernigoj *et al*., 2007). Other reactors with increased performance include the optical fiber reactor (Danion *et al*., 2004), corrugated plate reactor (Zhang *et al*., 2004), fountain reactor with a parabolic profile (Puma *et al*., 2001), Taylor vortex reactor (Dutta and Ray, 2004), fluidised photo reactors (Lee *et al*., 2003), Spinning disc reactor (Yatmaz *et al*., 2005) and labyrinth flow photoreactor with immobilised TiO_2 bed (Mozia *et al*., 2005). Most of the work to date on photoreactors has been on a laboratory scale, with only a limited number of large-scale applications of photocatalysis to wastewater treatment. Doll and Frimmel (2005a) investigated the combination of semiconductor photocatalysis with cross-flow microfiltration, which allowed the separation and reuse of TiO_2 after the photocatalytic degradation of clofibric acid, carbamazepine, and iomeprol. The majority of other pilot studies have been restricted to experiments with solar-type pilot plant apparatus, specifically those conducted at the Plataforma solar de Almeria (PSA) located in Europe. The efficiency achieved in the laboratory has not been achieved in these larger systems. One of the reasons for this is that small scale studies often fail to take into account the effect of other substances in the wastewaters (Doll and Frimmel, 2005b). Malato *et al*. (2002) described the experimental systems necessary for performing pilot-plant-scale solar photocatalytic experiments and outlined the basic components of these pilot plants and the fundamental parameters related to solar photocatalysis reactions. The pilot plant has been used successfully to treat pharmaceuticals along with other organic contaminants in wastewater (Perez-Estrada, *et al*., 2005b). The TiO_2 band-gap only represents 5 % of the solar spectrum. Other catalysts may be found which correspond better and could improve the efficiency of photo reactors. Other possibilities are changing catalyst structure and composition, the addition of electron acceptors or doping and deposition with metal ions and oxides (Rios-Enriquez and Shahin, 2004). Further research needs to be done in this area for pharmaceutical contaminated waters. In photocatalytic reactions, the contaminant substrate is oxidised by the photo-generated holes or by reactive oxygen species such as the $OH^{\bullet}$ and O^{-}_2 radicals formed on the surface of the catalyst. This mechanism requires that the contaminant adsorbs on the catalyst surface as a prerequisite for efficient oxidation (Serpone and Pelizzetti, 1989). Most researchers observe a Langmuir adsorption isotherm and describe the adsorption–desorption process and

the reaction rate constant based on the associated Langmuir-Hinshelwood (L-H) model (Xu and Langford, 2001; Rao *et al*., 2003), which is expressed as:

$$r = k\theta = -\frac{dC}{dt} = k(\frac{KC}{1+KC}) \quad (2)$$

Where r is the rate of mineralisation, k is the reaction rate constant, C is the concentration, K is the adsorption coefficient and θ is the fractional site coverage for the reactant (Herrmann, 1999). In general, adsorption studies are done in the dark and sometimes the adsorption capacity cannot be transferred quantitatively into irradiated systems (Xu and Langford, 2001). Studies indicated that increased adsorption to the catalyst surface translates to increased reaction rates (Xu and Langford, 2001; Rudder *et al*., 2004). However, it was found that with little difference in adsorption of carbamazepine on the surface of P25 and Hombikat UV100, the reaction rate and photo-adsorption was much higher with P25 as the catalyst (Doll and Frimmel, 2005b). Although the L-H model seems to adequately describe the macroscopic kinetics when dealing with very dilute aqueous solutions of photodegradable contaminants, some of the inherent assumptions of the model may not be valid at the microscopic level, which includes its failure to account for simultaneous adsorption (or desorption) of parent and intermediate compounds (Cunningham and Al Sayyed, 1990). Clearly, many different types of microscopic mechanisms could lead to the overall L-H type kinetic expression, but the derived kinetic parameters represent fundamentally different reactions and properties (Mandelbaum *et al*., 1999). Since most pharmaceuticals are present in trace concentrations, generally below 1μmol/L (KC<< 1), the L-H equation simplifies to a pseudo-first-order kinetic equation as follows:

$$r = -\frac{dC}{dt} = k_1 C \text{ or } C(t) = C_0 e^{-k_1 t} \quad (3)$$

Where k_1 is the Pseudo-first-order photo catalytic reaction rate constant. This Pseudo-first-order rate constant is often determined by observing the relative aqueous concentration changes of the contaminant as a function of time during experiments (Wei and Wan, 1992; Doll and Frimmel, 2005a; de Lasa *et al*., 2006; Tungudomwongsa *et al*., 2006).

Electrochemical treatment options

Electrochemistry is a relatively new method for the treatment of wastewater (Chen, 2004). The treatment of acetaminophen using anodic oxidation with a Boron-doped diamond (BDD) electrode has been successful during small scale investigations (Brillas *et al*., 2005). This process allows complete mineralisation of the acetaminophen due to the generation of large concentrations of hydroxyl radicals by the electrode. The BDD electrode was efficient even at low concentrations. BDD has high thermal conductivity, wide band gap, high e^- and hole mobilities, high breakdown electric fields, hardness, optical transparency and chemical inertness (Chen, 2004). Ultrasonic irradiation has been considered as a means of removing estrogenic compounds from contaminated water (Belgiorno *et al*., 2007; Suri *et al*., 2007). Hormones, for example, estradiol, estrone and ethinylestradiol, were examined in single component batch and flow through reactors using 0.6, 2 and 4 kW ultrasound sources (Suri *et al*., 2007). Results showed 80-90 % reduction in the hormones within a 40-60 min period (Suri *et al*., 2007). Further investigations in this area would be useful to determine the toxicity of breakdown products and to examine the feasibility of larger scale applications of the technology. Diamond anodes may produce $OH^\cdot$ radicals with high current efficiency. This is dependent on the mass transport of organic compounds to the anode not being a limiting factor.

CONCLUSION

Various treatment methods for pharmaceuticals in water and wastewater found in the literature have contributed greatly to our knowledge regarding the fate of these compounds in different treatment systems. Generalising compound behaviour in these systems would allow further characterisation of the fate and risk associated with pharmaceuticals in the environment, yet this description of trends is hindered by the wide variation in removal efficiencies across therapeutic classes, treatment processes, and even among separate studies for the same individual compounds. The majority of studies summarised used "removal" to describe the elimination of parent pharmaceuticals. The mere disappearance of the parent compound cannot be considered synonymous with complete removal. If adequate controls for physical and chemical removal mechanisms are in place, the loss of the parent compound indicates biotransformation of an unknown degree and not necessarily mineralisation. Only monitoring for metabolites or end

products of mineralisation can provide information about the degree of biotransformation.

The wastewater from pharmaceutical production facilities and municipal wastewater treatment plant are the primary source of APIs in the environment. A significant amount of research in the area has focused on municipal wastewater, as data from municipal wastewater plants are relatively accessible. However, research into wastewaters from pharmaceutical manufacturing plants is more problematic due to difficulties in accessing information. Nevertheless, treatment technologies that work for municipal wastewaters should also be suitable with modification for industrial wastewaters. There are a number of promising new treatments including AOPs such as oxidation, ozonation, perozonation, direct photolysis, TiO_2 photocatalysis, solar photocatalysis, Fenton reactions and ultrasonic irradiation. These significantly enhance the removal rate of pharmaceuticals from wastewaters. Comparisons among these technologies are problematic since most researchers used synthetic water rather than actual wastewater samples. Research is required in this area to improve treatment efficiencies, identify degradation compounds and to determine the cost and feasibility of full-scale applications. There is also interest in coupling AOPs with more conventional treatments such as activated carbon, which is the focus of ongoing research at Dublin City University (Keane *et al.*, 2011; Basha *et al.*, 2010). Finally, the problem of pharmaceuticals in wastewaters cannot be solved - even if it is considerably alleviated - merely by adopting end-of-pipe measures. At-source measures like replacement of critical chemicals, reduction in raw material consumption should continue to be pursued as the top priority.

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