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Fate and Occurrences of Pharmaceuticals and Their Remediation from Aquatic Environment

Ardhendu Sekhar Giri

Abstract

Pharmaceuticals have been present in our world's waters since humans began experimenting with medicines; however, product propagation and ready access to pharmaceuticals coupled with burgeoning human population have significantly increased the loading of these compounds into the environment. Pharmaceutically active compounds (PhACs) are considered to produce a biological activity on humans and animals. Drugs manufacturing processes lead to release of toxic organic compounds and their metabolites into the environment. Safety and toxicology studies have used to investigate the side effects of pharmaceuticals on human and animal health. Treatment processes can and do reduce the concentrations of pharmaceuticals in water, however, the degree of efficacy is often a function of chemical structure, cost, and energy. All treatment processes have some degree of side effects, such as generation of residuals or by-products. This paper provides a concise report on removal of PhACs by recent advances oxidation processes (AOPs) where hydroxyl radicals (HO $\cdot$) acts as a common oxidant and the improvement of biodegradability to a level amicable for subsequent biological treatment.

Keywords: pharmaceuticals, metabolites, toxicity, wastewater, biological treatment

1. Introduction

Pharmaceutical compounds are released widely into the environment without proper treatment. Proper elimination of Pharmaceutically active compound (PhACs) present in aquatic system plays an important role for preventing of diseases both in humans and animals. PhACs are structurally complex in nature and these organic compounds have some intrinsic characteristics so that treatment of drug contaminated water using conventional treatment processes namely, membrane-based separations, adsorption, ion-exchange and biological treatment are not that efficient for the industrial applications [1]. Researchers have been continuously working to progress technically, environmentally and economically comprehensive treatment techniques.

To quantify the impact of PhACs on the environment several attempts have been made in the past few years. Low levels of PhACs including antibiotics, analgesics, anti-depressants, beta-blockers, and hormones & hormone mimics are detected in

Parameters	Typical values
pH	6.5–7.0
BOD, mg/L	1,200–1,700
COD, mg/L	2,000–3,000
BOD/COD	0.57–0.6
Suspended solids, mg/L	300–400
Volatile acids, mg/L	50–80
Alkalinity as CaCO ₃ , mg/L	50–100
Phenols, mg/L	65–72

Table 1.
Characteristics of pharmaceutical industry wastewater producing allopathic medicines [2].

surface, ground and drinking water resources apart from wastewater effluent Globe [2]. However, the removal efficiency is highly variable, and it can be substantially less than 100%. Carballa et al. (2005) suggested that due to their relatively long environmental half-life, many PhACs may be accumulated to the measurable levels in aquatic ecosystems. Concentrations of PhACs were found to be less than one ppb, while the combined concentrations beat ppm ranges [2]. These drugs are highly active and interactive with receptors in humans and animals and are toxic in nature towards health threatening organisms such as bacteria, fungi and parasites. Moreover, human and animal health are affected by various types of organisms and also targeted by PhACs. Therefore, PhACs may have some potential effect on the aquatic and terrestrial organisms [3]. They are usually uncovered as waste for a long time. Therefore, many scientists have started to discover the effects of organisms to various PhACs [4]. Some drugs like an analgesic and anti-inflammatory are universal for their applicability in the medical field and in effluents of WWTPs. They are discharge recipient water at concentrations range of $\mu\text{g/L}$. For an example, the concentration of diclofenac is found in WWTP as $1.4 \mu\text{g/L}$ [5].

Due to presence of carboxylic moieties ($-\text{COOH}$) and one or two phenolic hydroxyl groups ($-\text{OH}$) most of these types of drugs are acidic in nature. Antibiotics are used generally to prevent bacterial infections and they are used in veterinary applications as food additives at sub-therapeutic doses to treat food efficiency and promote growth [6]. Carballa et al. [7] reported that wide application of antibiotics may lead to bacterial resistances. The occurrence of different drugs in sewage sludge of WWTPs and surface is well reported [8, 9]. Common PhACs present in various industrial effluents is summarized in **Table 1**.

2. Sources of PhACs in water and wastewater

2.1 Agriculture and agriculture industry

Variety of PhACs made from recombinant proteins potentially has greater efficacy and fewer side effects than small organic molecules [10]. Bacteria or yeast commonly produced the recombinant proteins [11]. However, pharming does not require expensive for the production of proteins or their metabolic products. Also, the production capacity can be rapidly climbed up to meet the demand. It is projected that the expense of producing a recombinant protein via pharming will be less than 60–70% of the current cost [12]. Uses of large amount of water and causes

extensive pollution are found in agricultural industry. Overflow from agricultural fields often contains fertilizers, eroded soil, pesticides and pharmaceuticals that could able to form a major source of water pollution [13].

2.2 Health care facilities

Varieties of antibiotics have been isolated from urban and hospital wastewater [14]. It has been found that they simply could pass through aquatic environment and be transferred to surface water [15]. Kim and Tanaka [16] suggested that both wastewater treatment processes and the microbial ecology in surface water were disturbed by antibiotics and disinfectants.

Chang et al. [17] found different PhACs including analgesics, beta-blockers, non-steroidal anti-inflammatories, alpha-antidepressants, anti-cancer drugs, anti-fungal agents, opiates, antibiotics, anti-coagulants, diuretics, anti-anginals, anti-diabetics and hypolipidemics are detected by in hospitals effluents. Unregulated disposal of unused and expired medicines is the primary inception of PhACs into the environment from hospitals and health care facilities [17]. Rejection of syringe into the hospital drain off after application on the patient’s body also an important source of PhACs is [18].

Figure 1. Pathways for inception of pharmaceuticals and their metabolites in the environment [20].

Parameters	Typical values
Drinking water, µg/L	0.3
Surface water, µg/L	2
Ground water, µg/L	1
Municipal sewage (treated), µg/L	10
Biosolids (treated), µg/kg	10000
Agricultural soils, µg/kg	10

Table 2. Concentrations of pharmaceuticals in water and solid wastes [2].

2.3 Surface water and ground water

Due to incomplete elimination pharmaceutical products, the residues of these products can enter the aquatic environment [19]. The typical concentration of PhACs in water and solid wastes is summarized in **Table 1**. However, the concentration in untreated industrial wastewater varies from ppb to ppm levels. Different pathways for initiation of pharmaceuticals and their metabolites in the environment are shown in **Figure 1**. The typical values of different parameters of pharmaceutical industry wastewater are shown in **Table 2**.

3. Techniques for treatment of pharmaceutical wastewater

3.1 Adsorption technique

The efficiency of adsorption process is studied by numerous workers for treatment of wastewater containing varieties of drugs. Especially the porosity and surface area of adsorbent shows the extent of adsorption [19]. Dutta et al. [21] reported that both adsorption and desorption efficiency of 6-aminopenicillanic acid (6-APA) in aqueous effluent using activated carbon as an adsorbent was found to be 93% and the process is highly reversible in nature. About greater than 90% of oestrogens is removed from both powdered activated carbon (PAC) (5 mg/L) and granular activated carbon (GAC) can remove [22]. However, dissolved organic compounds (DOC), surfactants and humic acids participate with binding sites to block the pores within activated carbon structures [22]. A filtration step is important to increase removal efficiency before treating micro pollutants using PAC [23, 24].

High molecular weight compounds reduce the blocking of micropores that leads to decrease in carbon demand. Thus, PAC will be suitable for the treatment of pre-treated effluent with a low organic loading [23]. Separation of fine carbon particles is the general difficulty with PAC treatment. An additional step of separation is usually needed such as sedimentation, which necessitates the use of precipitants, or via (membrane) filtration.

3.2 Membranes processes

Membrane-based separation methods like MBR (membrane bioreactor), MBR/RO (MBR followed by reverse osmosis) and UF/RO (ultra-filtration followed by RO) are used for the removal of PhACs from wastewater [22]. Maeng et al. [25] suggested that PhACs like ibuprofen, naproxen, caffeine and acetaminophen and can be expressively removed using MBR and the degradation efficiency can be as high as 82%. However, the adaptation of microorganisms to less degradable compounds can occur due to its enhanced sludge retention time (SRT) in MBRs. MBR treatment has a better performance (removal >80%) than the conventional processes for diclofenac, ketoprofen, ranitidine, gemfibrozil, bezafibrate, pravastatin and ofloxacin. Chang et al. [17] obtained about 95% COD and 99% BOD reduction from a 10 m³ per day capacity MBR operated at a pharmaceutical facility. Nano filtration (NF) and RO membranes are more efficient in eliminating PhACs having different physico-chemical properties. The removal using NF is mostly over 85%, except for gemfibrozil (50.2%), bezafibrate (71.8%), atenolol (66.6%), mefenamic acid (30.2%) and acetaminophen (43%) [26]. Short circuiting of membrane or failure of membrane support is responsible for the reduction of permeate quality. However, the retentate must be treated further to degrade the more concentrated form of PhACs.

3.3 Biological treatment

These processes use to remove contaminants by assimilating them and it has long been a support of wastewater treatment in chemical industries using bacteria and other microorganisms. In any biological system, the main factor is the supply of an adequate oxygen as cells need not only organic materials as food but also oxygen to breathe. A wide range of natural and xenobiotic chemicals in pharmaceutical wastewater are recalcitrant and non-biodegradable in nature. Anaerobic processes are not always effective in removing such substances [23]. Conventional activated sludge treatment (AST) with a long hydraulic retention time (HRT) generally is the choice for pharmaceutical industry wastewater [27]. It needs a lower capital cost than advanced treatment methods and a limited operational requirement. However, it suffers from the production of large amounts of sludge [22]. Removal efficiencies are decreased due to development of more resistant microorganisms towards many PhACs [28]. Ibuprofen, naproxen, bezafibrate and estrogens (estrone, estradiol and ethinylestradiol) showed a high degree of removal while sulfamethoxazole, carbamazepine and diclofenac displayed limited removal efficiency [29]. A few studies are carried out using sequence batch reactors (SBRs) and MBRs to improve the efficiency of AST [29]. Ileri et al. [30] achieved removal efficiency of 82% biochemical oxygen demand (BOD), 88% chemical oxygen demand (COD), 96% NH₃ and 98% suspended solids (SS) from domestic and pharmaceutical wastewater in a SBR operated for 4 h aeration followed by 60 min sedimentation. In another study, slightly lower COD removal efficiencies between 63 and 69% are reported [31]. MBRs are known to be effective for the removal of bulk organics and can replace traditional methods when operated in combination with a conventional AST [32]. The main advantage of MBRs over AST is that they require less space and can also treat variable wastewater compositions [17]. Biologically active filters are also used for pharmaceutical wastewater treatment and can remove PhACs [33].

3.4 Advanced oxidation processes (AOPs)

Advanced Oxidation Processes (AOPs) those are generating the very reactive radicals, such as hydroxyl radicals (HO[•]) which are able to react with most of the organic compounds. The pollutants and by-products are degraded through a series of complex reactions. In the first step, HO[•] radicals react with organic compounds through electron transfer leading to formation of organic intermediates and after that species react with dissolved oxygen to form peroxy (ROO[•]) radicals which undergo rapid decomposition. The overall process leads to partial or total mineralization of pollutants [34].

3.4.1 Fenton processes (FP)

Fenton's reagent, a mixture of Fe²⁺ (catalyst) and hydrogen peroxide (H₂O₂) which produces HO[•] radical, a strong oxidizing agent (E⁰ = 2.8 vs. NHS). The mechanism of FP is studied by several workers [17, 35]. The main reactions occurring in Fenton oxidation of organics are appended below (Eqs. 1–4):

where, $R^{\bullet}$ is alkyl free radical.

The major parameters like solution pH, amount of ferrous ion, concentration of H_2O_2 , initial concentration of pollutants/ PhACs and presence of other background ions [36] that are affecting FP. The optimum pH for FP generally ranges from 2 to 4. At $pH > 4$, Fe^{2+} ions are unstable, and they are easily transformed to Fe^{3+} forming complexes with hydroxyl ion. Moreover, under alkaline conditions H_2O_2 loses its oxidative power as it breakdowns to water [17]. An effluent pH was Adjusted usually before addition of Fenton reagent. Increase of Fe^{2+} ions and H_2O_2 concentration boosts up the degradation rate [37]. The use of excess amount of H_2O_2 can deteriorate the overall degradation efficiency of FP coupled with biological treatment due to toxic nature of H_2O_2 to microorganisms [38]. Fenton oxidation of organics/ PhACs can be inhibited by PO_4^{3-} , SO_4^{2-} , F^{-} , Br^{-} and Cl^{-} ions. The inhibition may be due to precipitation of iron, scavenging of $HO^{\bullet}$ radicals or coordination with Fe^{3+} to form a less reactive complex [39].

3.4.2 Photo-Fenton processes (PFP)

Photo-Fenton process ($H_2O_2/Fe^{2+}/UV$) involves formation of $HO^{\bullet}$ radicals through photolysis of hydrogen peroxide (H_2O_2/UV) by UV-irradiation along with the Fenton reaction (H_2O_2/Fe^{2+}). In presence of UV irradiation, ferric ions (Fe^{3+}) are also photo-catalytically converted to ferrous ions (Fe^{2+}) with formation of additional $HO^{\bullet}$ radicals (Eq. 5) [40].

Likewise, PFP gives faster rates and higher degree of mineralization compared to conventional FP [39]. The reaction can be driven by low energy photons and it also can be achieved using solar irradiation [39]. The employment of solar light significantly reduces the operational cost. Another important advantage of PFP is that iron-organic complexes formed during Fenton oxidation can be broken under the illumination of UV light [41].

3.4.3 UV/ H_2O_2 photolysis (UVP)

UVP includes H_2O_2 injection with continuous mixing in a reactor equipped with UV irradiation system (wavelength 200 to 280 nm). UV light is used to cleave O-O bond of H_2O_2 forming $HO^{\bullet}$ radicals. The reactions describing UVP are presented below (Eqs. 6–11) [42]:

Reaction 6 is the rate limiting because the rates of other reactions are much higher. In UVP, a higher initial H_2O_2 concentration produces higher $\text{HO}^\bullet$ radical concentration (Eq. 6), which decomposes the target compounds. However, an optimal H_2O_2 concentration exists because overdosing of H_2O_2 leads to reaction with $\text{HO}^\bullet$ radicals leaving off $\text{HO}_2^\bullet$ (Eq. 7). UVP is quite efficient in mineralizing PhACs [42]. A disadvantage of UVP is that it cannot utilize solar light as the source of UV illumination. The required UV irradiation for the photolysis of H_2O_2 is not available in the solar spectrum [43]. H_2O_2 has poor UV absorption characteristics and input irradiation to the reactor is wasted if the water matrix absorbs UV light.

3.4.4 UV/ TiO_2 photo catalysis (UVPC)

Photocatalysis is the acceleration of a photoreaction using a catalyst in presence of light/photon. It is a well-recognized approach where light energy is employed to excite the semiconductor material producing electron (e^-_{cb})/hole (h^+_{vb}) pair (Eq. 12) which eventually involves in the detoxification of pollutants (in water or air). e^-_{cb} from the valence band (VB) is promoted to the conduction band (CB) of the semiconductor and a h^+_{vb} is created in the VB. The photo generated e^- migrates to the surface without recombination can reduce and oxidize the contaminants adsorbed on the surface of the semiconductor [44]. e^-_{cb} react with surface adsorbed molecular oxygen to yield superoxide radical anions (Eq. 13), while h^+_{vb} react with water to form $\text{HO}^\bullet_{\text{ad}}$ radicals on the surface of the catalyst (Eq. 14) [45].

TiO_2 is widely used as a photocatalyst due to high photo-catalytic activity, low cost, low toxicity, high oxidation power, easy availability and chemical stability under UV light ($\lambda < 380 \text{ nm}$) [46]. TiO_2 has two common crystal structures i.e., rutile and anatase. TiO_2 Degussa 25 consisting of 20% rutile and 80% anatase is considered as a standard photocatalyst. Organic compounds can undergo oxidative degradation through reactions with h^+_{vb} , $\text{HO}^\bullet_{\text{ad}}$, and $\text{O}_2^{\bullet -}$ radicals as well as through reductive cleavage by e^-_{cb} . The key advantages of UVPC are treatment at ambient conditions, lower mass transfer limitations using nanoparticles and possibility of use of solar irradiation. UVPC is capable for destruction of a wide range of organic chemicals into harmless compounds such as CO_2 and H_2O [47]. The major factors affecting UVPC are initial pollutant load, amount of catalyst, reactor design, irradiation time, temperature, solution pH, light intensity and presence of ionic species. The use of excess catalyst may reduce the amount of photon transfer into the medium due to opacity offered by the catalyst particles [36]. The design of reactor should assure uniform irradiation of the catalyst [48].

3.5 Advantages and limitations of AOPs

AOPs using H_2O_2 and Fe^{2+} suffer from the requirement of acidic conditions, interference by inorganic ions, iron-organic complexation and formation of iron sludge. Some of the above limitations can be overcome when heterogeneous

photocatalytic treatments like UVPC is used. However, uniform illumination of UV light and separation of catalyst particles could limit the application. Application of artificial UV light increases the cost of treatment and also poses health hazard to the working personnel.

The typical advantages of iron based AOPs are:

- i. The process is capable to destroy a wide variety of organic compounds even without formation of toxic intermediates.
- ii. It offers a cost-effective source of HO[•] radicals using easy-to-handle reagents.
- iii. In FP and PFP, both oxidation and coagulation take place simultaneously.
- iv. Effective in destruction of refractory PhACs to improve biodegradability and produce an effluent that can be treated biologically as a finishing step.

4. Conclusions

AOPs undergo through different reacting systems such as homogeneous or heterogeneous phases and in light or dark. It causes consecutive unselective degradation of organic materials. Complete mineralization occurs even at very low concentration and the byproducts formed may be environmentally non-hazardous. Biological treatment is recognized as the cheapest available technology to remove and degrade organic contaminants. However, advanced separation technology gives very inefficient degradation of PhACs because they are usually resistant to biodegradation and characterized by low BOD/COD ratio. Partial Fenton oxidation yields more biodegradable products together with the destruction of inhibitory effect towards microorganisms in the downstream biological treatment. It also increases the overall treatment efficiencies compared to the efficiency of individual process. AOPs can be employed for the detoxification of PhACs until the biodegradability is improved to a level amicable for subsequent biological treatment.

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