sciendo

CIVIL AND ENVIRONMENTAL ENGINEERING REPORTS

E-ISSN 2450-8594

CEER 2019; 29 (3): 001-033
DOI: 10.2478/ceer-2019-0021
Original Research Article

PHOTOCATALYTIC DEGRADATION OF PHARMACEUTICALS USING TiO_2 BASED NANOCOMPOSITE CATALYST- REVIEW

Omar FAWZI SULEIMAN KHASAWNEH[2], Puganeshwary PALANIANDY[1],
School of Civil Engineering Campus, Universiti Sains Malaysia, Malaysia

A b s t r a c t

The occurrence of contaminants of emerging concern (CECs) such as pharmaceutical compounds (PhACs) is becoming a major global issue due to the persistence, bioaccumulation, and toxicity of these pollutants. Human and animal consumption was recognized as the major sources for pharmaceutical pollution. Existent conventional treatment processes have shown low degradation efficiencies towards PhACs. In this regard, TiO_2 based nanocomposite photocatalysis process has presented effective degradation towards PhACs. Operational parameters such as dopant content, catalyst loading, and initial pH were the major factors in the photocatalysis system. In this review, we discuss the recent studies that have employed TiO_2 based nanocomposite for the degradation of PhACs. Future research recommendations have also been elaborated.

Keywords: nanocomposite catalyst, photocatalysis, TiO_2, pharmaceutical compounds, photocatalytic process, titanium dioxide

[1] Corresponding author: Universiti Sains Malaysia, Civil Engineering Campus, 14300 Nibong Tebal, Penang, Malaysia, email: cepuganeshwary@usm.my, tel. +60164431545
[2] Student of the Universiti Sains Malaysia, Civil Engineering Campus, 14300 Nibong Tebal, Penang, Malaysia

1. PHARMACEUTICAL COMPOUNDS

Over recent years, the appearance of micropollutants in the aquatic environment became a major worldwide disquiet. Micropollutants which are also termed as emerging contaminants (ECs), consist of different and various amount of anthropic and natural substances, including pharmaceuticals, personal care products, agrochemicals, steroid hormones, and drugs of abuse (Luo et al., 2014; Ribeiro et al., 2015). Pharmaceutical compounds (PhACs) are chemical compounds that are used to diagnose, cure, and prevent the occurrence of diseases (Quesada et al., 2019). Furthermore, PhACs can be defined as prescriptions obtained over the counter and veterinary drugs which are used to cure human and fauna (Ebele et al., 2017). One of the significant issues with these substances is that they are commonly present in water bodies at low concentration, ranging from the nanogram to the microgram per liter, and each of these substances differs in their chemical nature, making their detection, analysis, and even removal from water and wastewater treatment plants a challenging quest (Luo et al., 2014).

Moreover, pharmaceutical compounds are developed to be biologically active and persistent in order to maintain their therapeutic activity in human and animals (Lee et al., 2017b). Hence, they can escape conventional biological treatment processes. In addition, the physiochemical properties of pharmaceuticals, such as lipophilicity, polarity, volatility, adsorption properties, and persistence (Farré et al., 2011; Geissen et al., 2015; Lee et al., 2017b), means that they are not completely and easily removed from by traditional water and wastewater treatment processes, which can induce the bioaccumulation of these compounds in the aquatic environment, causing negative effects towards to the aquatic organisms, environment, and the public health (Lee et al., 2017b; Ebele et al., 2017).

Various types of human medicines, such as antibiotics, synthetic hormones, statins, anti-inflammatories, and cytotoxins are continuously produced and consumed in large amounts, reaching thousands of tons per year (Quesada et al., 2019). It has also been documented that approximately about 3000 different substances are being used as ingredients for the manufacturing of pharmaceuticals, including painkillers, antibiotics, β-blockers, lipid regulators, impotence drugs, and antidepressants (Rodriguez-Narvaez et al., 2017). As a result, numerous pharmaceuticals, such as paracetamol, carbamazepine, and caffeine, have been detected in the sewage effluents and river systems of Australia as well as New Zealand, at maximum concentrations of 7150 ng/L, 682 ng/L, and 3770 ng/L, respectively (Scott et al., 2014). Moreover, several PhACs such as acetaminophen, cimetidine, and sulfamethoxazole, at concentration levels of 34.8, 281, and 26.9 ng/L have been reported in the surface water of Han River in Korea (Choi et al., 2008).

The presence of PhACs in water compartments has raised significant concerns due to their potential risk on humans and the aquatic environment (Tran et al., 2018; Quesada et al., 2019). Although the potential risks on human health and environment from direct exposure to pharmaceuticals residuals are very low, however, exposure to pharmaceuticals can indirectly impact the environment (Boxall, 2018). In the case of acetaminophen (ACT), it has been reported that overdosing on ACT can cause potentially fatal liver damage and rare skin reactions such as Steven-Johnson syndrome (Thi and Lee, 2017). Furthermore, the existence of antibiotics, such as tetracycline, ampicillin, and trimethoprim in the aquatic environment, could potentially create antibiotic-resistant strains in the natural bacteria population (Ebele et al., 2017). Moreover, pharmaceuticals, such as ciprofloxacin, oxolinic acid, and fluoroquinolone have been reported to cause adverse effects on aquatic organisms, such as toxicity towards green algae (Halling-Sørensen et al., 2000), *Daphnia magna*, *Microcystis aeruginosa*, etc. (Robinson et al., 2005; Ebele et al., 2017). In addition, antibiotics such as tetracycline have shown to cause toxic effects towards the plants as well as on the aquatic organisms in their early stage (Lee et al., 2017b). Existence of pharmaceuticals in the aquatic environment has also been found to prompt endocrine or hormonal disruption problems (Khataee et al., 2013). An experimental study conducted by Kidd et al. (2007) in a pristine lake in Canada, revealed that addition of some pharmaceuticals such as estrogen ethinyl estradiol (EE2) can potentially induce the feminization of males and can cause the collapse of the fish population.

As a consequence, several approaches have been adopted in the USA, United Kingdom, and Australia, in order to assess the health risks resulting from exposure to pharmaceuticals in water (WHO, 2012). According to the World Health Organization (WHO), the potential health risks from pharmaceuticals in drinking water can be assessed by employing the minimum therapeutic dose (MTD) as the selected point of departure (PoD) (Watts and Maycock, 2007; WHO, 2012). The MTD, is usually equal to the recommended or lowest prescribed dose, taking into account the number of daily doses. Another approach, which is based on ranking the pharmaceuticals and personal care products (PPCPs) according to their relative potential risk on the aquatic environment has also been adopted by the Environmental Agency (EA) of England and Wales (Ebele et al., 2017). The proposed ranking system employs a conventional risk assessment procedures, namely as: persistence, bioaccumulation, and toxicity (PBT). Based on these criteria, top compounds that can pose potential risk were identified (Ashton et al., 2004; Ebele et al., 2017). In spite of the fact that there are no legal discharge limits for emerging contaminates, however, some regulations have been issued (Barbosa et al., 2016). For example, the European

water policy has published the first regulation "Directive 2000/60/EC", which uses a strategy that prioritizes substances that can pose high risks (Directive, 2000). Eight years later, a group of 33 priority substances and respective environmental quality standards (EQS) were regulated by the Directive 2008/105/EC (Directive, 2008). Followed by the new Directive 2013/39/EC that recommended the monitoring and treatment for another set of 45 substances (Directive, 2013). Recently, it has been reported that the standard environmental regulation permits a maximum total pharmaceutical waste concentration of only 50 ng/L in discharge water (Rosman et al., 2018).

1.1. Fate and occurrence of pharmaceuticals

Although the growth rate of the financial disbursement per person of pharmaceutical compounds (PhACs) has declined. However, due to the decrease in the production cost and development of generic drugs, the price for PhACs became more affordable and accessible. Subsequently, the consumption rate has steadily increased in recent years. Furthermore, the continuous demand for the treatment of common illnesses, such as chronic diseases and aging disorders has also contributed to the increasing consumption in pharmaceuticals (Quesada et al., 2019).

The routes and fates of pharmaceutical compounds have been discussed in several literatures (Rosman et al., 2018; Lee et al., 2017b; Quesada et al., 2019). Fig. 1 depicts the possible fate and pathways for the occurrence of pharmaceutical compounds in the aquatic environment. Generally, PhACs are introduced into the aquatic environment either in their parent form or as metabolites form via various routes. As shown in Fig. 1, pharmaceutical residuals can be discharged and enter the surface water, groundwater, and soil via human and animal excretion after their consumption and metabolism. Basically, healthcare facilities, including hospitals and clinics, as well as private households, are considered among the major sources of pharmaceutical pollution. Hospitals contribute to major release of pharmaceuticals to the environment through patients' excretions (Bagheri et al., 2016). This is followed by private household consumption of pharmaceuticals. Human excreted residue (feces and urines) may then enter sewage treatment plants (STPs) either in their parent compound or metabolite (Helwig et al., 2016). Depending on the STPs and properties of pharmaceuticals, only parts of the PhACs are treated, whereas the remaining residues are introduced into the aquatic environment (Lee et al., 2017b), such as surface and ground water. In contrast, improper waste disposal of pharmaceuticals by human into toilets or sinks can also result in contamination of the environment (Lee et al., 2017b). In addition, medicinal products for veterinary use are also considered a significant source of pharmaceutical pollution (Lee et al., 2017b). Numerous drugs for veterinary are used in husbandry sector, mainly as growth promoters, breeding, and therapeutic

purposes (Bundschuh et al., 2016). After the consumption of pharmaceuticals by animals and livestock, pharmaceuticals are then excreted through feces and urines, either in their parent or metabolite form. The excreted drugs can then enter the soil and groundwater, causing contamination towards the environment (Lee et al., 2017b). Moreover, livestock's manure, which is often used as a fertilizer in the agriculture industry, can sometimes contain pharmaceutical residues that could be introduced into surface water or groundwater through infiltration (Abellán et al., 2007; Ebele et al., 2017) as illustrated in Fig. 1. Since Conventional wastewater treatment plants are not designed for the degradation of micropollutants (Lee et al., 2017b), hence, these pharmaceutical compounds are not biodegraded in conventional wastewater treatment plants. As a result, they are discharged with the treated effluent into water bodies, such as rivers and lakes. Further, reports have stated that these pharmaceuticals can still exist in drinking water, even after conventional water treatment (Rosman et al., 2018; Quesada et al., 2019).

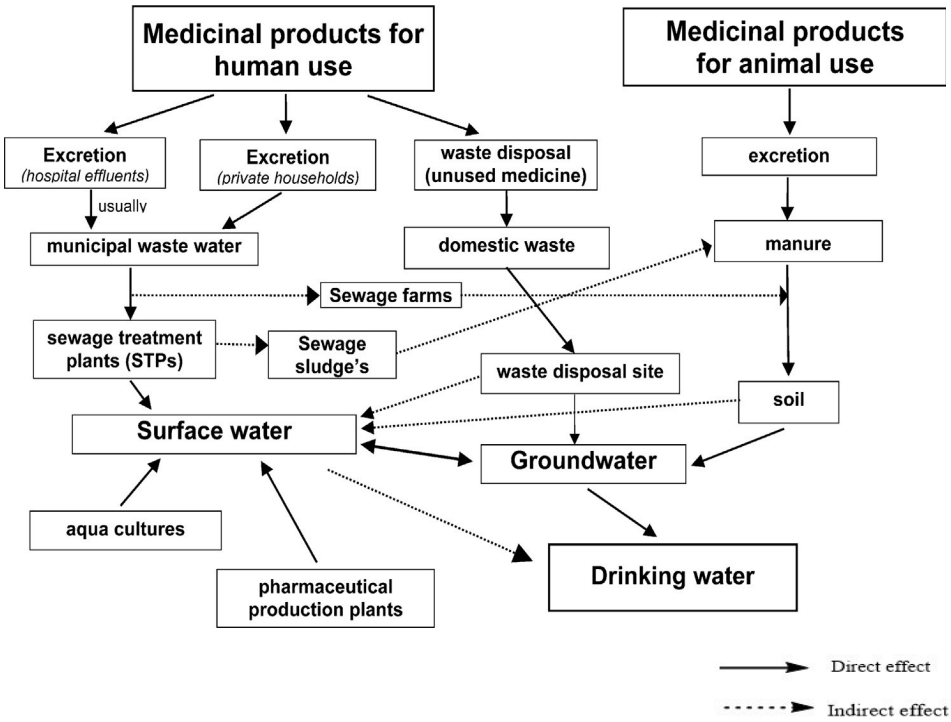

Fig. 1. Possible fate and pathways for the occurrence of pharmaceutical compounds in aquatic environment (Rosman et al., 2018)

The occurrence of pharmaceutical compounds in water bodies is raising significant concerns as it's becoming a global issue. However, determining the global consumption of pharmaceuticals is of great difficulty. This is due to the fact that the number of compounds used differ locally, depending on the lifestyles, accessibility, location, and population (Quesada et al., 2019). Table 1 summarizes some of the frequent detected pharmaceutical compounds in different countries. From Table 1, it can be noticed that acetaminophen (paracetamol), which is often used as a painkiller, or for the treatment of headaches and fevers, showed the highest concentration among the other PhACs. This could be attributed to the popularity of this compound and because of its lower risk of gastrointestinal toxicity (e.g., ulceration, bleeding) and so may be better tolerated (Schilling et al., 2010; Chun-Te Lin et al., 2016).

Table 1. Detected pharmaceutical compounds in different countries

Compound	Concentration (ng L^{-1})	Mean (ng L^{-1})	Country	Reference
Acetaminophen	0 – 9.61	3.18	China	Yang et al. (2018)
	354.00 – 508.00	430.00	Mexico	Rivera-Jaimes et al. (2018)
	0 – 69.15	38.18	Portugal	Pereira et al. (2017)
	0 – 9822.00	209.00	UK	Burns et al. (2018)
	-	34.8	South Korea	Choi et al. (2008)
	-	89.60	Poland	Caban et al. (2015)
	-	85.00	Japan	Komori et al. (2013)
Nitrofurazone	32.43 – 41.93	38.37	Malaysia	Praveena et al. (2018)
Ibuprofen	0 – 846.00	317.80	South Africa	Matongo et al. (2015)
	0.40 – 86.90	29.51	Portugal	Pereira et al. (2017)
	-	55.4	Poland	Caban et al. (2015)
Diclofenac	0 – 15.49	3.95	Malaysia	Praveena et al. (2018)
	258.00 – 352.00	313.00	Mexico	Rivera-Jaimes et al. (2018)
	25.13 – 51.24	33.56	Portugal	Pereira et al. (2017)
	0.02 – 1.49	-	Sweden	Lindim et al. (2016)

Ciprofloxacin	52.50 – 138.17	112.4	Malaysia	Praveena et al. (2018)
Carbamazepine	0 – 5.80	3.3	France	Celle-Jeanton et al. (2014)
Naproxen	834.00 – 986.00	911.00	Mexico	Rivera-Jaimes et al. (2018)
	0 – 7189.00	278.00	Spain	Carmona et al. (2014)
Erythromycin	0 – 6.46	1.31	Bangladesh	Hossain et al. (2018)
	0 – 263.00	-	UK	Burns et al. (2018)
Sulfamethoxazole	0 – 33.20	-	UK	Burns et al. (2018)
	19.26 – 75.48	61.49	Malaysia	Praveena et al. (2018)
	0 – 14.73	-	USA	Bean et al. (2018)
Ketoprofen	-	21.00	USA	Ferrer and Thurman (2012)
	0.03 – 1.27	-	Sweden	Lindim et al. (2016)

1.2. Removal of pharmaceuticals

Biological treatment technologies including activated sludge, constructed wetlands, aerobic bioreactor, trickling filter, membrane bioreactor (MBR), etc. are considered the most widely used treatment technologies for the removal of emerging contaminants (ECs), mainly, by the mechanism of biodegradation (Ahmed et al., 2017). The biodegradation mechanism is a process by which ECs are decomposed by microorganisms such as, bacteria, fungi, and algae, to simple inorganic matter, such as carbon dioxide and water (Garcia-Rodríguez et al., 2014). In the case of traditional biodegradation process, microorganisms employ organic matter as essential substrates for their growth and promotion of enzymes for their ingestion (Tran et al., 2013). However, the toxicity and persistence of some ECs towards cell and microbial growth can restrain and inhibit their biodegradation process (Ahmed et al., 2017). Nevertheless, it has been reported that some microorganisms can still biodegrade ECs by producing specific enzymes. For instance, some types of fungi can produce extracellular enzymes that exhibit low substrate specificity, rendering it suitable for the degradation of some ECs (Cajthaml et al., 2009).

Several reports (Svenson et al., 2003; Kasprzyk-Hordern et al., 2009) have stated that the use of activated sludge is more efficient and cheaper than the trickling filter. It has been reported that activated sludge treatment resulted in higher

removal efficiency of over 85%, compared to less than 70% removal rate when using trickling filter as the treatment system. As a result, in order to employ such treatment technologies, the present biological systems should be developed and modified to be able to degrade persistent micropollutants (Ahmed et al., 2017). Also, another disadvantage of using biological treatment systems is that they are very slow, and they contribute to the disposal of large quantities of sludge. Moreover, they require proper control over the temperature and the pH of the system (Ollis and Al-Ekabi, 1993; Kumar and Pandey, 2017).

Furthermore, conventional wastewater treatment technologies are fashioned to degrade a variety of pollutants, such as carbonaceous matter, pathogens, nutrient, and particulates (Luo et al., 2014). However, they are insufficient for the removal and degradation of micropollutants such as pharmaceuticals. Due to this fact, conventional treatment processes are sometimes considered the major route for the occurrence of pharmaceuticals in the environment (Lee et al., 2017b). It is worth to mention that, biological or chemical reactions that occur in the secondary clarifiers of conventional wastewater treatment plants (WWTPs) can result in the generation and accumulation of by-products (Oulton et al., 2010). As a result, some pharmaceutical compounds can exist in higher concentrations at the effluents of WWTPs than in the respective influents, which is attributed to the PhACs excretion as conjugates in the WWTPs. Generally, these released conjugates are metabolized during the biological treatment process and the origin compounds is emitted, which often results in increasing the concentration of the parent compound(s) at the effluent of WWTPs (Barbosa et al., 2016).

For instance, Verlicchi et al. (2012) reported that E1 was detected at higher concentrations in the effluent of a WWTP than the respective raw influent of the WWTP, which may be ascribed to the oxidation of E2 entering the treatment plant (Verlicchi et al., 2012; Barbosa et al., 2016). Moreover, the transformation of parent compounds during wastewater treatment process has also been reported (Zwiener et al., 2002; Ebele et al., 2017). Basically, when the parent compound(s) breakdown during the treatment process, it can experience complete degradation or partial transformation to metabolites, or in some cases left unchanged (Xia et al., 2005). It is noteworthy that the transformation or breakdown of pharmaceuticals does not necessarily mean the elimination of toxicity. In fact, the by-products can have unknown toxicity as well as stay persistence and present in the effluent of WWTPs (Hughes et al., 2012). For instance, Zwiener et al. (2002) have investigated the transformation of ibuprofen. They observed that hydroxy-ibuprofen (OH-Ibu), carboxy-hyratropic acid (CA-HA), and carboxy-ibuprofen (CA-Ibu) were identified as the major metabolite/by-products. These generated metabolites can also increase their presence in the environment (Ebele et al., 2017). Similarly, the metabolism and transformation of valsartan was also studied by Helbling et al. (2010). They revealed that the metabolism of valsartan followed

a sequence of transformation steps. Forming different by-product: dealkylated valsartan, amino-valsartan, and valsartan acid. Unlike ibuprofen and valsartan, some pharmaceuticals such as diatrizole, are not transformed and left unchanged during the wastewater treatment (Redeker et al., 2014). Hence, advanced oxidation processes (AOPs) must be employed to treat such persistent pollutant to avoid contamination of the land and aquatic environment (Aguilar et al., 2011).

1.3. Advanced oxidation processes for the removal of pharmaceuticals

Among the treatment technologies used for the removal of pharmaceuticals, advanced oxidation processes (AOPs) are considered the most effective processes as they present a significant potential for the treatment of a wide variety of emerging contaminants. The AOPs involves the in-*situ* generation of the highly reactive oxygen species (ROS), as well as hydroxyl radicals (•OH), hydrogen peroxides (H_2O_2), O_3, and superoxide anion radicals ($O^{\bullet-}_2$). These generated oxidants can provide complete mineralization of the micro-pollutants to CO_2, H_2O, and organic ions or acids (Dalrymple et al., 2007; Kanakaraju et al., 2018). In recent years, various advanced oxidation processes have been employed and investigated for the removal of several pharmaceuticals. Table 2 summarizes some of the latest publications that investigated the use of advanced oxidation processes for the removal of pharmaceuticals from contaminated water.

Table 2. Recent studies on the removal of pharmaceuticals using AOPs

AOPs applied	Pharmaceutical	Findings	ROS applied	Reference
Ozonation	Tetracycline	Direct ozonation showed complete removal of tetracycline.	H_2O_2 and •OH	Wang et al. (2011)
	Amoxicillin	The pseudo-first-order reaction rates for amoxicillin by ozonation at pH 3, pH 7 and pH 10 were 0.064 min^{-1}, 0.321 min^{-1} and 1.970 min^{-1}, respectively, with pH 10 being the optimum one.		Kıdak and Doğan (2018)
	Salicylic acid	95% removal was observed at pH 4 with 1 mg/L of ozone.		Hu et al. (2016)
Photo-Fenton	5-Fluorouracil	Solar-simulated Fenton-like treatment ($Fe_3/S_2O_8^{2-}$) resulted in a higher degradation rate and dissolved organic carbon (DOC) removal than	•OH, O^{-}_2, HO_2, and O_2	Koltsakidou et al. (2017)

		Fe_3/H_2O_2 for the degradation of 5-fluorouracil.		
	Antipyrine	Complete degradation was observed after 2.5 min, while 93% of TOC removal was obtained after 60 min		Davididou et al. (2017)
TiO_2 photocatalysis	Paracetamol	82% of paracetamol removal was obtained under optimum conditions and under 6 h of natural sunlight irradiation.	•OH, $O_2^{\bullet -}$ and h^+	Vasiliu et al. (2009)
	Tetracycline	75% of tetracycline removal was obtained under optimum conditions and under 30 min of natural sunlight irradiation.		Lee et al. (2017a)
Sonolysis	Piroxicam	The reaction rates of piroxicam (640 mg/L) at power density of 20, 36 and 60 W/L were 0.1157 min^{-1}, 0.1695 min^{-1} and 0.1967 min^{-1}, respectively.	•OH	Lianou et al. (2018)
	Ibuprofen	Increase degradation was observed with the application high single ultrasonic frequencies.		Ziylan-Yavas and Ince (2018)
Ultrafiltration	acetaminophen, metoprolol, caffeine, antipyrine.	Retention coefficients in municipal secondary effluent were higher than those obtained with ultrapure water, due to adsorption of hydrophobic compounds on the NOM of the secondary effluent or by the formation of the cake layer.	nd	Acero et al. (2010)

2. HETEROGENEOUS PHOTOCATALYSIS AS AN ADVANCED OXIDATION PROCESS

Heterogeneous photocatalysis is an appealing low-temperature and pressure technology for its promising applications in the area of solar energy, green chemistry, and environmental remediation (Bellardita et al., 2018). The potential of harnessing photocatalysis for the treatment of water was first discovered in 1972 by (Fujishima and Honda, 1972) which was founded based on the photo-

electrochemical water splitting by using titania as the semiconductor catalyst. Photocatalysis may be defined as the acceleration of a photoreaction in the presence of a catalyst. Heterogeneous photocatalysis, in most cases, is referred to as "semiconductor photocatalysis" (Mills and Le Hunte, 1997; Singh et al., 2018). The photocatalytic oxidation is considered one of the advanced oxidation processes (AOPs) and certainly one of the most promising (AOPs) for the treatment of wastewater containing toxic and unbiodegradable substances such as pharmaceuticals (PhACs) and dyes. Heterogeneous photocatalysis oxidation is beneficial for the removal of hazardous and non-hazardous contaminates and persistent organic micropollutants in water and wastewater (Qu et al., 2013). Numerous studies have investigated the employment of heterogeneous photocatalysis for the degradation and removal of various persistent pollutants and emerging contaminants of concern (ECC) such as, endocrine disrupting compounds (EDCs) (Mboula et al., 2013; Gmurek et al., 2017), pharmaceutical compounds (PhACs) (Dalida et al., 2014; Choi et al., 2014; He et al., 2016), and dyes (Akpan and Hameed, 2009; Li et al., 2015). The photocatalytic activity and degradation efficiency of the abovementioned pollutants show a promising future for the utilization of the heterogeneous photocatalysis as an advanced oxidation process (AOP) for water/wastewater treatment.

Photocatalysis process has several advantages over the other advanced oxidation technologies (AOTs) such as biological treatment, chemical oxidation, activated carbon adsorption, ozonation, etc. (Kumar et al., 2017; Miklos et al., 2018).

Generally, the chemical oxidation technology is only appropriate for the degradation of pollutants that exist at high concentrations, and no complete removal of organics is achieved in this process (Kumar and Pandey, 2017). Other chemical oxidation methods, such as ozonation, requires high energy, and it forms oxidative by-products (Ahmed et al., 2017). Biological treatment methods (i.e., activated sludge) removal kinetics are very slow, result in a large amount of sludge containing ECs that needs to be disposed of, and proper control over the pH and temperature is required. In addition, the activated sludge process have very low efficiencies towards the degradation of pharmaceuticals (Kumar and Pandey, 2017). Activated carbon adsorption is very effective; however, its main disadvantage is that the pollutants are transferred without decomposition, and hence, another pollution issue emerges (Kumar and Pandey, 2017).

Moreover, it has a relatively high operation and maintenance cost as well as issues related to the regenerations and disposal of high sludge (Sreekanth et al., 2009; Ahmed et al., 2017). On the other hand, the photocatalytic oxidation process is capable of degrading pollutants even at low concentrations and achieving complete oxidation of pollutants in a short period even at low concentration levels (ppb). Moreover, the photooxidation is accomplished without the formation of

secondary pollutants using cheap and highly active catalyst (Kumar et al., 2017). Further, sunlight can also be used in the photocatalysis process for the activation of the catalyst to degrade persistent contaminates (Prieto-Rodriguez et al., 2012; Ahmed et al., 2017).

3. TITANIUM DIOXIDE (TiO_2) AS A PHOTOCATALYST

Titanium dioxide (TiO_2) which also known by titania is the most widely used and researched catalyst, mainly because of its high stability, high photocatalytic activity, non-toxicity, physical and optical properties (Akpan and Hameed, 2009). Numerous investigations and reviews have been published on the photocatalytic activity and the chemical structure of titania (Zaleska, 2008; Mital and Manoj, 2011; Schneider et al., 2014; Lee et al., 2017b; Lee et al., 2017a). Basically, TiO_2 exhibits ideal properties, such as high UV absorption, resistance to photo-corrosion, low energy band gap, eco-friendly, and can be employed without any additives (Lee et al., 2017b). Further, TiO_2 is considered a naturally occurring mineral with optical and electronic properties that render it suitable for the application in photovoltaics field, sensors, and photocatalysis. In contrast with other semiconductors, such as Fe_2O_3 and CdS, that can operate both under UV and visible region, however, TiO_2 is considered highly stable and can only operate in the UV spectrum (Aziz et al., 2016). This clearly shows the importance of such material in many applications, such as water purification, sterilization, and H_2 generation (Robinson et al., 2001).

Titanium dioxide is a semiconductor that falls under the transition metal oxides family. Fig. 2 displays the crystalline structure of the three typical polymorphs phases of titania; brookite, anatase, and rutile, respectively. Titania constitutes of four mineral forms, namely: brookite (orthorhombic), anatase (tetragonal), rutile (tetragonal), and TiO_2 (B) known as (monoclinic) (Carp et al., 2004; Gupta and Tripathi, 2011). Moreover, Simons and Dachille (1967) have reported another two additional forms of TiO_2 that have been synthesized from the rutile phase structure of titania: TiO_2 (II) with PbO_2 structure and TiO_2 (H) with hollandite structure. Subsequently, TiO_2 contains 60 % and 40 % of Ti and O, respectively. The bandgap (*Eg*) of TiO_2 is an important optical characteristic that affects the photocatalytic activity of titanium dioxide.

Generally, depending on the phase structure, titania exhibits a band gap of 3.0 eV for rutile and 3.2 eV for anatase. The main standard for an ideal semiconductor photocatalyst is related to the redox potential of the charge carriers (Mital and Manoj, 2011). For instance, the electron-hole recombination should lie within the band-gap domain of the catalyst. The reducing ability of the photoelectrons is determined by the energy level located at the bottom of the conduction band,

while the oxidizing capacity of the photogenerated holes is evaluated based on the energy level located at the top of the valence band (Carp et al., 2004).
Several authors have observed that the anatase phase of titania presents higher photocatalytic activity (Hoffmann et al., 1995; You et al., 2005a; Khaki et al., 2017). This is attributed to the fact that anatase exhibits higher conduction band (E_{CB}) energy of (~0.2 eV). The high (E_{CB}) of anatase and (E_{CB}) position can affect the electron transfer rate and hence the charge recombination rate (Khaki et al., 2017) and because of the higher specific surface area (SSA) of anatase. However, this may result in higher recombination rate. Thence, the presence of rutile phase is recommended to lower and minimize the electron-hole recombination which results in higher photocatalytic activity (Hoffmann et al., 1995). In addition, the higher photocatalytic activity of anatase is related to its slightly higher Fermi level and a higher degree of hydroxylation (generation of hydroxyl groups) (Mital and Manoj, 2011). However, it may be concluded that it is not a necessity that the anatase phase has a higher photocatalytic activity over the rutile phase. Serpone et al. (1996) and Tryba et al. (2017) reported that the type of the substrate employed in the treatment process can also influence the photocatalytic activity of anatase and rutile. It is noteworthy that the rutile structure also has a smaller band gap than the anatase structure which can improve the photocatalytic activity of the catalyst.

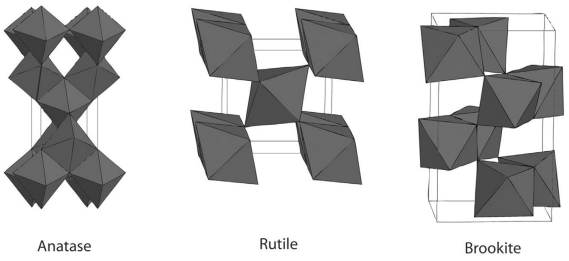

Fig. 2. Crystalline structure of TiO_2 (Khaki et al., 2017)

3.1. Usage of TiO_2 as a photocatalyst in pharmaceuticals removal

The ideal photocatalyst should possess several properties such as stability, non-toxicity, low-cost, photoactivity, and abundancy. Although there are various semiconductor photocatalysts such as CeO, Fe_2O_3, WO_3, TiO_2, ZnO and SnO_2 that meet all the requirements of an ideal photocatalyst, however, TiO_2 is the most widely investigated and selected catalyst for the degradation of pharmaceutical compounds (Kanakaraju et al., 2014a). The employment of titanium dioxide semiconductor as a heterogeneous photocatalysis has proven to be very effective for the degradation of different micro-pollutants. The favor of TiO_2 over other photocatalysts is because titania is inexpensive, abundant, photoreactive, non-

toxic, chemically, and biologically inert (Friedmann et al., 2010). Generally, most of the studies that included TiO_2 as a photocatalyst for the decomposition of pharmaceutical compounds have focused on determining the best-operating factors to yield the highest degradation efficiency (Kanakaraju et al., 2014a).
The photocatalytic activity of non-steroidal anti-inflammatory drugs (NSAIDs), analgesic, antibiotics, and antiepileptics is the most discussed because such pharmaceutical compounds are relevant to the environment (Kanakaraju et al., 2014a) and can be detected in both drinking water and river water. Moreover, majority of the studies that employed TiO_2 photocatalysis process for the removal of pharmaceuticals focused on optimizing the operating parameters that can yield the highest degradation efficiency towards pharmaceuticals (Lee et al., 2017b). This is mainly because the degradation of pharmaceuticals is highly dependent on the operational parameters of the system. Operating parameters such as initial pH, initial concentration of the pollutant, catalyst loading, and irradiation time can influence the removal rate of pollutants (Akpan and Hameed, 2009; Lee et al., 2017b). These operating parameters have been investigated by several authors (Dalida et al., 2014; Lee et al., 2017a; Bianchi et al., 2017). Furthermore, other operating factors such as the geometry and design of the photoreactor can also impact the degradation rate of pharmaceuticals (Kanakaraju et al., 2014b).
Table 3 presents some of the studies that employed bare TiO_2 as a photocatalyst for the degradation of pharmaceutical compounds. It can be noted from Table 3, that the findings from these investigations were related to obtaining the optimum operating parameters to yield the highest removal rate of pharmaceuticals. In addition, one can notice that these investigations were focused on the degradation of pharmaceuticals in synthetic conditions (not real wastewater). However, due to the difference in optimum operating parameters between these studies, we observe that further studies on optimizing the operational parameters are required. Additionally, more studies on the degradation of pharmaceuticals in real wastewater conditions using bare TiO_2 photocatalyst are also recommended.

3.2. Drawbacks of TiO_2 as a photocatalyst

Although titanium dioxide is an ideal photocatalyst for the degradation of pharmaceutical compounds and other micro-pollutants. However, the use of a single bare photocatalyst is associated with some drawbacks that hinder its use on a wide scale. These drawbacks include: (i) rapid recombination rate for the photo-induced e^-/h^+ pairs, (ii) small amounts of visible light photons are absorbed, (iii) low stability, (iv) agglomeration of particles, and (v) low photocatalytic activity in the presence of visible solar radiations (Mital and Manoj, 2011; Singh et al., 2018). Another limitation associated with using bare TiO_2 is that titania can only absorb wavelengths in the UV spectra. Meaning that it can only be photo-activated by light with wavelengths less than 388 nm (Lee et al., 2017b).

Furthermore, the recombination of generated charge carries is considered another major limitation when using bare TiO_2 catalyst. Basically, when the photogenerated electron-hole pair recombines, the excited electrons will return to the valence band (V_B) without reacting with absorbed contaminates on the surface

Table 3. Summary of work done on the degradation of pharmaceuticals using TiO_2 photocatalysis

Pharmaceutical	Water matrix	Reactor	Irradiation source	Findings	Reference
Acetaminophen (paracetamol)	Deionized water Tap water	Batch reactor	UV-A lamp with wavelength range of 315-400 nm	Deionized water: - Paracetamol was totally degraded after 6 hours - 98% removal of ACT was achieved using micro-sized TiO_2. Tap water: The matrix complexity in tap water hindered the degradation of paracetamol.	Bianchi et al. (2017)
	Distilled water	Batch reactor with magnetic stirrer	Five LED lamps with wavelength 440-490 nm	Optimal conditions for 100% degra-dation of acetaminophen was achieved by using 0.1 mM PARA initial concentration, pH of 9.0, system temperature of 22°C, and catalyst dose of 1 g L^{-1}	Chun-Te Lin et al. (2016)
	Ultra-pure water	Jacketed reactor (600 mL)	HG500 lamp (30 mW cm^{-2}).	The undoped (T) nano-particles showed degradation rate between 70 and 80% and revealed to be the most efficient in mineralization.	Rimoldi et al. (2017)
	Milli-Q water	Annular cylindric-cal	UVA of (8W) and UVC of (15 W).	Effective and rapid mineralization and degradation was observed in the presence of UVC radiations	Yang et al. (2008)

Table 3. Cont'd Summary of work done on the degradation of pharmaceuticals using TiO_2 photocatalysis

Pharmaceutical	Water matrix	Reactor	Irradiation source	Findings	Reference
Diclofenac (DCF) and ibuprofen (IBP)	Aqueous solution	Planar falling reactor	UV-A lamps with maximum wavelength of 350 nm	-The photocatalytic degradation of IBP is enhanced using photocatalysis ozonation. Due to generation of hydroxyl free radicals which promote oxidation of IBP.	Aziz et al. (2017)
Ibuprofen	Ultra-pure water	250-mL batch reactor	UV-vis solarium lamp (15 W), nm	-Complete removal of the antibacterial activity using TiO_2 as a catalyst. In the presence of ZnO, higher degradation rates were observed	Choina et al. (2013)
	Milli-Q water	Annular reactor	Solar radiations simulator (Xe-OP lamp, 1 kW)	-The optimum TiO_2 loading rate for the degradation of IBP was found to be at 1 g L^{-1} -The amount of dissolved oxygen affected the degradation of IBP	Méndez-Arriaga et al. (2008)
Tetracycline	Aqueous solution	Annular reactor	Mercury lamp model (TQ 718 Z1 700 W)	-The toxicity test was carried out on Pseudomonas and the results showed a decline in toxicity during the photocatalytic process.	Mboula et al. (2012)

of the semiconductor (Pelaez et al., 2012; Schneider et al., 2014). The aforementioned drawbacks of bare TiO_2 can reduce the quantum efficiency and thus, resulting in adverse effects on the photocatalytic performance of the photocatalyst (Singh et al., 2018).

4. NANOCOMPOSITE MATERIALS

Nanocomposite materials are considered as solid structures with nanometer-scale dimensional distances between the various phases that comprise the structure. Typically, nanocomposites are formed by the coupling of two or more different materials at the nanoscale size into a matrix that constitutes of inorganic/organic standard materials in order to properly control and develop new and enhanced structures and properties. Hence, nanocomposite materials can consist of at least two phases which might include: an amorphous phase and a crystalline phase, or two crystalline phases. Generally, the properties of the nanocomposite materials depend on the individual characteristics of the matrix components as well as on the morphology and interfacial features (Ajayan et al., 2006; Öchsner et al., 2009). The photocatalytic degradation of contaminants in the presence of nanocomposite catalysts based on the heterogeneous photocatalysis process has been shown to have significant potential as an effective, low-cost, and environmentally sustainable advanced technology for the purification of contaminated water (Pawar and Lee, 2015). Several studies have discussed the design and development of various nanocomposite catalysts for the degradation of organic pollutants and carcinogenic materials (Pawar and Lee, 2015; Mirzaei et al., 2016; Yu et al., 2018a; Yu et al., 2018b; Payan et al., 2019).

5. TiO_2 BASED NANOCOMPOSITE CATALYSTS FOR THE PHOTODEGRADATION OF PHARMACEUTICALS

In recent years, nanocomposite catalysts based on TiO_2 have been intensively developed and researched for the photocatalytic degradation of pharmaceutical compounds (Abdel-Wahab et al., 2017; Nasr et al., 2019; Mugunthan et al., 2019). As discussed previously, using titania as a bare catalyst is associated with some drawbacks. The major drawback is related to the wide bandgap of TiO_2 (3.2 eV) which hinders its activation to only under wavelengths located in the UV region ($\lambda < 400$ nm). Thus, it has been reported that doping and/or coupling metal oxides with TiO_2 can significantly enhance the optical and structural properties of titanium dioxide by extending the light absorption of titania from the UV to the visible region (Zaleska, 2008), hence improving its photocatalytic activity under visible light. The improvement in the optical properties of TiO_2 nanocomposite is

ascribed by the new energy level in the band gap of TiO_2 matrix (Zaleska, 2008). As illustrated in Fig. 3, electrons are excited from the defect state to the conduction band (C_B) of TiO_2 by photons having energy equal or larger than hv_2. In addition, doping metal oxides with TiO_2 matrix can noticeably enhance interfacial electron transfer rates, promote electron-hole trapping, and decrease recombination of electron-hole pairs (Zaleska, 2008; Gupta and Tripathi, 2011; Khaki et al., 2017).

Doping TiO_2 with transition metals (i.e., Fe, Mo, and V) can also extend the spectral response of titania into the visible light spectrum, which improve its photocatalytic activity (Murakami et al., 2010; Pelaez et al., 2012). This is because transition metal can supply additional energy level in the band gap of TiO_2. Hence, the electron transfer from one of the new additional energy levels to the conduction band requires lesser photon energy than the undoped semiconductor (Gupta and Tripathi, 2011). Doping and (or) coupling with noble metals (i.e., Ag, Au, and Pt) also improves the photocatalytic activity of TiO_2 nanocomposite under visible light irradiations. This explained by the electron trapping and enhanced interfacial charge transfer, which inhibits electron-hole pairs recombination (You et al., 2005b; Pelaez et al., 2012). Furthermore, doping titania with non-metallic materials (anions) has also been reported to shift the valence band edge of TiO_2 upwards as shown in Fig. 3, and thus narrowing the energy bandgap of TiO_2, which is attributed to the mixing between the p states of anions with the 2p states of O atoms (Ni et al., 2007; Gupta and Tripathi, 2011; Bignozzi, 2011).

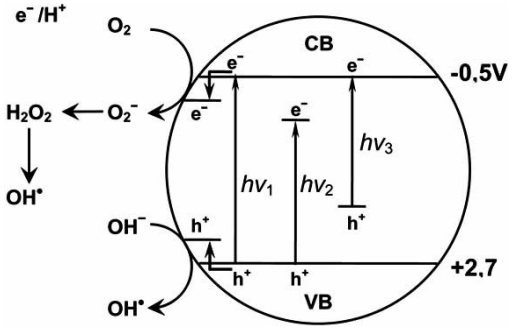

Fig. 3. Mechanism of TiO_2 photocatalysis: hv_1: pure TiO_2; hv_2: metal-doped TiO_2 and hv_3: non-metal-doped TiO_2 (Zaleska, 2008)

In the past five years, several authors have investigated the photodegradation of various pharmaceutical compounds using TiO_2 based nanocomposite photocatalysts. Table 5 presents some of the work done on the photocatalytic degradation of pharmaceuticals using TiO_2 based nanocomposite photocatalyst. For example, Nasr et al. (2019) have successfully loaded Ag, Au, and Pt noble

metals into the TiO_2 structure. The prepared nanocomposite photocatalysts were tested for the photocatalytic degradation of acetaminophen (AP) under solar irradiations and compared with UV light. Their results revealed improved photocatalytic degradation of AP under solar light and on a wide pH range (4.2 – 8.0) as well as under the presence of various interferences such as binding materials, surfactants, and drug excipients. Furthermore, Pt/TiO_2 nanocomposite catalyst showed the highest photocatalytic activity; this was attributed to the fact that doping Pt with TiO_2 can promote better trapping of electrons than loaded Au and Ag. Moreover, they concluded that the photocatalytic activity was influenced by light intensity, irradiation time, and type of photocatalyst. They also observed that the major degradation by-products generated were 4-acetamidocatechol, 4-acetamidoresorcinol, and hydroquinone. In the case of UV and solar irradiations, the proposed mechanism was predominated by hydroxyl radicals (OH) attack into the aromatic ring.

The photodegradation of acetaminophen under visible light was further investigated by using WO_3/TiO_2 nanocomposites. Namshah and Mohamed (2018) successfully coupled tungsten oxide-transition metal into the structure of TiO_2 nanowires via the sol-gel method. Their results showed that WO_3/TiO_2 with 3wt.% of WO_3 fully degraded AP. This was ascribed to the improvements in optical properties and delay in e^-/h^+ recombination rate. The synthesized nanocomposite exhibited excellent stability for the degradation of AP after five times. Further, the improvements in the optical properties of WO_3/TiO_2 nanocomposites can be explained by the electrons generated from the valence band (VB) of TiO_2 to its conduction band (CB), and since the CB level of tungsten (+0.475) is higher than the CB level of TiO2 (-0.29) in the nanocomposite matrix, this would result in trapping the excited electron from the conduction band of titania by WO_3.

The photocatalytic degradation of other pharmaceutical compounds such as ketoprofen, ibuprofen, tetracycline, amoxicillin, and naproxen have also been investigated using titania-based nanocomposites (Table 4). For instance, the photo-degradation of carbamazepine (CBZ), which is anti-epileptic drug used in the treatment of epilepsy been studied using graphene-TiO_2-P25 nanocomposite catalyst under UV-A radiations. The degradation efficiency of CBZ was found to be affected by the graphene content in the titania lattice. The optimum weight percentage of graphene was 1.5Gr, as it yielded the best removal efficiency for CBZ (Appavoo et al., 2014).

From Table 4, one can notice that the degradation of pharmaceutical compounds was very effective by using TiO_2 based nanocomposite catalyst. In addition, the synthesized nanocomposites exhibited enhanced structural and optical properties compared to the bare TiO_2 photocatalyst. Further, it was shown in the majority of

these investigations that the reusability of the nanocomposites was possible, even after several trials. Last, it is noteworthy that the dopant content in the TiO_2 lattice and other operating parameters played a major in the degradation of these pharmaceuticals.

Table 4. Summary of work done on the degradation of pharmaceuticals using TiO_2 based nanocomposite catalyst

Nanocomposite	Pharmaceutical	Light source	Major findings	Reference
- Ag/TiO_2 - Au/TiO_2 - Pt/TiO_2	-Acetaminophen (AP)	- Solar simulator - UV light	-Pt/TiO_2 showed the highest photocatalytic activity. -Improved degradation of AP under solar light.	Nasr et al. (2019)
WO_3/TiO_2		-500 W Xenon lamp	- Reduction in the bandgap to 2.62 eV and promoted electron trapping. - Complete degradation of AP was achieved using TiO_2-WO_3-3 wt.% and 30 min irradiation time with an optimum catalyst dose of 1.5 g/L.	Namshah and Mohamed (2018)
$FeNi_3/SiO_2/TiO_2$	-Tetracycline (TC)	-UV lamp (18 W), wavelength 254 nm and intensity of (2500 W/cm^{2}µ)	-Complete degradation was achieved under optimum conditions (catalyst dose 0.005 g/L, pH 9, UV irradiation 200m min, TC concentration 10 mg/L). -Prepared nanocomposite could be recovered and used frequently.	Khodadadi et al. (2018)
Diode/Carbon modified TiO_2		-RGD-LED (25 W)	-Degradation of tetracycline was achieved under initial pH 7. -The optimum light intensity for the degradation of tetracycline was at level 3 (46.00 W/m^2).	Oseghe et al. (2018)

Table 4. Cont'd Summary of work done on the degradation of pharmaceuticals using TiO_2 based nanocomposite catalyst

Nanocomposite	Pharmaceutical	Light source	Major findings	Reference
Bi_2S_3/TiO_2 Montmorillonite	Ketoprofen (KP)	Heraeus TQ150 medium-pressure Hg-vapor lamp (λ = 254 – 546 nm).	-Total degradation achieved using Bi_2S_3/TiO_2(25/75)– Montmorillonite under pH 11 and after 120 min or irradiation. -Disappearance of KP followed pseudo-first-order kinetics.	Djouadi et al. (2018)
PANI supported Ag/TiO_2	Bisphenol (BPA)	Mercury lamp (400 W) for UV. Halogen 500 W for visible light.	-The prepared nanocomposite showed high degradation rate (99.8%) of BPA in 110 min under UV and visible light. -Good reusability at least four times.	Sambaza et al. (2019)
Co-doped TiO_2	Amoxicillin (AMX)	Xe Lamp and UV-C filter	-More than 90% degradation of AMX was achieved using the 0.4% wt/v Co-doped TiO_2 nanocomposite. -The photodegradation was attained within 240 min under UV light and 300 min under visible light.	Çağlar Yılmaz et al. (2019)
TiO_2-SnO_2	Diclofenac	UV lamp	-Optimum operating parameters for were achieved at (pH 5, initial diclofenac concentration 20 mg/L, and catalyst dose 0.8 g/L). -nanocomposite showed good reusability with only 17% reduction in performance after three cycles.	Mugunthan et al. (2019)

6. CONCLUSIONS

Pharmaceuticals have been detected in wastewater effluents as well as in other water sources and even in drinking water. The appearance of pharmaceuticals is mainly due to their physiochemical properties, which hinder their natural biodegradation. The major route for the occurrence of pharmaceuticals in the aquatic environment was related to the insufficiency of conventional wastewater treatment processes. Present conventional wastewater treatment processes cannot fully degrade PhACs. As a result, numerous advanced oxidation technologies (AOTs) have been developed. Photocatalysis based on titanium dioxide showed a promising future for the degradation of pharmaceuticals. TiO_2 photocatalysis has several advantages over the AOTs, such as the ability to fully degrade pharmaceuticals, low-cost, and recovery as well as reusability of the photocatalyst. However, using TiO_2 as a bare catalyst is associated with some drawbacks that hinder its application on a wide scale. Several researchers have fabricated and developed numerous nanocomposite catalysts based on TiO_2. The novel synthesized TiO_2 based nanocomposites exhibited enhanced optical and structural properties. Most important, the ability to utilize the nanocomposite catalysts under visible light and solar irradiations, rendering it more environmentally friendly, sustainable, and effective for the degradation of pharmaceuticals. Another advantage was the possibility to reuse the nanocomposite for several times. Because of the many factors that can affect the photodegradation of pharmaceuticals, such as dopant content, catalyst loading, initial pH, etc. and because of the various pharmaceuticals that exist in the aquatic environment, additional studies are required to obtain the optimum conditions for the degradation of PhACs. In addition, more studies regarding the mineralization of the pharmaceuticals is also required using TiO_2 based nanocomposite. Furthermore, the review above leads us to the fact that more pilot-scale and large-scale studies and investigations are required to test the degradation of various pharmaceuticals under real conditions using practical and cheap TiO_2 based nanocomposite photocatalysts.

7. ACKNOWLEDGEMENTS

The authors would like to acknowledge Universiti Sains Malaysia for providing the funding for this study under grant RU (i) 1001/PAWAM/ 8014039.

REFERENCES

1. Abdel-Wahab, AM, Al-Shirbini, AS, Mohamed, O and Nasr, O 2017. Photocatalytic degradation of paracetamol over magnetic flower-like

TiO_2/Fe_2O_3 core-shell nanostructures. *Journal of Photochemistry and Photobiology A: Chemistry,* 347**,** 186-198.

2. Abellán, M, Bayarri, B, Giménez, J and Costa, JJACBE 2007. Photocatalytic degradation of sulfamethoxazole in aqueous suspension of TiO_2. 74**,** 233-241.
3. Acero, JL, Benitez, FJ, Teva, F and Leal, AI 2010. Retention of emerging micropollutants from UP water and a municipal secondary effluent by ultrafiltration and nanofiltration. *Chemical Engineering Journal,* 163**,** 264-272.
4. Aguilar, C, Montalvo, C, Ceron, J and Moctezuma, E 2011. Photocatalytic degradation of acetaminophen. *International Journal of Environmental Research,* 5**,** 1071-1078.
5. Ahmed, MB, Zhou, JL, Ngo, HH, Guo, W, Thomaidis, NS and Xu, J 2017. Progress in the biological and chemical treatment technologies for emerging contaminant removal from wastewater: a critical review. *Journal of hazardous materials,* 323**,** 274-298.
6. Ajayan, PM, Schadler, LS and Braun, PV 2006. *Nanocomposite science and technology*, John Wiley & Sons.
7. Akpan, UG and Hameed, BH 2009. Parameters affecting the photocatalytic degradation of dyes using TiO2-based photocatalysts: a review. *Journal of hazardous materials,* 170**,** 520-529.
8. Appavoo, IA, Hu, J, Huang, Y, Li, SFY and Ong, SLJW 2014. Response surface modeling of Carbamazepine (CBZ) removal by Graphene-P25 nanocomposites/UVA process using central composite design. 57**,** 270-279.
9. Ashton, D, Hilton, M and Thomas, KJS o. t. t. e. 2004. Investigating the environmental transport of human pharmaceuticals to streams in the United Kingdom. 333**,** 167-184.
10. Aziz, KHH, Miessner, H, Mueller, S, Kalass, D, Moeller, D, Khorshid, I and Rashid, MAM 2017. Degradation of pharmaceutical diclofenac and ibuprofen in aqueous solution, a direct comparison of ozonation, photocatalysis, and non-thermal plasma. *Chemical Engineering Journal,* 313**,** 1033-1041.
11. Aziz, NAA, Palaniandy, P, Aziz, HA and Dahlan, IJJ o. CR 2016. Review of the mechanism and operational factors influencing the degradation process of contaminants in heterogenous photocatalysis. 40**,** 704-712.
12. Bagheri, H., Afkhami, A, Noroozi, AJA and Research, BC 2016. Removal of pharmaceutical compounds from hospital wastewaters using nanomaterials: a review. 3**,** 1-18.

13. Barbosa, MO, Moreira, NF, Ribeiro, AR, Pereira, MF and Silva, AMJW 2016. Occurrence and removal of organic micropollutants: an overview of the watch list of EU Decision 2015/495. 94**,** 257-279.
14. Bean, TG, Rattner, BA, Lazarus, RS, Day, DD, Burket, SR, Brooks, BW, Haddad, SP and Bowerman, WWJEP 2018. Pharmaceuticals in water, fish and osprey nestlings in Delaware River and Bay. 232**,** 533-545.
15. Bellardita, M, Di Paola, A, Megna, B and Palmisano, L 2018. Determination of the crystallinity of TiO2 photocatalysts. *Journal of Photochemistry Photobiology A: Chemistry,* 367**,** 312-320.
16. Bianchi, CL, Sacchi, B, Pirola, C, Demartin, F. Cerrato, G, Morandi, S and Capucci, V 2017. Aspirin and paracetamol removal using a commercial micro-sized TiO_2 catalyst in deionized and tap water. *Environmental Science Pollution Research,* 24**,** 12646-12654.
17. Bignozzi, CA 2011. *Photocatalysis*, Springer Science & Business Media.
18. Boxall, AB 2018. Pharmaceuticals in the Environment and Human Health. *Health Care and Environmental Contamination.* Elsevier.
19. Bundschuh, M, Hahn, T, Ehrlich, B, Höltge, S, Kreuzig, R, Schulz, RJB o. e. c. and toxicology 2016. Acute toxicity and environmental risks of five veterinary pharmaceuticals for aquatic macroinvertebrates. 96**,** 139-143.
20. Burns, EE, Carter, LJ, Kolpin, DW, Thomas-Oates, J and Boxall, AB 2018. Temporal and spatial variation in pharmaceutical concentrations in an urban river system. *Water research,* 137**,** 72-85.
21. Caban, M, Lis, E, Kumirska, J and Stepnowski, PJS o. t. TE 2015. Determination of pharmaceutical residues in drinking water in Poland using a new SPE-GC-MS (SIM) method based on Speedisk extraction disks and DIMETRIS derivatization. 538**,** 402-411.
22. Çağlar Yılmaz, H, Akgeyik, E, Bougarrani, S, El Azzouzi, M, Erdemoğlu, SJJ o. DS & Technology 2019. Photocatalytic degradation of amoxicillin using Co-doped TiO_2 synthesized by reflux method and monitoring of degradation products by LC–MS/MS. 1-12.
23. Cajthaml, T, Křesinová, Z, Svobodová, K and Möder, MJC 2009. Biodegradation of endocrine-disrupting compounds and suppression of estrogenic activity by ligninolytic fungi. 75**,** 745-750.
24. Carmona, E, Andreu, V and Picó, YJS o. t. t. e. 2014. Occurrence of acidic pharmaceuticals and personal care products in Turia River Basin: from waste to drinking water. 484**,** 53-63.
25. Carp, O, Huisman, CL and Reller, A 2004. Photoinduced reactivity of titanium dioxide. *Progress in solid state chemistry,* 32**,** 33-177.
26. Celle-Jeanton, H, Schemberg, D, Mohammed, N, Huneau, F, Bertrand, G, Lavastre, V and Le Coustumer, PJE i. 2014. Evaluation of pharmaceuticals in surface water: Reliability of PECs compared to MECs. 73**,** 10-21.

27. Choi, J, Lee, H., Choi, Y, Kim, S, Lee, S, Lee, S, Choi, W end Lee, J 2014. Heterogeneous photocatalytic treatment of pharmaceutical micropollutants: Effects of wastewater effluent matrix and catalyst modifications. *Applied Catalysis B: Environmental,* 147**,** 8-16.
28. Choi, K, Kim, Y, Park, J, Park, CK, Kim, M, Kim, HS. and Kim, PJS o. t. t. E 2008. Seasonal variations of several pharmaceutical residues in surface water and sewage treatment plants of Han River, Korea. 405**,** 120-128.
29. Choina, J, Kosslick, H, Fischer, C, Flechsig, GU, Frunza, L and Schulz, A 2013. Photocatalytic decomposition of pharmaceutical ibuprofen pollutions in water over titania catalyst. *Applied Catalysis B: Environmental,* 129**,** 589-598.
30. Chun-Te Lin, J de Luna, MDG, Aranzamendez, GL and Lu, MC 2016. Degradations of acetaminophen via a $K_2S_2O_8$-doped TiO_2 photocatalyst under visible light irradiation. *Chemosphere,* 155**,** 388-394.
31. Dalida, MLP, Amer, KMS, Su, CC and Lu, MC 2014. Photocatalytic degradation of acetaminophen in modified TiO_2 under visible irradiation. *Environmental Science Pollution Research,* 21**,** 1208-1216.
32. Dalrymple, OK, Yeh, DH and Trotz, MA 2007. Removing pharmaceuticals and endocrine‐disrupting compounds from wastewater by photocatalysis. *Journal of Chemical Technology Biotechnology: International Research in Process, Environmental Clean Technology,* 82**,** 121-134.
33. Davididou, K, Monteagudo, JM, Chatzisymeon, E, Durán, A and Expósito, AJ 2017. Degradation and mineralization of antipyrine by UV-A LED photo-Fenton reaction intensified by ferrioxalate with addition of persulfate. *Separation Purification Technology,* 172**,** 227-235.
34. Directive, EJE 2008. 105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy, amending and subsequently repealing Council Directives 82/176. 83**,** 84-97.
35. Directive, EJLOJ o. t. EU 2013. 39/EU of the European Parliament and of the Council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. 24.
36. Directive, WFJO j. o. t. E c. 2000. Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy. 22**,** 2000.
37. Djouadi, L, Khalaf, H, Boukhatem, H, Boutoumi, H, Kezzime, A, Santaballa, JA and Canle, MJACS 2018. Degradation of aqueous ketoprofen by heterogeneous photocatalysis using Bi_2S_3/TiO_2–Montmorillonite nanocomposites under simulated solar irradiation. 166**,** 27-37.

38. Ebele, AJ, Abdallah, MAE and Harrad, S 2017. Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. *Emerging Contaminants,* 3**,** 1-16.
39. Farré, M, Sanchís, J and Barceló, DJTT i. AC 2011. Analysis and assessment of the occurrence, the fate and the behavior of nanomaterials in the environment. 30**,** 517-527.
40. Ferrer, I and Thurman, EMJJ o. CA 2012. Analysis of 100 pharmaceuticals and their degradates in water samples by liquid chromatography/quadrupole time-of-flight mass spectrometry. 1259**,** 148-157.
41. Friedmann, D, Mendive, C and Bahnemann, D 2010. TiO_2 for water treatment: parameters affecting the kinetics and mechanisms of photocatalysis. *Applied Catalysis B: Environmental,* 99**,** 398-406.
42. Fujishima, A and Honda, K 1972. Electrochemical photolysis of water at a semiconductor electrode. *Nature,* 238**,** 37.
43. Garcia-Rodríguez, A, Matamoros, V, Fontàs, C, Salvadó, VJES and Research, P 2014. The ability of biologically based wastewater treatment systems to remove emerging organic contaminants—a review. 21**,** 11708-11728.
44. Geissen, V, Mol, H, Klumpp, E, Umlauf, G. Nadal, M. van der Ploeg, M, van de Zee, SE, Ritsema, CJJIS and Research, WC 2015. Emerging pollutants in the environment: a challenge for water resource management. 3**,** 57-65.
45. Gmurek, M, Olak-Kucharczyk, M and Ledakowicz, S 2017. Photochemical decomposition of endocrine disrupting compounds–A review. *Chemical Engineering Journal,* 310**,** 437-456.
46. Gupta, SM and Tripathi, M 2011. A review of TiO_2 nanoparticles. *Chinese Science Bulletin,* 56**,** 1639.
47. Halling-Sørensen, B, Lützhøft, HCH, Andersen, HR and Ingerslev, FJJ o. a. c. 2000. Environmental risk assessment of antibiotics: comparison of mecillinam, trimethoprim and ciprofloxacin. 46**,** 53-58.
48. He, Y, Sutton, NB, Rijnaarts, HH and Langenhoff, AA 2016. Degradation of pharmaceuticals in wastewater using immobilized TiO2 photocatalysis under simulated solar irradiation. *Applied Catalysis B: Environmental,* 182**,** 132-141.
49. Helbling, DE, Hollender, J, Kohler, H.PE, Singer, H, Fenner, KJE s. and technology 2010. High-throughput identification of microbial transformation products of organic micropollutants. 44**,** 6621-6627.
50. Helwig, K, Hunter, C, McNaughtan, M, Roberts, J, Pahl, OJE t.and chemistry 2016. Ranking prescribed pharmaceuticals in terms of environmental risk: inclusion of hospital data and the importance of regular review. 35**,** 1043-1050.

51. Hoffmann, MR, Martin, ST, Choi, W and Bahnemann, DW 1995. Environmental applications of semiconductor photocatalysis. *Chemical reviews,* 95**,** 69-96.
52. Hossain, A, Nakamichi, S, Habibullah-Al-Mamun, M, Tani, K, Masunaga, S and Matsuda, H. 2018. Occurrence and ecological risk of pharmaceuticals in river surface water of Bangladesh. *Environmental research,* 165**,** 258-266.
53. Hu, R, Zhang, L and Hu, J 2016. Study on the kinetics and transformation products of salicylic acid in water via ozonation. *Chemosphere,* 153**,** 394-404.
54. Hughes, SR, Kay, P, Brown, LEJE s. and technology 2012. Global synthesis and critical evaluation of pharmaceutical data sets collected from river systems. 47**,** 661-677.
55. Kanakaraju, D, Glass, BD and Oelgemöller, M 2014a. Titanium dioxide photocatalysis for pharmaceutical wastewater treatment. *Environmental Chemistry Letters,* 12**,** 27-47.
56. Kanakaraju, D, Glass, BD and Oelgemöller, M 2018. Advanced oxidation process-mediated removal of pharmaceuticals from water: A review. *Journal of environmental management,* 219**,** 189-207.
57. Kanakaraju, D, Glass, BD and Oelgemöller, MJE c. l. 2014b. Titanium dioxide photocatalysis for pharmaceutical wastewater treatment. 12**,** 27-47.
58. Kasprzyk-Hordern, B, Dinsdale, RM and Guwy, AJ 2009. The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. *Water research,* 43**,** 363-380.
59. Khaki, MRD, Shafeeyan, MS, Raman, AAA and Daud, WMAW 2017. Application of doped photocatalysts for organic pollutant degradation-A review. *Journal of environmental management,* 198**,** 78-94.
60. Khataee, A, Fathinia, M, Joo, SJSAPAM and Spectroscopy, B 2013. Simultaneous monitoring of photocatalysis of three pharmaceuticals by immobilized TiO_2 nanoparticles: chemometric assessment, intermediates identification and ecotoxicological evaluation. 112**,** 33-45.
61. Khodadadi, M, Ehrampoush, M, Ghaneian, M, Allahresani, A and Mahvi, AJJ o. ML 2018. Synthesis and characterizations of $FeNi_3$@ SiO_2@ TiO_2 nanocomposite and its application in photo-catalytic degradation of tetracycline in simulated wastewater. 255**,** 224-232.
62. Kıdak, R and Doğan, Ş 2018. Medium-high frequency ultrasound and ozone based advanced oxidation for amoxicillin removal in water. *Ultrasonics sonochemistry,* 40**,** 131-139.

63. Kidd, KA, Blanchfield, PJ, Mills, KH, Palace, VP, Evans, RE, Lazorchak, JMand and Flick, RWJP o. t. NA o. S 2007. Collapse of a fish population after exposure to a synthetic estrogen. 104**,** 8897-8901.
64. Koltsakidou, A, Antonopoulou, M, Sykiotou, M, Evgenidou, E, Konstantinou, I and Lambropoulou, D 2017. Photo-Fenton and Fenton-like processes for the treatment of the antineoplastic drug 5-fluorouracil under simulated solar radiation. *Environmental Science Pollution Research,* 24**,** 4791-4800.
65. Komori, K, Suzuki, Y, Minamiyama, M, Harada, AJE m. and assessment 2013. Occurrence of selected pharmaceuticals in river water in Japan and assessment of their environmental risk. 185**,** 4529-4536.
66. Kumar, A and Pandey, G 2017. A review on the factors affecting the photocatalytic degradation of hazardous materials. *Material Sci & Eng Int J 1,* 3**,** 106-114.
67. Kumar, A, Pandey, GJMS and JEI 2017. A review on the factors affecting the photocatalytic degradation of hazardous materials. 1**,** 106-114.
68. Lee, C, Nurul, A, Puganeshwary, P and Amr, S 2017a. Performance of natural sunlight on paracetamol removal from synthetic pharmaceutical wastewater using heterogeneous TiO2 photocatalyst. *Desalination Water Treatment,* 78**,** 341-349.
69. Lee, CM, Palaniandy, P and Dahlan, I 2017b. Pharmaceutical residues in aquatic environment and water remediation by TiO_2 heterogeneous photocatalysis: a review. *Environmental Earth Sciences,* 76**,** 611.
70. Li, R, Jia, Y, Bu, N, Wu, J and Zhen, Q 2015. Photocatalytic degradation of methyl blue using Fe_2O_3/TiO_2 composite ceramics. *Journal of Alloys Compounds,* 643**,** 88-93.
71. Lianou, A, Frontistis, Z, Chatzisymeon, E, Antonopoulou, M, Konstantinou, I and Mantzavinos, D 2018. Sonochemical oxidation of piroxicam drug: Effect of key operating parameters and degradation pathways. *Journal of Chemical Technology Biotechnology,* 93**,** 28-34.
72. Lindim, C, Van Gils, J, Georgieva, D, Mekenyan, O and Cousins, ITJS o. t. TE 2016. Evaluation of human pharmaceutical emissions and concentrations in Swedish river basins. 572**,** 508-519.
73. Luo, Y., Guo, W., Ngo, H. H., Nghiem, L. D., Hai, F. I., Zhang, J., Liang, S. & Wang, X. C. 2014. A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Science of the total environment,* 473**,** 619-641.
74. Matongo, S, Birungi, G, Moodley, B and Ndungu, P 2015. Pharmaceutical residues in water and sediment of Msunduzi River, kwazulu-natal, South Africa. *Chemosphere,* 134**,** 133-140.

75. Mboula, VM, Héquet, V, Andres, Y, Pastrana-Martínez, L M, Doña-Rodríguez, JM, Silva, AM. and Falaras, P 2013. Photocatalytic degradation of endocrine disruptor compounds under simulated solar light. *Water research,* 47**,** 3997-4005.
76. Mboula, VM, Hequet, V, Gru, Y, Colin, R and Andres, Y 2012. Assessment of the efficiency of photocatalysis on tetracycline biodegradation. *Journal of hazardous materials,* 209**,** 355-364.
77. Méndez-Arriaga, F, Gimenez, J and Esplugas, S 2008. Photolysis and TiO_2 photocatalytic treatment of naproxen: degradation, mineralization, intermediates and toxicity. *Journal of Advanced Oxidation Technologies,* 11**,** 435-444.
78. Miklos, DB, Remy, C, Jekel, M, Linden, KG, Drewes, JE and Hübner, U 2018. Evaluation of advanced oxidation processes for water and wastewater treatment–A critical review. *Water research*.
79. Mills, A and Le Hunte, S 1997. An overview of semiconductor photocatalysis. *Journal of photochemistry photobiology A: Chemistry,* 108**,** 1-35.
80. Mirzaei, A, Chen, Z, Haghighat, F, Yerushalmi, LJS c. and society 2016. Removal of pharmaceuticals and endocrine disrupting compounds from water by zinc oxide-based photocatalytic degradation: a review. 27**,** 407-418.
81. Mital, G. S. & Manoj, T. 2011. A review of TiO_2 nanoparticles, Phys. Springer.
82. Mugunthan, E, Saidutta, M and Jagadeeshbabu, PJE t. 2019. Photocatalytic degradation of diclofenac using TiO2–SnO2 mixed oxide catalysts. 40**,** 929-941.
83. Murakami, N, Ono, A, Nakamura, M, Tsubota, T and Ohno, TJACBE 2010. Development of a visible-light-responsive rutile rod by site-selective modification of iron (III) ion on {1 1 1} exposed crystal faces. 97**,** 115-119.
84. Namshah, KS and Mohamed, RMJAN 2018. WO_3–TiO_2 nanocomposites for paracetamol degradation under visible light. 8**,** 2021-2030.
85. Nasr, O, Mohamed, O, Al-Shirbini, AS and Abdel-Wahab, AM 2019. Photocatalytic degradation of acetaminophen over Ag, Au and Pt loaded TiO_2 using solar light. *Journal of Photochemistry Photobiology A: Chemistry,* 374**,** 185-193.
86. Ni, M, Leung, MK, Leung, DY and Sumathy, K 2007. A review and recent developments in photocatalytic water-splitting using TiO_2 for hydrogen production. *Renewable Sustainable Energy Reviews,* 11**,** 401-425.
87. Öchsner, A, Ahmed, W and Ali, N 2009. *Nanocomposite coatings and nanocomposite materials*.

88. Ollis, DF and Al-Ekabi, H 1993. *Photocatalytic purification and treatment of water and air: proceedings of the 1st International Conference on TiO₂ Photocatalytic Purification and Treatment of Water and Air, London, Ontario, Canada, 8-13 November, 1992*, Elsevier Science Ltd.
89. Oseghe, EO, Ofomaja, AEJJ. o. P and Chemistry, PA 2018. Study on light emission diode/carbon modified TiO_2 system for tetracycline hydrochloride degradation. 360**,** 242-248.
90. Oulton, RL, Kohn, T and Cwiertny, DMJJ o. EM 2010. Pharmaceuticals and personal care products in effluent matrices: a survey of transformation and removal during wastewater treatment and implications for wastewater management. 12**,** 1956-1978.
91. Pawar, R and Lee, CS 2015. *Heterogeneous Nanocomposite-Photocatalysis for Water Purification*, William Andrew.
92. Payan, A, Isari, AA and Gholizade, NJCEJ 2019. Catalytic decomposition of sulfamethazine antibiotic and pharmaceutical wastewater using Cu-TiO_2@ functionalized SWCNT ternary porous nanocomposite: Influential factors, mechanism, and pathway studies. 361**,** 1121-1141.
93. Pelaez, M, Nolan, NT, Pillai, SC, Seery, MK, Falaras, P, Kontos, AG, Dunlop, PS, Hamilton, JW, Byrne, JA. and O'shea, K 2012. A review on the visible light active titanium dioxide photocatalysts for environmental applications. *Applied Catalysis B: Environmental,* 125**,** 331-349.
94. Pereira, AM, Silva, LJ, Laranjeiro, CS, Meisel, LM, Lino, CM and Pena, A 2017. Human pharmaceuticals in Portuguese rivers: The impact of water scarcity in the environmental risk. *Science of the Total Environment,* 609**,** 1182-1191.
95. Praveena, SM, Shaifuddin, SNM, Sukiman, S, Nasir, FAM, Hanafi, Z, Kamarudin, N, Ismail, THT. and Aris, AZ 2018. Pharmaceuticals residues in selected tropical surface water bodies from Selangor (Malaysia): Occurrence and potential risk assessments. *Science of the total environment,* 642**,** 230-240.
96. Prieto-Rodriguez, L, Miralles-Cuevas, S, Oller, I, Agüera, A, Puma, G. and Malato, SJJ o. h. m. 2012. Treatment of emerging contaminants in wastewater treatment plants (WWTP) effluents by solar photocatalysis using low TiO_2 concentrations. 211**,** 131-137.
97. Qu, X, Alvarez, PJ and Li, Q 2013. Applications of nanotechnology in water and wastewater treatment. *Water research,* 47**,** 3931-3946.
98. Quesada, HB, Baptista, ATA, Cusioli, LF, Seibert, D, de Oliveira Bezerra, C. and Bergamasco, R 2019. Surface water pollution by pharmaceuticals and an alternative of Removal by low-cost adsorbents: a review. *Chemosphere*.

99. Redeker, M, Wick, A, Meermann, B r. Ternes, TAJES and Technology 2014. Removal of the iodinated X-ray contrast medium diatrizoate by anaerobic transformation. 48**,** 10145-10154.
100. Ribeiro, AR, Nunes, OC, Pereira, MF and Silva, AMJE i. 2015. An overview on the advanced oxidation processes applied for the treatment of water pollutants defined in the recently launched Directive 2013/39/EU. 75**,** 33-51.
101. Rimoldi, L, Meroni, D, Falletta, E, Ferretti, AM, Gervasini, A, Cappelletti, G and Ardizzone, S 2017. The role played by different TiO_2 features on the photocatalytic degradation of paracetamol. *Applied Surface Science,* 424**,** 198-205.
102. Rivera-Jaimes, JA, Postigo, C, Melgoza-Alemán, RM, Aceña, J, Barceló, D and de Alda, ML 2018. Study of pharmaceuticals in surface and wastewater from Cuernavaca, Morelos, Mexico: occurrence and environmental risk assessment. *Science of the Total Environment,* 613**,** 1263-1274.
103. Robinson, AA, Belden, JB, Lydy, MJJET and Journal, CAI 2005. Toxicity of fluoroquinolone antibiotics to aquatic organisms. 24**,** 423-430.
104. Robinson, T, McMullan, G, Marchant, R and Nigam, P 2001. Remediation of dyes in textile effluent: a critical review on current treatment technologies with a proposed alternative. *Bioresource technology,* 77**,** 247-255.
105. Rodriguez-Narvaez, O. M., Peralta-Hernandez, J. M., Goonetilleke, A. & Bandala, E. R. 2017. Treatment technologies for emerging contaminants in water: A review. *Chemical Engineering Journal,* 323**,** 361-380.
106. Rosman, N, Salleh, W, Mohamed, MA, Jaafar, J, Ismail, A and Harun, Z 2018. Hybrid membrane filtration-advanced oxidation processes for removal of pharmaceutical residue. *Journal of colloid interface science,* 532**,** 236-260.
107. Sambaza, S, Maity, A & Pillay, KJJ o. ECE 2019. Enhanced degradation of BPA in water by PANI supported Ag/TiO_2 nanocomposite under UV and visible light. 7**,** 102880.
108. Schilling, A, Corey, R, Leonard, M and Eghtesad, BJCC j. o. m. 2010. Acetaminophen: old drug, new warnings. 77**,** 19-27.
109. Schneider, J, Matsuoka, M, Takeuchi, M, Zhang, J, Horiuchi, Y, Anpo, M and Bahnemann, DWJC r. 2014. Understanding TiO2 photocatalysis: mechanisms and materials. 114**,** 9919-9986.
110. Scott, PD, Bartkow, M, Blockwell, SJ, Coleman, HM, Khan, SJ, Lim, R, McDonald, JA, Nice, H, Nugegoda, D and Pettigrove, VJJ o. e. q. 2014. A national survey of trace organic contaminants in Australian rivers. 43**,** 1702-1712.
111. Simons, P and Dachille, F 1967. The structure of TiO2II, a high‐pressure phase of TiO_2. *Acta Crystallographica,* 23**,** 334-336.

112. Singh, P, Shandilya, P, Raizada, P, Sudhaik, A, Rahmani-Sani, A and Hosseini-Bandegharaei, A 2018. Review on various strategies for enhancing photocatalytic activity of graphene based nanocomposites for water purification. *Arabian Journal of Chemistry*.
113. Sreekanth, D, Sivaramakrishna, D, Himabindu, V a Anjaneyulu, YJB t. 2009. Thermophilic treatment of bulk drug pharmaceutical industrial wastewaters by using hybrid up flow anaerobic sludge blanket reactor. 100**,** 2534-2539.
114. Svenson, A, Allard, AS and Ek, M 2003. Removal of estrogenicity in Swedish municipal sewage treatment plants. *Water Research,* 37**,** 4433-4443.
115. Thi, VHT and Lee, BK 2017. Effective photocatalytic degradation of paracetamol using La-doped ZnO photocatalyst under visible light irradiation. *Materials Research Bulletin,* 96**,** 171-182.
116. Tran, NH, Reinhard, M and Gin, KYHJW r. 2018. Occurrence and fate of emerging contaminants in municipal wastewater treatment plants from different geographical regions-a review. 133**,** 182-207.
117. Tran, NH, Urase, T, Ngo, HH, Hu, J and Ong, SLJB t. 2013. Insight into metabolic and cometabolic activities of autotrophic and heterotrophic microorganisms in the biodegradation of emerging trace organic contaminants. 146**,** 721-731.
118. Tryba, B, Toyoda, M, Morawski, AW, Nonaka, R and Inagaki, M 2007. Photocatalytic activity and OH radical formation on TiO_2 in the relation to crystallinity. *Applied Catalysis B: Environmental,* 71**,** 163-168.
119. Vasiliu, F, Diamandescu, L, Macovei, D, Teodorescu, C, Tarabasanu-Mihaila, D, Vlaicu, A and Parvulescu, V 2009. Fe-and Eu-doped TiO_2 photocatalytical materials prepared by high energy ball milling. *Topics in Catalysis,* 52**,** 544-556.
120. Verlicchi, P, Al Aukidy, M and Zambello, EJS o. t. t. e. 2012. Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment—a review. 429**,** 123-155.
121. Wang, Y, Zhang, H, Zhang, J, Lu, C, Huang, Q, Wu, J and Liu, F 2011. Degradation of tetracycline in aqueous media by ozonation in an internal loop-lift reactor. *Journal of hazardous materials,* 192**,** 35-43.
122. Watts, C and Maycock, D 2007. Desk Based Review of Current Knowledge on Pharmaceuticals in Drinking Water and Estimation of Potential Levels, Final Report to Drinking Water Inspectorate, 2007, Watts and Crane Associates, United Kingdom. WT02046/DWI70/2/213.
123. WHO, WHO 2012. Pharmaceuticals in drinking-water.
124. Xia, K, Bhandari, A, Das, K and Pillar, GJJ o. e. q. 2005. Occurrence and fate of pharmaceuticals and personal care products (PPCPs) in biosolids. 34**,** 91-104.

125. Yang, L, Liya, EY and Ray, MB 2008. Degradation of paracetamol in aqueous solutions by TiO2 photocatalysis. *Water research,* 42**,** 3480-3488.
126. Yang, YY, Zhao, JL, Liu, YS, Liu, WR, Zhang, QQ, Yao, L, Hu, LX, Zhang, JN, Jiang, YX and Ying, GG 2018. Pharmaceuticals and personal care products (PPCPs) and artificial sweeteners (ASs) in surface and ground waters and their application as indication of wastewater contamination. *Science of the Total Environment,* 616**,** 816-823.
127. You, X, Chen, F and Zhang, J 2005a. Effects of calcination on the physical and photocatalytic properties of TiO_2 powders prepared by sol–gel template method. *Journal of sol-gel science technology,* 34**,** 181-187.
128. You, X, Chen, F, Zhang, J and Anpo, MJCL 2005b. A novel deposition precipitation method for preparation of Ag-loaded titanium dioxide. 102**,** 247-250.
129. Yu, JY, Chen, ZJ, Zeng, XY, Liu, C, Cai, FY, Cao, HL and Lü, JJICC 2018a. Morphological control of CdS@ AC nanocomposites for enhanced photocatalytic degradation of tetracycline antibiotics under visible irradiation. 95**,** 134-138.
130. Yu, S, Wang, Y, Sun, F, Wang, R and Zhou, YJCEJ 2018b. Novel mpg-C_3N_4/TiO_2 nanocomposite photocatalytic membrane reactor for sulfamethoxazole photodegradation. 337**,** 183-192.
131. Zaleska, A 2008. Doped-TiO_2: a review. *Recent patents on engineering,* 2**,** 157-164.
132. Ziylan-Yavas, A and Ince, NH 2018. Single, simultaneous and sequential applications of ultrasonic frequencies for the elimination of ibuprofen in water. *Ultrasonics sonochemistry,* 40**,** 17-23.
133. Zwiener, C, Seeger, S, Glauner, T, Frimmel, FJA and chemistry, b. 2002. Metabolites from the biodegradation of pharmaceutical residues of ibuprofen in biofilm reactors and batch experiments. 372**,** 569-575.

Editor received the manuscript: 12.08.2019