

Acetaminophen micropollutant: Historical and current occurrences, toxicity, removal strategies and transformation pathways in different environments

Hoang, Nam Nhat; Ky Le, Gia; Minh Hong Nguyen, Thi; Bui, Xuan Thanh; Nguyen, Khanh Hoang; Rene, Eldon R.; Vo, Thi-Dieu-Hien; Thanh Cao, Ngoc-Dan; Mohan, Raj

Published in: Chemosphere

Link to article, DOI: /10.1016/j.chemosphere.2019.124391

Publication date: 2019

Document Version Peer reviewed version

Link back to DTU Orbit

Citation (APA):

Hoang, N. N., Ky Le, G., Minh Hong Nguyen, T., Bui, X. T., Nguyen, K. H., Rene, E. R., Vo, T-D-H., Thanh Cao, N-D., & Mohan, R. (2019). Acetaminophen micropollutant: Historical and current occurrences, toxicity, removal strategies and transformation pathways in different environments. *Chemosphere*, 236, Article 124391. https://doi.org//10.1016/j.chemosphere.2019.124391

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.

- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Accepted Manuscript

Acetaminophen micropollutant: Historical and current occurrences, toxicity, removal strategies and transformation pathways in different environments



Hoang Nhat Phong Vo, Gia Ky Le, Thi Minh Hong Nguyen, Xuan-Thanh Bui, Khanh Hoang Nguyen, Eldon R. Rene, Thi-Dieu-Hien Vo, Ngoc-Dan Thanh Cao, Raj Mohan

PII:	S0045-6535(19)31612-1
DOI:	10.1016/j.chemosphere.2019.124391
Article Number:	124391
Reference:	CHEM 124391
To appear in:	Chemosphere
Received Date:	14 April 2019
Accepted Date:	16 July 2019

Please cite this article as: Hoang Nhat Phong Vo, Gia Ky Le, Thi Minh Hong Nguyen, Xuan-Thanh Bui, Khanh Hoang Nguyen, Eldon R. Rene, Thi-Dieu-Hien Vo, Ngoc-Dan Thanh Cao, Raj Mohan, Acetaminophen micropollutant: Historical and current occurrences, toxicity, removal strategies and transformation pathways in different environments, *Chemosphere* (2019), doi: 10.1016/j. chemosphere.2019.124391

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1	Acetaminophen micropollutant: Historical and current occurrences, toxicity, removal
2	strategies and transformation pathways in different environments
3	Hoang Nhat Phong Vo ¹ , Gia Ky Le ² , Thi Minh Hong Nguyen ² , Xuan-Thanh Bui ^{3,*} , Khanh Hoang
4	Nguyen ⁴ , Eldon R. Rene ⁵ , Thi-Dieu-Hien Vo ^{6,*} , Ngoc-Dan Thanh Cao ⁶ , Raj Mohan ⁷
5	Q
6	¹ Institute of Research and Development, Duy Tan University, Da Nang, Viet Nam.
7	² Environmental Engineering and Management Program, Asian Institute of Technology (AIT), P.O. Box
8	4, Klong Luang, Pathumthani 12120, Thailand.
9	³ Faculty of Environment and Natural Resources, Ho Chi Minh City University of Technology, VNU-
10	HCM, Viet Nam.
11	⁴ National Food Institute, Denmark Technical University, 2800 Kgs. Lyngby, Denmark.
12	⁵ Department of Environmental Engineering and Water Technology, IHE - Delft, Institute of Water
13	Education 2601 DA, Delft, the Netherlands.
14	⁶ NTT Institute of Hi-Technology, Nguyen Tat Thanh University, Ho Chi Minh City, Viet Nam.
15	⁷ National Institute of Technology Karnataka, Surathkal, Karnataka, Dakshina Kannada – 575025, India.
16	
17	
18	*Corresponding author:
19	Xuan-Thanh Bui, PhD
20	Email: bxthanh@hcmut.edu.vn
21	Ÿ

22 Abstract

Acetaminophen (ACT) is commonly used as a counter painkiller and nowadays, it is 23 increasingly present in the natural water environment. Although its concentrations are usually 24 at the ppt to ppm levels, ACT can transform into various intermediates depending on the 25 environmental conditions. Due to the complexity of the ACT degradation products and the 26 intermediates, it poses a major challenge for monitoring, detection and to propose adequate 27 28 treatment technologies. The main objectives of this review study were to assess (i) the occurrences and toxicities, (2) the removal technologies and (3) the transformation pathways 29 30 and intermediates of ACT in four environmental compartments namely wastewater, surface water, ground water, and soil/sediments. Based on the review, it was observed that the ACT 31 concentrations in wastewater can reach upto several hundreds of ppb. Amongst the different 32 countries, China and the USA showed the highest ACT concentration in wastewater (≤ 300 33 μ g/L), with a very high detection frequency (81-100%). Concerning surface water, the ACT 34 concentrations were found to be at the ppt level. Some regions in France, Spain, Germany, 35 Korea, USA, and UK comply with the recommended ACT concentration for drinking water 36 (71 ng/L). Notably, ACT can transform and degrade into various metabolites such as aromatic 37 derivatives or organic acids. Some of them (e.g., hydroquinone and benzoquinone) are toxic to 38 human and other life forms. Thus, in water and wastewater treatment plants, tertiary treatment 39 systems such as advanced oxidation, membrane separation, and hybrid processes should be 40 used to remove the toxic metabolites of ACT. 41

42 Keywords

43 Micropollutant, acetaminophen, pharmaceutical and personal care products, intermediates,

44 wastewater treatment

45 1. Introduction

In recent years, acetaminophen (ACT) is one of the most consumed pharmaceutical and 46 personal care products (PPCPs) in many countries. For instance, in 2009, ~ 54.3 and 22.6 g 47 ACT/inhabitant per year was reported in France and Spain, respectively (Ortiz de García et al., 48 2013). Likewise, the Taiwan citizens used ~580 million ACT doses in 2004 (Lin and Tsai, 49 2009). After consumption, ACT is excreted in both native and metabolized forms to the sewer 50 51 systems, wastewater treatment plants (WWTPs) and other aquatic/natural environments. ACT in wastewater has been detected frequently in various countries from Asia, Europe and 52 53 Americas. It inflicts significant negative impacts to the aquatic and ecological systems. Additionally, through drinking water and food consumption, it can enter the human body and 54 cause significant health effects (Baron et al., 2014). The long-term exposure would result in 55 cancer, endocrine disruption, antibiotic-resistant and several chronic diseases (Fisher and 56 Curry, 2019). Therefore, the proper removal of ACT and its metabolites/degradation products 57 from water, prior to being discharged to the environment, is important in order to preserve the 58 environmental quality. 59

For the removal of ACT from water, numerous treatment technologies have been developed 60 and tested both at the laboratory and pilot scales. These include biological processes, advanced 61 oxidation processes (AOP), constructed wetlands (CWs), adsorption and membrane processes. 62 Evidently, the principles and working mechanisms of these technologies are different and they 63 64 remove ACT at different efficiencies depending on the concentration of ACT, its source, geographical and environmental conditions. For example, biological processes are green and 65 safe, but high concentrations of ACT can inhibit the microbial activity. In turn, AOPs are rather 66 fast and efficient for high concentrations of ACT; however, AOPs consume more chemicals 67 and they are energy intensive. The degradation mechanism is also different for a biological 68 process and a AOP. For instance, in the case of AOPs, the hydroxyl radicals ('OH), in the 69

presence of photon energy would create chemical breakdown of the ACT molecules and transform them into different ACT metabolites. In a biological process, the microorganisms or the biocatalyst degrade/mineralize the ACT by enzyme mediated biochemical reactions the and convert ACT into metabolites. Consequently, the different treatment technologies should be differentiated clearly and selected depending on the level of treatment required.

After degradation by the different treatment technologies, intermediates/by products are 75 76 formed which entail another issue of secondary ACT pollution. The transformation pathway, and the metabolites of ACT occur synergistically in wastewater treatment systems and other 77 78 aquatic environments. In essence, several transformation processes have been proposed and more than 20 by-products have been identified during the past 15 years (Andreozzi et al., 2003; 79 de Luna et al., 2013). However, these metabolites pose different toxicities. Some of them are 80 more detrimental than the parent forms such as *N*-acetyl-*p*-benzoquinone imine (Liang et al., 81 2016). From a health viewpoint, such aromatic intermediates can result in failure of liver 82 functions in humans (Fisher and Curry, 2019). Hence, the transformation pathways and by-83 products of ACT should be identified and studied systematically. 84

From all the above concerns, this review study aims to assess the following aspects: (i) the occurrences and toxicities, (ii) the different treatment/removal technologies, and (iii) the transformation pathways and intermediates of ACT in four environmental compartments (i.e. wastewater, surface water, ground water, and soil/sediments). By clarifying such stated issues, this review delineates and proposes a sustainable management and treatment option for ACT pollution.

91 2. Occurrences of acetaminophen in various environments

Human wastes, domestic and industrial wastewater are the major sources of ACT, a persistent
micropollutant in the natural environment. Various household activities dispose ACT to the
sewage systems and ACT is collected in the WWTPs. After the treatment process(es) in

WWTPs, ACT still remains in the effluent and is released to water reservoirs and contaminates
soil, sediment and groundwater. Thus, ACT occurs mainly in four environments: sewage and
WWTPs, surface water, groundwater and soil and sediments.

98 2.1 Sewage and wastewater treatment plants

In 1998, a number of WWTPs in Germany were examined if the treatment systems contained ACT; however, surprisingly, it was not detected (Ternes, 1998). Although it could one isolated finding, ACT has been detected across continents, at varying concentrations and detection frequencies (Fig. 1). In 2006, ACT in wastewater was investigated in South Korea, China, United States of America (USA), France, United Kingdom (UK) and many other countries worldwide. The concentration of ACT ranged from 0.1 to 300 µg/l and its detection frequency reached up to 100%.

In Asia, several countries reported their wastewater being contaminated by ACT such as South 106 Korea, China and Taiwan. From Fig. 1, it is evident that the documented sites were mostly in 107 mega cities and their nearby regions (e.g., Busan, Ulsan and Xiamen) with high-density 108 population. In the case of South Korea, ACT accounted for 18 - 80% of the total PPCPs in 109 wastewater in the year 2007 (Kim et al., 2007a; Sim et al., 2010). From the year 2008 to 2012, 110 ACT concentration in sewages and WWTPs increased by ~11-fold from 6.8 to 75 µg/l (Sim et 111 al., 2010; Kim et al., 2012). The main reason was attributed to the high ACT consumption rate 112 in South Korea. In the year 2004, Korean consumed 9 tons ACT and the ACT consumption 113 rate only started to rise from 2008 to 2012 (Sim et al., 2010). Similarly, in China, the ACT 114 concentration was recorded at 3.4 µg/l in sewages and WWTPs and it was ranked as the highest 115 amongst all the assessed PPCPs (Sun et al., 2016b). Therefore, researchers suggested ACT as 116 the marker for PPCPs pollution in China. In comparison with the Korean survey, the Chinese 117 citizens also used ACT widely and the survey showed values ranging from 10 - 18 g/d per 1000 118 inhabitants (Gao et al., 2016). In Taiwan, ACT was the most detected compound in WWTPs 119

120 effluent because the Taiwanese citizens have consumed 579 million doses of ACT (different

- forms) in 2004 (Lin and Tsai, 2009). This was 4 times higher than the propanolol dose of 156
- 122 millions, being the second most-consumed PPCPs.

In Europe, the pattern of ACT contamination differed from those observed in Asia. Countries 123 such as Greece and France showed 100% ACT detection frequency in WWTPs (Gros et al., 124 2010; Papageorgiou et al., 2016). Although its detection frequencies were higher than in Asia, 125 nevertheless, the total amount of ACT accounted for only 1 - 2% of the total PPCPs in 126 wastewater compared with 18 - 80% in Asia (Rabiet et al., 2006). These values can be 127 128 considered to be acceptable because European citizens used 320 mg/d per 1000 inhabitants, much less than the values of 10 - 18 g/d per 1000 inhabitants of the Asian region (Kosma et 129 al., 2010). 130

Concerning the United States, the ACT concentration in WWTPs was more pronounced than 131 other countries. For example, in the year 2006, $\sim 0.96 \,\mu g$ ACT/L was reported in Baltimore, 132 and these values subsequently increased 100-fold μ g/l after 2012 (Hedgespeth et al., 2012; 133 Blair et al., 2013; Kosma et al., 2014). Besides, in the United States, ACT accounted for ~ 45% 134 of the total PPCPs present in the hospital effluent (Oliveira et al., 2015). Its concentration was 135 $\sim 220 \,\mu$ g/l and the highest values were observed during the winter season due to the pattern of 136 consumption (Yu et al., 2013). ACT is being used in hospitals; thus, its concentration in 137 wastewater was 3-fold higher than those observed normally in municipal WWTPs. In the case 138 of Colombia, ACT concentration in sewage and WWTPs varied from 9.2 to 39.2 µg/l (Botero-139 Cov et al., 2018), which is nearly similar to the amounts reported in WWTPs samples from the 140 Asian region. 141

During 8 years, from 1998 to 2006, ACT was detected increasingly in many countries and regions. Since the invention of ACT in 1955 for medication purposes, ACT was consumed even more. Although it was not detected in German WWTPs in the year 1998, it might be

possible that the ACT concentration was below the detection limit in that study. In the following years, modern analytical techniques, tools and technologies are well-developed and these instruments can detect even low concentrations. Additionally, micropollutants have attracted a growing interest amongst researchers from various disciplines, ranging from public health, engineering, geochemistry to policy and governance.

150

[Insert Fig. 1]

151 **2.2 Surface water**

In developing countries, industrial effluent, municipal wastewater, hospital wastewater and septic tank effluent are often not collected and treated properly. This causes the wide spread prevalence of ACT in surface water. Unlike in the case of sewage and WWTPs, the concentration of ACT in surface water reduced chronologically with respect to the years. At the early stage, ACT was detected in surface water at the ppb concentration levels (10 μ g/l in 2002) (Kolpin et al., 2002). In recent reports, the concentration of ACT decreased to ppt levels

158 (Lv et al., 2014; You et al., 2015; Lin et al., 2016c).

Similar to sewage and WWTPs, ACT was detected in surface water of several Asian countries 159 such as South Korea, China, Taiwan and Singapore. In South Korea, ACT was present in many 160 rivers with the highest occurrence frequency (80%) and concentration (33 ng/l) than other 161 PPCPs (Kim et al., 2007a). For example, they existed in the three biggest rivers in South Korea: 162 Han, Nakdong and Youngsan, respectively. Particularly, they were present in 9/12 of the water 163 samples collected from rivers (Choi et al., 2008); 6/8 of the water samples collected from 164 wastewater treatment plants and surface waters (Kim et al., 2007a), and 2/5 of the river water 165 samples (Sim et al., 2010). In China, ACT concentration in surface water was comparable to 166 the values reported from South Korea. Specifically, ACT existed in the range of 9.8 to 197 ng/l 167 in Taihu lake and Jiulong river, while other PPCP concentrations were found to be below the 168 detection limit (Lv et al., 2014; Lin et al., 2016c; Sun et al., 2016b). In Taiwan and Singapore, 169

ACT was dominant (33 - 95%) among the total PPCPs in surface waters (Lin and Tsai, 2009; 170 You et al., 2015). Incidentally, these water reservoirs received discharges from various 171 industrial activities and supplied drinking water to the local communities in the region. 172 Concerning Europe, in France and Spain, the ACT detection frequency in surface water was in 173 the range of 28 - 41% (Vulliet and Cren-Olivé, 2011; Vazquez-Roig et al., 2012) and its 174 concentration varied from 0.4 to 71 ng/l. However, the studied (sampled) regions were remote 175 areas like national parks and mountain lakes. Elsewhere, the Ensanche region of Northwest 176 Spain recorded a maximum ACT concentration of 5.71 µg/l (wet weather) and 0.72 µg/l (dry 177 weather), respectively (Del Río et al., 2013). This area was used as a catchment for wastewater 178

179 discharge by the local communities.

In United States, the ACT concentration and detection frequency in Michigan lake was 2.5 -180 17 ng/l and 25%, respectively (Ferguson et al., 2013). Michigan lake was the catchment serving 181 drinking water for a larger part of the community in the region. It also received wastewater 182 from the local communities. Thus, ACT concentration in these densely populated areas 183 overtook the open water/catchment sites. In the Mississippi river, ACT concentration ranged 184 from 24.7 - 65.2 ng/L, which was higher than the values reported from Michigan lake (Zhang 185 et al., 2007). The Mississippi river carried $\sim 66\%$ suspended solids (SS) from the mainland of 186 the United States to the ocean. Interestingly, the presence of suspended solids adsorbed and 187 reduced a significant amount of ACT and other PPCPs present in the river water. Previously, 188 Boyd et al. (2003) tested water samples collected from the Mississippi river and Pontchartrain 189 lake and reported that ACP were below the detectable levels. 190

In general, ACT detection frequencies (< 50%) and ACT concentrations in surface waters of Europe and America was less than those reported in Asia. In surface water, ACT concentration is usually influenced by several environmental, geographical and social factors. The most important parameter was, however, the polulation - given that Europe and United States has

less population density compared to Asia. Geographical condition such as rainfall also affected 195 the ACT concentration in surface water. For example, according to a field study, Michigan lake 196 received runoff and rainfall that diluted the ACT concentration several fold after the monsoon 197 season (Ferguson et al., 2013). Neverhtless, from the yearly trends, it is evident that the ACT 198 concentration in surface water has reduced in recent years. Such drop in the ACT levels can be 199 attributed to the better performance of WWTPs, innovations in research, awareness and 200 enactment of policies and regulations. Besides, the discharge standards for micropollutant have 201 been gradually been established in many countries. In 2008, the United States Environmental 202 203 Protection Agency (USEPA) developed a "White Paper Aquatic Life Criteria for Contaminants of Emerging Concern: Part I Challenges and Recommendations" and, in the meantime, 204 Directive 2000/60/EC and 2008/105/EC were published by the European Commission. In Asia, 205 discharge standards for micropollutants is still scarce or they are still at the policy approval 206 level. Some of the new treatment technologies and discharge standards have compromised 207 ACT concentration < 71 ng/l that makes the water suitable for drinking purposes (Vulliet and 208 Cren-Olivé, 2011). However, in the case of European countries, although the levels of ACT 209 were reported to be high in some reports, the policies and guidelines are substantially stronger 210 and well-implemented than in many Asian countries. 211

212 2.3 Groundwater

The sources of ACT pollution in ground water are similar to those observed in surface water, industrial effluent, municipal WWTP, septic tank and landfill. The leakage of septic tank and landfill can contain concentrated pollutants in the range of 100 - 1000 ng/l of ACT (Lapworth et al., 2012). ACT contaminated ground water has been reported in many countries and regions. In France and Serbia, ACT appeared in 17% and 15% of the groundwater samples tested (Grujić et al., 2009; Vulliet and Cren-Olivé, 2011). In the Tennessee River basin (USA), ACT concentration was in the range of 2.1 - 12.3 ng/l and it was present in ~ 13% of the groundwater

samples (Conley et al., 2008). In California, the ACT detection frequency and maximum 220 concentration were 0.32% and 1.89 µg/l, respectively (Fram and Belitz, 2011). Thus, ground 221 222 water is less contaminated than wastewater and surface water because the ACT containing stream is usually filtered by the soil layers as it penetrates gradually into the soil layers (He et 223 al., 2016). Nevertheless, studies related to the identification/quantification of ACT in ground 224 water is scarce compared to wastewater and surface water. Hence, the available reports related 225 226 to ground water contamination due to ACT might not reflect the actual problem adequately. In developing countries, septic tanks are used widely but their quality and durability still remains 227 228 a challenge and persisting problem. Anew, the management policies concerning landfills in Asia is rather poorly defined and incomplete. Those must be considered for micropollutant 229 control in the future. 230

231 2.4 Sediment and soil

Similar to drinking water, ACT has also contaminated the soil and sediment environments, e.g. 232 the Pego-Oliva marsh in Spain. ACT was detected in 87% of the soil and 91% of the sediment 233 samples with maximum concentrations of 15.1 ng/l and 1.8 ng/g, respectively (Vazquez-Roig 234 et al., 2012). Notably, ACT settles and accumulates in sediment and soil faster than in surface 235 water. In samples collected from the Masan Bay in South Korea, ACT was an indicator of 236 micropollutant pollution. It was detected in > 50% of the sediment samples with a concentration 237 of ~ 2.2 ng/g sediment (Choi et al., 2014). The Masan Bay was one of the most polluted coastal 238 area in South Korea due to effluent discharges from heavy industries and highly urbanized 239 cities. According to the authors, the ACT detection frequencies in soil and sediment were high 240 because ACT could adsorb onto the solid phase and settle easily than in surface waters. 241 Although its concentration in sediment and soil still remained at the ppt level, it could increase 242 gradually in the next coming years due to (bio)accumulation and (bio)magnification. 243

The salient observations can be summarized as follows: (i) ACT concentration in wastewater 244 is constantly increasing since 1998 to the present values of several 100 ppb; (ii) in surface 245 water, ACT concentration decreased to ppt from the same time but has contaminated the larger 246 surface areas, (iii) groundwater is less polluted with ACT than surface water, and (iv) soil and 247 sediment environments accumulated ACT from surface water. These evidences clearly 248 illustrate that ACT can be an indicator for the presence of micropollutants in several countries. 249 250 Although the pattern of ACT contamination in those countries were different, China and the USA showed the highest ACT detection frequency ranging from 81 - 100%, compared to 22 -251 252 73% in France, Spain and Singapore. In some reports from United States, UK, Colombia and Taiwan, ACT concentrations were > 300 μ g/l. France recorded the lowest ACT detection 253 frequency (< 39%) and concentration < 0.1 μ g/l. Table 1 classifies the countries depending on 254 their levels of ACT contamination. 255

256

[Insert Table 1]

257 **3. Toxicities of acetaminophen**

ACT is toxic to both aquatic and human life. It causes genetic code damage, oxidative degradation of lipids and denaturation of protein in cells. The toxicity of ACT can vary from low to moderate depending on acute and chronic exposure conditions (Kosma et al., 2010). The effective concentration (EC₅₀) and exposure time to ACT are summarized in Table 2.

262

[Insert Table 2]

The toxicity of ACT has been studied in several hosts such as bacteria, algae, macrophytes, protozoan and fish. Amongst those, the freshwater invertebrate and cell *in-vitro* showed the lowest effective concentration, i.e. < 50 mg/l (Henschel et al., 1997; Kim et al., 2007b). This implies that these species were sensitive to ACT. In turn, bacteria and macrophyte species were recalcitrant to ACT. Most of the authors have reported that their EC_{50} values were > 400 mg/l (Henschel et al., 1997; Kim et al., 2007b).

ACT can be present in drinking water and it would endanger public health. However, the risk 269 assessment method of PPCPs in drinking water has not been established officially. Instead, two 270 main procedures have been proposed in the literature, i.e. the measured and predicted 271 concentrations. For instance, Vulliet and Cren-Olivé (2011) followed this approach to estimate 272 the maximum levels of ACT in drinking water. The maximum value for drinking water was 273 reported as 71 ng/l and the daily ACT intake was 142 ng/l. The ACT concentrations of some 274 surface water sources have reported to be > 71 ng/l, such as the Hérault River Basin of France 275 River Taff and River Ely of the UK, Sindian and Dahan river of Taiwan, Jiulong River of China 276 277 and many areas of the United States (Rabiet et al., 2006; Kasprzyk-Hordern et al., 2008; Lin and Tsai, 2009; Lv et al., 2014). 278

279 4. Removal technologies for acetaminophen (ACT)

Several technologies have been developed, both at the laboratory and field scale, for the 280 removal of micropollutants. They range from biological, physical, chemical to hybrid and 281 advanced technologies. The common technologies for ACT removal including biological 282 processes, AOPs, plant uptake, adsorption, membrane processes, hybrid processes and other 283 technologies were reviewed and discussed. In essence, they differ from originalities and 284 mechanisms. For example, the AOPs are regulated by chemical reactions and physical 285 processes, e.g, Fenton's reagent/photo-Fenton process. The adsorption and membrane 286 processes are largely physical treatments, while plant uptake (phytoremediation), activated 287 sludge process and anaerobic process refer to biological treatment. 288

289 4.1 Biological processes

Biological processes refer to the removal of micropollutants using suitable biocatalysts under
aerobic or anaerobic environments. The pollutant removal mechanisms of biological processes
comprise of biosorption, biodegradation and bioaccumulation. In practice, the commonly used
biological processes include the activated sludge process, anaerobic process, microalgae based

294 photobioreactor and microalgae based pond system. However, during wastewater treatment,

these technologies yield different advantages and limitations for ACT removal.

Activated sludge process has proven to be effective for the removal of ACT from wastewater.
For example, in the Baltimore WWTP (USA), it could remove 99% ACT in 14 d (Yu et al.,
2006). A half of ACT dose was biotransformed within 4 d. In the Coslech WWTP (UK), an
activated sludge process eliminated 100% ACT from wastewater (Kasprzyk-Hordern et al.,

2009). Although ACT was removed efficiently in the system, according to the authors, it was

not mineralized completely and bioaccumulation, physical adsorption and biodegradation

302 contributed to > 99% removal efficiency. After treatment, the wasted sludge can be composted,

303 incinerated or treated in an anaerobic digester.

301

Similar to an activated sludge process, anaerobic systems could also remove > 75% ACT from wastewater. According to a recent study, ACT was retained in the anaerobic sludge biomass to a value of 35 g/kg (Narumiya et al., 2013). The superiority of anaerobic process(es) compared to a conventional anaerobic process is that this process could tolerate high dose of ACT, ranging from 50 to 1000 mg/l. Over this dose, ACT would inhibit the anaerobic microbial community in the reactor (Alvarino et al., 2014). In addition, ACT concentrations > 250 mg/l could hamper/inhibit the nitrification and denitrification rates.

Regarding microalgae, a high rate algae pond could handle wastewater containing 9 µg ACT/l from 4 to 8 d (Matamoros et al., 2015). When compared to the microorganisms present in the activated sludge process and the anaerobic process, microalgae are less tolerant to ACT stress. The effective ACT concentration causing toxicity to algae ranges from 134 - 240 mg/l; whereas the inhibitory concentration for certain bacteria ranged between 550 and 650 mg/l (Table 2). Hence, in order to enhance the overall removal efficiency, algal cells were immobilized to intert matrices such as sponge, bead and nanoparticles. As a result, the immobilized algal cells were

able to tolerate ACT, achieving 100% efficiency at a concentration of 100 μ g/l in 8 d (Yu et al., 2011).

From these previous reports, it is clearly evident that biological processes could treat 320 wastewater containing high levels of ACT, upto hundreds of ppb. From a practical viewpoint, 321 in WWTPs, biological processes are prone to receive fluctuating concentrations/loading rates 322 of wastewater. In order to withstand the shock load effects on the biological system, the 323 application of an equalization tank will help to maintain the ACT concentrations at values < 50324 mg/l for anaerobic treatment and 500 µg/L for aerobic treatment, respectively. Algal pond 325 326 systems can still be considered as a post-treatment step because it can easily tolerate low ACT concentrations present in wastewater. However, some of these biological processes require 327 long start-up or acclimation time, high surface (land) area, long solids and hydraulic retention 328 time and the removal efficiency depends on the composition and concentration of pollutant(s) 329 present in the wastewater. Nevertheless, complete mineralization of the ACT is still not 330 accomplished in biological treatment systems, thus, a tertiary treatment step as AOPs, plant 331 uptake, adsorption and/or membrane processes are usually required. The tertiary treatment step 332 could also be used as a pre-treatment step to reduce the load of wastewater to the biological 333 process, thereby reducing the size of bioreactors and completely eliminate ACT from the 334 treated effluent. 335

336 **4.2 Plant uptake processes**

Plant can uptake organics, inorganics and a wide variety of recalitrant pollutants present in wastewater (Vo et al., 2018). Thus, it can also be considered as an option for ACT removal. In natural/constructed wetlands, the plants uptake ACT via the root, and its accumulated and thereafter translocated. In addition, the plant rhizosphere offers co-benefits for other removal processes, by promoting microbial growth in the wetland and alleviating clogging of the media bed. Although plant contributes greatly to the removal of ACT, depending on the plant species,

the removal efficiency could vary largely. For instance, *P. australis* removed ~51 - 99% ACT
from contaminated water, while *T. latifolia* reduced 46.7 - 99.9% ACT (Ranieri et al., 2011).
Some plant species could also contribute to the transformation of ACT (Huber et al., 2009; Wu
et al., 2013).

The fate and metabolism of ACT was investigated in the tissues of Armoracia rusticana (Huber 347 et al., 2009). After 6 h of incubating the plant species in ACT containing wastewater, ACT and 348 349 its metabolites were detected in the plant tissues. The metabolites consisted of 18% ACT, 64% paracetamol glucoside, 17% paracetamol glutathione and 1% cysteine conjugate, respectively. 350 351 However, after 168 h, 88% ACT in the plant root system had reduced and transformed to other metabolities. Similarly, Brassica juncea was able to uptake 22% ACT within 3 d. The authors 352 confirmed that the shoot was responsible for determining the fate of ACT transformation and 353 its metabolites (Bartha et al., 2010). The conjugation of ACT - glutathione and glucose 354 occurred in the plant tissues and these mechanisms are somewhat similar to those occurring in 355 mammals. The transformation process of ACT in plant tissues depends on the plant species, 356 lasting from 6 h to 3 d. Using plants, wastewater containing ACT < 5 μ g/l can be handled 357 effectively and this technique can be used as a post-treatment step to reduce ACT to ppt levels. 358

359 4.3 Advanced oxidation processes

360 4.3.1 Chemical-based Fenton processes

Chemical-based Fenton reaction is one of the commonly reported AOP. The chemical-based Fenton includes classical Fenton, Fenton-like and bio-Fenton processes. It produces hydroxyl radical groups that plays a major role in the degradation/mineralization of ACT (Eq. 1 & 2):

364

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^- + OH \dots (Eq. 1)$$

365
$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HO_2 + H^+ \dots(Eq. 2)$$

The ACT removal efficiency of chemical-based Fenton process is affected by the pH, H_2O_2 and Fe²⁺ concentrations. The importance of those parameters varies in the order: Fe²⁺ > H_2O_2 >

pH (Su et al., 2012). The increase of Fe^{2+} and H_2O_2 concentration can enhance the ACT 368 removal efficiency, whereas the prevailing pH conditions can also synergistically or 369 antagonistically affect the ACT removal. At higher pH conditions, Fe³⁺ precipitates to 370 amorphous $Fe(OH)_3$ and reduces the regeneration of Fe^{2+} . In a recent study, the optimal 371 conditions were reported to be: pH - 3.0, H_2O_2 - 25 mM and Fe²⁺ - 0.1 mM, to remove 5 mM 372 of ACT from contaminated water (Su et al., 2013a). The amorphous form of iron present in 373 sludge damages the equipments in WWTPs. The type of iron sources used in the chemical 374 based Fenton process is also important in the Fenton reaction. For example, artificial ferrous 375 iron removes ACT 5% higher than the iron source present in laterite soil (Basavaraju et al., 376 2011). 377

Referring to the mechanism, Fenton reaction degrades ACT in 2 stages including an initially occuring reaction at higher rates, followed by a reaction at slower rates (de Luna et al., 2013). In the first stage, Fe^{2+}/H_2O_2 reaction occurs within 30s to generate large amount of •OH, while the second stage of Fe^{3+}/H_2O_2 occurs after 30s in which the Fe^{3+} combines with H_2O_2 to degrade ACT. Depending on the degree of treatment required, the reaction time of a Fenton's process could be optimized.

The chemical-based Fenton's reaction has been performed in different reactors such as an 384 aerated reactor, fluidized-bed reactor and wetlands. In an aerated reactor, it removed 99% ACT 385 at an initial concentration of 5 mM (Su et al., 2012). In a fluidized-bed reactor, 99.6% ACT 386 removal was observed at an initial concentration of 5 mM, within 40 min (de Luna et al., 2013). 387 Bio-Fenton's process has also emerged as a novel technology as it uses the iron present in 388 laterite soil environments and H₂O₂ from the plant rhizosphere of a constructed wetland (Phong 389 et al., 2016). The H₂O₂ of the root tissue and iron species of laterite soil activated bio-Fenton 390 reaction and degraded 99.5% of ACT at a concentration of 100 μ g/l. 391

The chemical-based Fenton's reaction is almost instantaneous and highly efficient for ACT removal. The ACT removal efficiency of a chemical-based Fenton's process is typically > 75% (Table 3). As seen from Table 3, depending on the degree of treatment required, the retention times have been varied from 40 to 120 min in order to remove high concentrations of ACT (10 mg/l) at pH 3.0. Besides, a wide range of $[Fe^{2+}]:[H_2O_2]$ ratios has been reported in the literatures, varying from 1:40 to 1:250.

398

[Insert Table 3]

399 4.3.2 Photo-based Fenton processes

400 The conventional Fenton's reaction can be modified as the photo-based Fenton's process when coupled to a light source. The photo-based Fenton's process degrades ACT 2-fold faster than 401 the traditional Fenton's reaction (Manu and Mahamood, 2011). The photo-based Fenton's 402 process encompasses both photolysis and photocatalytic oxidation. Commonly, the photo 403 Fenton's reaction uses a light source such as as monochromatic UV, metal halide and xenon 404 lamp. The light emitting diode (LED) with polychromatic function is commercially available 405 and it is more advantageous than traditional UV lamps. TiO₂-based and carbon-based materials 406 are the preferred photocatalysts used in this process. 407

The photo Fenton's process removes ACT depending on the wavelength of the incident UV 408 light source. The shorter wavelenghts offer higher energy to create the required 'OH radicals 409 and degrades ACT more efficiently. For example, Kim and Tanaka (2009) tested two UV 410 systems encompassing a UV/lamp 1 (254 nm) and a UV/lamp 2 (254 nm and 185 nm). 411 According to the authors, the UV/lamp 1 degraded 20% ACT and UV/lamp 2 removed 40% 412 ACT, respectively. Similarly, UVA of wavelength 360 nm removed 99% ACT at an initial 413 concentration of 5 mM within 40 min (Su et al., 2013b). In the case of UV-LED, it provides 414 higher light intensity compared to the traditional UV mercury lamp. Thus, it creates a stronger 415

416 oxidation state and removes ACT with high efficiency (Xiong and Hu, 2012). The UVA-LED,

417 at a wavelength 365 nm was able to remove 200 ppb of ACT completely within 15 min.

418 The photocatalytic Fenton's process involves the use of a suitable, inert catalyst in the photo Fenton system. Catalysts would increase the amount of 'OH group and provide sufficient surface 419 area for the adsorption of the pollutant. Hence, it improves the ACT removal efficiency. The 420 common catalysts used in this process are carbon-based and TiO₂-based materials, such as 421 BiOCl_xI_v nanospheres (Wang et al., 2016b), modified reticulated vitreous carbon (Arredondo 422 Valdez et al., 2012), nano-porous TiO₂ (Xie et al., 2016) and BaTiO₃/TiO₂ (Kurniawan et al., 423 424 2018). The photocatalytic systems could remove > 95% ACT, at concentrations as high as 96 mg/l (Arredondo Valdez et al., 2012). Among the different operation parameters, pH is 425 important and its optimum value depends on the type and physico-chemical properties of the 426 catalyst used. For example, a pH of 3.5 was found to be the optimal for TiO₂ catalysts (Yang et 427 al., 2008; Zhang et al., 2008), whereas it was 7.0 for BaTiO₃/TiO₂ (Kurniawan et al., 2018), or 428 9.0 for $WO_3/TiO_2/SiO_2$ (Yanyan et al., 2017). 429

For a photo-based Fenton process, proper light source and catalyst are key operational 430 parameters that affects the performance. An UV light source is preferable than a metal halide 431 or xenon lamp source (Table 4). Compared with these light sources, UV handles higher ACT 432 load, with shorter exposure times. Among the UV light source, UVC wavelength was two-fold 433 better than the conventional UVA process (Yang et al., 2008). The exposure time of an UVC 434 process is also 4-fold lower than the UVA process. This was presumably because ACT 435 absorbed the photon energy of UVC better than UVA. If the UV light source and catalyst dose 436 is optimized, the ACT removal efficiency can be improved. For example, a stand-alone process 437 without a light source requires $\sim 20 - 25$ d to remove 100 mg ACT/l (He et al., 2015), or it just 438 could remove little doses of 3 µM ACT within 30 min (Im et al., 2015). However, the integrated 439 system could remove 96 mg ACT/l within a short contact time of 60 min (Arredondo Valdez 440

et al., 2012). From a practical viewpoint, the economics of the process should be considered as
it is a rather expensive process and generates secondary pollutant such as iron containing
sludge.

444

[Insert Table 4]

445 **4.3.3 Electro-based Fenton processes**

The electro-based Fenton is another modification of the conventional Fenton's process. This 446 electro-based Fenton's process uses electrodes to generate the 'OH radicals and subsequently 447 removes ACT from wastewater. Compared to the chemical-based and photo-based Fenton's 448 449 processes, it does not produce iron oxyhydroxide sludge and the overdose of H_2O_2 is controlled. The electrodes of the electro-based Fenton's processes act as the electron donor and acceptor 450 for the Fenton reaction. However, the efficiency relies on the characteristics of the electrode 451 materials. Choosing an appropriate material for the electrode is important since after prolong 452 operation, the electrode can be deteriorated. Some typical examples of electrodes include Pt 453 and Ti-based, porous Ti/boron-doped diamond, Pt sheet and Pt gauze. These materials have 454 demonstrated good ACT removal efficiencies. For example, the planar and porous Ti/boron-455 doped diamond (BDD) electrodes mineralized 100 mg ACT/l (He et al., 2015). The porous 456 electrode was superior to the planar type because it offers high surface area and active sites for 457 the electrochemical reaction to occur. To enhance the ACT removal efficiency, catalyst dose 458 and a light source could also be integrated with the electro-based Fenton process. For example, 459 system with nano-schwertmannite and nano-goethite catalysts removed 500 µg ACT/kg of 460 sediment, completely within 3 d (Yang et al., 2016). Concerning the light source, it has been 461 reported to have a very low effect in enhancing the ACT removal efficiency (de Luna et al., 462 2012). For instance, the electro-Fenton and photoelectro-Fenton processes removed $\sim 97 - 98\%$ 463 of the ACT present in polluted water environments. 464

The electro-based Fenton's process includes the MFC Fenton system, cross-flow-electro 465 Fenton system, and the double cathode electro Fenton system, respectively. Compared with 466 other reactor types and processes, MFC Fenton is more environmentally friendly, although it 467 requires longer reaction times (Zhang et al., 2015). Similar to the photo-based Fenton process, 468 the electro-based Fenton process can also remove ACT from high (ppm) concentrations to the 469 ppt levels. The electro based Fenton process can be applied as a tertiary treatment option in 470 WWTPs. Nevertheless, it is noteworthy to mention that the electro based Fenton process is 471 rather expensive compared to other processes described herein, because it consumes a lot of 472 473 electricity, chemicals and catalysts. Anew, periodic maintenance is required for this process since the amorphous Fe(OH)₃ adheres to the electrodes and decreases the overall ACT removal 474 efficiency. 475

476 **4.3.4 Ozonation**

Ozonation is an established AOP used commonly in drinking water treatment. The ozonation 477 process and its reactions generate free radical groups of O₃⁻ HO₂• and O₂• that has high 478 oxidation states and the spontaneous reactions mineralizes the pollutants. Ozonation has been 479 used extensively for both surface water and wastewater treatment (Trang et al., 2014; Vo et al., 480 2019). For surface water, ozone dose of 5 mg/l can completely remove ACT within 30 min 481 (Lutpi et al., 2015). However, the removal rates achieved in this process (0.7 to 45.7 per mM.s) 482 depends on the water quality. The higher dissolved organic carbon (DOC) concentration and 483 alkalinity increases the removal rate of ACT (Lutpi et al., 2015). In another study, wastewater 484 containing ACT was removed at the rate of 0.2 mg ACT/l within 25 min (Quiñones et al., 485 2015). Similar to the Fenton's process, the presence of a suitable (inert) catalyst also supports 486 ozonation and increases the ACT removal efficiency. According to a recent report, by applying 487 a modified MgO catalyst, the MgO/O₃ process showed ACT degradation and mineralization 488 efficiencies that were 18.8 and 7.8-fold higher than the sole ozonation process (Mashayekh-489

Salehi et al., 2017). Ozonation could also eliminate ACT entirely to the ppt level, but the operation cost of ozonation is comparable to the Fenton's process. The cost of a photo-based Fenton process is $1.56 \notin /m^3$, whereas the ozone-based process costs ~ 0.49-0.59 \notin /m^3 (Quiñones et al., 2015). Fenton process, when incorporated with modified TiO₂ based catalysts can increase the operational costs. In comparision, MgO is a relatively low-cost and environmentally friendly catalyst that has also been extensively used in the field of environmental engineering.

497 **4.4 Adsorption processes**

498 The efficiency of adsorption based processes can be governed by the physico-chemical properties of the adsorbent as well as the chemical reactions occurring at the surface of the 499 adsorbent. Typically, activated carbon is the most commonly used adsorbent that yields 500 relatively stable ACT removal efficiencies. Modified activated carbon based adsorbent 501 includes, chitosan-nano (Amouzgar et al., 2017), granular type (Yanyan et al., 2018) and 502 phosphoric acid modified (Wong et al., 2018) for ACT removal from wastewater. In practice, 503 the adsorption process is assisted with sonication, ozonation and constructed wetlands to 504 enhance the ACT removal efficiency. 505

Concerning the chitosan nano activated carbon, 94.7% of ACT, at a concentration of 0.2 mg/l 506 can be removed from the aqueous solution when its supported by a sonication step (Amouzgar 507 et al., 2017). Another modified activated carbon media is the granular form that is usually 508 derived from coconut shell (Yanyan et al., 2018). In both cases, the breakthrough capacities of 509 the media were reached within 26 - 48 h of operation, at a concentration of 40 - 120 mg ACT/l. 510 The activated carbon developed from spent tea leaves have also been tested for ACT treatment 511 and removal efficiencies > 99% at an initial concentration of 10 mg/l was reported (Wong et 512 al., 2018). In large scale systems, a WWTP when combined with a horizontal sub-surface flow 513 wetland removed > 98% ACT (Verlicchi et al., 2013). In that study, the influent and effluent 514

concentrations of ACT were 30 ± 20 and 16 ± 6 ng/l, respectively. In this combined removal 515 process, other removal pathways such as biodegradation, sedimentation and plant uptake are 516 also involved. In a recent study that was aimed at the removal of ACT from drinking water, 517 20% ACT was removed in a sand filter and a granular activated carbon (GAC) filter, 518 respectively (Lin et al., 2016c). For a conventional drinking water treatment plant, the average 519 ACT removal efficiency is usually > 96% (Boleda et al., 2011). Therefore, adsorption is a 520 promising and feasible treatment option that contributes to the good removal of ACT in major 521 drinking water treatment plants. 522

523 4.5 Membrane processes

Membrane separation process is an emerging technology for ACT removal from different water 524 environments. It is categorized based on the pore size of the membrane and the material of 525 construction. For the pore size, the nanofiltration and reverse osmosis membranes are effective 526 to retain the ACT molecules/particles, rather than the ultrafiltration and microfiltration 527 modules. The pore sizes of nanofiltration and reverse osmosis membranes are less than the size 528 of the ACT molecules. Regarding the fabricated materials, they can either natural or synthetic. 529 The natural material include wool, ceramics, rubber and cellulose. The synthetic membrane 530 include polyethylene amine, metal-organic frameworks (MOF), laccase and polydopamine, 531 polyvinylidene difluoride, hydroxyapatite, cellulose triacetate and polyamide composite. The 532 membrane process can be combined with biological treatment in a membrane bioreactor 533 (MBR). For ACT contaminated ground water, nanofiltration and RO membrane rejected 44.8 534 - 73% ACT (Radjenović et al., 2008). Similarly, hollow fiber MBR removed ACT at lower 535 efficiencies, i.e. < 20% (Nguyen et al., 2013). The single process of MF can remove 50 - 90% 536 of ACT from different water environments (Ba et al., 2014). However, if they are supported by 537 an integrated UV process, NF and RO can completely remove ACT from water. Therefore, a 538

stand-alone MBR or a microfiltration membrane process is not highly efficient for the treatmentof ACT at high concentrations.

Another improved membrane process is a novel enzyme coating on the surface of membranes to achieve high ACT removal efficiencies. For example, cross-linked enzyme aggregates of laccase were doped on a polysulfone hollow fiber MF membrane to remove ACT (> 99%) at concentrations < 0.1 mg/l (Ba et al., 2014).

545 **4.6 Hybrid processes**

The hybrid process (treatment train) incorporates different technologies such as a biological process, plant uptake, membrane filtration, adsorption and AOPs. In this combined process, the biological processes such as anaerobic/aerobic/oxic (A_2O) would be placed first (as a pretreatment step) to reduce the pollutant load, followed by either AOP, plant uptake, adsorption and membrane process.

As an example, at the Alcalá de Henares WWTP (Madrid, Spain), the A₂O process was coupled 551 with ozonation to eliminate ACT from wastewater (Rosal et al., 2010). For this case, the A₂O 552 process removed ACT to below detection limits, thus, ozonation was rarely used. Similarly, an 553 integrated system of anoxic/aerobic process and MFC was able to remove > 98% ACT at a 554 concentration of 30 mg/l (Chang et al., 2014). In another study, at the pilot scale, the integrated 555 process removed ~ 94 - 99.9% ACT at initial concentrations varying between 2.6 - 300 μ g/l 556 (Gallardo-Altamirano et al., 2018). According to the authors, long-term experiments confirmed 557 that the operating and environmental conditions of A₂O did not affect the ACT removal 558 efficiency. It is noteworthy to mention that, for the hybrid system, each technology contributes 559 differently during the ACT removal process. For example, A_2O contributes to ~ 77% of the 560 97% ACT removed during the entire process, whereas chlorine disinfection accounted for the 561 remaining 20% ACT removed (Kosma et al., 2010). In a case study involving five WWTPs 562 from Ulsan city (South Korea), the primary treatment process removed 28% of the total PPCPs, 563

including ACT, and the biological treatment process used in the WWTP was recognized as the

main process that ensured > 99% ACT removal in the WWTPs (Behera et al., 2011).

566 **4.7 Other processes**

Apart from the above mentioned and illustrated technologies, the non-conventional 567 technologies include ultrasonic treatment (Villaroel et al., 2014) and zero valent aluminum 568 (Zhang et al., 2012). Ultrasonic treatment could degrade ACT to inorganic compounds 569 competitively when compared to other technologies (Villaroel et al., 2014). For instance, ACT 570 was completely removed after 180 min at initial concentrations varying between 33 to 1323 571 572 µmol/l. In the case of zero valent aluminium technology, the commercial zero valent aluminum under air-equilibrated acidic conditions eliminated > 99% ACT, at a concentration of 2 mg/l 573 and a contact time of 16 h (Zhang et al., 2012). Although these processes are applicable for 574 ACT removal from contaminated water sources, full-scale applications of this process has 575 never been demonstrated due to cost and scale-up implications. 576

577 4.8 Comparison of technologies

In practice, all the technologies mentioned in this review could be a part of the WWTP train. 578 Their application would depend on the characteristics of the wastewater, initial ACT 579 concentration, local environmental conditions and the effluent discharge standards. Overall, 580 the biological process (aerobic/anaerobic) is suitable for secondary treatment and it can reduce 581 the ACT concentration from the ppm to ppb levels. The adsorption, AOP, membrane process 582 and plant uptake are rather meant specifically for tertiary treatment. These technologies can act 583 as a post-treatment or polishing step to reduce the ACT concentration from the ppb to ppt level. 584 When space is a constraint at the field-scale, membrane, AOP and adsorption technologies are 585 feasible options. However, in the case of membrane reactors, fouling is a major concern and it 586 also requires high operation and maintanence skills. In the case of AOP and adsorption, 587 chemical consumption and secondary pollution (e.g. due to metabolites) are the major concerns 588

that will add to the operating costs. In a spacious WWTP, CWs can be considered as adependable solution.

Most technologies remove ACT efficiently in the range of 80 - 100% (Fig. 2). However, plant 591 uptake and membrane process perform less with average removal efficiencies in the range of 592 \sim 60%. For example, at a ACT concentration of 1200 mg/l, an external airlift membrane 593 bioreactor (MBR) removed ACT better than an activated sludge process (Shariati et al., 2010). 594 Within 2 d of continuous operation, the external airlift MBR treated 100% ACT, while the 595 activated sludge was able to perform only with 50% efficiency. The mechanism of the MBR 596 597 system involves biodegradation, adsorption and filtration process, whereas biological activity was the sole mechanism governing the removal of ACT in the activated sludge process. 598

Nevertheless, high removal efficiency does not necessarily mean that ACT is removed 599 600 completely from the aqueous (water) phase because it can be degraded and transformed into other less toxic or more toxic metabolites. In brief, the following salient features were 601 recognized based on this review on ACT: (i) biological processes can deal with high 602 concentrations of ACT in wastewater (1200 mg/l), however, the biodegradation process 603 requires more time and ACT is not reduced to the ppt levels; (ii) AOPs can degrade ACT at 604 high degradation rates to the ppt levels, but they are rather expensive and might lead to the 605 formation of toxic intermediates, and (iii) other technologies such as plant uptake, adsorption 606 and membrane processes can be integrated with biological process to reduce ACT to the desired 607 608 ppt levels.

609

[Insert Fig. 2]

610 5. By-products transformation and degradation pathways

During wastewater treatment, ACT can be degraded/transformed to several metabolites. As
explained previously, some of these intermediates can be more detrimental to human health
and the ecological system than the parent ACT compound (Bedner and MacCrehan, 2006). By

applying the existing analytical technologies, some of these metabolites are not adequately detected in the influent wastewater and the treated effluent. Thus, identification of ACT intermediates and their metabolic pathways is essential to evaluate their potential impacts on human health, the environment and other aquatic life forms.

5.1 Mechanisms of acetaminophen transformation

ACT molecules consist of an aromatic phenol ring with an acetamido substitution at the paraposition (Fig. 3). These components are targets for the invasion of oxidizing agents such as
OH, CO₃- and ClO-, photon energy and ferrate (VI).

622

[Insert Fig. 3]

The most striking oxidative agent that helps in breaking the aromatic ring is 'OH. It would 623 invade the aromatic bonds first during the photo-Fenton process (Trovó et al., 2012). Similarly, 624 O₃ and/or 'OH agents can attack the aromatic ring through normal and ipso mechanisms, 625 following by a series of oxidation processes (Zhang et al. 2008; de Luna et al., 2012; Wang et 626 al., 2016a). These processes open the ring core and cleave the phenol-acetamido bond. Similar 627 to hydroxyl radicals, ClO⁻ and ferrate (VI) can also attack the benzene ring or the phenol-628 acetamido bonds (Bedner and MacCrehan, 2006; Wang et al., 2016a). This gives rise to a wide 629 range of ACT metabolites such as hydroquinone, 2-hydroxy-4-(N-acetyl)-aminophenol, or 630 dicarboxylic acids. These metabolites can exhibit both toxic and non-toxic characteristics 631 (Table 5). In addition, the phenol-acetamido and NH-CO amide bonds are also the targets of 632 the oxidative agents. The phenol-acetamido bond can be invaded by CO₃⁻, ClO⁻ and ferrate 633 (VI), while the ferrate (VI) and photon energy breaks down the NH-CO bond (Bedner and 634 MacCrehan, 2006; De Laurentiis et al., 2014; Chang et al., 2015; Wang et al., 2016a). 635 Thereafter, acetamide and/or acetamide derivatives are formed from the acetamido group of 636 ACT. 637

Unlike chemical treatment where oxidizing reagents are employed, bioenzymes are the driving 638 agents to degrade or transform ACT in biological treatment systems. For instance, 639 monooxygenases such as flavin-containing hydroxylases or cytochromes P-450 could degrade 640 ACT efficiencely in different water environments (Li et al., 2014). While the biodegradation 641 intermediates and/or end-products of ACT are somewhat similar to chemical degradation 642 processes, the mechanism involved in these two processes are entirely different. For example, 643 in a microbial fuel cell (MFC) - Fenton system, the acetamido moiety was the preferable target 644 of bioenzymes rather than the aromatic ring (Zhang et al., 2015). Firstly, the phenol-acetamido 645 646 bond was hydrolyzed by bio-electrons and protons to form p-aminophenol and acetic acid, respectively. Subsequently, *p*-aminophenol was oxidized by the 'OH radicals forming various 647 by-products (Zhang et al., 2015). 648

In brief, the exact intermediates and end-products of ACT formed largely depends on the degradation mechanism and the pathway. Therefore, one should consider what treatment system would be employed to predict the transformation pathways and intermediates of ACT. These information are essential to evaluate the suitability and sustainability of such systems in full-scale applications.

654 **5.2 Aromatic intermediates**

The first point of attack during ACT degradation often takes place on the aromatic ring or the acetamido moiety as discussed earlier. In this stage, ring cleavage does not occur and the byproducts are often of aromatic nature (Fig. 4). However, the exact intermediates formed depend only on the treatment (physical/chemical or biological) system used.

659

[Insert Fig. 4]

During the AOP processes, 1,4-benzoquinone, hydroquinone and amides were the main intermediates of ACT regardless of the applied technologies (Andreozzi et al., 2003; de Luna et al., 2012; Chang et al., 2015). However, other intermediates were also reported to be formed

in different technologies, especially alcoholic substances. For example, in a photocatalytic 663 treatment process, the major intermediates were hydroquinone, 1,4-benzoquinone, 1-(2-664 hydroxyphenyl-5-amino) ethanone and 1-(2-amino-5-hydroxyphenyl) ethanone (Chang et al., 665 2015). On the other hand, H₂O₂/UV systems generated 1-(2-amino-5-hydroxyphenyl) 666 ethanone, (N-(3,4-dihydroxyphenyl) acetamide, and 1-(2-amino-5-hydroxyphenyl) ethanone 667 (Andreozzi et al. 2003; Feng et al., 2015). Notably, the H₂O₂/UV system did not generate the 668 toxic compound N-acetyl-para-benzoquinone imine (NAPQI). Therefore, it is a recommended 669 technology to avoid the formation of NAPQI. In turn, hypochlorination disinfection should be 670 671 applied cautiously since at least 11 by-products of ACT were reported including two toxic compounds 1,4-benzoquinone and NAPQI (Bedner and MacCrehan, 2006). As reported in the 672 liteatures, these compounds are even more toxic than ACT. 673

On the other hand, when the MBR technology was applied, sulfate-related intermediates of ACT were identified: acetaminophen-O-sulphate ($C_8H_9O_5NS$), acetaminophen-glutathione ($C_{18}H_{24}O_8N_4S$), and transformation product ($C_{12}H_{10}O_2N$) of acetaminophen-glutathione (Tambosi et al., 2010). These compounds are popular intermediates in WWTPs and also formed from human detoxification and excretion processes. In contrast, De Gusseme et al. (2011) reported that hydroquinone was the only by-product of ACT degradation in a membrane reactor.

In soil environments, microorganisms play a critical role as a biocatalyst for ACT mineralization. Li et al. (2014) detected 8 aromatic intermediates of ACT in soil such as 3hydroxyacetaminophen, hydroquinone and 1,4-benzoquinone, respectively. Similar mechanism can also potentially occur in ACT contaminated sludge of WWTPs. Interestingly, in both environments, hydroquinone and 1,4-benzoquinone are the most commonly detected intermediates.

687 5.3 Ring-opening and inorganic intermediates

During the first step of the degradation stage, oxidative agents attack the different functional 688 groups and bonds of the ACT molecule including the hydroxyl group, acetamido group and the 689 phenolic ring. For example, 'OH in a bio-electrochemical system oxidizes the hydroxyl group 690 of the phenol ring creating intermediates such as maleic, malonic, malic and lactic acid, 691 respectively (Zhang et al., 2015). Organic carboxylic acids were also observed to be 692 intermediates of the ACT degradation process by other researchers (Andreozzi et al., 2003; de 693 Luna et al., 2012; de Luna et al., 2013). In a fluidized-bed reactor employing the Fenton's 694 695 process, NH₄⁺, formic acid and 1,2-pentanediol were identified as the main ACT degradation products (de Luna et al., 2013). Similarly, ferrate (VI) reacts with the acetamido group and the 696 aromatic intermediates of ACT to form NO3⁻, maleic acid, oxalic acid and formic acid, 697 respectively (Wang et al., 2016a). Following the oxidation of ACT to organic acids, CO₂ was 698 ascertained as a final mineralized product (Zhang et al., 2012). Thus, briefly stating, ring-699 opening of ACT and ACT by-products will eventually lead to the formation of different types 700 of organic acids. Further oxidation of these acids, acetamide, and acetamide derivatives would 701 only result in complete mineralization of ACT into NH₄⁺, NO₃⁻, and CO₂, respectively. 702

703 **5.4 Polymeric intermediates**

Polymeric intermediates are usually prevalent and noticed in soil environments (Liang et al., 704 2016). ACT molecules can interact with each other at either the ortho, para, or amide bonding 705 706 positions giving rise to numerous dimer and trimer intermediates. For example, nine dimer and trimer intermediates of ACT were discovered in soil (Li et al., 2014). Importantly, a low pH 707 and warm environmental condition will accelerate the ACT polymerization reaction (Xiao et 708 709 al., 2013). The degradation process would be largely dependent on the soil types, activity of the microorganism, enzymes secreted during the biodegradation processes, pH, moisture 710 content of soil, soil porosity, oxygen availability, and the initial ACT concentration. 711

Recently, more than 20 intermediates formed during the ACT removal process was reported in 712 the literature. Compounds such as 4-benzoquinone and NAPQI are more toxic than ACT, while 713 some compounds such as NH_4^+ , CO_2 , and NO_3^- are rather less toxic. As observed from the 714 review, the dimer and trimer by-products were also detected, particularly in the soil 715 environment. According to the information presented in Table 5, AOP was the only technology 716 that is capable of degrading ACT to innocuous inorganic end-products. Thus, AOP can be 717 recommended to be applied in WWTPs as a tertiary treatment step. The salient remarks on 718 ACT transformation products and metabolites in environments can be stated as follows: (i) the 719 oxidative agents capable of removing ACT include 'OH, O₃ ClO', photon energy and 720 bioenzymes; (ii) the oxidative agents attack and cleave the aromatic ring and acetamido moiety 721 of ACT to form more than 20 aromatic and inorganic intermediates; and (iii) polymeric 722 intermediates are only formed in soil environments. 723

724

726

6. Conclusions 725

Historically, ACT pollution has occurred in many countries, at various concentrations and

[Insert Table 5]

detection frequencies and ACT concentration in wastewater has increased significantly since 727 the year of 1998. China and the USA are the two countries with concerned ACT levels and 728 detection frequencies in wastewater. However, ACT concentration in drinking water has 729 decreased significantly from ppb to ppt levels due to advancements in wastewater treatment 730 systems. Concerning the implementation of policies, European countries and the United States 731 have developed different management policies and legislations/standards for the discharge of 732 micropollutants and their prevention, while the legislation are rather not stringent in most of 733 the Asian countries due to lack of reliable historic data. In addition, to ensure ACT free drinking 734 water source, the application of advanced and hybrid technologies is urgently required at the 735 field scale because ACT can transform to more than 20 different intermediates and end-736

737	prod	ucts. Anew, ensuring ACT levels less than 71 ng/l in drinking water is still a challenging							
738	task as it will require extensive investment costs, technical and management expertise.								
739	Ack	nowledgements							
740	The	authors would thank IHE-Delft (The Netherlands) for providing staff time support to							
741	colla	borate with researchers from Vietnam under the project "Support to Society". Also, the							
742	auth	or would like to thank Ms. Khanh-Dieu Hoang for her support in data collection.							
743	Refe	erences							
744	1.	Alvarino, T., Katsou, E., Malamis, S., Suarez, S., Omil, F., Fatone, F., 2014. Inhibition							
745		of biomass activity in the via nitrite nitrogen removal processes by veterinary							
746		pharmaceuticals. Bioresource Technology, 152, 477-483.							
747	2.	Amouzgar, P., Chan, ES., Salamatinia, B., 2017. Effects of ultrasound on development							
748		of Cs/NAC nano composite beads through extrusion dripping for acetaminophen removal							
749		from aqueous solution. Journal of Cleaner Production, 165, 537-551.							
750	3.	Andreozzi, R., Caprio, V., Marotta, R., Vogna, D., 2003. Paracetamol oxidation from							
751		aqueous solutions by means of ozonation and H_2O_2/UV system. Water Research, 37(5),							
752		993-1004.							
753	4.	Arredondo Valdez, H.C., García Jiménez, G., Gutiérrez Granados, S., Ponce de León, C.,							
754		2012. Degradation of paracetamol by advance oxidation processes using modified							
755		reticulated vitreous carbon electrodes with TiO ₂ and CuO/TiO ₂ /Al ₂ O ₃ . Chemosphere,							
756		89(10), 1195-1201.							
757	5.	Ba, S., Jones, J.P., Cabana, H., 2014. Hybrid bioreactor (HBR) of hollow fiber microfilter							
758		membrane and cross-linked laccase aggregates eliminate aromatic pharmaceuticals in							

wastewaters. Journal of Hazardous materials, 280, 662-670.

760	6.	Baron, P.A., Love, D.C., Nachman, K.E., 2014. Pharmaceuticals and personal care
761		products in chicken meat and other food animal products: A market-basket pilot study.
762		Science of the Total Environment, 490, 296-300.

- 763 7. Bartha, B., Huber, C., Harpaintner, R., Schröder, P., 2010. Effects of acetaminophen in *Brassica juncea* L. Czern.: investigation of uptake, translocation, detoxification, and the
 induced defense pathways. Environmental Science and Pollution Research, 17(9), 15531562.
- 8. Basavaraju, M., Mahamood, S., Vittal, H., Shrihari, S., 2011. A novel catalytic route to
 degrade paracetamol by Fenton process. International Journal of Research in Chemistry
 and Environment, 1(1), 157-164.
- 9. Bedner, M., MacCrehan, W.A., 2006. Transformation of Acetaminophen by Chlorination
 Produces the Toxicants 1,4-Benzoquinone and N-Acetyl-p-benzoquinone Imine.
 Environmental Science & Technology, 40(2), 516-522.
- Behera, S.K., Kim, H.W., Oh, J.-E., Park, H.-S., 2011. Occurrence and removal of
 antibiotics, hormones and several other pharmaceuticals in wastewater treatment plants
 of the largest industrial city of Korea. Science of the Total Environment, 409(20), 43514360.
- Blair, B.D., Crago, J.P., Hedman, C.J., Klaper, R.D., 2013a. Pharmaceuticals and
 personal care products found in the Great Lakes above concentrations of environmental
 concern. Chemosphere, 93(9), 2116-2123.
- Blair, B.D., Crago, J.P., Hedman, C.J., Treguer, R.J.F., Magruder, C., Royer, L.S.,
 Klaper, R.D., 2013. Evaluation of a model for the removal of pharmaceuticals, personal
 care products, and hormones from wastewater. Science of the Total Environment, 444,
 515-521.

784	13.	Boleda, M.R., Galceran, M.T., Ventura, F., 2011. Behavior of pharmaceutics	als and drugs
785		of abuse in a drinking water treatment plant (DWTP) using combined conv	rentional and
786		ultrafiltration and reverse osmosis (UF/RO) treatments. Environmental Pollu	tion, 159(6),
787		1584-1591.	

- Botero-Coy, A., Martínez-Pachón, D., Boix, C., Rincón, R., Castillo, N., Arias-Marín,
 L., Manrique-Losada, L., Torres-Palma, R., Moncayo-Lasso, A., Hernández,
 F.J.S.o.T.T.E., 2018. An investigation into the occurrence and removal of
 pharmaceuticals in Colombian wastewater. 642, 842-853.
- Boyd, G.R., Reemtsma, H., Grimm, D.A., Mitra, S., 2003. Pharmaceuticals and personal
 care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario,
 Canada. Science of the Total Environment, 311(1), 135-149.
- Cantwell, M.G., Katz, D.R., Sullivan, J.C., Shapley, D., Lipscomb, J., Epstein, J., Juhl,
 A.R., Knudson, C., O'Mullan, G.D., 2018. Spatial patterns of pharmaceuticals and
 wastewater tracers in the Hudson River Estuary. Water Research, 137, 335-343.
- Chang, C.-T., Wang, J.-J., Ouyang, T., Zhang, Q., Jing, Y.-H., 2015. Photocatalytic
 degradation of acetaminophen in aqueous solutions by TiO₂/ZSM-5 zeolite with low
 energy irradiation. Materials Science and Engineering: B, 196, 53-60.
- 18. Chang, Y.-T., Yang, C.-W., Chang, Y.-J., Chang, T.-C., Wei, D.-J., 2014. The Treatment
 of PPCP-Containing Sewage in an Anoxic/Aerobic Reactor Coupled with a Novel
 Design of Solid Plain Graphite-Plates Microbial Fuel Cell. BioMed Research
 International, 2014, 13.
- 19. Choi, K., Kim, Y., Park, J., Park, C.K., Kim, M., Kim, H.S., Kim, P., 2008. Seasonal
 variations of several pharmaceutical residues in surface water and sewage treatment
 plants of Han River, Korea. Science of the Total Environment, 405(1–3), 120-128.

808	20. Choi, M., Furlong, E.T., Werner, S.L., Pait, A.S., Lee, IS., Choi, HG., 2014.
809	Cimetidine, acetaminophen, and 1,7-dimethylxanthine, as indicators of wastewater
810	pollution in marine sediments from Masan Bay, Korea. Ocean Science Journal, 49(3),
811	231-240.

- Conley, J.M., Symes, S.J., Schorr, M.S., Richards, S.M., 2008. Spatial and temporal
 analysis of pharmaceutical concentrations in the upper Tennessee River basin.
 Chemosphere, 73(8), 1178-1187.
- 22. Daniel, C.-Y.W., Wan-Loy, C., Yih-Yih, K., 2015. Assessment of Paracetamol
 (Acetaminophen) Toxicity in Microalgae. Polish Journal of Environmental Studies 24(2),
 735-741.
- 23. De Gusseme, B., Vanhaecke, L., Verstraete, W., Boon, N., 2011. Degradation of
 acetaminophen by *Delftia tsuruhatensis* and *Pseudomonas aeruginosa* in a membrane
 bioreactor. Water Research, 45(4), 1829-1837.
- 24. De Laurentiis, E., Prasse, C., Ternes, T.A., Minella, M., Maurino, V., Minero, C.,
 Sarakha, M., Brigante, M., Vione, D., 2014. Assessing the photochemical transformation
 pathways of acetaminophen relevant to surface waters: Transformation kinetics,
 intermediates, and modelling. Water Research, 53, 235-248.
- 825 25. de Luna, M.D.G., Briones, R.M., Su, C.-C., Lu, M.-C., 2013. Kinetics of acetaminophen
 826 degradation by Fenton oxidation in a fluidized-bed reactor. Chemosphere, 90(4), 1444827 1448.
- de Luna, M.D.G., Veciana, M.L., Su, C.-C., Lu, M.-C., 2012. Acetaminophen
 degradation by electro-Fenton and photoelectro-Fenton using a double cathode
 electrochemical cell. Journal of Hazardous Materials, 217–218, 200-207.

- 27. Del Río, H., Suárez, J., Puertas, J., Ures, P., 2013. PPCPs wet weather mobilization in a
 combined sewer in NW Spain. Science of the Total Environment, 449, 189-198.
- 833 28. Feng, S., Zhang, X., Liu, Y., 2015. New insights into the primary phototransformation
- of acetaminophen by UV/H_2O_2 : photo-Fries rearrangement versus hydroxyl radical induced hydroxylation. Water Research, 86, 35-45.
- Ferguson, P.J., Bernot, M.J., Doll, J.C., Lauer, T.E., 2013. Detection of pharmaceuticals
 and personal care products (PPCPs) in near-shore habitats of southern Lake Michigan.
 Science of the Total Environment, 458–460, 187-196.
- 839 30. Fisher, E.S., Curry, S.C. 2019. Evaluation and Treatment of Acetaminophen Toxicity.
 840 in: *Adv. Pharmacol.*, Academic Press.
- 841 31. Fram, M.S., Belitz, K., 2011. Occurrence and concentrations of pharmaceutical
 842 compounds in groundwater used for public drinking-water supply in California. Science
 843 of the Total Environment, 409(18), 3409-3417.
- 32. Gallardo-Altamirano, M.J., Maza-Márquez, P., Peña-Herrera, J.M., Rodelas, B., Osorio,
- F., Pozo, C., 2018. Removal of anti-inflammatory/analgesic pharmaceuticals from urban
 wastewater in a pilot-scale A2O system: Linking performance and microbial population
- dynamics to operating variables. Science of The Total Environment, 643, 1481-1492.
- 33. Gao, J., O'Brien, J., Du, P., Li, X., Ort, C., Mueller, J.F., Thai, P.K., 2016. Measuring
 selected PPCPs in wastewater to estimate the population in different cities in China.
 Science of the Total Environment, 568, 164-170.
- 34. Gros, M., Petrović, M., Ginebreda, A., Barceló, D., 2010. Removal of pharmaceuticals
 during wastewater treatment and environmental risk assessment using hazard indexes.
 Environment International, 36(1), 15-26.

- 35. Grujić, S., Vasiljević, T., Laušević, M., 2009. Determination of multiple pharmaceutical
 classes in surface and ground waters by liquid chromatography–ion trap–tandem mass
 spectrometry. Journal of Chromatography A, 1216(25), 4989-5000.
- 36. He, K., Echigo, S., Itoh, S., 2016. Effect of operating conditions in soil aquifer treatment
 on the removals of pharmaceuticals and personal care products. Science of the Total
 Environment, 565, 672-681.
- 860 37. He, Y., Dong, Y., Huang, W., Tang, X., Liu, H., Lin, H., Li, H., 2015. Investigation of
 861 boron-doped diamond on porous Ti for electrochemical oxidation of acetaminophen
 862 pharmaceutical drug. Journal of Electroanalytical Chemistry, 759, Part 2, 167-173.
- 38. Hedgespeth, M.L., Sapozhnikova, Y., Pennington, P., Clum, A., Fairey, A., Wirth, E.,
 2012. Pharmaceuticals and personal care products (PPCPs) in treated wastewater
 discharges into Charleston Harbor, South Carolina. Science of the Total Environment,
 437, 1-9.
- 39. Henschel, K.P., Wenzel, A., Diedrich, M., Fliedner, A., 1997. Environmental Hazard
 Assessment of Pharmaceuticals. Regulatory Toxicology and Pharmacology, 25(3), 220225.
- 40. Huber, C., Bartha, B., Harpaintner, R., Schröder, P., 2009. Metabolism of acetaminophen
 (paracetamol) in plants—two independent pathways result in the formation of a
 glutathione and a glucose conjugate. Environmental Science and Pollution Research,
 16(2), 206-213.
- 41. Im, J.-K., Yoon, J., Her, N., Han, J., Zoh, K.-D., Yoon, Y., 2015. Sonocatalytic-TiO₂
 nanotube, Fenton, and CCl4 reactions for enhanced oxidation, and their applications to
 acetaminophen and naproxen degradation. Separation and Purification Technology, 141,
 1-9.

- Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2008. The occurrence of
 pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface
 water in South Wales, UK. Water Research, 42(13), 3498-3518.
- 43. Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 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(2), 363-380.
- Kim, I., Tanaka, H., 2009. Photodegradation characteristics of PPCPs in water with UV
 treatment. Environment International, 35(5), 793-802.
- Kim, J.W., Yoon, S.M., Lee, S.J., Narumiya, M., Nakada, N., Han, I.S., Tanaka, H. 2012.
 Occurrence and Fate of PPCPs Wastewater Treatment Plants in Korea. in: *2nd International Conference on Environment and Industrial Innovation*, Vol. 35, IACSIT
 Press, Singapore.
- 46. Kim, S.D., Cho, J., Kim, I.S., Vanderford, B.J., Snyder, S.A., 2007a. Occurrence and
 removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking,
 and waste waters. Water Research, 41(5), 1013-1021.
- Kim, Y., Choi, K., Jung, J., Park, S., Kim, P.-G., Park, J., 2007b. Aquatic toxicity of
 acetaminophen, carbamazepine, cimetidine, diltiazem and six major sulfonamides, and
 their potential ecological risks in Korea. Environment International, 33(3), 370-375.
- Kolpin, D.W., Furlong, E.T., Meyer, M.T., Thurman, E.M., Zaugg, S.D., Barber, L.B.,
 Buxton, H.T., 2002. Pharmaceuticals, Hormones, and Other Organic Wastewater
 Contaminants in U.S. Streams, 1999–2000: A National Reconnaissance. Environmental
 Science & Technology, 36(6), 1202-1211.

- 49. Kosma, C.I., Lambropoulou, D.A., Albanis, T.A., 2010. Occurrence and removal of
 PPCPs in municipal and hospital wastewaters in Greece. Journal of Hazardous materials,
 179(1–3), 804-817.
- 50. Kosma, C.I., Lambropoulou, D.A., Albanis, T.A., 2014. Investigation of PPCPs in
 wastewater treatment plants in Greece: Occurrence, removal and environmental risk
 assessment. Science of the Total Environment, 466–467, 421-438.
- 51. Kurniawan, T.A., Yanyan, L., Ouyang, T., Albadarin, A.B., Walker, G., 2018.
 BaTiO₃/TiO₂ composite-assisted photocatalytic degradation for removal of
 acetaminophen from synthetic wastewater under UV–vis irradiation. Materials Science
 in Semiconductor Processing, 73, 42-50.
- 52. Lapworth, D.J., Baran, N., Stuart, M.E., Ward, R.S., 2012. Emerging organic
 contaminants in groundwater: A review of sources, fate and occurrence. Environmental
 Pollution, 163, 287-303.
- 53. Li, J., Ye, Q., Gan, J., 2014. Degradation and transformation products of acetaminophen
 in soil. Water Research, 49, 44-52.
- 54. Liang, C., Lan, Z., Zhang, X., Liu, Y., 2016. Mechanism for the primary transformation
 of acetaminophen in a soil/water system. Water Research, 98, 215-224.
- 55. Lin, A.Y.-C., Tsai, Y.-T., 2009. Occurrence of pharmaceuticals in Taiwan's surface
 waters: Impact of waste streams from hospitals and pharmaceutical production facilities.
 Science of the Total Environment, 407(12), 3793-3802.
- 56. Lin, C.J., Yang, W.-T., Chou, C.-Y., Liou, S.Y.H., 2016a. Hollow mesoporous TiO₂
 microspheres for enhanced photocatalytic degradation of acetaminophen in water.
 Chemosphere, 152, 490-495.

924	7. Lin, J.CT., de Luna, M.D.G., Aranzamendez, G.L., Lu, MC., 2016b. Degrad	lations of
925	acetaminophen via a $K_2S_2O_8$ -doped TiO ₂ photocatalyst under visible light ir	radiation.
926	Chemosphere, 155, 388-394.	

- 58. Lin, T., Yu, S., Chen, W., 2016c. Occurrence, removal and risk assessment of
 pharmaceutical and personal care products (PPCPs) in an advanced drinking water
 treatment plant (ADWTP) around Taihu Lake in China. Chemosphere, 152, 1-9.
- 59. Lutpi, N.A.A., Yuzir, M.A.M., Yong, E.L., Salim, M.R., Yusop, Z., Salmiati, 2015. The
 effect of water quality on removal of acetaminophen in surface water by ozonation
 process. Jurnal Teknologi, 74(11), 1-7.
- 60. Lv, M., Sun, Q., Hu, A., Hou, L., Li, J., Cai, X., Yu, C.-P., 2014. Pharmaceuticals and
 personal care products in a mesoscale subtropical watershed and their application as
 sewage markers. Journal of Hazardous materials, 280, 696-705.
- Manu, B. and Mahamood, 2011. Degradation of paracetamol in aqueous solution by
 Fenton Oxidation and photo-Fenton Oxidation processes using iron from Laterite soil as
 catalyst. International Journal of Earth Sciences and Engineering, 4(6), 1103-1110.
- 939 62. Mashayekh-Salehi, A., Moussavi, G., Yaghmaeian, K., 2017. Preparation,
 940 characterization and catalytic activity of a novel mesoporous nanocrystalline MgO
 941 nanoparticle for ozonation of acetaminophen as an emerging water contaminant.
 942 Chemical Engineering Journal, 310, 157-169.
- 63. Matamoros, V., Gutiérrez, R., Ferrer, I., García, J., Bayona, J.M., 2015. Capability of
 microalgae-based wastewater treatment systems to remove emerging organic
 contaminants: A pilot-scale study. Journal of Hazardous materials, 288, 34-42.

- 64. Narumiya, M., Nakada, N., Yamashita, N., Tanaka, H., 2013. Phase distribution and
 removal of pharmaceuticals and personal care products during anaerobic sludge
 digestion. Journal of Hazardous materials, 260, 305-312.
- 65. Nguyen, L.N., Hai, F.I., Kang, J., Price, W.E., Nghiem, L.D., 2013. Removal of emerging
 trace organic contaminants by MBR-based hybrid treatment processes. International
 Biodeterioration & Biodegradation, 85, 474-482.
- 952 66. Nunes, B., Pinto, G., Martins, L., Goncalves, F., Antunes, S.C., 2014. Biochemical and
 953 standard toxic effects of acetaminophen on the macrophyte species Lemna minor and
 954 Lemna gibba. Environ Sci Pollut Res Int, 21(18), 10815-22.
- 955 67. Oliveira, T.S., Murphy, M., Mendola, N., Wong, V., Carlson, D., Waring, L., 2015.
 956 Characterization of Pharmaceuticals and Personal Care products in hospital effluent and
 957 waste water influent/effluent by direct-injection LC-MS-MS. Science of the Total
 958 Environment, 518-519, 459-478.
- 68. Ortiz de García, S., Pinto Pinto, G., García Encina, P., Irusta Mata, R., 2013.
 Consumption and occurrence of pharmaceutical and personal care products in the aquatic
 environment in Spain. Science of the Total Environment, 444, 451-465.
- 962 69. Papageorgiou, M., Kosma, C., Lambropoulou, D., 2016. Seasonal occurrence, removal,
 963 mass loading and environmental risk assessment of 55 pharmaceuticals and personal care
 964 products in a municipal wastewater treatment plant in Central Greece. Science of the
 965 Total Environment, 543, 547-569.
- 966 70. Pedrouzo, M., Reverte, S., Borrull, F., Pocurull, E., Marce, R.M., 2007. Pharmaceutical
 967 determination in surface and wastewaters using high-performance liquid
 968 chromatography-(electrospray)-mass spectrometry. Journal of Separation Science, 30(3),
 969 297-303.

- 970 71. Phong, V.H.N., Koottatep, T., Chapagain, S.K., Panuvatvanich, A., Polprasert, C., Ahn,
- 971 K.-H., 2016. Removal of acetaminophen from wastewater by constructed wetlands with

972 *Scirpus validus*. Environmental Engineering Research, 21(2), 164-170.

- 973 72. Quiñones, D.H., Álvarez, P.M., Rey, A., Beltrán, F.J., 2015. Removal of emerging
 974 contaminants from municipal WWTP secondary effluents by solar photocatalytic
 975 ozonation. A pilot-scale study. Separation and Purification Technology, 149, 132-139.
- 976 73. Rabiet, M., Togola, A., Brissaud, F., Seidel, J.L., Budzinski, H., Elbaz-Poulichet, F.,
- 977 2006. Consequences of treated water recycling as regards pharmaceuticals and drugs in978 surface and ground waters of a medium-sized Mediterranean catchment. Environmental
- 979 Science and Technology, 40(17), 5282-8.
- 74. Radjenović, J., Petrović, M., Ventura, F., Barceló, D., 2008. Rejection of
 pharmaceuticals in nanofiltration and reverse osmosis membrane drinking water
 treatment. Water Research, 42(14), 3601-3610.
- 75. Ranieri, E., Verlicchi, P., Young, T.M., 2011. Paracetamol removal in subsurface flow
 constructed wetlands. Journal of Hydrology, 404(3–4), 130-135.
- 76. Roberts, P.H., Thomas, K.V., 2006. The occurrence of selected pharmaceuticals in
 wastewater effluent and surface waters of the lower Tyne catchment. Science of the Total
 Environment, 356(1–3), 143-153.
- 77. Rosal, R., Rodríguez, A., Perdigón-Melón, J.A., Petre, A., García-Calvo, E., Gómez,
 M.J., Agüera, A., Fernández-Alba, A.R., 2010. Occurrence of emerging pollutants in
 urban wastewater and their removal through biological treatment followed by ozonation.
 Water Research, 44(2), 578-588.

- 992 78. Shariati, F.P., Mehrnia, M.R., Salmasi, B.M., Heran, M., Wisniewski, C., Sarrafzadeh,
- 993 M.H., 2010. Membrane bioreactor for treatment of pharmaceutical wastewater 994 containing acetaminophen. Desalination, 250(2), 798-800.
- 995 79. Sim, W.-J., Lee, J.-W., Oh, J.-E., 2010. Occurrence and fate of pharmaceuticals in
 996 wastewater treatment plants and rivers in Korea. Environmental Pollution, 158(5), 1938997 1947.
- 80. Su, C.-C., Bellotindos, L.M., Chang, A.-T., Lu, M.-C., 2013a. Degradation of
 acetaminophen in an aerated Fenton reactor. Journal of the Taiwan Institute of Chemical
 Engineers, 44(2), 310-316.
- 1001 81. Su, C.-C., Cada Jr, C.A., Dalida, M.L.P., Lu, M.-C., 2013b. Effect of UV light on
 1002 acetaminophen degradation in the electro-Fenton process. Separation and Purification
 1003 Technology, 120, 43-51.
- 1004 82. Su, C.-C., Chang, A.-T., Bellotindos, L.M., Lu, M.-C., 2012. Degradation of
 1005 acetaminophen by Fenton and electro-Fenton processes in aerator reactor. Separation and
 1006 Purification Technology, 99, 8-13.
- Sun, Q., Li, M., Ma, C., Chen, X., Xie, X., Yu, C.-P., 2016a. Seasonal and spatial
 variations of PPCP occurrence, removal and mass loading in three wastewater treatment
 plants located in different urbanization areas in Xiamen, China. Environmental Pollution,
 208, Part B, 371-381.
- 1011 84. Sun, Q., Li, Y., Li, M., Ashfaq, M., Lv, M., Wang, H., Hu, A., Yu, C.-P., 2016b. PPCPs
 1012 in Jiulong River estuary (China): Spatiotemporal distributions, fate, and their use as
 1013 chemical markers of wastewater. Chemosphere, 150, 596-604.

- 1014 85. Tambosi, J.L., de Sena, R.F., Favier, M., Gebhardt, W., José, H.J., Schröder, H.F.,
- 1015 Moreira, R.d.F.P.M., 2010. Removal of pharmaceutical compounds in membrane
- 1016 bioreactors (MBR) applying submerged membranes. Desalination, 261(1–2), 148-156.
- 1017 86. Ternes, T.A., 1998. Occurrence of drugs in German sewage treatment plants and rivers.
 1018 Water Research, 32(11), 3245-3260.
- 1019 87. Trang, V.N., Dan, N.P., Phuong, L.D., Thanh, B.X., 2014. Pilot study on the removal of
- TOC, THMs and HAAs in drinking water using ozone/UV BAC, Desalination and
 Water Treatment, 52(4-6), 990-998.
- 1022 88. Trovó, A.G., Pupo Nogueira, R.F., Agüera, A., Fernandez-Alba, A.R., Malato, S., 2012.
- Paracetamol degradation intermediates and toxicity during photo-Fenton treatment using
 different iron species. Water Research, 46(16), 5374-5380.
- 1025 89. Vazquez-Roig, P., Andreu, V., Blasco, C., Picó, Y., 2012. Risk assessment on the
 1026 presence of pharmaceuticals in sediments, soils and waters of the Pego–Oliva
 1027 Marshlands (Valencia, eastern Spain). Science of the Total Environment, 440, 24-32.
- 1028 90. Verlicchi, P., Galletti, A., Petrovic, M., Barceló, D., Al Aukidy, M., Zambello, E., 2013.
- 1029 Removal of selected pharmaceuticals from domestic wastewater in an activated sludge

system followed by a horizontal subsurface flow bed — Analysis of their respective

1031 contributions. Science of the Total Environment, 454–455, 411-425.

- 1032 91. Villaroel, E., Silva-Agredo, J., Petrier, C., Taborda, G., Torres-Palma, R.A., 2014.
 1033 Ultrasonic degradation of acetaminophen in water: Effect of sonochemical parameters
 1034 and water matrix. Ultrasonics Sonochemistry, 21(5), 1763-1769.
- 1035 92. Vo, T.D.H., Bui, X.T., Nguyen, D.D., Nguyen, V.T., Ngo, H.H., Guo, W., Nguyen, P.D.,
- 1036 Nguyen, C.N., Lin, C., 2018. Wastewater treatment and biomass growth of eight plants
- 1037 for shallow bed wetland roofs, Bioresource Technology, 247, 992-998.

- 1038 93. Vo, T.K.Q., Bui, X.T., Chen, S.S., Nguyen, P.D., Cao, N.D.T., Vo, T.D.H., Nguyen,
- 1039 T.T., Nguyen, T.B., 2019. Hospital wastewater treatment by sponge membrane 1040 bioreactor coupled with ozonation, Chemosphere, 230, 377-383.
- 1041 94. Vulliet, E., Cren-Olivé, C., 2011. Screening of pharmaceuticals and hormones at the
 1042 regional scale, in surface and groundwaters intended to human consumption.
 1043 Environmental Pollution, 159(10), 2929-2934.
- Wang, H., Liu, Y., Jiang, J.-Q., 2016a. Reaction kinetics and oxidation product formation
 in the degradation of acetaminophen by ferrate (VI). Chemosphere, 155, 583-590.
- Wang, X., Bi, W., Zhai, P., Wang, X., Li, H., Mailhot, G., Dong, W., 2016b. Adsorption
 and photocatalytic degradation of pharmaceuticals by BiOCl_xI_y nanospheres in aqueous
 solution. Applied Surface Science, 360, Part A, 240-251.
- 1049 97. Wong, S., Lim, Y., Ngadi, N., Mat, R., Hassan, O., Inuwa, I.M., Mohamed, N.B., Low,
- J.H., 2018. Removal of acetaminophen by activated carbon synthesized from spent tea
 leaves: equilibrium, kinetics and thermodynamics studies. Powder Technology, 338,
 878-886.
- 1053 98. Wu, C., Huang, X., Witter, J.D., Spongberg, A.L., Wang, K., Wang, D., Liu, J., 2014.
 1054 Occurrence of pharmaceuticals and personal care products and associated environmental
 1055 risks in the central and lower Yangtze river, China. Ecotoxicology and Environmental
 1056 Safety, 106, 19-26.
- 1057 99. Wu, X., Ernst, F., Conkle, J.L., Gan, J., 2013. Comparative uptake and translocation of
 1058 pharmaceutical and personal care products (PPCPs) by common vegetables.
 1059 Environment International, 60, 15-22.

- 1060 100. Xiao, H., Song, H., Xie, H., Huang, W., Tan, J., Wu, J., 2013. Transformation of
- 1061 acetaminophen using manganese dioxide mediated oxidative processes: Reaction rates

and pathways. Journal of Hazardous materials, 250–251, 138-146.

- 1063 101. Xie, G., Chang, X., Adhikari, B.R., Thind, S.S., Chen, A., 2016. Photoelectrochemical
- degradation of acetaminophen and valacyclovir using nanoporous titanium dioxide.Chinese Journal of Catalysis, 37(7), 1062-1069.
- 1066 102. Xiong, P., Hu, J., 2012. Degradation of acetaminophen by UVA/LED/TiO₂ process.
 1067 Separation and Purification Technology, 91, 89-95.
- 103. Xiong, P., Hu, J., 2017. Decomposition of acetaminophen (Ace) using TiO₂/UVA/LED
 system. Catalyst Today, 282, 48-56.
- 1070 104. Yang, G.C.C., Huang, S.-C., Wang, C.-L., Jen, Y.-S., 2016. Degradation of phthalate
 1071 esters and acetaminophen in river sediments using the electrokinetic process integrated
 1072 with a novel Fenton-like process catalyzed by nanoscale schwertmannite. Chemosphere,
 1073 159, 282-292.
- 1074 105. Yang, L., Yu, L.E., Ray, M.B., 2008. Degradation of paracetamol in aqueous solutions
 1075 by TiO₂ photocatalysis. Water Research, 42(13), 3480-3488.
- 106. Yanyan, L., Kurniawan, T.A., Ying, Z., Albadarin, A.B., Walker, G., 2017. Enhanced
 photocatalytic degradation of acetaminophen from wastewater using WO₃/TiO₂/SiO₂
 composite under UV–VIS irradiation. Journal of Molecular Liquids, 243, 761-770.
- 1079 107. Yanyan, L., Kurniawan, T.A., Zhu, M., Ouyang, T., Avtar, R., Dzarfan Othman, M.H.,
 1080 Mohammad, B.T., Albadarin, A.B., 2018. Removal of acetaminophen from synthetic
 1081 wastewater in a fixed-bed column adsorption using low-cost coconut shell waste
 1082 pretreated with NaOH, HNO₃, ozone, and/or chitosan. Journal of Environmental
 1083 Management, 226, 365-376.

- 1084 108. You, L., Nguyen, V.T., Pal, A., Chen, H., He, Y., Reinhard, M., Gin, K.Y.-H., 2015.
- Investigation of pharmaceuticals, personal care products and endocrine disrupting
 chemicals in a tropical urban catchment and the influence of environmental factors.
 Science of the Total Environment, 536, 955-963.
- 1088 109. Yu, J.T., Bouwer, E.J., Coelhan, M., 2006. Occurrence and biodegradability studies of
 selected pharmaceuticals and personal care products in sewage effluent. Agricultural
 Water Management, 86(1–2), 72-80.
- 1091 110. Yu, T.-H., Lin, A.Y.-C., Panchangam, S.C., Hong, P.-K.A., Yang, P.-Y., Lin, C.-F.,
- 2011. Biodegradation and bio-sorption of antibiotics and non-steroidal anti-inflammatory
 drugs using immobilized cell process. Chemosphere, 84(9), 1216-1222.
- 1094 111. Yu, Y., Wu, L., Chang, A.C., 2013. Seasonal variation of endocrine disrupting
 1095 compounds, pharmaceuticals and personal care products in wastewater treatment plants.
 1096 Science of the Total Environment, 442, 310-316.
- 1097 112. Zhang, H., Cao, B., Liu, W., Lin, K., Feng, J., 2012. Oxidative removal of acetaminophen
 using zero valent aluminum-acid system: Efficacy, influencing factors, and reaction
 mechanism. Journal of Environmental Sciences, 24(2), 314-319.
- 1100 113. Zhang, L., Yin, X., Li, S.F.Y., 2015. Bio-electrochemical degradation of paracetamol in
 a microbial fuel cell-Fenton system. Chemical Engineering Journal, 276, 185-192.
- 1102 114. Zhang, S., Zhang, Q., Darisaw, S., Ehie, O., Wang, G., 2007. Simultaneous quantification
 1103 of polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and
 1104 pharmaceuticals and personal care products (PPCPs) in Mississippi river water, in New
- 1105 Orleans, Louisiana, USA. Chemosphere, 66(6), 1057-1069.

- 1106 115. Zhang, X., Wu, F., Wu, X., Chen, P., Deng, N., 2008. Photodegradation of
- acetaminophen in TiO₂ suspended solution. Journal of Hazardous materials, 157(2–3),
- **1108 300-307**.

1109 Table 1. Classification of ACT levels in WWTPs and surface water of countries

ACT concentration	Countries	ACT concentration range	Countries
range - detection		compared with	
frequency in WWTPs		recommended level for	
		drinking water (71 ng/l)**	
Beyond 100 µg/l - 80-	China, USA, Greece,	Higher than	China, USA,
100%	UK, Korea, Taiwan	recommendation	Taiwan, UK,
			Spain, Serbia
Below 100 µg/l – below	France, Spain,	Lower than	France, Spain,
50%	Columbia	recommendation	USA, Singapore,
			Germany, UK,
			Korea

1110 *Data from appendix

1111 ** (Vulliet and Cren-Olivé, 2011)

1113 Table 2. EC₅₀ of aquatic species exposing to ACT

Species	Effective concentration (mg/L)	Exposure time	Reference
Algae			
Scenedesmus subspicatus	134	72 h	Henschel et al. (1997)
Pseudokirchneriella subcapitata	Over 240	96 h	Daniel et al. (2015)
Scenedesmus dimorphus			
Stichococcus bacillaris			
Chlorella vulgaris			
Chlamydomonas reinhardtii			
Macrophyte species (Lemna minor	446.6	46.6 7 d	
and <i>Lemna gibba</i>)			
Protozoan (Ciliates)	112	48 h	Henschel et al. (1997)
Fishes			
Brachydanio rerio	378	48 h	Henschel et al. (1997)
Oryzias latipes	Over 160	48-96 h	Kim et al. (2007b)
Freshwater invertebrate (Daphnia	50	24 h	Henschel et al. (1997)
magna)	26.6 - 30.1	48 - 96 h	Kim et al. (2007b)
Marine bacterium (Vibrio fischeri)	650	30 min	Henschel et al. (1997)
	549.7	15 min	Kim et al. (2007b)
Cells in vitro	19	18 h	Henschel et al. (1997)

1115

Process	[Fe ²⁺]	[H ₂ O ₂]	рН	Initial ACT concentratio n	Removal efficienc y (%)	Retentio n time	References
Photo- Fenton	$H_2O_2/Laterit$ e iron =	30 mg/L ACT/H ₂ O ₂	3	10 mg/L	79	- 120 min	Manu and Mahamoo
Fenton	(w/w)	(w/w)		-	76		d (2011)
Fenton with artificial ferrous catalyst (FeSO ₄)	[H ₂ O ₂]:[Fe ²⁺]	= 60:1	2	10 mg/I	80		Basavaraju
Fenton with iron source from laterite soil	[H ₂ O ₂]:[Lateri 40:1	H ₂ O ₂]:[Laterite soil] = 0:1		10 mg/L	75	ou min	(2011)
Fenton Electro- Fenton	0.1 mM	15 mM (fixed value)	2	5mM	<u>99</u> 100	120 min	Su et al. (2012)
Novel Fenton aerated reactor	0.1 mM	25 mM	3	5 mM	99	40 min	Su et al. (2013a)
Fluidized -bed Fenton	0.06 mM*	19.87 mM *	3	5 mM	99.6	40 min	de Luna et al. (2013)
Bio- Fenton (Phyto- Fenton)	n.d	200-800 nmol g ⁻¹ fresh weight	n. d	1 &100 ppb	55-99.8%	5 d	Phong et al. (2016)

1116 Table 3. Summary of chemical-based Fenton reaction

1117 Remark: n.d: no data; *treated solution

Process	Light source	Catalyst dose	pН	Initial ACT concentration	Removal efficienc y (%)	Retention time	References
Suspended TiO ₂	Metal halide lamp 250 W, ≥ 365nm)	1.0 g/l	3.5	100 µmol/l	95	100 min	Zhang et al. (2008)
Suspended	UVA (8W, 365 nm)	- 0.4 g/l	95	2 mM	50	300 min	Yang et al.
TiO ₂	UVC (15W, 254nm)	0.1 8/1).5	4 mM	95	80 min	(2008)
TiO ₂ / reticulated vitreous carbon assisted UV	UV mercury vapor lamp (350 nm peak)	l g binding on reticulat ed vitreous carbon anode	n.d	96 mg/l	95	60 min	Arredondo Valdez et al. (2012)
Non-porous TiO ₂ -P25	UVA/LED (365 nm) 1-3 mW/cm ²	0.2 mg/l	5.6	200 ppb	100	15 min	Xiong and Hu (2012)
ZSM-5 supported TiO ₂	UV lamp (254 nm) 0.97 mW/cm ²	TiO ₂ : ZSM-5 as 40 wt%	6.8	15 mg/l	96.6	180 min	Chang et al. (2015)
Planar and porous Ti/ BDD electrodes	None	-		100 mg/l	100	20 – 25 h	He et al. (2015)
US/Fenton/TiO ₂ NT	None	TiO ₂ NT as anode US 1000 kHz	3	3 μΜ	85.3	30 min	Im et al. (2015)
Non-porous TiO ₂ -P25	UVA/LED (365 nm) 5 mW/cm ²	10 ppm	5.6	200 ppb	-	20 min as 20% time of periodic illumination	Xiong and Hu (2016)
Carbon self- doped (C- doped) TiO ₂	LED (440–490 nm)	100 ppm 1.0 g/l	6.9	20 ppm 0.1 mM	70-100* 94	60 min 30 min for adsorption 9 h for photo- degradation	de Luna et al. (2016)
Nano-porous TiO ₂	UV visible lamp (365, 405 and 435 nm) 130 mW/cm ²	-	-	40 ppm	86.96	60 min	Xie et al. (2016)
Hollow core- shell mesoporous	UV mercury vapor lamp	0.1 g/l	-	50 mg/l	94	60 min	Lin et al. (2016a)

1119Table 4. Summary of photo-based and electro-based Fenton process

TiO ₂	(500W, 245						
microspheres	nm)						
	LED (450						
TiO ₂ doping	nm peak)	1 g/l	9	0.1 mM	100	9 h	Lin et al.
$K_2S_2O_8$	16.85	1 8/1	-	011 11111	100	, 1	(2016b)
Fonton like	$\frac{\text{mW/cm}^2}{5.621 \times 10^{-6}}$	1.106	A	500 ~/1-~	100	14 am 29 d	Var a at al
with nano-	$5.051 \times 10^{\circ}$	1.120×10^{-4} to	Ano de	500 μg/kg	100	14 01 28 U	(2016)
Schwertmannit	$10^{-5} \text{ mol g}^{-1}$	$2253 \times$	as 2	seament			(2010)
e catalyst,	10 11018	10-4	Cat				
assisted EK		mol/g	hod				
			e as				
			12				
			Sed				
			ime				
			as				
			6-				
			12				
	Full						
	waveband						
	xenon lamp						
WO ₂ /TiO ₂ /SiO ₂	with a cutoff	15 σ/Ι	0	5 mg/l	95	1 h	Yanyan et
W 03/ 1102/ 5102	filter (500	1.5 8/1)	5 mg/1))	7 11	al. (2017)
	W, 800 nm						
	$>\lambda>200$						
	nm)						
	Xenon lamp						Kurniawan
BaTiO ₃ /TiO ₂	(500 W, 200	1 g/l	7	5 mg/l	95	4 h	et al.
	$1111 < \chi < 800 \text{ nm}$						(2018)
* Retrieved from graph							
		\land					

1122 Table 5. Main metabolites of ACT degradation

1124 List of Figures



1125

Fig. 1. Occurrence of ACT in various environments in (a) America, (b) Asia and (c) Europe



1127

1128Fig. 2. Comparison of ACT removal efficiency by technologies. X-axis exhibits the1129technologies and their mean ACT removal efficiencies and standard deviations (in the1130brackets). Error bars represent the standard deviations of the data.

(Amouzgar et al., 2017; Arredondo Valdez et al., 2012; Ba et al., 2014; Behera et al., 2011; 1131 Boleda et al., 2011; Chang et al., 2015; Chang et al., 2014; de Luna et al., 2013; de Luna et al., 1132 2016; Gallardo-Altamirano et al., 2018; Gros et al., 2010; He et al., 2015; Huber et al., 2009; 1133 Im et al., 2015; Kasprzyk-Hordern et al., 2009; Kim and Tanaka, 2009; Kurniawan et al., 2018; 1134 Lin et al., 2016a; Lin et al., 2016b; Lutpi et al., 2015; Manu and Mahamood, 2011; Manu et al., 1135 2011; Mashavekh-Salehi et al., 2017; Narumiya et al., 2013; Nguyen et al., 2013; Phong et al., 1136 2016; Quiñones et al., 2015; Radjenović et al., 2008; Ranieri et al., 2011; Rosal et al., 2010; Su 1137 1138 et al., 2013a; Su et al., 2013b; Su et al., 2012; Verlicchi et al., 2013; Villaroel et al., 2014; Wong et al., 2018; Xie et al., 2016; Xiong and Hu, 2017; Yang et al., 2016; Yang et al., 2008; Yanyan 1139 et al., 2017; Yanyan et al., 2018; Yu et al., 2006; Yu et al., 2011; Zhang et al., 2012; Zhang et 1140 1141 al., 2008)





Highlights

- China and the USA showed the highest acetaminophen (ACT) concentration
- Advanced oxidation processes (AOPs) removed ACT to the ppt level
- More than 20 by-products and intermediates of ACT were detected
- Treated wastewater was not totally free from the toxic effects due to ACT metabolites

Acetaminophen





By-products Transformation

ACT

Metabolites





China and the USA: highestACT concentration in WWTPs influent (300 µg/l) AOP degraded ACT to non-toxic intermediates

More than 20 intermediates detected