Review Article

A review on comparative study between the physicochemical and biological processes for paracetamol degradation

Abstract Paracetamol has emerged as one of the most frequent pharmaceuticals that found in natural waters and even in drinking water due to its high consumption and therefore deserves a review on the possible treatments for its remediation. The purpose of this review work is to give a compare between the physicochemical and biological processes for removing paracetamol from aquatic environment. Different types of processes are described in this review: from physicochemical process such as membrane filtration, chlorination, activated carbon, and advance oxidation, which applied for pracetamol degradation, to biological process such as microbial, membrane bioreactor, aerobic and anaerobic degradation, which are more recently focused on the degrading paracetamol. Physical processes, that eliminate the pollutant without degrade it, are not efficient enough to completely remove paracetamol from aquatic environment. While the chemical processes that are shown to be fast and efficient to remove paracetamol substance possess some drawbacks representing in high operational cost which make them not a desirable choice for treating wastewater. Biological process receives currently a significant attention for the removal of pollutants because it is found to be the most efficient technology which can be applied in degrading different pollutants. Regardless of its disadvantages, it have been found more efficient on degrading the paracetamol when compared to physicochemical processes. Furthermore, the combination between the biological and physicochemical processes overcome all of the problems of processes that presented during treatment. Also, the combined processes improve the paracetamol degradation rate and reduce the treatment costs.

Keywords: Biodegradation, Paracetamol, Biological and Physicochemical process

Introduction

Paracetamol, also known as acetaminophen, 4-acetamidophenol, N-(4-hydroxyphenyl) acetamide ($C_8H_9NO_2$) fig. (1), and consists of a benzene ring core substituted by one hydroxyl group and the nitrogen atom of an amide group in the *para* (1,4) pattern. It is very common over the counter analgesic used for fever, headaches, and other minor pain (Martindale, 2009).

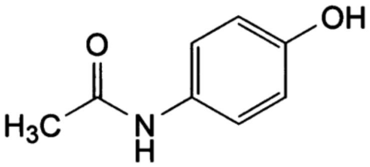


Figure (1). Chemical structure of paracetamol (Martindale, 2009)

Paracetamol is one of the most frequently used drugs worldwide (Kim et al., 2007). It is ranked as one of the top three drugs prescribed in England and one of the top 200 prescriptions in USA (Sebastine and Wakeman, 2003; Zhang et al., 2008). In Yemen, it is ranked as first of top ten drugs produced by local industrial and one of the top ten drugs imported (SBDMA, 2013). Also, it was consumed as the second pharmaceutical products during the year 2008 in Kuwait (Alajmi, 2014).

68–85% of paracetamol excreted from the body during therapeutic use as parent compound was recorded by Muir et al., (1997); Schowanek and Webb (2005). Moreover, it is known to exhibit virtually no sorption and no retardation in aquifer sand studies (Lorphensri et al., 2007). Also, paracetamol is easily accumulated in aquatic environment due to their high solubility and hydrophilicity. Although it is one of the most frequently detected in surface waters, wastewater, groundwater, and drinking water which making it a high priority trace pollutant (Li et al., 2007; Wu et al., 2012).

Paracetamol has been found with a concentration of up to 6 µg/L in European sewage effluents (Ternes, 1998), up to 10 µg/L in USA natural waters (Kolpin et al., 2002), and more than 65 µg/L in Tyne river in the UK (Roberts and Thomas 2006). Rabiet et al., (2006) detected 0. 211 µg/L in a well supplying drinking water. Also, it was reported from 0.101–20.86 µg/L in the wastewater in Kuwait by Alajmi (2014) and 12 ug/L in hospital wastewater treatment in Saudi Arabia (Al-Qarni et al., 2016).

Paracetamol is continuously introduced into the aquatic environment as parent compound, metabolites or conjugates by manufacturing wastes, consumer use and disposal and hospital waste (Langford and Thomas, 2009; Philips et al., 2010). Frequent occurrence of this compound in environment and drinking water has raised a concern about their potential effects on environment and human health (Wu et al., 2012).

Different reports mentioned that it is capable of causing skin eruptions, hemolytic anemia, hypoglycemia, jaundice, hepatotoxicity, and hepatic failure (Sally et al., 2004), as well as causing DNA strand breaks, and inhibition of replication and DNA repair systems (Rannug et al., 1995), and induces breast cancer cell proliferation (Theophilus et al., 1999).

Previous studies on removal of paracetamol from wastewater mainly focused on chemical methods including oxidation processes such as electrochemical (Brillas et al., 2005), ozonation and H_2O_2/UV oxidation (Andreozzi et al., 2003), TiO_2 photocatalysis (Yang et al., 2008), solar photoelectro-Fenton oxidation (Li et al., 2007). Although these treatment methods may be available for treating this pollutant, the harsh reaction conditions, the generation of secondary pollutants, and the high operational cost associated with these methods have often made them not a desirable choice (Li et al., 2007; Trovo et al., 2008).

The objective of this review work is to compare between physicochemical and biological treatment methods efficiency for paracetamol remove and degradation in aquatic environment. Moreover, it will serve as a valuable source of data and literature for paracetamol degradation and remove from aquatic environment. Meanwhile this review will open the door to meaningful discussion on the application of physicochemical and biological methods in removing paracetamol from environment as well as advantages and disadvantages, and degradation routes for paracetamol.

Paracetamol degradation by physicochemical processes

The physicochemical treatment technologies have been explored with the intention of finding suitable for polishing techniques to further remove paracetamol concentrations from wastewater, surface water, and drinking water. These technologies include sand filtration, membrane separation, activated carbon, chlorination and oxidation processes (Andreozzi et al., 2003; Snyder et al., 2007; Snyder, 2008).

Nowadays, more attention has been paid towards chemical oxidation processes such as ozonation (Andreozzi et al., 2003; Skoumal et al., 2006), and advanced oxidation processes like H_2O_2/UV (Andreozzi et al., 2003), O_3/Fe^{2+}/UV (Skoumal et al., 2006), TiO_2

photocatalysis (Yang et al., 2008), sonolysis (Quesada et al., 2009), anodic oxidation with BDD anode (Brillas et al., 2005; Waterston et al., 2006), and solar photoelectro-Fenton oxidation (Almeida et al., 2011) that have been studied for removal of paracetamol from wastewater and drinking water.

Physical treatments include methods such as coagulation, flocculation, sedimentation, flotation, filtration, adsorption onto activated carbon and air striping. The physical methods are losing acceptance since their main drawbacks are the transfer of pollutants from the liquid phase to a new phase instead of their elimination (Chiron et al., 2000).

Alajmi (2014) reported that the paracetamol was removed by 57%, with mean and median concentrations in the sand filtration effluent of 8.58 ng/L and 4.5 ng/L, respectively. Also, Lorphensri et al., (2007) examined the sorption and transport of paracetamol by batch sorption experiments and solute displacement in columns of silica, alumina, and low organic carbon aquifer sand at neutral pH. It was found that the paracetamol exhibited virtually no sorption and no retardation in aquifer sand studies.

Thus, physical wastewater treatment methods require post-treatments to remove the pollutant from the newly contaminated environment, enhancing in this way operational costs and diminishing effective viability (Chiron et al., 2000).

Membrane processes

The use of membrane technology, particularly in wastewater treatment and reuse has received much attention since early 1990s. Membrane processes can be categorized into four classes according to the size of particles that can be retained, namely, reverse osmosis (RO), ultrafiltration (UF), microfiltration (MF), and nanofiltration (NF). NF and RO are widely used in water reuse industry due to their high contaminant removal efficiency, but they are still somewhat permeable to some relatively small micropollutants whereas MF and UF cannot remove dissolved organic matter due to their relatively larger pore sizes (Wang et al., 2005; Steinle-Darling et al., 2010).

All types of membrane were evaluated for the removal to paracetamol from wastewater treatment plant (WWTP) and drinking water treatment plant (DWTP) (Snyder et al., 2007; Boleda et al., 2011). The experiment on Al-Rifai et al., (2007) employed the RO technology to remove the paracetamol (23.3 µg/L) from WWTP and found that the more than 70% of paracetamol was removed. Snyder et al., (2007) used the UF membrane to remove the paracetamol from WWTP and found that the paracetamol decreased from 0.018 µg/L to 0.017 µg/L. Another study by Yoon et al., (2007) applied the NF and UF membrane to retention the paracetamol and found that the <10% of paracetamol was retained by NF and UF.

Radjenovic et al., (2008) investigated the removal of paracetamol (0.034 µg/L) during NF and RO which applied in a full-scale DWTP using groundwater. Deteriorations in retentions on NF and RO membranes were 44.8% and 73%, respectively, observed for paracetamol. Also, Yangali-Quintanilla et al., (2011) used two types of NF (N200 and N90) to remove the paracetamol from water reuse and 23% and 67% of paracetamol removed by N200 and N90, respectively.

Han et al., (2006) indicated the removal efficiency 8.7% of paracetamol from WWTP equipping with sand filtration. In contrast, Wilcox et al., (2009) applied the sand filtration to remove paracetamol from WWTP. It was found that the paracetamol was decreased from >500µg/L to 1.3µg/L with efficiency 99% remove. Boleda et al., (2011) used the dioxychlorination and sand filtration as a conventional treatment and UF, UV and RO as an advanced treatment to remove the paracetamol from DWTP (0.26 µg/L). It was 14% removal of paracetamol found by conventional treatment and 99% by advanced treatment.

The retention of micropollutants in membrane processes can generally achieved by size exclusion, adsorption onto membrane, and charge repulsion. These removal mechanisms are largely dependent on a number of factors such as membrane process type, membrane characteristics, operating conditions, specific micropollutant characteristics and membrane fouling (Xu et al., 2005; Schäfer et al., 2011).

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 WWTP or for treating saline groundwater (Nghiem et al., 2005; Yoon et al., 2006; Snyder et al., 2007). The removing efficiency of substance by MF and UF depend on the substance size and pore size of membrane filtration (Watkinson et al., 2007).

Due to the low removal efficiency, MF or UF alone is not feasible for micropollutant removal. Hence, the combination of MF or UF with other processes (e.g. NF or RO) is essential for enhanced elimination of different micropollutants (Garcia et al., 2013) Although membrane processes such as OR and NF could in theory remove all pollutants, including dissolved organics, their operational costs are high because of high-energy requirements and membrane fouling. MF and UF are cost-effective options. Therefore, in water-reuse applications, UF or MF needs to be combined with biological processes (Wang et al., 2005).

Although the technical feasibility of membranes has been proven, high investment and operational costs keep their application very limited (Lu et al., 2007). Currently membrane filtration, NF and RO are almost exclusively applied in drinking water treatment facilities whereas their application during wastewater treatment is scarce. In addition, the combination of MF or UF with RO as secondary effluent post-treatment seems to be efficient for the removal of pharmaceuticals (Stoquart et al., 2012). In Singapore and few cities in Australia, a combination of MF or UF with RO is to perform the biological treatment in a membrane bioreactor (MBR) followed by an RO system at full scale, which has been operated at pilot scale first by (Snyder et al., 2007).

Furthermore, the combination between the biological process and membrane filtration have been employed. Xu et al., (2014) aimed to use immobilized horseradish peroxidase (HRP) on poly (vinyl alcohol)/poly(acrylic acid)/SiO_2 (PVA/PAA/SiO_2) nanofibrous membranes (PPSiNFM-HRP) to biotransform paracetamol catalytically. Paracetamol removal rate by immobilized HRP (83.5%) was similar to that of free HRP (84.4%) at 0.8 mM of initial H_2O_2 concentration after 60 min, but immobilized HRP showed excellent reusability. The results signify that enzyme immobilized on nanofibers has great application potential in water treatment.

Activated carbon (AC)

AC is a recognized conventional technology for the removal of both natural and synthetic organic contaminants and commonly employed for controlling taste and odor in drinking water (Hrubec et al., 1983; Annesini et al., 1987). It is most commonly applied as a powdered activated carbon (PAC) or in granular activated carbon (GAC) form in packed bed filters. Both PAC and GAC can be affected by the properties of both adsorbate (KO_W, Pk_a, molecular size, aromacity versus aliphaticity, and presence of specific functional groups) and adsorbent (surface area, pore size and texture, surface chemistry, and mineral matter content) (Kovalova et al., 2013).

GAC is used worldwide at many water treatment plants as a replacement for anthracite media in conventional filters providing both adsorption and filtration (Moore et al., 2001). The AC was employed the adsorb and remove the paracetamol compound from wastewater, surface water, and drinking water (Westerhoff et al., 2005; Rossner et al., 2009).

Snyder et al., (2007) applied the PAC to remove the paracetamol concentration from wastewater. The paracetamol was reduced from 10.65 µg/L to 0.047 µg/L with >90% removal. Also, Westerhoff et al., (2005) applied the AC to remove the paracetamol (0.020 µg/L) from DWTP. It was 72% removed from this substance after 4 h. Similarly, Rossner et al., (2009) observed that the 58% of paracetamol concentration (0.200 µg/L) was removed by the AC from surface water.

The experiment on Suntisukaseam et al., (2007) used the polymeric resins and AC to adsorb the paracetamol in batch experiment within 24 h. It was observed that the AC produced much higher sorption than the polymeric resins for paracetamol. It can adsorb onto both polar and nonpolar surfaces due to their amphiphilic characteristic. Sim et al., (2010) pointed out that the decrease rate of paracetamol was 38% by a chemical flocculation system and 74% by a sand/activated carbon filter recorded in hospital WWTP. Boleda et al., (2011) used the GAC filtration in DWTP to remove the paracetamol. The paracetamol concentration 0.26 µg/L which detected in source water was 69% removed by GAC filtration. Mestre et al., (2011) prepared sisal-based AC with K_2CO_3 to remove paracetamol from liquid phase. It was more than 65% removal of paracetamol found.

A study by Quesada et al., (2012) investigated the catalytic wet air oxidation of paracetamol on AC. It was found that the paracetamol has been removed at concentration 126.1 mg after 2 h. The basic idea is to take advantage of both operations: (1) efficient and cheap water purification at room temperature by adsorption, (2) effective pollutant degradation by catalytic air oxidation achieving simultaneously AC regeneration for the next adsorption.

The main advantage of using AC to remove pharmaceuticals is that it does not generate toxic or pharmacologically active products (Reungoat et al., 2010). It enhances the buffer capacity of a biological treatment system due to adsorption of the toxic compounds present, thereby decreasing the toxicity toward the microorganisms. Mensah and Forster (2003) concluded that a combination of AC and anaerobic treatment was required to overcome toxicity problems investigated the toxicity of wastewater from a detergent manufacturing process.

However, it was found that counter-current use of PAC by recycling waste PAC from post-treatment tank to biological treatment tank could enhance micropollutant removal by 10 to 50% in comparison with the application without recycling. PAC addition in WWTP was shown to be able to reduce micropollutant 25 levels by more than 80% (Boehler et al., 2012).

Despite the effectiveness of AC, the major drawbacks for the use of AC is a poor economic feasibility required a lot of energy and short lifetime, often due to low and expensive regeneration capacities (Cabrita et al., 2010). However, its efficacy might be significantly lowered by presence of natural organic matter which competes for binding sides, thereby resulting in blocked pores (Luo et al., 2014).

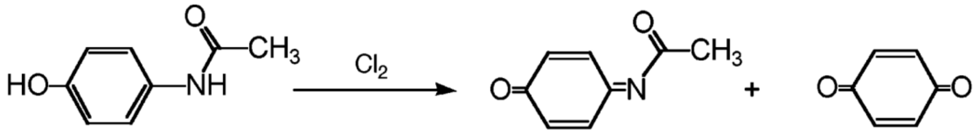
Furthermore, it is quite expensive, non-selective and ineffective against certain pollutants, such as, disperse and vat dyes. The regeneration of adsorbent after its use has several problems as it dose not cost effective and not a straight forward method which results in loss of adsorbent. It should be noted that the adsorption capacity of any carbon depends on several parameters, such as, the source of raw material, type of preparation, pyrolysis temperature and activation. In addition to these factors, surface chemistry, surface charge and nature of pore also influence the adsorption capacity (Babel and Kurniawan, 2003).

Moreover, the production of AC is also non-environmentally friendly, as its dust might be emitted to the environment during production and the chemicals used will contaminate the water source and affect the aqua ecosystem (Cetin and Pehlivan, 2007). Despite such features, the implementation of AC on large scale industrial processes is limited due to a poor economic feasibility associated with its manufacture, maintenance, and regeneration costs (Roskill, 1998). Consequently, AC is often replaced by costly effective adsorbents in many industrial applications, even if their removal efficiency is much lower from that of AC (Cabrita et al., 2010).

Chlorination

Chlorination is one of the most common treatment processes for disinfecting wastewater and drinking water. Therefore, many pharmaceutical compounds are further subjected to chlorination treatment processes. Chlorine is strong oxidant on pharmaceutical compounds containing aromatic like paracetamol that rapidly react to form chlorinated compounds by the other substituents on the ring (Pinkston and Sedlak, 2004; Bedner and Maccrehan, 2006).

The presence of paracetamol in wastewater and drinking water raises the concern of whether or not the compound persist during chlorination treatment. Bedner and Maccrehan, (2006) reported that during chlorination of paracetamol, 11 different chlorination products were observed including the toxic substances N-acetyl-p-benzoquinone imine and 1,4-benzoquinone fig. (2), the latter being a toxicant associated with lethality in paracetamol overdoses. Although these toxicants may exist only at very low levels in drinking water and wastewater. Their presence along with multiple other pharmaceuticals deserves further consideration (Bedner and Maccrehan, 2006).



Paracetamol

N-acetyl-p-benzoquinone imine

1,4-benzoquinone

Figure (2). Effect of chlorination on paracetamol (Bedner and Maccrehan, 2006)

A study by Glassmeyer and Shoemaker (2005) revealed that the 76.2% of paracetamol was degraded during the chlorination treatment. The experiment on Stackelberg et al., (2007) applied the chlorination treatment methods in the removal of paracetamol from DWTP. The maximum concentration of paracetamol found in this study was 0.12 µg/L and greater than 90% removed of these concentration by chlorination methods. Also, Snyder (2008) pointed out that the more than 70% of paracetamol was removed by using the free chlorine (3.5 mg/L dose).

Advanced oxidation processes (AOPs)

Advanced oxidation processes (AOPs) are relatively new and effective technologies which have gained a lot of attention in the field of water and wastewater treatment in the past 30 years. AOPs are oxidation methods which degrade a wide range of pollutants by in situ formation of highly reactive radicals such as hydroxyl radical (Gogate and Pandit, 2004).

The major advantage of AOPs is their capability to destroy the organic pollutants completely without transferring them to another phase or producing secondary waste disposal troubles. The term “Advanced” is given to these processes due to the fast reaction of the organic matters with hydroxyl radicals (Bolton and Cotton, 2008). AOPs consist of four main groups; (1) photochemical processes such as UV/H_2O_2, UV/O_3, and $UV/O_3/H_2O_2$, (2) photocataytic processes such as photo-Fenton and UV/TiO_2, (3) chemical oxidation such as ozonation (O_3), O_3/H_2O_2 and H_2O_2/Fe^{2+}, and (4) sonolytic processes such as ultrasound (US) (Oppenländer, 2003; Tchobanoglous et al., 2003).

Furthermore, several previous publications have been devoted to the study of paracetamol degradation in water using different AOPs like ultrasound, UV radiation, gamma radiation, electrochemistry, pulsed corona discharge and their combination with catalysts and chemical oxydants as ozone, hydrogen peroxide and Fenton reactive (Andreozzi et al., 2003; Jordá et al., 2011; Jagannathan et al., 2013; Panorel et al., 2013).

Ozonation

Ozone technology has been employed to the treatment of waters primarily due to its strong disinfection and sterilization properties (Araña et al., 2002). 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). The reaction of the aromatic ring is independent of solution pH. While, the reactivity of amines strongly depends on the pK_a of the amine and the pH of the solution (Andreozzi et al., 2006; Ikehata et al., 2006).

The use of ozone as a means of breaking down paracetamol in water has been the subject of numerous studies over the last ten years including (Andreozzi et al., 2003; Snyder, 2008; Boleda et al., 2011). The oxidative system is able to destroy the aromatic ring of the paracetamol with a partial conversion of the initial carbon content into carbon dioxide (Andreozzi et al., 2003).

Andreozzi et al., (2003) applied the ozonation and H_2O_2/UV systems for the complete mineralization of paracetamol (5.0×10^{-3} mol dm^{-3}) in aqueous solutions. After 120 min, the paracetamol mineralization was 30% by ozonation at pH 2.0 and 40% by H_2O_2/UV at pH 7.0 recorded. In similar, Westerhoff et al., (2005) used the oxidize system to treatment the pharmaceuticals and personal care products in drinking water. The paracetamol was 94% degraded in 24 h by this system.

Snyder et al., (2006) evaluated the oxidative removal of paracetamol (0.117 µg/L) from Colorado river water by using O_3 (2.5 mg/L) and O_3 combined with H_2O_2 (0.5 mg/L). The paracetamol was >99% removed from river water after 24 min by O_3/H_2O_2. Skoumal et al., (2006) reported a detailed study on the mineralization of paracetamol (157 mg/L) in pH 3.0 by the use O_3, O_3/UV, O_3/Fe^{2+}/UV and $O_3/Fe^{2+} + Cu^{2+}$/UV systems. The paracetamol was completely degraded in 6 min. The coupling of ozone with UV or $/Fe^{2+}$ can efficiently increase the mineralization yield of the oxidation process.

Garrido et al., (2007) studied the degradation of paracetamol (157 mg/L) by direct ozonation and ozonation catalyzed with Fe^{2+}, Cu^{2+} and/or UV light at pH 3.0. 83% of paracetamol was mineralized in 4 h. Similarity, Snyder, (2008) observed that the more than 70% of paracetamol was removed by using the ozone (2.5 mg/L dose). Boleda et al., (2011) found that the paracetamol was removed from DWTP after ozonation with a varying efficiency 68%.

Panorel et al., (2013) studied the oxidation of paracetamol (100 mg/L) in aqueous solution by using pulsed corona discharge as a means for advanced oxidation. Pulse repetition frequency, the delivered energy dose, and oxidation media were the main parameters evaluated. The pulsed corona discharge treatment appeared to be effective in oxidation of paracetamol: complete degradation of target pollutant together with partial mineralization was achieved at moderate energy consumption; oxidation proceeds faster in alkaline media, the fastest oxidation rate was observed in oxygen-enriched air.

The main disadvantage of ozonation is that in general the target compounds are not completely mineralized, but merely transformed, and so even more harmful substances can be produced as a result (Deegan et al., 2011). Also, production of ozone is an energy intensive process making it costly to appliance and may increase the energy demand over a conventional wastewater treatment plant by 40-50% as a treatment system (Cokgor et al., 2004).

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).

Fenton reactions

The Fenton and photo-Fenton process involves the reaction of ferrous ions (Fe^{2+}) as a catalyst and hydrogen peroxide (H_2O_2) as an oxidizing agent under UV/visible radiation to form active oxidant species, mainly hydroxyl radical, which oxidize organic compounds when they are present in aqueous solution. Compared to other oxidants, hydrogen peroxide is not expensive, not dangerous, easy to handle and poses no lasting environmental threat since it readily decomposes to water and oxygen. In addition, iron is also reasonably priced, safe and environmentally friendly. Such an easy and economical mode to generate hydroxyl radicals has promoted this oxidation method for wastewater treatment. Another important advantage of the photo-Fenton process is the inexistence of mass transfer limitations due to its homogeneous catalytic nature (Neyens and Baeyens, 2003; Pignatello et al., 2006).

Fenton process has been used and applied for the degradation and mineralization the paracetamol in aquatic and wastewater. Sirés et al., (2004) studied the paracetamol (150 mg/L) mineralization at pH 3.0 using electrochemical variants of Fenton and photo-Fenton processes with a Pt anode and an O_2-diffusion cathode for H_2O_2 electrogeneration. The complete removal of paracetamol was found after 25 min. Also, Almeida et al., (2011) studied the degradation of 10 L of 157 mg/L paracetamol solutions in 0.05 M of Na_2SO_4 by the solar photoelectro-Fenton method. After 60 min, the completely degradation (100%) of paracetamol was recorded at 35°C and pH 3.0.

A study on the use of solarphoto-Fenton to remove paracetamol (0.1mg/L) resulted in a removal efficiency of 16.3% (Klamerth et al., 2010). Also, Luna et al., (2012) investigated the applicability of the electro-Fenton and photoelectro-Fenton processes using a double cathode electrochemical cell in the treatment of wastewater containing 5 mM of paracetamol. The paracetamol removal efficiency was 89% by the electro-Fenton and 97% by photoelectro-Fenton method.

Quesada et al., (2009) aimed to evaluate the influence of several parameters of the ultrasound process on the degradation of paracetamol. After 4 h of sonolysis, the extent of degradation was 95%, 82%, 70% and 56%, respectively, for the reaction mixture initially containing 25, 50, 100 and 150 mg/L of paracetamol. Similarity, Su et al., (2012) observed that the 5 mM of paracetamol was 72% degraded by Fenton at pH 2.0 and 74% by electro-Fenton processes at pH 2.0 in aerator reactor in wastewater.

A study by Su et al., (2013) assessed the degradation of paracetamol using a novel Fenton aerated reactor. The removal efficiencies of paracetamol was 99% at 40 min with degradation rate 0.449 mM/min, when optimum conditions for 5 mM paracetamol, 25 mM H_2O_2 and 0.1 mM Fe^{2+} were used at pH 3. The results indicate that a novel Fenton aerated reactor was successfully performed to degrade paracetamol.

Manu and Mahamood (2011) studied the photo-Fenton oxidation and classic Fenton oxidation process for the paracetamol treatment in water. The optimum conditions observed for 10 mg/L initial paracetamol concentration are influent pH 3, initial H_2O_2 dosage 30 mg/L, [paracetamol]/[H_2O_2] ratio 1:3 (w/w) and [H_2O_2] [Laterite iron] ratio 30:0.75 (w/w). At the optimum conditions, for 10 mg/L of initial paracetamol concentration , 76% paracetamol reduction removal by Fenton oxidation and 79% paracetamol reduction removal by UVC Fenton process are observed in 120 minutes reaction time.

Recently, studies aiming at the application of Fenton's oxidation process into pretreatment of non-biodegradation industrial wastewaters have been reported (Chen et al., 2009, Padoley et al., 2011). In a Fenton's oxidation pretreatment process, the initially non-biodegradable organic compounds can be converted into more biodegradable intermediates, thus greatly enhancing the biodegradability of raw wastewaters (Zhang et al., 2013a). And then the effluent from the pretreatment system was further treated in a biological oxidation process with a potentially lower cost. The feasibility of combination process of Fenton's oxidation coupled with biological oxidation for the treatment of non-biodegradation industrial wastewater has been demonstrated in the literature (Lodha and Chaudhari, 2007; Oller et al., 2011).

In the Fenton's oxidation followed by biological oxidation process, non-biodegradable organic compounds can be partially oxidized to easy biodegradable organic intermediates and then be completely degraded in biological treatment system (Zou et al., 2016).

The experiment on Jordá et al., (2011) combined between the solar photo-Fenton process, 20 mg/L of Fe^{2+} and 200 mg/L of H_2O_2, and biological treatment, using the *Pseudomonas putida* bacteria, for degrading paracetamol (157.5 mg/L) in 25 min. Firstly, biodegradability enhancement with photo-Fenton treatment time has been evaluated; the minimum mineralization level should be at least 18.6% where paracetamol has been degraded and biodegradability efficiency is higher than 40%. 20 mg/L of Fe^{2+} and 200 mg/L of H_2O_2 were selected in a lab-scale study looking at paracetamol's degradation rate and organic carbon mineralization rate. As a result of scaling up the process at a pilot plant, 157.5 mg/L of paracetamol was treated in 25 min of photo-Fenton treatment achieving the desired biodegradability. A further economic evaluation shows how the proposed treatment strategy markedly increases plant efficiency, resulting in an 83.33% reduction in reagent cost and a 79.11% reduction in costs associated with reaction time. Total cost is reduced from 3.4502 €/m^3 to 0.7392 €/m^3.

Zhang et al., (2012) investigated the oxidative removal of paracetamol by zero valent aluminum under air-equilibrated acidic conditions (ZVAl)/H^+/air system. More than 99% of paracetamol was eliminated within 16 h in pH 1.5 reaction solutions initially containing 2.0 mg/L paracetamol at 25±1°C. Higher temperature and lower pH facilitated paracetamol removal. It was suggested that ZVAl/H^+/air system may be potentially employed to treat paracetamol–contaminated water.

Xiong and Hu (2012) evaluated the photocatalytic degradation of paracetamol (100–385 ppb) in aqueous solution using TiO_2-P25 as the catalyst and UVA/LED as the light source. It was found that the chosen UVA/LED alone negligible amount of paracetamol was degraded, while in the presence of TiO_2, the concentration of paracetamol decreased substantially. Also, the paracetamol could be degraded to non-detectable level within 20 min. The apparent degradation rate increased dramatically when the concentration of TiO_2-P25 increased from 5 to 20 ppm. However, the degradation rate decreased with the increase of the initial paracetamol concentration.

Valdez et al., (2012) applied the electrochemical and photoelectrochemical process to degrade the paracetamol (96 mg/L) in aqueous solution using modified 100 pores per inch reticulated vitreous carbon electrodes (RVC) at pH 5.0. The paracetamol concentration was 90% degraded by the electrolysis RVC in 4 h, 90% by the electrolysis with the modified electrode TiO_2/RVC in 2 h, and 98% by the electricatalysis ($CuO/TiO_2/Al_2O_3$/RVC) in I h. In photoelectrocatalysis, representing 95% of paracetamol was degraded by TiO_2/RVC/UV process after 1 h and 99% was removed of this substance by $CuO/TiO_2/Al_2O_3$/RVC/UV process after less than 1 h of reaction.

Sirés et al., (2013) evaluated the efficiency of the electro-oxidation and electro-Fenton with a boron-doped diamond (BDD) anode for the treatment of solutions containing 1 mg/L paracetamol at pH 3.0. Electro-oxidation was performed in a BDD/Pt cell, whereas electro-Fenton was carried out in a BDD/air-diffusion cell to electrogenerate H_2O_2 at the cathode. It was found that the paracetamol was completely removed in synthetic solutions by electro-oxidation with a BDD anode, in 45 min at pH 3.0 and more slowly, in 60 min, at pH 6.0. While, in the electro-Fenton process performance in solution in containing 0.15 mmol/L of Fe^{2+} at of pH 3.0, the paracetamol was 100% removed after 60 min.

Villaroel et al., (2014) studied the effect of ultrasonic power (20–60W), initial paracetamol concentration (33–1323µmol/L), pH (3–12) and water matrix at 600 kHz on paracetamol degradation. High ultrasonic powers (60 W) and, low and natural acidic pH values favored the efficiency of the treatment. In similar, Cruz-González et al., (2015) studied the paracetamol degradation (100 mg/L) in aqueous solution by ultrasound/H_2O_2 and ultrasound/Fenton processes. The total degradation of paracetamol is obtained at 60 min for all studied concentrations of H_2O_2 and ferrum salt. The optimal conditions of sono-Fenton process guarantee a mineralization higher than 60% are 4.7 mmol/L of Fe^{2+} and 14.4 mmol/L H_2O_2.

Despite the effectiveness of Fenton and photo-Fenton, the main drawbacks of these technologies as a wastewater treatment system are mainly related to the need for pH control and the problem of sludge generation. In order to solve these weaknesses, Fenton and photo-Fenton modified technologies where iron is used as heterogeneous catalyst, have been developed (Maletzky et al., 1999; Yuranova et al., 2004; Martínez et al., 2007).

However, Fenton and photo-Fenton reactions are inhibited by inorganic ions. In particular, ferric ion forms complexes with phosphate that are quite insoluble in neutral or mildly acidic solution. Moreover, sulphate, chloride and fluoride inhibit the process because these ions reduce the reactivity of ferric ion through coordination to form less reactive complexes (De Laat et al., 2004).

TiO_2 photocatalysis

Photocatalysis is the acceleration of a photochemical transformation by the action of a catalyst such as titanium dioxide (TiO_2) or Fenton's reagent (Chatterjee and Dasgupta, 2005; Herrmann, 2005). TiO_2 photocatalysis, one of the most promising AOPs, receives significant attention for the treatment of contaminated streams because of its chemical stability, nontoxicity, and low cost (Carp et al., 2004).

The major disadvantage of using TiO_2 in photocatalysis is its applicability to UV irradiation (λ <380 nm) only due to its wide band gap (3.2 eV). Sunlight is composed of 2% ultra-violet light, hence expensive light sources are often needed to activate TiO_2 and enable oxidation reactions (Klosek and Raftery, 2001). However, compared with other conventional chemical oxidation methods, photocatalysis may be more effective because semiconductors are inexpensive and capable of mineralizing various refractory compounds (Bernabeu et al., 2011).

This type of treatment has been applied to remove the paracetamol from aquatic environment (Yang et al., 2008). A study by Dalmázio et al., (2008) evaluated the efficiency of the photocatalysis (TiO_2/UV) system in promoting the degradation of paracetamol (1.0×10^{-4} mol/L) in aqueous solution. It was about 90% of paracetamol removed after a reaction time of 160 min. Trovo et al., (2008) assessed the influence of the iron source (FeOx or $Fe(NO_3)_3$) on the photo-Fenton degradation of paracetamol (15 mg/L). When using a FeOx a removal of 98% for paracetamol was achieved after 5 min irradiation as opposed to using $Fe(NO_3)_3$ where 53% of the initial concentration of these compound was removed after the same irradiation times.

Yang et al., (2008) studied the photo/photocatalytic oxidation of paracetamol in aqueous TiO_2 suspension using UV irradiation. It was found that more than 95% of 2.0 mM paracetamol was degraded within 80 min, whereas at an initial concentration of 10 mM, less than 20% of substance was removed. Zhang et al., (2008) investigated the photodegradation of paracetamol in 1.0 g/L TiO_2 suspended solution and found that able to remove 95% of paracetamol (50 µM) in 100 min. Similarity, Aguilar et al., (2011) evaluated the photocatalytic degradation of paracetamol solutions (20–200 mg/L) with TiO_2 catalyst (2 g/L) illuminated with UV-light. The paracetamol was (100%) completely degraded at concentration 120 mg/L in 300 min.

Yang et al., (2009) applied the photocatalysis (UV/TiO_2) to remove the paracetamol (4 mM) and found that more than 80% of paracetamol was degraded after 30 min. Also, Valdez et al., (2012) carried out the degradation of paracetamol (96 mg/L) in aqueous solutions in the presence of H_2O_2 by photolysis and photocatalysis. After 6 h of reaction, 20% of paracetamol concentration was degraded by UV light, 80% by TiO_2/UV, and 60% by $CuO/TiO_2/Al_2O_3$/UV.

Desale et al., (2013) investigated the influences of dosage TiO_2 on paracetamol degradation. The degradation of paracetamol were found 100%, 80% and 50% at initial concentration of paracetamol 100, 200, and 500 mg/L respectively at 240 min. Degradation of paracetamol increased with increasing TiO_2 loading in the range 1 to 4 g/L. It is observed that as the pH decreases from alkaline to acidic the rate of photocatalytic degradation of paracetamol increases.

Jagannathan et al., (2013) studied the degradation of paracetamol by sonolysis, photocatalysis and sonophotocatalysis in the presence of homogeneous (Fe^{3+}) and heterogeneous (TiO_2) photocatalysts using 213 kHz ultrasound. The degradation rates obtained for sonolysis, photocatalysis and sonophotocatalysis using TiO_2 (1 g/L) were about 8.3, 30.2 and 40.2 x 10^{-7} M/min, respectively. In the case of reactions involving Fe^{3+}, the degradation rates obtained were 26.1, 18.6 and 46.7x10^{-7} M/min for sonolysis, photocatalysis and sonophotocatalysis, respectively. In sonophotocatalysis, higher degradation was produced by Fe^{3+} compared to that of TiO_2. There was no synergistic effect in total organic carbon removal during sonophotocatalysis with TiO_2 catalyst while Fe^{3+} produced the synergistic effect on mineralization during sonophotocatalysis.

Luna et al., (2014) investigated the effects of important parameters, Fe^{2+}, H_2O_2 and initial paracetamol concentrations, on the initial rate and efficiency of paracetamol degradation in the electro-Fenton and photoelectro-Fenton processes. It was observed that the initial rate and removal efficiency of paracetamol in the electro-Fenton and photoelectro-Fenton processes varied insignificantly with Fe^{2+} concentration. The initial rate and removal efficiency of paracetamol in the photoelectro-Fenton process were higher than those in the electro-Fenton process.

Dalida et al., (2013) investigated the photocatalytic degradation of paracetamol in synthetic TiO_2 solution under a visible light (λ >440 nm). The TiO_2 photocatalyst was synthesized via sol–gel method and doped with $KAl(SO_4)_2$ and $NaAlO_2$. The results showed that LED alone degraded negligible amount of paracetamol but with the presence of $TiO_2/KAl(SO_4)_2$, 95%

removal of 0.10 mM paracetamol in 540 min irradiation time was achieved. The optimal operational conditions were obtained in pH 6.9 with a dose of 1.0g/L$TiO_2/KAl(SO_4)_2$ at 30°C.

França et al., (2016) evaluated the mineralization of paracetamol (10 mg/L) by the photocatalytic performance of a composite based on the association of TiO_2 and 2.5 wt.% of zinc(II) phthalocyanine (TiO2/ZnPc) in different pH and H_2O_2 concentrations. It found that the photocatalytic performances were influenced by the pH. Mineralization efficiencies between 86-91% was obtained using TiO_2/ZnPc in pH 5.5–6.8, with 33 mg/L of H_2O_2, ca. 15% higher than that observed with TiO_2. Above pH 6.8, the mineralization efficiencies decrease for both photocatalysts, although the consumption of H_2O_2 remains above 90%, due to its decomposition in alkaline pH. It concluded that the TiO_2/ZnPc nanocomposite is an effective catalyst to promote paracetamol mineralization under a wide pH range.

Electrochemical treatment

Electrochemical technology can be defined as an anodic oxidation that is able to attain the oxidation of pollutants from water or wastewater, either by direct or by mediated oxidative processes originated on the anode surface of an electrochemical cell (Chen, 2004; Panizza and Cerisola, 2009).The electrochemical methods are very promising alternatives for organics degradation because of their environmental compatibility, versatility, simplicity, and easy possibility of automation (Ratiu et. al., 2010).

The treatment of paracetamol using anodic oxidation with a Boron-doped diamond (BDD) electrode has been successful investigated in small scale. This process allows complete mineralization of the paracetamol due to the generation of large concentrations of hydroxyl radicals by the electrode. The BDD electrode was efficient even at low concentrations (Brillas et al., 2005).

A first work reporting the use of anodic oxidation with a BDD electrodes was done by Brillas et al., (2005) and the focus was on the oxidation of paracetamol. It was found that anodic oxidation with BDD was a very effective method for the complete mineralization of paracetamol up to 1 g/L in aqueous medium within the pH range 2.0–12.0. Also, Sirés et al., (2006) applied the electrochemical degradation of paracetamol from water by catalytic action of Fe^{2+}, Cu^{2+}, and UV light on electrogenerated H_2O_2. Total mineralization of paracetamol (157 mg/L) is achieved when Fe^{2+}, Cu^{2+}, and UV light are combined at pH 3.0 and 35°C in 6 h.

The electrochemical oxidation of paracetamol (2.0 mM) at BDD and at Ti/SnO_2 anodes was applied by Waterston et al., (2006). At the BDD, the efficiency of degradation of paracetamol was increased. Also, Garrido et al., (2007) carried out a study on the mineralization of solutions containing 157 mg/L of paracetamol at pH 3.0 using a Pt anode and an O_2-diffusion cathode in the presence and in the absence of Fe^{2+}, Cu^{2+} and/or UV light as catalysts. It was observed the complete (100%) degradation of paracetamol in 75 min. The use of electrochemical as a pre-treatment step, enhance the biodegradability of wastewater containing recalcitrant or inhibitory compounds, by resulting intermediate is easily degraded in subsequent biological treatment (Mouli et al., 2004).

Paracetamol degradation by biological processes

Biological processes most frequently use microorganisms, plants, and adsorption on living or dead biomass. Microbes degrade or convert the pollutants in an effective way. In both cases, whether it is a degraded or converted product, it is very important to confirm that the end product is more stable than the parent compound and less toxic (Misal et al., 2011; Rana et al., 2014).

Biodegradation will generally occur during secondary treatment in the WWTP. The biodegradation of compound depends on a number of factors, such as: stereochemistry, toxicity, structure, and concentration of the compound, efficiency of the microbial strain, conditions during degradation, retention time, and presence of other compounds and their concentration. Compounds with a large number of branched side chains are less probable to biodegraded than unbranched compounds with short side chains (Jones et al., 2005; Misal et al., 2011).

The advantage of biological treatment is the enormous adaptability of microorganisms to a wide variety of substrate media (O'Neils et al., 1999; Bitton, 2005), but this is a long term treatment in large physical areas and leads to the generation of non-biodegradable, soluble, and cellular residues, and also the high salinity of the effluent inhibit the microbial growth. Furthermore, high molecular weight fractions present in some types of aqueous effluents found in several industries tend to be resistant to biodegradation and inhibition (Archibald and Roy-Arcand, 1995; Dalmacija et al., 1995).

Moreover, the drawbacks of biological in WWTP are based on the requirement of a long residence time to degrade the pollutants because microorganisms are affected by the toxicity of the herbicides (Pera-Titus et al., 2004). Hence the overall efficiency of the biological treatment, even after employing well-acclimatized microorganisms is far from satisfactory (Lin et al., 1998).

It is essential to enhance the biodegradability of the effluent by breaking the refractory chemicals prior to the biological process to enhance the biodegradability which can be achieved by proper application of physico-chemical or chemical or advanced oxidation methods (Mouli et al., 2004).

A few research on the removal of paracetamol in WWTPs have been focused on biological treatment processes. According to these research, the paracetamol is known to show good removal efficiencies by biological treatment processes due to its high biodegradability (Yu et al., 2006; Jones et al., 2007; Gomez et al., 2007; Wu et al., 2012). Biological degradation of paracetamol can be achieved by anaerobic, aerobic, microorganisms (bacteria and fungi), membrane bioreactor, and phytoremediation.

Anaerobic treatment

Anaerobic technology was used earlier for treating wastewaters of different industries (Rao et al., 2004). In anaerobic treatment, the high organic content in industrial wastewater decomposes into methane and CO_2 with the help of microorganisms. The advantages of anaerobic treatment are very little sludge production, with lower energy inputs, operation at high organic loading rate, operating cost, need of low nutrient amount and production of biogas which can be utilized for energy production in this treatment process (Nandy et al., 2002).

High bacterial sensitivity to some environmental conditions (mainly pH, temperature, and toxic compounds), long starting processes, not good at removing non-organic pollution within wastewater, and the production of malodorous compounds, have been commonly cited as disadvantages of anaerobic treatment (Jewell, 1987). Various reactor configurations such as anaerobic contact reactor, upflow anaerobic sludge blanket reactor, fluidized bed reactor and anaerobic fixed film reactor have been developed to treat wastewaters from different industries (Rao et al., 2004).

The experiment on Weirong et al., (2007) studied the anaerobic biodegradation of paracetamol by using sludge enriched with humic acid in WWTP. The degradation efficiency of paracetamol for half a year with pH (7.0) exceeded 90%. Another study by Dutta et al., (2014) used two-stage anaerobic fluidized membrane bioreactor (AFMBR) and anaerobic fluidized bed reactor (AFBR) to remove paracetamol from wastewater. It was found that the 87.8% of paracetamol (2.70 µg/L) was removed by AFBR and 97.9% by AFMBR. Similarly, Abdullah et al., (2016) employed the an anaerobic packed-bed reactor (APBR) to treatment the brewery wastewater containing paracetamol concentration from 5 to 15 mg/L. It was found that the APBR has a good ability to remove the paracetamol.

Aerobic treatment

Aerobic condition accelerate biodegradation at a much faster rate and to a greater than anaerobic condition in a given time period (Murphy et al., 1995). Advantages of aerobic systems include higher ability of elimination of soluble biodegradable organic matters and lower suspended solid concentration in the effluent (Grady et al., 1999). In aerobic methods, generally aerobic sequencing batch reactor (ASBR) and AC have been used for removing paracetamol from aquatic environment (Fang et al., 2011a).

A study by Wilcox et al., (2009) applied the aerobic treatment in WWTP to remove the paracetamol (0.013-1000 µg/L) from wastewater. It was found the efficiency of this system to reduce the paracetamol concentration less than 0.010 µg/L. Also, Fang et al., (2011a) achieved the treatment of paracetamol by sequencing batch reactor (SBR) with aerobic granular sludge that consisted of a wide variety of bacteria, mainly including coccoid-like and rod-shaped bacterium. The Michaelis-Menten equation could be fitted to the experimental data of paracetamol degradation by 0.31 g-paracetamol/(g- volatile suspended solids (VSS)·h).

In experiment on Hu et al., (2012) carried out studies on biodegradation of paracetamol by aerobic granules using SBR. The aerobic granules are consisted of consortia of coccus and bacillus bacteria which isolated from SBR. The granular sludge on day 80 and 200 degraded paracetamol (1000 mg/L) completely in 48 h and 28 h, respectively, indicating that granulation contributed to paracetamol degradation. The specific paracetamol degradation rate was observed to increase with increasing paracetamol initial concentration from 500 to 5000 mg/L, peaked at 1200 mg- tert-butyl ether (MTBE)/g-VSS·h, and declined with further increases in MTBE concentration as substrate inhibition effects became significant. Paracetamol up to 1000 mg/L could be effectively degraded and mineralized by this consortium. It was further suggested that the granular sludge had a good degradation performance and high mineralization degree of paracetamol.

In aerobic processes, the disadvantages are: (1) usually produce a digested sludge with very poor mechanical dewatering characteristics, (2) have high power costs to supply oxygen, even for very small plants, (3) are significantly influenced in performance by temperature, location, and type of tank material, (4) no heavy metal removal, and (5) lack of useful by-product (Wang et al., 2009).

Activated sludge (AS) process

This process is the most common one utilized biological process in many WWTPs as a secondary treatment. It is capable of converting most organic wastes to stable inorganic forms by oxidizing organic matter into CO_2 and H_2O, NH_4 and new biomass under aerobic conditions (Bitton, 2005; Francisco et al., 2006). The new biomass production excess is the main drawback of biological treatment since a posterior management is required prior to its disposal (Suh and Rosseaux, 2002).

A number of reports have been published about the degradation rate and remove of paracetamol by AS in WWTP and sewage treatment plant (STP). The paracetamol concentration between (0.96 µg/L to 100 mg/L) have been removed completely (100%) or more than 90% by AS process (Yu et al., 2006; Andrew, 2009).

Gomez et al., (2007) investigated that the paracetamol was reduced from 246 µg/L to 4.3µg/L by AS process in STP. Also, Yu et al., (2006) reported that the paracetamol concentration (0.96 µg/L) has been removed with efficiency 99% in WWTP by AS. Another study by Roberts and Thomas (2006) revealed that the paracetamol (69.57 µg/L), which presented in the raw effluent, was completely eliminated by AS. Also, Joss et al., (2006) inducted that the paracetamol was fast degraded by AS in 0.15 day.

Benotti and Brownawell (2007) reported that the AS efficiency removal of paracetamol (61µg/L) was 99% found in WWTP. Similarly, Jones et al., (2007) studied the remove of paracetamol from STP by AS. The medium rate removal of paracetamol was 91.93% observed in 4 days. In similar, Foster (2007) revealed that the paracetamol was removed completely 100% in San Marco WWTP contained AS. Also, Choi et al., (2008) reported that the paracetamol was totally removed in STP in in Han River, Korea. Miege et al., (2008) demonstrated the paracetamol concentration has been removed (292 µg/L) in WWTP with AS process. Another study by Munoz et al., (2008) reported that the more than 40 mg/L of paracetamol was (>99%) removed in STP by AS.

The experiment on Andrew (2009) applied the AS for paracetamol (100 mg/L) degradation and found that the 100% of paracetamol concentration was removed during 8 days. In study by Kasprzyk-Hordern et al., (2009) reported the 92% removal of paracetamol in WWTP with cilfynydd-trickling filters and almost 100% removal of paracetamol in WWTP with AS. Also, Radjenovic et al., (2009) recorded that the paracetamol was 100% removed in full-scale AS during the pharmaceutical wastewater treatment.

Kosmaa et al., (2010) reported that the highest mean removal of paracetamol was 97% found in the municipal and hospital WWTPs in Western Greece. In similar, Gros et al., (2010) found that the removal rate for paracetamol was up to 99% in WWTP with conventional AS system in Barcelona, Spain. The experiment on Lin et al., (2010) showed that the 99% of paracetamol was removed in WWTP by AS system. Similar results were also reported by Sim et al., (2010) and Nödler et al., (2010) demonstrated the concentration of paracetamol decrease rate over 99% in WWTP by AS process.

Rosal et al., (2010) recorded that the removal of paracetamol (23 µg/L) was completely eliminated by biological treatment. In similar, Pedrouzo et al., (2011) revealed that the paracetamol (19.850 µg/L) was completely eliminated in STP by AS system. Falas et al., (2012) used AS system for removal of some pharmaceuticals. The paracetamol was 100% removed by this system. Gracia-Lor et al., (2012) found that the concentration 201µg/L of paracetamol in WWTP influent has been removed effectively during treatment with AS system.

Membrane bioreactor (MBR)

The MBR has been used for the large-scale wastewater treatment of industrial wastewater and have become an alternative to conventional activated sludge (AS) processes for wastewater treatment (Yang et al., 2006; Trinh et al., 2012). MBR technology is considered the most promising development in biological wastewater treatment (Petrovic et al., 2009).

The advantages of MBR are full removal of suspended solids, compact plant size, efficiently in degradation, flexibility in operation, little sludge production, disinfection and odor control, prolonged microorganisms retention time and treatment of toxic organic and inorganic contaminants (Rana et al., 2014). The main disadvantage of MBR is high energy usage to reduce the fouling problem. Coupling of fluidized bed reactor with membrane reactor was found to potentially reduce the membrane energy cost (Kim et al., 2011).

Several reports have explored the removal of paracetamol from WWTP or STP to evaluate the MBR system efficiency. Brun et al., (2006) reported that the paracetamol was totally removed in STP in Atlantic Canada. Similar results were also reported by Snyder et al., (2006) and Joss et al., (2006) revealed that the biodegradation of paracetamol was completely degraded by MBR.

Kim et al., (2007) studied the removal of pharmaceuticals in municipal STP in a MBR pilot plant and obtained a removal efficiency of 99% for paracetamol. Also, Thomas et al., (2007) recorded that the paracetamol was reduced from 43.223 µg/L to 0.031µg/L in WWTP. Stackelberg et al., (2007) reported that the paracetamol was decreased from 0.015 µg/L in source drinking water to 0.0003 µg/L in finished drinking water with the efficiency 98% removal. Radjenovic et al., (2007) found the removal efficiency 98.6% of paracetamol in a laboratory-scale MBR.

Biological treatment combined with membrane filtration is also employed for treating wastewater. Radjenovic et al., (2009) applied the MBR equipped with hollow-fibre (HF) UF membrane in in WWTP with using pilot-scale to remove the paracetamol from the aqueous phase. It was showed that the paracetamol was completely removed from wastewater.

The experiment on Shariati et al., (2010) compared between the efficiency of the external loop airlift membrane bioreactor (ELAMBR) system and the AS for treatment the wastewater containing paracetamol. After 2 days, the concentration 1000 mg/L of paracetamol was 100% removed by ELAMBR system, whereas by AS process, it was reduced from 1200 mg/L to 445 mg/L. Lin et al., (2010) paracetamol was detected at the highest concentrations (33.4 µg/L) and was effectively removed 99% by MBR system.

Lubliner et al., (2010) reported that the concentration which ranged between 182 to 233 µg/L in wastewater influent has been 100% removed in secondary treatment with biological treatment. In study by Behera et al., (2011) indicated that the 99.9% of paracetamol was removed in WWTP with biological treatment. In similar, Gros et al., (2012) revealed that the paracetamol was decreased from 18.7 µg/L to zero during the biological treatment.

Kovalova et al., (2012) found that the paracetamol (107.1 µg/L) was removed with efficiency 99% from hospital wastewater by MBR. Also, Verlicchi et al., (2012) reported the removal of paracetamol (246 µg/L) with efficiency 93% in AS, and 99% in MBR. Schröder et al., (2012) applied the MBR to evaluate the treatment of wastewater containing paracetamol. After 14 days, it was 100% of paracetamol removed. Santos et al., (2013) recorded that the (13.03–58.85 µg/L) of paracetamol was eliminated with efficiency 96.1% by biological treatment in WWTP. Also, Kim et al., (2014) applied the MBR to remove the paracetamol (1000 µg/L) from WWTP. The degrading paracetamol was >97% observed by MBR.

Lu et al., (2009) coupled the laccases enzymes with completely mixed batch reactors (CMBRs) in 50 mL glass flasks. The reaction solution was prepared in 0.01 M phosphate buffer (pH 7.0) containing 50 µM paracetamol. It was found that paracetamol could be effectively transformed and removed from water by laccase-mediated oxidative coupling processes. These findings demonstrated that laccase-mediated oxidative coupling can potentially serve as an alternative strategy to control certain micropollutants in water/wastewater treatment and reuse.

Microorganisms degradation of paracetamol

Microorganisms play a vital role in the degradation of xenobiotics and in maintaining the steady-state concentration of chemicals in the environment (Misal et al., 2011). Microorganisms in the biological treatment oxidize organics into more simple constituents. The microorganisms are also used to remove nitrogen through nitrification and denitrification (Metcalf and Eddy, 2003).

The microorganisms require a range of nutrients to grow. Beyond nutrient requirements, other factors can affect the effectiveness of microbial degradation such as the nature of organic matter and the environmental conditions. Also, the presence some toxic and non-biodegradable compounds that cannot be assimilated by the biomass without the presence of specific previously adapted microorganisms (González et al., 2006). On the other hand, pH and temperature are other environmental factors affecting biodegradability. Moreover, the presence of high concentration of suspended solids or turbidity in wastewater influence the ability of microorganisms for survival and proliferation (Stephenson and Blackburn, 1998; Jang et al., 2013).

Microorganisms have established effective strategies involving specialized enzyme systems and metabolic pathways to access paracetamol as a carbon and energy source. Thus, such microorganisms are capable of degrading paracetamol and converting them to easily metabolizable substrates (Wu et al., 2012).

The essential characteristics of aerobic microorganisms degrading organic pollutants are:1) metabolic processes for optimizing the contact between the microbial cells and the organic pollutants. (2) The initial intracellular attack of organic pollutants is an oxidative process, the activation and incorporation of oxygen is the enzymatic key reaction catalyzed by oxygenases and peroxidases. (3) Peripheral degradation pathways convert organic pollutants step by step into intermediates of the central intermediary metabolism. (4) Biosynthesis of cell biomass from the central precursor metabolites (Fritsche and Hofrichter, 2005).

Some of bacteria and fungi which are capable of using paracetamol as carbon and energy source have been described. Further, a microbial consortia involving fungal and bacterial cultures for treatment were found effective in removing the paracetamol (Fang et al., 2011a; Zhang et al., 2013b). The advantages of microbial degradation and mineralization of paracetamol are representing in the producing nontoxic byproducts and reducing the environmental impact of the treated water on the receiving surface and drinking water supplies (Gusseme et al., 2011).

Bacterial treatment

Some bacteria have been reported to use the paracetamol as the sole carbon, nitrogen, and energy resource for growth as well as capable of degrading and converting it to nontoxic compounds. A listing of isolated bacterial strains characterized for the degradation of the paracetamol is presented in table (1) (Wu et al., 2012). Also, the biodegradation performance of patacetamol by bacterial consortia were much better than any pure bacterial strain due to a potential complementary interaction among the different bacterial strains (Fang et al., 2011a; Zhang et al., 2013b).

The first study by Ahmed et al., (2001) aimed to isolate and characterize of a new paracetamol and 4-aminophenol degrading microorganism from wastewater contaminated site of a pharmaceutical plant. Detailed studies identified the organisms as *Pseudomonas* sp. strain ST-1 and capable of using phenol 4-aminophenol (4000 mg/L) and paracetamol (4000 mg/L) as sole source of carbon and energy. The optimal conditions for growth were recorded at 30°C and pH 7. Non growing suspended cells of strain degraded 68% of 4-aminophenol and 76.8% of paracetamol in 72 h. This strain may contribute to efforts on phenolic bioremediation, particularly in an environment with very high levels of paracetamol and 4-aminophenol.

The experiment on Khan et al., (2006) recorded that the *Pseudomonas* sp. strain ST-4 was grown on mineral salt media plates containing 400 ppm of 4-aminophenol as growth substrate and found to be able to degrade it up to 84%. Biodegradation was found to be more effective than autoxidation of 4-aminophenol, indicating bioremediation as main process to eliminate aromatic amines.

A study by Gusseme et al., (2011) reported that two paracetamol degrading strains were isolated from the membrane bioreactor biomass and identified as *Delftia tsuruhatensis* and *Pseudomonas aeruginosa*. It was found that the 97% and 40% of paracetamol concentration were removed by *D. tsuruhatensis* and *P. aeruginosa*, respectively, in 48 h. Also, it was recommended that the specific enrichment of a microbial consortium in an MBR operated at a high sludge age might be a promising strategy for post-treatment of WWTP effluents containing pharmaceuticals.

Furthermore, three bacterial strains which capable of degrading paracetamol were isolated from a high efficiency paracetamol degrading aerobic granules by Fang et al., (2011a). These strains were identified and assigned to be *Cupriavidus* sp. strain F1, *Lysobacter* sp. strain F2 and *Pseudomonas* sp. strain Fg-2. The optimal conditions for the growth of the strains were all at 25~35℃ and pH 7~8. The strains F1, F2, and Fg-2 were able to degrade paracetamol up to 400 mg/L, 2500 mg/L and 2000 mg/L, respectively. The hydroquinone 1,2-dioxygenase and catechol 1,2-dioxygenase enzyme were found with high activities in all strains extracts which suggested these enzymes might play important roles in degrading paracetamol. It was suggested that the synergistic effect exerted by different strains in the microbial consortia possibly strengthened biodegradation of paracetamol.

Another study by Fang et al., (2011b) isolated the paracetamol degrading bacteria from activated sludge samples and identified as *Cupriavidus necator*. The optimal pH 7.0 and temperature 30℃ were found for *C. necator* biodegradation in shaking flasks. This strain was found completely degrading of paracetamol at the initial concentration of 400 mg/L in 48 h. The degrading process of the strain F1 followed the Haldane kinetic model. The maximum specific growth rate and yield coefficient were 0.097 h^{-1} and 0.21 mg/mg recorded, respectively. The results indicated that this strain had a high mineralization extent for paracetamol.

Hu et al., (2013) isolated the *Pseudomonas aeruginosa* strain HJ1012 from stable microbial aggregate in a sequencing batch reactor treating paracetamol contaminated wastewater. This organism could completely degrade paracetamol as high as 2200 mg/L within 75 h of reaction. Haldane’s equation adequately described the relationship between the specific growth rate and substrate concentration. The maximum specific growth rate and yield coefficient were 0.201 g-paracetamol/g- VSS·h and 0.101 mg of biomass yield/mg of paracetamol consumed, respectively. It is degraded predominantly via p-aminophenol to hydroquinone with subsequent ring fission, suggesting partially new pathways for paracetamol degrading bacteria.

Zhang et al., (2013b) isolated three bacterial strains from a paracetamol degrading aerobic aggregate, and assigned to species of the genera *Stenotrophomonas* sp. strain Fg-2 and *Pseudomonas* sp. strain F1 and F2. The *Stenotrophomonas* sp. was the first time known to be as the paracetamol degraders. In batch cultures, the strain F1, F2, and Fg-2 could perform complete degradation of paracetamol at concentrations of 400, 2500, and 2000 mg/L or below in 116 h, 60 h, 45 h, respectively. A combination of three microbial strains resulted in considerably enhanced degradation and mineralization of paracetamol. These strains were able to use up to 4000 mg/L, and mineralized 87.1% of the added paracetamol at the initial of 2000 mg/L. A combination of the three microbial strains recovered from the same culture was shown to be necessary for complete paracetamol degradation and mineralization, suggesting a possible complementary interaction among the various isolates.

Mixed microbial communities have the most powerful biodegradative potential because the genetic information of more than one organism is necessary to degrade the complex mixtures of organic compounds present in contaminated areas. The genetic potential and certain environmental factors such as temperature, pH, and available nitrogen and phosphorus sources, therefore, appear to determine the rate and the extent of degradation (Fritsche and Hofrichter, 2005).

Therefore, the synergistic effects on the paracetamol degradation in the co-culture of microorganisms may be attributed to their metabolic products in the consortia. The synergistic enhancement of degradation efficiency in consortia can result from the cooperative effects as a result of different complementary biochemical compound degradation pathways in the strains, assimilation of compound onto cell membrane and changes of cell hydrophobicity by excreted substances, removal of compound metabolites by one strain that inhibit other strains, and significant increase of biomass using surfactants as a primary carbon source.

Mutnur (2014) isolated the *Pseudomonas mendocina* from wastewater and applied to degrade the paracetamol. It was found that this strain able to grow in paracetamol concentration from 500 to 1000 mg/L and degraded it in 48 h. *Pseudomonas* species are environmental organisms known for their ability to degrade aromatic compounds of environmental concern (Neumann et al., 2004; Cámara et al., 2009). The adaptability of *Pseudomonas* species to different organic compounds makes it an attractive organism for its use in biodegradation for a wide ranges of organic substances that present in WWTP.

Table (1). Bacterial strains capable of utilizing paracetamol as a sole carbon source.

Species, strain	Isolated from	Concentration (mg/L^{-1})	Performance	References
Stenotrophomonas sp. f1	Paracetamol-degrading aerobic aggregate	400	100% degradation in 116 h	Zhang et al., (2013b)
Pseudomonas sp. f2	Paracetamol-degrading aerobic aggregate	2500	100% degraded in 70 h	Zhang et al., (2013b)
Pseudomonas sp. fg-2	Paracetamol-degrading aerobic aggregate	2000	100% degraded in 45 h	Zhang et al., (2013b)
Delftia tsuruhatensis	In a membrane bioreactor biomass	100	Shaking flask, 97 % degraded in 48 h	Gusseme et al., (2011)
Pseudomonas aeruginosa	In a membrane bioreactor biomass	16	Shaking flask, 40 % degraded in 48 h	Gusseme et al., (2011)

Cupriavidus necator F1	Activated sludge samples	400	Completely degradation in 48 h	Fang et al., (2011b)
Pseudomonas sp. ST-4	Activated sludge samples (4-aminophenol as substrates)	200 ppm	Shaking flask, 80 % degraded in 72 h	Khan et al., (2006)
Pseudomonas sp. strain ST-1	wastewater contaminated site of a pharmaceutical plant	4000	76.8% degraded in 72 h	Ahmed et al., (2001)
Pseudomonas aeruginosa strain HJ1012	In a sequencing batch reactor treating	2200	99% degraded in 75 h	Hu et al., (2013)
Pseudomonas sp. strain Fg-2	In sequencing batch reactor	2500	100% degraded	Fang et al., (2011a)
Lysobacter sp. strain F2	In sequencing batch reactor	2000	100% degraded	Fang et al., (2011a)
Pseudomonas mendocina	Wastewater	500-1000	Growth and utilized in 48 h	Mutnur (2014)

Fungal treatment

Fungi are known to degrade a wide variety of materials and compounds, process known as mycodegradation (Singh, 2006). Living fungi are employed in degradation of persistent organic pollutants due to their unspecific oxidative enzymatic system, which includes ligninolytic extracellular enzymes as laccase and peroxidases, as well as intracellular enzymes as the cytochrome P450 system (Asgher et al., 2008; Kues, 2015).

Few studies up to now have been reported about the use of fungi and their enzymes to remove or degrade the paracetamol. Hart and Orr (1975) recorded the first studies of paracetamol removal with fungi strains which isolated from a solution of paracetamol and identified as a *Penicillium* sp. This strain was found to possess the ability to utilize a paracetamol as sole carbon sources for growth. Studies with washed-cell suspensions indicated that growth of the *Penicillium* sp. isolate in the presence of paracetamol induced the respective enzyme systems for the degradation of this compound to acetate and 4-aminophenol.

Cruz-Morató et al., (2014) carried out the treatment paracetamol using a *Trametes versicolor* pellets fungi in a batch fluidized bed bioreactor under sterile and non-sterile conditions. The initial total amount of paracetamol into the reactor was between 109.3 µg/L–114.4 µg/L. The paracetamol concentration was completely removed after 8 days. Also, Ba et al., (2014) used the two fungal enzymes, laccase (*Trametes versicolor*) and tyrosinase (mushroom), and combined into crosslinked enzyme aggregates by using a chitosan that was applied to the transformation of paracetamol from wastewater samples. The paracetamol transformation was achieved of more than 80% to nearly 100% from the municipal wastewater and of more than 90% from the hospital wastewater by crosslinked enzyme.

Phytoremediation

Phytoremediation technology, green bioremediation, is a developing low-cost technique for removal of heavy and hazardous metal ions from industrial wastewater. In such case, phytoremediation that use the natural or transgenic plants proves a better treatment tool for bio-treatment is able to bioaccumulate the toxins (Amin et al., 2013).

Plant roots release substances, which may interact with contaminants and decompose them to non-toxic, low molecular substances, which can be degraded by microorganisms easily. By using plants, one can avoid introducing additional, potentially harmful chemicals into the environment. Phytoremediation techniques are relatively manageable and allow a fast adaption to a specific area as well as not require large investment to be practically introduced. Furthermore, they are cost friendly as they are able to remove several pollutants at once and can be applied at a small as well as at a large scale (Susarla et al., 2002; Kotyza et al., 2010).

Huber et al., (2009) used the a hairy root culture of horseradish (*Armoracia rusticana* L.) to remove the paracetamol with concentration 1 mM in the growth medium. The result showed that 70% of paracetamol concentration was decreased after 3 h of incubation.

Another study by Kotyza et al., (2010) carried out the treatment of paracetamol with the help of *Armoracia rusticana* and *Linum usitatissimum* in hairy root cultures and hydroponically cultivated with the *Lupinus albus*, *Hordeum vulgaris*, and *Phragmites australis* plants in laboratory conditions. It was found that 100% (160 mg/L) and 50% (30 mg/L) of starting amount were removed during 8 days by *A. rusticana* and *L. usitatissimum*, respectively. *A. rusticana* have been found the ability to remove paracetamol (600 mg/L) completely from the medium. The paracetamol in concentrations of 0.1 mM (15.12 mg/L) was 100% by *L. luteolus*, 83% by *H. vulgare* and 16% by *P. australis* removed from media during 4 days.

In the case of *Hordeum*, paracetamol was fully removed during 2 days and partially released back to the media at the end of experiment. Based on this observation, it is possible to suppose, that paracetamol is stored in vacuole and released because of toxic effect of paracetamol to *Hordeum* plant (Kotyza et al., 2010)

The experiment on Ribeiro et al., (2011) evaluated the efficiency of sugar cane bagasse (SCB) and vegetable sponge (VS) (*Luffa cylindrica*) plants and compared with AC for removing paracetamol (100 µM) from aqueous media. The results showed that SCB was more attractive than AC in terms of price and efficiency (60% against 45% adsorption, respectively), while VS was responsible for removing 40% of paracetamol dissolved in the enriched water samples. Similarly, Lee (2013) carried out the remove of paracetamol from contaminated water with the help of plants duckweeds, *Lemna minor* and *Spirodela polyrhizza*. There was totally (100%) removed of the paracetamol after 7 days by duckweeds.

Conclusion

The physical processes described previously has shown limited success for the treatment of paracetamol from aquatic environment. The regeneration of membrane filtration and activated carbon after use has several problems representing which effect on efficiency to reject and adsorb the paracetamol and disposable it again to environment as parent compound without degradation.

The chemical processes such as advanced oxidation processes has effectively degraded paracetamol from the aquatic environment in few hours. The cost of chemical agents and the energy sources are the major disadvantage on using chemical methods to remove the paracetamol from wastewaters. However, the natural compounds may lead to a reduction in treatment efficiency as these compound may act as antioxidants. The interaction condition and chemical concentration that lead to precipitate almost all the byproducts present in the wastewater are also drawbacks on using the chemical as management tool for remove micropollutants.

Methods which produce fewer intermediates must to allow for effective modeling and application are being developed to implementation the industrial wastewater treatment. However, the combination between physicochemical processes accelerate the paracetamol degradation and reduce the cost of the treatment process.

Biological process is considered to be the most crucial process for the removal of paracetamol present to a large extent in the dissolved phase in WWTP. It is showing higher removal rates of paracetamol. In the biological process, the use microorganisms exhibited a highly selective removal efficiency towards the target pollutants and it can be stated that is more appropriate for environment cleanup of pollutants. So by developing an understanding of microbial communities and their response to the natural environment and pollutants, expanding information of genetics of the microbes to increase capabilities to degrade pollutants, researching for new biodegradation techniques which are cost effective, these opportunities offer potential for significant advances.

The drawbacks of use biological process are take more period for degradation, seasonal variation of the microbial activity as a result by direct exposure to changes in environmental factors that cannot be regulated and problematic application of treatment additives. As biodegradation can be effective only where environmental conditions permit microbial growth and activity. Therefore, the capacity of degradation by microorganisms decreased when the nutrients and energy sources are not enough. However, the biological process is often highly specific and limited to some compounds that are biodegradable.

Regardless of which aspect of biodegradation that is used, this technology offers an efficient and cost effective way to treat contaminated ground water and soil. Its advantages generally outweigh the disadvantages, which is evident by the number of sites that choose to use this technology and its increasing popularity. The combination between the physicochemical and biological processes has increased attention recently. The combined process enhance the degradation rate and complete degradation the non-biodegradability as well as reduce the treatment process cost.

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