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Review of advanced oxidation processes (AOPs) for treatment of pharmaceutical wastewater

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Abstract. Pharmaceutically active compounds (PhACs) have become an environmental havoc in last few decades with reported cases of antibiotic resistant bacteria (ARB) and antibiotic resistant genes (ARGs), lethal effects over aquatic organisms, interference in natural decomposition of organic matter, reduced diversity of microbial communities in different environmental compartments, inhibition of growth of microbes resulting in reduced rate of nutrient cycling, hormonal imbalance in exposed organisms etc. Owing to their potential towards bioaccumulation and persistent nature, these compounds have longer residence time and activity in environment. The conventional technologies of wastewater treatment have got poor efficiency towards removal/degradation of PhACs and therefore, modern techniques with efficient, cost-effective and environment-friendly operation need to be explored. Advanced oxidation processes (AOPs) like Photocatalysis, Fenton oxidation, Ozonation etc. are some of the promising, viable and sustainable options for degradation of PhACs. Although energy/chemical or both are essentially required for AOPs, these methods target complete degradation/mineralization of persistent pollutants resulting in no residual toxicity. Considering the high efficiency towards degradation, non-toxic nature, universal viability and acceptability, AOPs have become a promising option for effective treatment of chemicals with persistent nature.

Keywords: pharmaceutical drugs; AOPs; fenton; photocatalysis; ultrasonication

1. Introduction

The pharmaceutical industrial wastewater generated from different manufacturing processes contains wide variety of products. The industrial processes use organics as well as inorganic raw materials to produce a variety of drugs like analgesics, antibiotics, antidepressant, antiepileptic etc. which can be of synthetic, vegetable, or animal origin (Raj *et al.* 2003). These processes also utilize distinct kind of catalysts, reactants, solvents, solids, and water, which are handled in special equipments/units. The Drug master file (DMF) specifies some strict regulations due to which ultrapure water used for solid cake washing and as extractant cannot be utilized again for any other purpose (Gadipelly *et al.* 2014). Most of the wastewater generated from these processes are

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disposed without any specific treatment (Lang *et al.* 2006, Enick *et al.* 2007). The concern towards pharmaceutical wastewater was increased when around 100 pharmaceuticals and their metabolites were observed in effluent and surface water in various countries (Aston *et al.* 2004, Ankley *et al.* 2005). The wastewater generated from pharmaceutical industry is characterized with a wide range of pH from 1 to 11 and also contains higher biochemical oxygen demand (BOD), Chemical oxygen demand (COD) and total suspended solids (TSS). The wastewater is not suitable for physical and/or chemical treatment because of its low efficiency for dissolved COD removal and high consumption of chemicals (Oktem *et al.* 2007). Wastes originating from these plants are highly alkaline or acidic in nature. Manufacturing of Sulfa drugs and Vitamin B12 leads to the generation of highly alkaline waste whereas highly acidic waste is generated from manufacturing of organic intermediates. The chemicals from pharmaceutical industry are released into the environment and cause deleterious effects on ecosystem, animals, as well as human health. At the same time, most of the pharmaceuticals reach to aquatic environment such as wastewater treatment plants (WWTP) effluent, groundwater, sludge, surface water, and even treated drinking water (Garoma *et al.* 2010, Deghani *et al.* 2013). Heavy rainfall over contaminated land (promote surface water runoff), industrial effluents, and untreated sewage are responsible for distributing the pharmaceutical drugs and their metabolites through different compartments of environment (Santos *et al.* 2010). Some of the most common drugs found in aquatic environment are amoxicillin, atenolol, diclofenac, ibuprofen, ciprofloxacin, carbamazepine, ofloxacin, gemfibrozil, erythromycin, propranolol, and sulfamethoxazole (Fatta-Kassinos *et al.* 2011). Conventional technologies like flocculation, coagulation, sedimentation, filtration and disinfection are generally used to remove contaminants in drinking water treatment facilities but these are unable to degrade chemicals present in pharmaceutical wastewater. Microbial degradation is also not effective as these pharmaceutical drugs primarily resist microbes. Therefore, oxidation technologies known as advanced oxidation technology (AOT) is broadly evaluated for the degradation of pharmaceutical drugs. Advanced oxidation processes (AOPs) involve the in-situ production of powerful oxidants as hydroxyl radical so that it can efficiently degrade complex organic compounds to carbon dioxide and water. One of the most important part of this technology is production of the hydroxyl radical. Some of the common techniques of AOPs are Fenton reaction, photo-Fenton, photocatalysis, ultrasonication, electrochemical methods, and ozonation (Brillas *et al.* 2009, Sunil *et al.* 2013).

2. Environmental fate of pharmaceutical wastewater

The pharmaceutical drugs enter into the environment from treated patients as parent compound or as metabolites, direct release of drug into wastewater system from manufacturing, hospitals or domestic discharges and also through leaching from terrestrial deposition (Corcoran *et al.* 2010). There are various classes of pharmaceuticals such as antibiotics, analgesics, lipid regulators, beta-blockers, anti-inflammatory, steroids and related hormones and cancer therapeutics which are usually observed in environment. The pharmaceutical compounds reach to aquatic environment through various routes and sources as shown in Fig. 1. These drugs bioaccumulate in freshwater compartments including biofilms, sediments, invertebrates like *Hyalella azteoa, D. magna, C. dubia* and fishes like rainbow trout *(Oncorhynchus mykiss)*, brown trout *(Salmo trutta, F. fario)* etc. As these drugs have potential to affect aquatic organisms, their influence also extends to ecological processes and ecosystem functions. These drugs also influence biogeochemical cycling

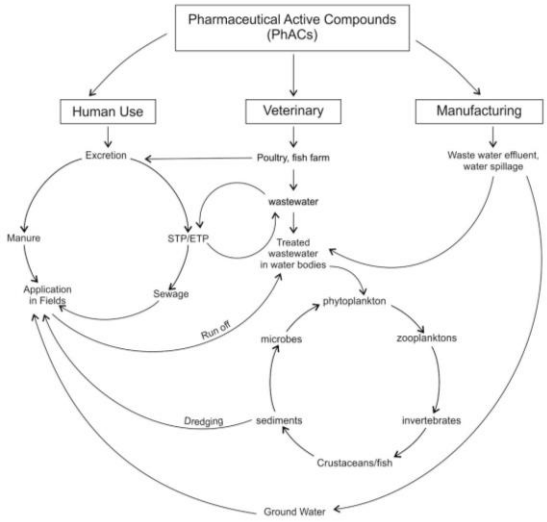

Fig. 1 Occurrence and fate of pharmaceutically active compounds (PhACs) in environment

of important elements through disruption of algal *(M. aeriginosa, S. acutus)* and bacterial *(V. fischeri, A. salmonicida)* communities. Ecosystem function such as organic matter decomposition, nutrient transformations, and invertebrate population dynamics, mediated by bacteria, fungi and invertebrate consumers are also influenced by these drugs (Fatta-Kassinos *et al.* 2011).

The persistence of drugs in soil or sediments is predominantly influenced by its photo stability, adsorption and binding capability, leaching in water, and rate of degradation. Strongly sorbing pharmaceuticals tend to accumulate in soil or sediments but most of the pharmaceuticals are highly mobile so they can leach into groundwater, and surface run-off to surface water (Diaz-Cruz *et al.* 2003). Presence of antibiotics in soil disrupts the soil microbial communities due to which development of plant is affected indirectly. It affects the soil ecosystem by decreasing the soil bacterial number which ultimately leads to food scarcity for soil fauna (nematodes, protozoa, micro-arthropods). It also slows the decomposition rate of plant residue and also slows the rate of denitrification due to which rate of recycling of nutrients reduces (Fatta-Kassinos *et al.* 2011).

Pharmaceutical drugs also enter in environment through fish farming. In aquaculture, drugs which are used as feed are additives directly discharged into the water. It was estimated that around 70% of drugs administrated were released into environment through over feeding, loss of appetite by diseased fish and poor adsorption of the drugs (Jacobsen *et al.* 1998). The veterinary drugs and active metabolites in huge amounts end up in sediments surrounded by aquaculture areas. A significant amount of these substances, available in sediments, is present in stable form and may lead to the development of antibiotic resistance, which ultimately leads to infections that are difficult to treat; simultaneously, the sediments behave as a reservoir for both, the compounds and the resistant bacteria (Silvia *et al.* 2003).

3. Characterization of pharmaceutical wastewater

Characteristics of wastewater play a significant role in selection of treatment process for the

Table 1 General characteristics of pharmaceutical wastewater

Parameters	India				Pakistan	Egypt	Korea	UK	China	
	Hussain *et al.* (2011)	Rana *et al.* (2014)	Raj *et al.* (2003)	Saravanane *et al.* (2001)	Saleem *et al.* (2007)	Badawy *et al.* (2009)	Behera *et al.* (2011)	Chelliapan *et al.* (2006)	Chen *et al.* (2008)	Madukasi *et al.* (2010)
pH	Alkaline	6.9	7.9	4	6.2-7.0	8.4	-	5.2-6.8	6.0-7.0	
TSS (mg/l)	-	370	7132	6000	690-930	133	109		-	8480
TDS (mg/l)	20000-35000	1550	28814	11000-18500	600-1300	17251	-		-	425
Total solids (mg/l)	-	1920	35886	-	-	-	-		-	
BOD (mg/l)	-	120	5992	2000	1300-1800	2650	84	3500	750-10800	534
COD (mg/l)	30000-42000	490	12378	12000-15000	2500-3200	9703	122	7000-8000	5000-60000	
Biodegradability (BOD/COD)	-	0.259			-	0.27	-	-	-	-
Alkalinity (mg/l)	-	130-564			90-180	518	-	-	-	-
Total nitrogen (mg/l)	-	-			-	764	29	364	560-980	1600
Ammonium nitrogen (mg/l)	-	-		15-40	-	296	-	-	36-261	-
Total phosphate (mg/l)	-	-			-	-	3.0	-	51.4-120.4	-
Turbidity (NTU)	-	-	-	-	2.2-3.0	-	-	-	-	-
Phenol (mg/l)	-	-	-	-	95-125	43	-	-	-	-

wastewater. The pharmaceutical wastewater originates from variety of processes and raw materials used in manufacturing of drugs differing in their volume and composition not only from plant to plant but also from section to section in plant (Davis *et al.* 1998). The waste water is characterized by high BOD, chemical oxygen demand (COD) and a low BOD/COD ratio because of which biological treatment is ineffective (Ferrari *et al.* 2003) (Table 1). Apart from it, there is significant concentration of antibiotics and other drugs which can kill microorganisms involved in wastewater treatment.

4. Treatment of pharmaceutical wastewater

Conventional treatment methods used for the treatment of pharmaceutical wastewater includes physicochemical and biological treatment methods. Earlier treatment of wastewater using biological method was most commonly used and economical method (Kulik *et al.* 2008) but it was found that these methods are not that much effective for the removal of persistant constituents present in wastewater (Clara *et al.* 2005). Biological methods are further classified as aerobic and anaerobic processes. Activated sludge method, membrane batch reactors and sequential batch reactors are included in aerobic methods (LaPara *et al.* 2002) while anaerobic methods includes anaerobic film reactors, anaerobic sludge reactors, and anaerobic filters (Gangagni *et al.* 2005,

Enright *et al.* 2005). Anaerobic treatment has more potential to treat high-strength wastewater compared to aerobic process with less energy input, operational cost, requirement of nutrients, sludge yield, recovery of biogas, and requirement of space. But, anaerobic processes are not as effective in treating the pharmaceutical wastewater that carries recalcitrant xenobiotic compounds which are non- biodegradable to microbial mass within the conventional treatment (Deegan *et al.* 2011). The other treatment technologies used for treatment of pharmaceutical wastewater are physico-chemical treatment methods such as membrane separation, chemical removal, activated carbon adsorption, air stripping etc. These methods are responsible for transferring the pollutant from one phase to another rather than destroying them completely (Elmolla *et al.* 2010).

AOPs, on the other hand, are found to be most effective treatment technology for completely mineralizing the pollutants to inorganic compounds, CO_2 and water (Poyatos *et al.* 2010). AOPs act as low cost, easy to operate and effective options for treatment of pharmaceutical wastewater and can also be coupled with biological or conventional physico-chemical processes to design cost effective solutions. AOPs are based on generation of highly reactive hydroxyl radical which can rapidly oxidize the target pollutants non-selectively (Chelliapan *et al.* 2013). Hydroxyl radicals have oxidation potential of 2.80 V vs NHE, second only to Fluorine. There are various technologies included in AOPs such as Fenton, photo-Fenton, ultrasonication, photo-catalysis, etc. which differ in mechanism of radical generation (Kim *et al.* 2011). It was also reported that the combinations of AOPs are more efficient in removal of organic compounds than that generated with individual techniques (Mendez-Arriagad *et al.* 2009). Various technologies included in AOPs are discussed below.

4.1 Photo-catalysis

Among the various AOPs, photocatalytic oxidation process is regarded as a promising technique for treatment of pharmaceutical wastewater due to its non-toxic nature, absence of mass transfer limitation, relatively cost-efficient, chemically stable and it can even be operated at ambient temperature (Elmolla *et al.* 2010, Sharma *et al.* 2015, Sharma *et al.* 2016). During Photo-catalysis, reaction is stimulated in the presence of photons and a catalyst. Homogenous and heterogenous photo-catalysis are the two main classes of photo-catalysis. In homogenous, catalyst and the substrate both appear in same phase while in heterogenous, process move at the periphery of two phases i.e., aqueous or gaseous phase and solid photo-catalyst phase (Brillas *et al.* 2009, Almeida *et al.* 2011). Various photo-catalysts which can be used for treatment of persistent pollutants are iron (III) oxide (Fe_2O_3), zinc oxide (ZnO), tungsten trioxide (WO_3), Titanium dioxide(TiO_2), zirconia (ZrO_2), and vanadium oxide (V_2O_5) (Kudo *et al.* 2009). A photo-catalyst can be considered as ideal when it has properties like photo-activity, biological and chemical inertness, stability toward photo corrosion, suitability towards visible or near UV light, low cost, lack of toxicity etc. (Bhatkhande *et al.* 2001). Among various photo-catalysts, TiO_2 and ZnO are found to be the most efficient catalysts for degrading recalcitrant pollutant. Titanium dioxide (TiO_2) is a mixture of anatase and rutile forms and possesses the properties like photostability, non-toxicity, inexpensive, photoreactive and chemical and biological inertness (Friedmann *et al.* 2010). At room temperature, ZnO is a n-type of semiconductor which possess a broad band gap of 3.2 eV and binding energy of 60 meV. It also provides good biocompatibility, piezoelectric characteristics and also the photochemical stability (Benhebal *et al.* 2010). Photocatalytic performances ZnO and TiO_2 are expected to be similar as both possess same band gap energy (Lee *et al.* 2016). Some of the factors like charge-transfer dynamics, morphology, and surface

interactions regulate the performance of semiconductors (Kamat *et al.* 2002). Photo-catalysis is initiated when the photo-catalyst particle gets excited with quantum of light. The particles get photo-excited by radiation having energy equal or higher than the band gap energy of semiconductor (Almeida *et al.* 2011). When the photon particles get absorbed, electron from the low-energy valence band moves to the high-energy conduction band transported with formation of electron-electron gap pairs and this starts a chain of redox reductions which lead to degradation of organic contaminants (Hoffmann *et al.* 1995). Light of wavelength 300-400 nm can be given by using UV lamps or by solar rays. In recent years, several studies have been focused on use of nano-sized TiO_2 and ZnO photo-catalysts in the form of nanorods, nanospheres, thin porous films, nano fibers and nanowires for treatment of recalcitrant compounds in wastewater because of their high activity, low-cost and environmentally safe nature. Nano particles have very high surface to volume ratio in nanostructures which makes them efficient for photo-catalysis (Mondal *et al.* 2013).

Various researchers have studied the degradation of pharmaceutical drugs using photocatalysis and observed complete degradation of drugs. Safari *et al.* (2015) studied the degradation of tetracycline antibiotic using TiO_2 photocatalysis and also added H_2O_2 to enhance the reaction. It was observed that the TiO_2 photocatalysis could efficiently degrade tetracycline at maximum concentration of 1.0 mg/l while addition of H_2O_2 reduces the time duration to completely degrade the tetracycline. Similarly, degradation of Metronidazole was studied by Farzadkia *et al.* (2015) and this study reported that with increase in dose of TiO_2, increases degradation of Metronidazole and the maximum degradation was achieved at 0.5 g/l at neutral pH within 180 minutes. Kaur *et al.* (2016) synthesized Bi_2WO_6 nano cuboids and studied the photocatalysis process using the synthesized Bi_2WO_6 nano cuboids to degrade levofloxacin and observed that more than 80% degradation was achieved within 150 minutes of reaction time. All such studies have confirmed that photocatalysis has got a significant potential towards treatment/mineralisation of PhACs.

4.2 Fenton like processes

Fenton process is another AOP which can efficiently degrade the pollutants. In Fenton process, under acidic conditions (pH 3.0), Ferrous ions (Fe^{2+}) combine with hydrogen peroxide (H_2O_2) to generate hydroxyl radicals ($OH^{\cdot}$) (Kavitha *et al.* 2004, Bagal *et al.* 2014, Verma *et al.* 2019). Fenton process preferably works at pH range of 2-4. Several studies reported the limitations of Fenton process like high hydrogen peroxide cost, iron sludge produced during process require additional treatment, storage risk, require neutralization of treated solution before disposal etc. (Bagal *et al.* 2014). To overcome the disadvantages of Fenton process, photo- assisted Fenton reaction can be used. Photo-Fenton process as compared to dark fenton reaction leads to rapid mineralization as well as higher rate of reaction (Vilar *et al.* 2012). During photo-Fenton process, H_2O_2 oxidizes Fe^{2+} ions to produce Fe^{3+} and also there is generation of one equivalent ($HO^{\cdot}$). The Fe^{3+} generated serve as an electron acceptor during the photo-exposed reaction and lead to production of one more radical whereas Fe^{2+} is reproduced in aqueous solutions as shown in Eqs. (1) and (2) (He *et al.* 2004)

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

$$Fe^{+3} + H_2O + h\upsilon \rightarrow Fe^{+2} + {}^{\cdot}OH + H^{+} \quad (2)$$

Several researchers have reported that the application of solar light as compared to UV lamps is

more economical and better alternative for the treatment of recalcitrant pollutants (Luna *et al.* 2014). It was also reported by several researchers that the Ferrioxalate (FeOx) can also be used for degradation of organic pollutants in photo-Fenton process. Ferrioxalate strongly absorbs between 250 and 500 nm and has high quantum efficiency so it is highly suitable for solar applications (Trovo *et al.* 2008).

During the past few years electrochemical advanced oxidation processes (EAOPs) has become more popular among the AOPs as these are more effective for degradation of refractory organic compounds. EAOPs are involved in production of strong oxidants like sulfate or hydroxyl radicals (in situ) in water medium. Various technologies involved in EAOPs are anodic Fenton, electro-Fenton and anodic oxidation. The degradation of compounds in EAOPs is carried out through direct electrolysis or indirect electrolysis. In direct electrolysis, there is direct exchange of electrons between the compounds and anodic surface and the participation of other substances is nil. In indirect electrolysis, there is reformation of electroactive species which behaves as a mediator for exchanging the electrons between the compounds and electrode. Efficiency of EAOPs can be increased by adding some external sources like UV light in photo-electro-Fenton or ultrasound in sono-electro-fenton or by combining it with other processes for improving degradation (Oturan *et al.* 2018).

Anodic oxidation is based on direct EAOPS in which origin of hydroxyl radicals takes place through the oxidation of water over the highly oxygen developing anodic surface (Panizza and Cerisola, 2009). Some of the electrode materials like platinum, Boron doped diamond (BD) etc. are considered as efficacious materials for electrode. In doped diamond, at the time of electrolysis, the area where the discharge of water takes place, the BD anodes encourage the generation of hydroxyl radicals which ultimately degrade the compounds with high current efficiency as shown in Eqs. (3) and (4).

$$BD + H_2O \rightarrow BDD(^{\bullet}OH) + H^+ + e^- \quad (3)$$

$$BD(^{\bullet}OH) + R \rightarrow BDD + CO_2 + H_2O \quad (4)$$

The degradation of antibiotic Trimethoprim (TMP) was studied by González *et al.* (2011), and the study reported complete degradation of TMP at flow rate $1.25 cm^3 min^{-1}$, pH 3 and the current density of 207 $mAcm^{-2}$. BDD can also be effective for degradation real pharmaceutical effluent. Based on experimental study done by Domínguez *et al.* (2011), almost complete removal of TOC was observed for real pharmaceutical effluent and the paramaters such as flow rate and current density show maximum degradation within residence time of 77minutes.

Degradation of amoxicillin (AMX) was carried out using nanoscale zero-valent iron (nZVI) can also be used as catalyst. It was observed that around 25% AMX was degraded using nZVI while more than 85% AMX was degraded using nZVI/H2O2 within 25 minutes at nZVI 500 mg/l, H_2O_2 6.6 mM, pH 3.0 and AMX 50 mg/l. A possible mechanism for Fenton-like degradation of AMX using nZVI/H_2O_2 was also proposed as shown in Fig. 2 (Zha *et al.* 2014).

Electro-Fenton process is indirect EAOPs in which production of hydrogen peroxide is carried out in-situ on the cathode surface in acidic medium. Then the fenton reaction takes place by combining the electrolytically produced hydrogen peroxide and externally added ferrous ions. Production of ferric ions takes place which further undergoes cathodic reduction and leads to regeneration of ferric ions as shown in Eqs. (5), (6), (7), and (8). During Electro-Fenton process pH remains under control because of production of protons at anode and production of carboxylic acids while in conventional Fenton's process pH is not controlled because of the production of

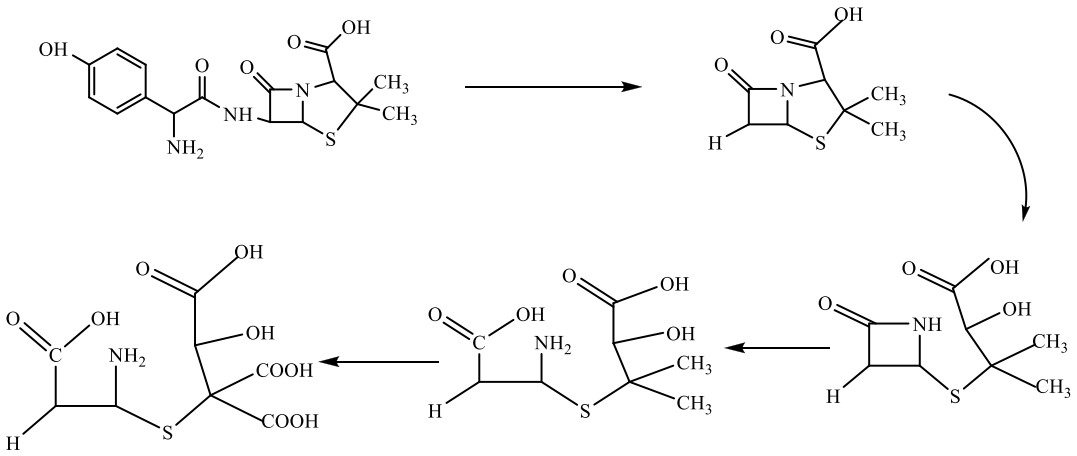

Fig. 2 Degradation pathway for amoxicillin (AMX)

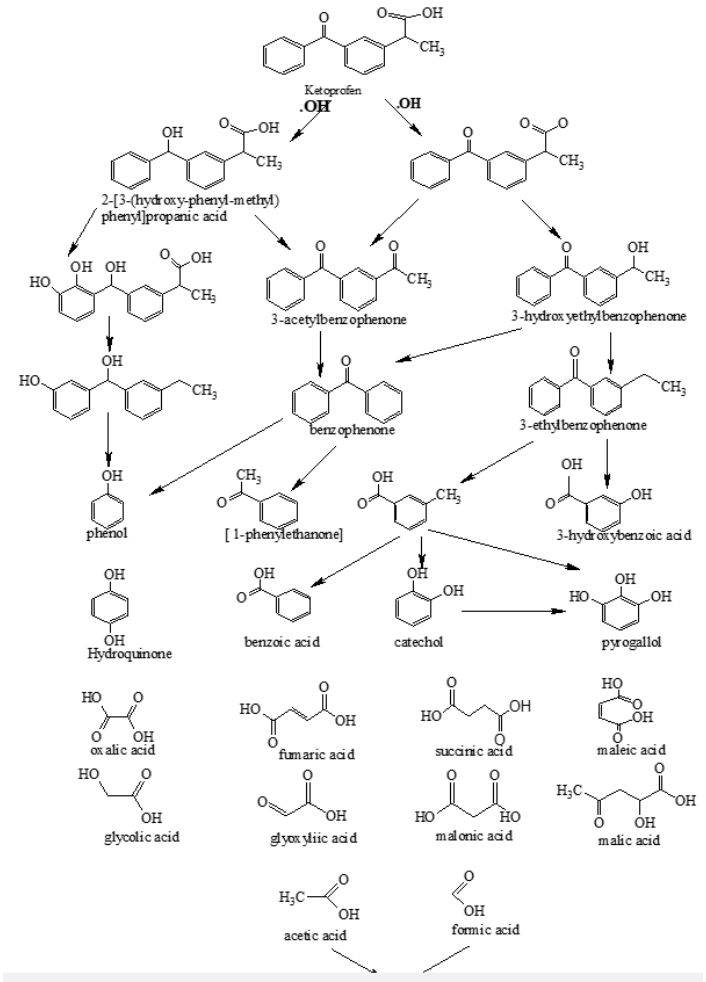

Fig. 3 A reaction pathway for mineralization of ketoprofen

hydroxyl ions in water. Electro-AOP was categorized into two types on the basis of catalyst physical nature: Homogenous and Heterogenous process. In homogenous process, iron like ferrous sulfate and ferric chloride are used in soluble form as a catalyst while in heterogenous process solid catalysts are used which are slightly soluble or insoluble in water.

$$BD + H_2O \rightarrow BDD(^{\bullet}OH) + H^+ + e^- \quad (5)$$

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + HO^{\bullet} \quad (6)$$

$$Fe^{3+} + e^- \longrightarrow Fe^{2+} \quad (7)$$

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \quad (8)$$

Electro-Fenton (EF) and anodic oxidation (AO) processes using platinium (Pt) and boron-doped diamond (BDD) anodes and carbon felt cathode was used to study the degradation of ketoprofen which is a non-steroidal anti-inflammatory drug. It was observed that rate of degradation was increased with increase in applied current and complete mineralization was achieved with Pt, BDD anodes and carbon felt cathode. The reaction pathway for mineralization of ketoprofen was studied by Feng *et al.* (2014) as shown in Fig. 3. Electro-Fenton process is advantageous as it is highly efficient in degradation, no sludge production, regeneration of ferrous ion is more and also production hydrogen peroxide is in-situ.

4.3 Ozonation

Ozonation is another type of AOP which is used for the treatment of recalcitrant pollutants (Gerrity *et al.* 2012, Hollender *et al.* 2009). There are two pathways through which ozone reacts with wastewater; one in which ozone directly attack on acidic points while in indirect action highly oxidizing radicals are produces which act as secondary oxidants (Hollender *et al.* 2009, Gamal *et al.* 2006). When the ozone reacts directly, it is accompanied by an electrophilic aromatic substitution and leads to selective processes (Gamal *et al.* 2006). There is an establishment of secondary oxidation pathway due the reaction of radical species mainly hydroxyl radicals which are generated from the decomposition of ozone (Staehelin *et al.* 1985). Although ozone can efficiently degrade different types of pharmaceuticals (Brosus *et al.* 2009), but even then ability of ozone to mineralize pharmaceuticals is limited (Vogan *et al.* 2004). In order to determine the effectiveness of ozonation on pharmaceutical waste water and also to decrease the risk of intermediates formed, it is important to analyze the toxicity of the water before and after the ozone treatment ((Brosus *et al.* 2009). Ozone is advantageous as it generates less noxious and more biodegradable by-products; able to completely mineralize the organic contaminants; and also able to handle varying compositions and flow rates (Ikehata *et al.* 2006, Zhu *et al.* 2001). Various studies reviewed by Ikehata *et al.* (2006) showed that ozonation and AOPs are highly efficient to degrade pharmaceutical compounds. Various pharmaceuticals such as carbamazepine, diclofenac, and estrogen 17b-estradiol show highest degree of reactiveness toward molecular ozone whereas some pharmaceutical compounds like clofibric acid, a lipid regulator metabolite, anti-anxiety diazepam, and ibuprofen, a NSAID, show resistance to ozonation. Ozonation process may not be able to completely mineralize the target compound, and may also lead to generation of harmful by-products from the compounds present in the pharmaceutical wastewater. (Larsen *et al.* 2004).

It was reported in various studies that combination of ozone with other AOPs enhances the

degradation rate. Combination of ozonation with sonolysis can efficiently mineralize the drugs like diclofenac. When sonolysis and ozonation are combined they show synergistic effect, and it is due to the increase in degradation of O_3 bubbles during sonolysis which leads to generation of more free radicals (Naddeo *et al.* 2015). Kim *et al.* (2010) studied the degradation of real pharmaceutical wastewater using O_3 and combination of O_3 processes (O_3, O_3/H_2O_2, and O_3/UV). It was observed that individual O_3 process may increase the concentration of bromate ion in effluent while O_3 process combined with H_2O_2 and UV may lead to generation of very less unconsumed dissolved ozone and prevents generation of bromate ion. So, it can be an effective option to degrade pharmaceutical compounds.

4.4 Ultrasonication

Ultrasound removes pollutants without the generation of contaminants and can be regarded as a 'green' technology. Under the periodic pressure variations, acoustic cavitation implies the formation and subsequent expansion of micro-bubbles which leads to production of ·OH radicals (Li *et al.* 2010, Eren 2012). Ultrasound carries out acoustic cavitation mainly above 20 kHz. When ultrasound irradiation propagates in solution, a sequence of compression and rarefaction waves occurs. Cavitation bubbles are formed which increase in size and reach to an unsteady size at sufficient high power causing the bubble to collapse violently. At high temperature and pressure of 2000℃ and 200 atm, respectively, the auxiliary liberation of heat leading to formation of 'hotspots' within the reaction mixture. At these extreme conditions of temperature and pressure, the bond of dissolved gases, organic substances and water vapors gets ruptured and ultimately leads to generation of hydroxyl radical from water dissociation as indicated in Eq. (9).

$$H_2O +))) \rightarrow {}^{\cdot}H + {}^{\cdot}O \quad (9)$$

The perhydroxyl radical is formed in presence of oxygen as shown in Eq. (10).

$$^{\cdot}H + O_2 \rightarrow {}^{\cdot}OOH \quad (10)$$

The radicals which are fabricated disperse in the suspension while at the same time hydrogen peroxide liberated from the incorporation of ·OOH and ·OH radicals.

$$2{}^{\cdot}OH \rightarrow H_2O_2 \quad (11)$$

$$2OOH \rightarrow H_2O_2 + O_2 \quad (12)$$

There are three zones which can be characterized in cavitation process i.e., bulk of dissolution, supercritical interface, and cavitation bubble (Mendez-Arriaga *et al.* 2008).

The degradation of pharmaceuticals drugs such as diclofenac (DCF), amoxicillin (AMX), carbamazepine (CBZ)) individually and by mixing them with urban wastewater effluent was studied by Naddeo *et al.* (2009). The initial substrate concentration was varied from 2.5-10mg/L and pH was varied from 3-11. It was observed that at lower frequency, with or without mixing the samples in wastewater, low frequency sonication can efficiently degrade the compounds by generating the hydroxyl radical and it acts as better pretreatment option for biological and other oxidation processes.

The degradation of amoxicillin using high frequency ultrasonic waves (2.4MHz) and without ultrasonic waves was studied by Matouq *et al.* (2014). The concentration of amoxicillin and concentration of outlet wastewater effluent was selected to be similar in pharmaceutical industry as

Table 2 Advantages and Disadvantages of different AOPs

Technologies	Advantages	Disadvantages
Photocatalysis	• Cost-efficient • Non-toxic • Mass transfer limitation is absent • Chemically stable and can be operated at ambient temperature	• Separation of catalyst is required if it is present in form of slurry • Requirement of UV light for surface activation
Fenton like processes	**Fenton** • Highly efficient • Easy to operate • Reaction time is less **Photo-Fenton** • Rapid mineralization • High rate of reaction • Reduced iron sludge production **Electro-Fenton Process** • Production of H_2O_2 is in-situ so risk of handling, storage and transportation can be avoided • Continuously regenerate Fe^{2+} on cathode which decreases iron sludge production • Higher degradation efficiency	**Fenton** • Generation of iron sludge • Low pH is required **Photo-Fenton** • High operation cost • Cost of UV-visible lamps **Electro-Fenton process** • Low conductivity • Low current density • H_2O_2 yield is low
Ultrasonication	• Initiates reaction without external reagents • Generates mass transfer effect at microscopic and macroscopic levels	• Full scale application is missing • Oxidation is needed to improve the efficiency of the treatment which increases the cost
Ozonation	• Generates less noxious and more biodegradable by-products • Able to handle varying compositions and flow rates • No sludge production	• Ability of ozone to mineralize pharmaceuticals are limited • Complex technology

50 and 100ppm. The rate of degradation of antibiotic amoxicillin was increased when ultrasound waves and hydrogen peroxide (H_2O_2) were applied together. It was observed that the ultrasound waves double the degradation of amoxicillin (90 minutes) than without ultrasonic waves.

5. Conclusions

In comparison to conventional technologies, AOPs are more efficient to degrade pharmaceutical drugs. Several advantages of AOPs include mild operation condition, low-cost, and complete mineralization of compounds. There are certain advantages/disadvantages associated with each of the processes; therefore, the selection of process/technique requires thorough analysis of all the input parameters associated and the kind of output desired during the treatment (Table 2). Combination of AOPs generates more $^{\cdot}OH$ radicals and improves the efficiency towards degradation of pharmaceutical drugs. AOPs are environment friendly as these

do not result in generation of any kind of waste, and are responsible for complete degradation pharmaceutical drugs. So, AOPs can also be called as 'green technology' or 'clean technology'. Complete mineralization of drugs helps overcome the problems related to drug resistance, environmental pollution and elimination of toxicity being induced in the environment.

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