Critical Review

Municipal solid waste landfills: An underestimated source of PPCPs in the water environment

Xia Yu, Qian Sui, Shuguang Lyu, Wentao Zhao, Jianguo Liu, Zhenxiao Cai, Gang Yu, and Damia Barcelo

Environ. Sci. Technol., **Just Accepted Manuscript** • DOI: 10.1021/acs.est.0c00565 • Publication Date (Web): 19 Jun 2020

Downloaded from pubs.acs.org on June 21, 2020

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

Municipal solid waste landfills: An underestimated source of PPCPs in the water environment

*Xia Yu*¹, *Qian Sui*^{1,5,*}, *Shuguang Lyu*^{1,5}, *Wentao Zhao*², *Jianguo Liu*³,
*Zhenxiao Cai*⁴, *Gang Yu*³, *Damia Barcelo*⁶

¹ State Environmental Protection Key Laboratory of Environmental Risk Assessment and Control on Chemical Process, School of Resources and Environmental Engineering, East China University of Science and Technology, Shanghai 200237, China

² State Key Laboratory of Pollution Control and Resource Reuse, College of Environmental Science and Engineering, Tongji University, Shanghai 200092, China

³ School of Environment, Tsinghua University, Beijing 100084, China

⁴ MicroHAOPs Inc., University of Washington, Seattle WA 98195, USA

⁵ Shanghai Institute of Pollution Control and Ecological Security, Shanghai 200092, China

⁶ Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research, Spanish Council for Scientific Research (CSIC), Barcelona 08034, Spain

* Corresponding authors:

Qian Sui (Tel: 86-21-64252139; Fax: 86-21-64252139; Email: suiqian@ecust.edu.cn)

Abstract: Pharmaceutical and personal care products (PPCPs) have been the focus of increasing concern in recent decades due to their ubiquity in the environment and potential risks. Out-of-date PPCPs are usually discharged into municipal solid wastes (MSWs), enter the leachates in MSW landfills and have serious adverse effects on the surrounding water environment. However, the occurrence and removal of PPCPs from landfill leachates have rarely been examined to date. This lack of knowledge makes landfill an underestimated source of PPCPs in the environment. In this review, we collected the relevant publications of PPCPs in landfill leachates, systematically summarized the occurrence of PPCPs in landfill leachates globally, evaluated the removal performances for various PPCPs by different types of on-site full-scale leachate treatment processes, and assessed the impacts of landfill leachates on PPCPs in the adjacent groundwater. In particular, influencing factors for PPCPs in landfill leachates, including the physicochemical properties of PPCPs, climate conditions, characteristics of landfill sites (i.e., landfill ages) as well as sociological factors (i.e., economic development) were extensively discussed to understand their occurrence patterns. Future perspectives were also proposed in light of the identified knowledge gaps. To the best of our knowledge, this is the first review regarding the occurrence and removal of PPCPs from landfill leachates worldwide.

Keywords: Pharmaceutical and personal care products (PPCPs); landfill leachates; occurrence; influencing factors; removal efficiency; groundwater

41 TOC

42

1. Introduction

In recent years, increasing attention has been paid to pharmaceutical and personal care products (PPCPs) due to their ubiquity in the environment and potential to cause undesirable ecological effects¹⁻⁹.

Normally, PPCPs enter the environment through three pathways. The manufacture of PPCPs is one of the three emission sources. During PPCP production, some active ingredients are released via the discharge of industrial wastewater¹⁰. PPCP consumption has been identified as the second source of PPCP contamination. After uptake by humans or animals, part of the PPCPs are excreted via urine or feces, delivered into domestic wastewater or livestock wastewater, and released to the receiving water due to the inefficient removal by conventional treatment processes¹¹. The disposal of out-of-date PPCPs in landfills is the third source of PPCPs in the environment^{11, 12}.

Lacking a proper recycling system, most unused PPCPs are discarded via municipal solid wastes (MSWs)¹³⁻¹⁶. Currently, landfills are still the primary disposal method for MSWs in many countries. Therefore, large amounts of PPCPs are expected to enter the MSW landfills. For instance, the total concentration of 22 pharmaceutical ingredients in MSWs measured in a landfill located in Florida was 8.1 mg/kg¹⁷. High concentrations of pharmaceuticals in MSWs were also detected in China. The average concentrations of oxytetracycline, tetracycline, and sulfamethoxazole were 100.9, 63.8, and 47.9 µg/kg, respectively¹⁸.

In landfills, PPCPs may undergo degradation, adsorption, or enter the leachates¹⁷. Although compared to other pollutants, such as ammonia and heavy metals, PPCPs are less abundant in landfill leachates. But considering that PPCPs cause unexpected consequences and unintended effects on non-target species, and induce undesirable effects on humans and ecosystems even at a low concentration level¹⁹, their occurrence in landfill leachates should also be concerned. In fact, landfill leachates are one of the representative sources of PPCPs in the environment^{20, 21}. Compared with other sources, PPCP concentrations in landfills are higher (even reaching mg/L levels) and fluctuating (varying by several orders of magnitude)²².

In most landfills, leachates are treated by either on- or off-site processes. During the leachate treatment process, traditional pollutants (such as heavy metals, chemical oxygen

demand (COD), biological oxygen demand (BOD) and ammonia nitrogen) were efficiently eliminated²³. However, the effectiveness of PPCP removal during the leachate treatment processes has not been clearly understood. A lack of legal requirements regarding PPCPs in wastewater emission standards is one of the reasons for their limited recognition. Recently, increased concerns about emerging organic contaminants (EOCs), including PPCPs, during wastewater treatment processes have facilitated the promulgation of new regulations. For example, in Switzerland, wastewater treatment plants (WWTPs) with a larger size or those that discharge effluent to sensitive receiving waters are required to reach removal efficiencies of 80% for 12 EOCs (11 PPCPs included) according to the new Waters Protection Ordinance implemented in 2016²⁴. Similarly, the newly established wastewater emission standard for Shanghai, China (DB 31/199-2018) also include EOCs, such as nonylphenol, for the first time. The treated landfill leachates in Shanghai that are either delivered to the municipal WWTPs or released to the environment should meet the requirement of the newly established emission standard. Therefore, there is an urgent need to track PPCP occurrence in landfill leachates and their removal during the current leachate treatment processes, to consider their environmental risks and potential regulation requirements in the future.

PPCPs have been detected in the groundwater near landfills in several countries²⁵⁻²⁷. Particularly for historical landfills, where no or insufficient composite liners and leachate-collection systems were installed, leachates were prone to leach into groundwater gradually and contribute to PPCP contamination in the adjoining groundwater^{26, 28, 29}.

Unfortunately, very few researchers have generated summaries on the above PPCP issues in landfill leachates. Only one review investigated the presence of emerging contaminants in landfill leachates³⁰ but was limited to their occurrence in China. Consequently, there is still a lack of comprehensive overview of PPCPs from a global perspective. Furthermore, the removal of PPCPs by landfill leachate treatment processes and the impacts on the surrounding environment should be evaluated. To fill this gap, we have systematically summarized the current studies on the occurrence of PPCPs in landfill leachates globally and proposed the factors that influence PPCP concentrations in landfill leachates. The second objective is to provide a snapshot of PPCP removal using different leachate treatment processes. Finally, the impacts of landfills on

PPCPs in the groundwater was elucidated. To the best of our knowledge, this is the first review on the occurrence and removal of PPCPs from landfill leachates worldwide.

2. Occurrences in landfill leachates

2.1 Overall occurrence

A total of 172 PPCPs were reported in landfill leachates globally over the last two decades (from 1993 to 2018, Table S1). They belong to various therapeutic classes, including antibiotics, anti-inflammatories, stimulants, beta-blockers, etc. Individual PPCPs were statistically analyzed for the number of times they were reported in the raw landfill leachates identified in 50 relevant papers (detailed methodologies for publication collection and data compilation are described in the supporting information), and the top 25 PPCPs, which were reported in more than four related papers, are illustrated in Figure 1a.

By and large, antibiotics comprise approximately half of the top 25 most frequently reported PPCPs in the leachates, reflecting considerable concerns about antibiotics. Antibiotics are widely used human and veterinary medicines. Global antibiotic consumption used for livestock was estimated to be 63,151 tons in 2010 and would rise by 67% between 2010 and 2030³¹. In China, a total of 150 to 200 kt of antibiotics are used every year³². The United States Food and Drug Administration estimated that 14.6 kt of antibiotics were sold for veterinary use in 2012 and 3.3 kt for human use in 2011 in the United States³³. High concentrations of antibiotics were subsequently detected in most PPCP emission sources, such as municipal wastewater^{34, 35} and livestock wastewater^{36, 37}. Additionally, the occurrence of antibiotics in the environment has led to the development of antibiotic resistant bacteria and resistance genes and has therefore adversely impacted the aquatic ecosystem and human health^{33, 38-40}. For these reasons, the occurrence of antibiotics in landfill leachates has been extensively studied in 24 out of the 50 articles on PPCPs in landfill leachates.

Figure 1. Top 25 PPCPs sorted by number of reported times (a) and by concentrations (maximum concentrations) (b) in landfill leachates (DEET: diethyltoluamide; DAS: diacetone sorbose; DAG: diacetone alpha-keto-gulonic acid; EATC: 4-epianhydrotetracycline)

However, several non-antibiotics were more focused on in the studies about PPCPs in landfill leachates. The most frequently reported PPCPs, namely, diethyltoluamide (DEET), caffeine, carbamazepine, and ibuprofen, are an insect repellent, stimulant, anticonvulsant and

133 anti-inflammatory, respectively. Special concerns about these non-antibiotics were consistent
134 with their high frequencies of detection in individual PPCP surveys in landfill leachates. For
135 example, DEET, the most frequently reported PPCP, was detected in 95% of leachate samples
136 from 19 landfills across the entire United States ⁴¹. In addition, these hot spot non-antibiotics
137 showed relatively higher concentrations in landfill leachates (Figure 1b), increasing their
138 opportunities to be selected as the target compounds in the following surveys for PPCPs in
139 landfill leachates. For example, the maximum concentration of DEET reached 52,800 µg/L ²⁵,
140 several orders of magnitude higher than that of other PPCPs. Ibuprofen and caffeine, which were
141 also included in the most frequently reported PPCPs, displayed maximum concentrations of 705
142 ⁴¹ and 430 µg/L ⁴², respectively, ranking No. 5 and 6 in the PPCP list when sorted by their
143 concentrations (Figure 1b). While in other emission sources (such as in municipal and livestock
144 wastewater), DEET, ibuprofen and caffeine exhibited a concentration level of ng/L to µg/L, much
145 lower than those in landfill leachates ⁴³⁻⁴⁵.

146 By contrast, although antibiotics were subject to special attention in raw landfill leachates,
147 they were present at markedly lower concentrations than these non-antibiotics. There are only
148 seven antibiotics among the top 25 PPCPs sorted by maximum concentration (Figure 1b). Even
149 for ofloxacin, the most abundant antibiotic in landfill leachates, the concentration was 1 to 2
150 orders of magnitude lower than the above hot spot non-antibiotics. Besides, compared to
151 municipal and livestock wastewater, the concentration of some antibiotics in landfill leachates
152 were even lower. Tetracycline and trimethoprim were detected up to 48 µg/L ⁴⁴ and 162 µg/L ⁴³ in
153 the municipal wastewaters, but their maximum concentrations in landfill leachates globally were
154 19 µg/L ⁴⁶ and 8.08 µg/L ⁴⁷, respectively. Sulfamethazine was found to be 324.4 µg/L ⁴⁸ in
155 livestock wastewaters and 16.17 µg/L ⁴⁹ in landfill leachates. Therefore, it could be concluded
156 that antibiotics were not predominant in landfill leachates, unlike the situation in the municipal
157 wastewater ⁴⁴ or livestock wastewater ⁴⁸.

158 The primary cause of the different occurrence patterns was the different sources of PPCPs
159 in landfill leachates from municipal or livestock wastewater. Antibiotic residues are detected
160 extensively in municipal wastewater because 50% - 90% of consumed antibiotics are excreted
161 via feces or urine ^{44, 50}. In livestock wastewater, high concentrations of antibiotics were detected

162 due to the broad application of antibiotics to livestock ^{51, 52}. In most cases, the antibiotics that
163 ended up in landfill leachates come from outdated or unused antibiotics discarded in MSWs.
164 Because antibiotics are prescription medicines, not over-the-counter (OTC) drugs, in most
165 countries, the amount of out-of-date antibiotics was much lower than that of some OTC non-
166 antibiotics. Thus, the focus on antibiotics in landfill leachates might be considered with too much
167 weight.

168 It also should be noted that PPCP metabolites in landfill leachates seemed to be
169 underestimated. Knowledge of PPCP metabolites in landfill leachates is very limited. Only one
170 metabolite (cotinine, a major nicotine metabolite) was included in the top 25 most frequently
171 reported PPCPs in landfill leachates. However, some PPCP metabolites were found to have very
172 high contamination levels, and three of them were involved in the top 25 PPCP list sorted by their
173 maximum concentrations (Figure 1b). Diacetone sorbose (DAS, vitamin C byproduct) exhibited
174 the second-highest maximum concentration in landfill leachates (2570 µg/L ⁵³). In addition, PPCP
175 metabolites could have equal or even higher toxicity than the parent products ^{54, 55}. Therefore,
176 further investigations of PPCP metabolites in landfill leachates should be undertaken to fill this
177 knowledge gap.

178 The physicochemical property, i.e., the hydrophobicity of PPCPs, is another influencing
179 factor on the contaminant levels in landfill leachates. The statistical analysis showed a significant
180 negative relationship ($r = -0.276$, $p < 0.01$) between the log concentrations of individual PPCPs in
181 landfill leachates and their octanol/water partition coefficients ($\text{Log } K_{ow}$) (Figure S1). This trend
182 indicated that PPCPs with lower K_{ow} values generally had more severe contamination levels in
183 landfill leachates. In the landfill, PPCPs in MSWs gradually percolated into the leachate, and
184 PPCPs with a hydrophilic nature have a higher leaching potential to facilitate their mobilization
185 from MSWs to water.

186 2.2 Geographic distribution

187 In total, the occurrence of PPCPs in landfill leachates has been reported in 18 countries located
188 in five continents (Figure S2). Before 2008, a large portion of publications originated from Europe,
189 accounting for 62% of early publications. Subsequently, the quantity of related publications from
190 North America and Asia has grown rapidly, reaching 12% and 46% of the total publications,

191 respectively. In Africa and Oceania, the occurrence of PPCPs in raw landfill leachates was only
192 reported in one country ^{56,57}, respectively. In other continents, no investigation was conducted for
193 the occurrence of PPCPs in landfill leachates.

194 The United States conducted the most comprehensive studies on PPCPs in landfill
195 leachates (Figure 2a). Overall, a considerable number ($n = 103$) of PPCPs was investigated in
196 landfill leachates in the United States. The United States Geological Survey (USGS) conducted a
197 program to sample fresh leachates from 19 landfills across the United States, and quantified 80
198 PPCPs in the raw landfill leachates, providing a comprehensive evaluation across the entire
199 United States ^{41, 58}. Sixty-seven PPCPs were determined in landfill leachates in China. Unlike the
200 situation in the United States, the studies in China were unevenly distributed. Thirteen out of
201 sixteen related studies were conducted in two provinces. Therefore, the current knowledge on
202 PPCPs in landfill leachates in China lacks representativeness. In other countries, due to the
203 limited sampling campaigns and analytical methods, only 1~19 PPCPs were reported in landfill
204 leachates.

205 Maximum concentrations of PPCPs in landfill leachates in various countries are depicted in
206 Figure 2b. Sixteen PPCPs exhibited more severe contamination levels with maximum
207 concentrations of $> 50 \mu\text{g/L}$. Nine of them were detected in landfill leachates in the United States,
208 with an extremely high contamination level for DEET (52.8 mg/L) ²⁵. Germany and Croatia also
209 had relatively severe PPCP contamination in their landfill leachates. Five highly contaminating
210 PPCPs were detected in German landfill leachates, and a very high concentration of DAS (2570
211 $\mu\text{g/L}$) was found in Croatia ⁵³.

Figure 2. Types of PPCPs reported (a) and maximum concentration of highly contaminating PPCPs (>50 µg/L) (b) in landfill leachates from different countries

Generally, the concentrations and numbers of highly contaminating PPCPs (Figure 2b) were higher and larger in developed countries, which seems to be related to the economic development levels in the investigated countries. Previous studies showed the local production and usage/consumption pattern determined the concentration levels of PPCPs reaching municipal wastewater ³⁴ and regions characterized by higher economic development levels had

higher PPCP contamination levels in their WWTPs ^{44, 59, 60}. Unlike PPCPs in municipal wastewater, the amount of discarded PPCPs entering the landfill was random. However, cities characterized by higher economic development levels have more opportunities to accumulate a larger population, and the overall amounts of PPCP consumption or discharge would be higher. Currently, few investigation was conducted to elucidate the relationship between PPCPs in landfill leachates and social development in the countries where the landfills were located, but higher levels of PPCPs in landfill leachates were found in urbanized areas ^{61, 62}.

Figure 2b also exhibits the distinct characteristics of PPCPs in individual landfill leachates. For example, in the United States and Poland, DEET was the most abundant PPCP in the leachates; nicotine was detected primarily in landfill leachates in Germany and Italy, while in China, Croatia, India and Norway, the landfill leachates were dominated by caffeine, DAS, diclofenac, and ibuprofen, respectively.

These regional differences in the dominant PPCPs may be associated with their consumption patterns. For instance, approximately one-third of the United States population was expected to use at least one DEET-containing products from the 524 commercial names referenced ⁶³, leading to an estimated nationwide DEET annual usage of approximately 1.1 kt ⁶⁴. In China, caffeine and ibuprofen were consumed in excess of 1 kt per year ⁶⁵. Ibuprofen was also identified as a high priority pharmaceutical and should receive attention primarily because of its large production ^{65, 66}. In Norway, the characteristic PPCP ibuprofen is among the top ten national nonprescription and prescription pharmaceuticals ²¹. In India, diclofenac is the characteristic PPCP matching national consumption ⁶⁷.

2.3 Other influencing factors

In addition to economic development and consumption patterns in the studied region, the substantial variation in the level of PPCPs could also be attributable to several other influencing factors, such as the climate conditions and the characteristics of the investigated landfills.

The climate conditions were found to affect the concentrations of PPCPs in raw landfill leachate in several cases ^{61, 68}. Rainfall can cause dilution, thus reducing the concentration of pollutants. For instance, concentrations of most PPCPs in spring (dry season) were higher than those in fall (wet season) in landfill leachates in Taiwan, China ⁶⁸. On the other hand, rainfall can

leach pollutants from MSWs, leading to an increased load of pollutants in landfill leachates. Therefore, a higher concentration of PPCPs was observed during the rainy seasons in some studies. For example, Masoner et al ⁴¹ investigated 19 landfill sites with different annual precipitation in the USA and demonstrated that landfills located in areas receiving greater amounts of precipitation were likely to produce leachates with higher frequency of detection and concentrations of pharmaceuticals. However, in some other cases, no significant differences in PPCP concentrations in landfill leachates were observed under dry weather and wet weather conditions ^{47, 69}. Thus, the influence of climate condition (rainfall) on the PPCP concentration levels in landfill leachate remains unclear, and more efforts need to be made to clarify the influence mechanisms.

The landfill age has a remarkable influence on the PPCP concentration in leachates. Using sulfonamides as an example, the leachates that generated in a landfill aged 6 years contained higher levels of sulfonamides than those in more aged landfill leachate (aged > 10 years) samples ^{70, 71}. During the lifespan of landfills, organic pollutants harbored in solid wastes enter the landfill leachate continuously over time and simultaneously undergo degradation. Therefore, middle-aged landfills were found to have elevated levels of PPCPs and other contaminants in landfill leachates ^{25,41}.

In addition, the landfill status (active or closed) is another factor affecting the PPCP concentrations in landfill leachates. Since closed landfills stop receiving wastes and have had more time for the natural attenuation of PPCPs, leachates from closed landfills have lower PPCP concentrations than those from active landfills. Masoner et al ⁵⁸ found that at 16 active landfills, the EOC (including PPCPs) levels (median: 65.6 µg/L) were significantly greater than those in 6 closed landfills (median: 32 µg/L). However, an exception was also observed by Chung et al ⁶¹; they reported elevated levels of four antibiotics in closed landfills relative to active landfills.

In summary, landfill leachates harbored abundant and diverse pollutants and acted as an underestimated source of PPCPs. The climate conditions, characteristics of landfill sites (i.e., landfill ages) as well as the sociological factors (i.e., economic development) were found to influence the PPCP contamination in landfill leachates. Nonetheless, contrasting observations on the influencing patterns in different landfills have been reported, which hinders the understanding

of PPCP behavior in landfill leachates. Furthermore, the influencing mechanisms involved in the fate of PPCPs in landfill leachates are far from clear. The identification of leading influencing factors and the elucidation of their mechanisms should be addressed in further studies on the occurrence of PPCPs in landfill leachates.

3. Removal of PPCPs in full-scale leachate treatment plants

In most landfills, leachates must be properly treated before being released into receiving waters. Commonly applied treatment processes are a combination of biological, physical and/or chemical treatment⁷²⁻⁷⁴. We reviewed the literature about the removal of PPCPs by on-site full-scale landfill leachate processes and revealed the removal of different PPCPs by various treatment processes.

3.1 Removal performance for different types of PPCPs

Table S2 summarizes the results of PPCP removal efficiencies in landfill leachate using different treatment processes. On the whole, only 35 PPCPs were investigated in the previous studies during the on-site full-scale leachate treatment processes. A high removal efficiency of > 90% was observed for 5 out of 35 PPCPs, namely, acetaminophen, bezafibrate, clofibric acid, DEET and metoprolol. Five PPCPs, such as trimethoprim and sulfadiazine, could be eliminated by 80 - 90%. There were seven PPCPs, such as amphetamine and ampicillin, that displayed a low removal efficiency of < 50%. Some PPCPs, i.e., chloramphenicol, sulfamethoxazole, and sulpiride, even showed negative removal elimination in some cases, similar to the observations in municipal WWTPs^{50, 75-77}.

Removal efficiencies of PPCPs in leachates varied from negative removal to 100% depending on the pollutants. Most PPCPs exhibited similar removal performance during the treatment of landfill leachate and municipal wastewater. For example, acetaminophen and DEET tended to be highly removed, while carbamazepine and sulpiride appeared to be persistent. However, some PPCPs showed different removal performances. Beta-lactam antibiotics (ampicillin and cephalexin) were prone to hydrolysis⁵⁰ and generally presented a high elimination efficiency (approximately 80%) without significant fluctuation in the municipal WWTPs^{11, 78}; while in landfill leachates, the beta-lactam antibiotics did not present such high elimination efficiencies (ampicillin was removed by less than 50%). On the contrary, trimethoprim showed an

unsatisfactory removal efficiency (69%) from municipal wastewater⁵⁰ but encouraging results (> 92%) from landfill leachate⁴⁷ using the same treatment process (full-scale membrane reactor).

Biodegradation and sorption are believed to be the key mechanisms for removing pollutants, including PPCPs, during wastewater treatment processes⁴. The removal performance depends on the properties of PPCPs, such as their hydrophilicity, solubility, and biodegradability¹¹. Several PPCPs with low biodegradability, such as carbamazepine and diclofenac, exhibited refractory behavior to biodegradation and escaped from the treatment process. The hydrophilicity and solubility of PPCPs are associated with their removal by sorption. Pollutants with a high K_{ow} and lower water solubility tended to accumulate onto the sludge^{79, 80}. For example, Jia et al⁸¹ found that the removal efficiencies for fluoroquinolone (FQ) antibiotics are significantly positively correlated with their K_d (solid-water partition coefficients) and suggested that sorption to sludge was the major removal mechanism of FQs from municipal wastewater. However, the data on the removal of PPCPs by leachate treatment processes are too limited to reach a firm conclusion on the relationship between PPCP properties and their removal efficiencies.

3.2 Removal performance by various treatment processes

The removal efficiencies of PPCPs also largely depend on the different treatment processes. Figure 3 summarizes the removal efficiency of PPCPs by different biological and combined landfill leachate treatment processes.

Generally, higher median removal efficiencies were obtained by constructed wetland system (CW) and membrane bioreactor (MBR). A CW, employed in a local old, closed landfill in Singapore, exhibited high removal efficiencies for most of the investigated pollutants, even for some persistent compounds such as diclofenac and gemfibrozil⁶⁹. A variety of removal pathways including photolysis, biodegradation, plant uptake, and sorption onto the bed were proposed for the efficient elimination of PPCPs by CW^{82, 83}. The MBR also exhibited good PPCP removal performance with a median elimination of > 80% for target PPCPs in landfill leachates^{47, 84}, probably ascribing to the membrane retention and enhanced biodegradation during the MBR process^{85, 86}. Additionally, the high hydraulic retention time adopted in the above CW (22.75 d) and MBR (9 d) was another cause for the good removal performance for PPCPs, due to the prolonged contact time between microorganisms and PPCPs.

Figure 3. Box-and-whisker plots showing the removal efficiencies of PPCPs by different biological (pink) and combined (blue) landfill leachate treatment processes (SBR: sequencing batch reactor, MBR: membrane bioreactor, CW: constructed wetlands system, A/N: anaerobic/nitrification process, N/A/O: nitrification/anaerobic/ozonation, and OD/GAC: oxidation ditch/granular activated carbon)

Advanced treatment techniques, such as granular activated carbon (GAC) adsorption, membrane filtration, and ozonation, were incorporated to enhance the removal of pollutants from landfill leachates. Some combined treatment processes exhibited superior performance for PPCP elimination. For instance, the nitrification/anaerobic/ozonation (N/A/O) process exhibited a larger PPCP removal capability than the anaerobic/nitrification (A/N) process⁶⁸. The median PPCP removal efficiency by the N/A/O process was 78%, significantly higher than that of the same group of PPCPs by the A/N process (28%) (Figure 3). However, not all the combined treatment processes exhibited better removal performances. Oxidation ditch/GAC processes, which were employed to treat 10 PPCPs in Taiwan⁶⁸, exhibited removal efficiencies ranging from 12% to 80%, which was lower than that of most reported biological treatment processes⁸⁷.

Nevertheless, it should be noted that the selected target PPCPs in the limited studies are quite different. Therefore, there are few target PPCPs in common in the related studies. The different choice of target PPCPs may also lead to some bias when the treatment processes are assessed. To make an accurate comparison, more comprehensive studies on the elimination of PPCPs by landfill leachate treatment processes should be conducted to explore the best

available technologies to meet the current discharge standards for landfill leachate and enhance the elimination of PPCPs simultaneously.

Although PPCPs were largely reduced by some leachate treatment processes, their residues in the effluent were still high in some cases due to their high contamination levels in raw landfill leachates. For most landfills, treated leachates are delivered to nearby municipal WWTPs for further elimination. However, since the flow rates of treated leachates usually are much lower than those of municipal WWTP influents, their impacts to receiving municipal WWTPs could not be easily figured out. To obtain a solid conclusion, we made an estimation about contribution of treated landfill leachates to PPCP load in the receiving WWTPs, according to the flowrate and concentrations of PPCPs in treated leachates and municipal wastewaters in the studied areas. Given the availability of required data, we selected landfills in Shanghai and Hong Kong as the case study areas. For PPCPs in treated leachate, PPCP concentrations in landfills were obtained from Sui et al ⁴⁷ and Chung et al ⁶¹, respectively. The relevant publications about PPCPs in raw municipal wastewater in Shanghai and Hong Kong were collected and the mean concentrations were used for estimation. The detailed information is compiled in Table S3, and the estimated contribution of treated landfill leachate on PPCP mass loads in the receiving municipal WWTPs are shown in Figure 4. For some PPCPs that were predominant in the municipal wastewaters, treated leachates showed negligible impacts on the mass load of PPCPs in the receiving WWTPs because of the relatively high concentrations of PPCPs in municipal wastewaters and the high flow rate of influents. For example, the mass loads of antibiotics in treated leachates in Hong Kong were 60-858 g/d, while in the raw municipal wastewater which did not include treated landfill leachates in the studies region, their average mass loads were 12-239 kg/d. For other PPCPs, of which the concentrations in municipal wastewater were much lower than those in treated leachates (such as diclofenac and gemfibrozil), the contribution of treated leachate accounted for approximately 40% of the total load in the case of Shanghai, indicating the treated leachate could still result in an increased load of these PPCPs to the receiving WWTPs. Additionally, in some landfills, leachate might be directly discharged into the adjoining water environment intentionally or unintentionally ^{27, 46}, posing a risk to nearby surface water and groundwater.

Figure 4. Estimated contribution of treated landfill leachate on PPCP mass loads in the receiving municipal WWTPs

4. Impacts on the adjacent groundwater

4.1 Overall occurrence in the surrounding groundwater

Groundwater is vulnerable to contaminants from different sources. In particular, groundwater adjacent to landfills undergoes more serious adverse impacts than other pollution sources^{88, 89}, since landfill leachates generally have higher contamination levels and long-term impacts on the surrounding environment^{90, 91}. High PPCP contamination level was detected in the groundwater downgradient of some landfills, especially unlined landfills, even after their closure for a prolonged duration of many years^{25, 88, 89, 92}. Thus, landfills pose an alarming threat of PPCP contamination to the adjoining groundwater environment.

The occurrence of PPCPs previously reported in groundwater related to landfills is collated in Table S4 (from 1993 to 2018). A total of 48 PPCPs have been detected and 14 PPCPs, as reported in more than two papers, are illustrated in Figure 5. DEET and Ibuprofen were chosen as target compounds in six and five out of the sixteen papers, respectively, being the most frequently reported PPCPs. The concentrations of 48 PPCPs in groundwater near landfills

ranged between 0.24 ng/L (sulfadiazine)⁹³ and 10.44 mg/L (sulfanilic acid)²⁹ (Table S4). A study in Denmark reported a high concentration level of sulfonamides (10-1000 µg/L²⁹), which was largely related to the disposal of pharmaceutical wastes containing sulfonamides in the investigated MSW landfill. Propyphenazone and sulfadiazine exhibited the highest median concentrations (170 and 140 µg/L, respectively), followed by DEET (6.1 µg/L).

Figure 5. Number of reported times (a) and concentrations of selected PPCPs (b) in the groundwater adjacent to the landfills

The most frequently reported PPCPs did not show a high concentration level in the groundwater (Figure 5). For instance, Ibuprofen is one of the most frequently reported PPCPs, and it displayed a maximum concentration of less than 3.1 $\mu\text{g/L}$ ²⁸, which was much lower than that of many other PPCPs. By contrast, although some PPCPs were only investigated in a limited number of studies, they exhibited very severe contamination levels. Nicotine was only investigated in one study (therefore was not involved in Figure 5) but was detected at an extremely high concentration (960 $\mu\text{g/L}$)⁹⁴.

PPCPs showing high concentrations in the raw landfill leachate have greater opportunities to be detected in the nearby groundwater. Besides, PPCP properties (e.g., biodegradability, distribution coefficient) also influence their natural attenuation in the aquifers and their concentrations in the groundwater. For example, caffeine and acetaminophen were abundant in the raw landfill leachates but showed much lower contamination levels (130 and 380 ng/L , respectively) in the nearby groundwater than other PPCPs²⁸. These two PPCPs are recognized as biodegradable compounds, and their biodegradation in the subsurface environment was the primary cause of this phenomenon¹⁹. For other relatively persistent PPCPs, such as diclofenac, DEET, and propyphenazone, the severe contamination levels in the groundwater near the landfills were consistent with their high concentrations in landfill leachates. In addition, aquifer properties (e.g., permeability, redox condition, groundwater seepage velocity) also contribute to the different concentrations of PPCPs in the groundwater in various studies.

4.2 Geographic distribution

Figure S3 shows that PPCPs occurred at significantly higher concentrations in the groundwater near landfills in Europe than those in other regions. Fourteen PPCPs were reported at relatively high concentrations ($> 10 \mu\text{g/L}$) in the groundwater globally, and seven and four of them were found in Denmark and Germany, respectively. Besides, in these two countries, their concentration levels were much higher (maximum concentration higher than 100 $\mu\text{g/L}$) than those in other countries. Many investigated European landfills, including the ones in Denmark and Germany, were established in the 1980s or even earlier when the regulations on modern landfill design and management practices were lacking, and therefore they had no liner and leachate collection system. The infiltration of heavily contaminated leachates could seriously

imperil the quality of groundwater near these old landfills, leading to an extremely high level of PPCP contamination in the groundwater^{29, 94, 95}. In other regions, although the overall PPCP contamination levels in the groundwater near the landfill were lower than those in European countries, the contribution of landfills to the groundwater was still significant. Lu et al⁶⁸ observed that concentrations of some nonsteroidal anti-inflammatory drugs in landfill leachates and the groundwater downstream of the landfill in Taiwan were of the same order of magnitude, suggesting the infiltration of landfill leachate into the groundwater. Nevertheless, there are still other cases demonstrating that landfills did not have significant impacts on the nearby groundwater^{49, 96, 97}. Unfortunately, the potential reasons for these negligible impacts were not discussed. It remains unclear whether modern landfills have an adverse influence on the PPCP contamination in their ambient groundwater. Efforts should be made to conduct investigations in more landfills to draw a firm conclusion on the influence of landfills on PPCP contamination in the adjacent groundwater.

4.3 Risk assessment

Ecosystems and humans have been reported to suffer from the PPCP contamination for decades^{11, 98}. Several PPCPs have been found in biota⁹⁹, indicating the risk that they can trigger various unexpected impacts. In some areas, groundwater is used as a source of public water. Therefore, the PPCP residues in the groundwater in those areas should be highly concerning^{89, 100}. Environmental and human health risk assessments were therefore conducted based on the reported PPCP concentrations in the groundwater near the landfills in this section.

4.3.1 Environmental risk assessment

The environmental risk assessment was performed using the risk quotient (RQ), the ratio between the maximum measured PPCP concentrations (MECs) in the groundwater adjacent to the landfill and their corresponding predicted no effect concentrations (PNECs) (Table S5). The risk levels are defined according to the RQ value, with $RQ < 0.1$ indicating low risk, $0.1 < RQ < 1.0$ indicating medium risk and $RQ > 1.0$ indicating high risk¹⁰¹.

Figure 6 illustrates the RQ values for 36 out of 48 PPCPs included in our review, considering the availability of their PNECs. Nineteen compounds pose a high risk, and the top three PPCPs were diclofenac, DEET, and sulfadiazine. The highest risk for diclofenac ($RQ > 10000$) was

attributed to its relatively high measured concentration (1390 $\mu\text{g/L}$ ²⁷) and low PNEC value (36 ng/L, Table S5). The overall high environmental risks are also because the maximum concentrations of individual PPCPs in the groundwater globally were used to calculate the RQs as a worst-case scenario. Thus, for groundwater in specific areas, the risks caused by individual PPCPs should be lower. However, because the groundwater in most studied areas contained several types of PPCPs, the risks caused by the PPCP mixture should be much higher than that caused by a single compound¹⁰².

Figure 6. Environmental risk assessment of PPCPs detected in groundwater adjacent to the landfill

4.3.2 Human health risk assessment

To evaluate the risk of exposure to PPCPs, potential non-carcinogenic risk was quantified using hazard quotient (HQ), a ratio of chronic daily intake value (CDI) to reference dose (RfD) or acceptable daily intake (ADI) value¹⁰³. The detailed health risk assessment method was described in the supporting information. $HQ > 1$ indicates a chance that non-carcinogenic risk may occur; $HQ > 0.2$ indicates the requirement for further investigation¹⁰⁴. Totally, among the PPCPs investigated in the groundwater near the landfills, 21 of them could be considered as

candidates in human risk assessment due to the availability of ADI values (Table S6). Therefore, HQ was estimated for thirteen different study regions located in seven countries (Table S7). For each study area, we calculated the total non-carcinogenic risk as the sum of HQ (Σ HQ) of individual PPCPs to assess the overall potential for non-carcinogenic risks posed by all the detected PPCPs.

Figure 7. Human risk assessment of PPCPs detected in groundwater adjacent to the landfills (A to M represents different study areas, as shown in Table S7. A: in India ²⁷; B: in Denmark ²⁹; C: in Germany ¹⁰⁵; D: in Poland ¹⁰⁶; E: in Germany ⁹⁴; F: in China ⁶⁸; G: in USA ²⁸; H: in Spain ¹⁰⁷; I: in China ⁴⁹; J: in Poland ¹⁰⁸; K: in USA ²⁶; L: in USA ⁸⁹; M: in China ⁹³)

The results (Figure 7) showed that Σ HQs were in the range of 6.78×10^{-6} - 1.39 for different study areas. The highest Σ HQ was observed in India (Figure 7) because the investigated landfill was claimed to be un-segregated and unscientific, and a high level of diclofenac was detected in the nearby aquifers, making a great contribution to the high Σ HQ. Except that, Σ HQs in other study areas were lower than 0.2, indicating that there was no immediate health risk. These results demonstrated that PPCPs detected in groundwater impacted by landfill leachates posed a potential risk to human health in some areas. Besides, the calculated Σ HQs might be underestimated because only PPCPs were considered as candidates to generate Σ HQs. In the reality, much more contaminants, such as other endocrine disrupting chemicals and persistent organic pollutants, are contained in the groundwater near the landfills, and a higher Σ HQ could

be expected due to the combination of risk caused by PPCPs and other pollutants. Thus, even these groundwater sites that were heavily affected by nearby landfills were not directly used for drinking water, as a precaution, there still remains a need for comprehensive studies since PPCPs in groundwater may undergo migration and transport processes and ultimately find their way into the drinking water supply^{92, 100, 109}.

5. Recommendations for future research

Landfill leachates are one of the important sources of PPCPs in the environment. In this paper, the occurrence of PPCPs in landfill leachates, their removal performance by on-site full-scale treatment processes as well as their impacts on nearby groundwater were comprehensively reviewed. Expanding research efforts should be made in the following respects:

(1) The current state-of-knowledge on PPCPs in landfill leachates in different geographical regions showed striking discrepancies. The occurrence of PPCPs in landfill leachates in most countries except the United States lacks representativeness in terms of the time period (Europe) or spatial distribution (China) or are even missing. Thus, there is a great need to conduct more studies to gain a comprehensive understanding of PPCPs in landfill leachates worldwide.

(2) Knowledge of the PPCP metabolites in landfill leachates is very limited. Further investigations of PPCP metabolites in landfill leachate should be undertaken to fill the knowledge gap.

(3) PPCPs in landfill leachates are influenced by many factors, such as the physicochemical properties of PPCPs, climate conditions, and the characteristics of landfill sites. To date, the key influencing factors and their mechanisms have not been identified and elucidated. Therefore, more representative landfills and their leachate samples should be investigated with the purpose of identifying the key influencing factor based on big data analysis.

(4) Comparisons of PPCP removal performance by various leachate treatment process could not be firmly made because few target PPCPs in common could be found over the limited number of studies. Studies involving more types of PPCPs in different landfill leachate treatment processes should be conducted to explore the best available technologies to meet the current emission standards for landfill leachate and enhance the elimination of PPCPs simultaneously.

(5) Contradictory results have been obtained for the influence of landfills on PPCP contamination in nearby groundwater. Efforts should be made to investigate more landfills with different construction and management levels and to draw a firm conclusion.

(6) The environmental and health risks of PPCP mixtures, not only individual PPCPs, in the groundwater adjacent to landfills in specific regions, should be assessed to more accurately reflect the real situation.

(7) Management for unused or out-of-date PPCPs, such as launching a recycling program with incentives, should be encouraged to reduce PPCPs in the MSWs.

Acknowledgments

This work was partly supported by the National Natural Science Foundation of China (21777042, 21577033, 51408425), the Major Science and Technology Program for Water Pollution Control and Treatment in China (2017ZX07202006), the Fundamental Research Funds for the Central Universities and Beijing Key Laboratory for Emerging Organic Contaminants Control.

Supporting Information Available

This information is available free of charge via the Internet at <http://pubs.acs.org>.

Reference:

1. Ashfaq, M.; Li, Y.; Rehman, M. S. U.; Zubair, M.; Mustafa, G.; Nazar, M. F.; Yu, C. P.; Sun, Q., Occurrence, spatial variation and risk assessment of pharmaceuticals and personal care products in urban wastewater, canal surface water, and their sediments: A case study of Lahore, Pakistan. *Science of the Total Environment* **2019**, *688*, 653-663.
2. Bu, Q.; Wang, B.; Huang, J.; Deng, S.; Yu, G., Pharmaceuticals and personal care products in the aquatic environment in China: A review. *Journal of Hazardous Materials* **2013**, *262*, 189-211.
3. Junaid, M.; Wang, Y.; Hamid, N.; Deng, S.; Li, W.-G.; Pei, D.-S., Prioritizing selected PPCPs on the basis of environmental and toxicogenetic Concerns: A toxicity estimation to confirmation approach. *Journal of Hazardous Materials* **2019**, *380*: 120828.
4. Liu, J. L.; Wong, M. H., Pharmaceuticals and personal care products (PPCPs): A review on environmental contamination in China. *Environment International* **2013**, *59*, 208-224.
5. Mei, X.; Sui, Q.; Lyu, S.; Wang, D.; Zhao, W., Pharmaceuticals and personal care products in the urban river across the megacity Shanghai: Occurrence, source apportionment and a snapshot of influence of rainfall. *Journal of Hazardous Materials* **2018**, *359*, 429-436.
6. Zhao, W.; Guo, Y.; Lu, S.; Yan, P.; Sui, Q., Recent advances in pharmaceuticals and personal care products in the surface water and sediments in China. *Frontiers of Environmental Science & Engineering* **2016**, *10*, 29-40.
7. Noguera-Oviedo, K.; Aga, D. S., Lessons learned from more than two decades of research on emerging contaminants in the environment. *Journal of Hazardous Materials* **2016**, *316*, 242-251.
8. Meyer, M. F.; Powers, S. M.; Hampton, S. E., An evidence synthesis of pharmaceuticals and personal care products (PPCPs) in the environment: Imbalances among compounds, sewage treatment techniques, and ecosystem types. *Environmental Science & Technology* **2019**, *53*, 12961-12973.
9. Meffe, R.; de Bustamante, I., Emerging organic contaminants in surface water and groundwater: A first overview of the situation in Italy. *Science of the Total Environment* **2014**, *481*, 280-95.
10. Ebele, A. J.; Abou-Elwafa Abdallah, M.; Harrad, S., Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. *Emerging Contaminants* **2017**, *3*, 1-16.
11. Yang, Y.; Ok, Y. S.; Kim, K.-H.; Kwon, E. E.; Tsang, Y. F., Occurrences and removal of pharmaceuticals and personal care products (PPCPs) in drinking water and water/sewage treatment plants: A review. *Science of The Total Environment* **2017**, *596-597*, 303-320.
12. Mompelat, S.; Le Bot, B.; Thomas, O., Occurrence and fate of pharmaceutical products and by-

- products, from resource to drinking water. *Environment International* **2009**, 35, 803-814.
13. Bound, J. P.; Voulvoulis, N., Household disposal of pharmaceuticals as a pathway for aquatic contamination in the United Kingdom. *Environmental Health Perspectives* **2005**, 113, 1705-1711.
14. Daughton, C. G., Cradle-to-cradle stewardship of drugs for minimizing their environmental disposition while promoting human health. II. Drug disposal, waste reduction, and future directions. *Environmental Health Perspectives* **2003**, 111, 775-785.
15. Sasu, S.; Kummerer, K.; Kranert, M., Assessment of pharmaceutical waste management at selected hospitals and homes in Ghana. *Waste Management & Research* **2012**, 30, 625-630.
16. Slack, R. J.; Gronow, J. R.; Voulvoulis, N., Household hazardous waste in municipal landfills: Contaminants in leachate. *Science of the Total Environment* **2005**, 337, 119-137.
17. Musson, S. E.; Townsend, T. G., Pharmaceutical compound content of municipal solid waste. *Journal of Hazardous Materials* **2009**, 162, 730-735.
18. Song, L.; Li, L.; Yang, S.; Lan, J.; He, H.; McElmurry, S. P.; Zhao, Y., Sulfamethoxazole, tetracycline and oxytetracycline and related antibiotic resistance genes in a large-scale landfill, China. *Science of the Total Environment* **2016**, 551-552, 9-15.
19. Sui, Q.; Cao, X.; Lu, S.; Zhao, W.; Qiu, Z.; Yu, G., Occurrence, sources and fate of pharmaceuticals and personal care products in the groundwater: A review. *Emerging Contaminants* **2015**, 1, 14-24.
20. Clarke, B. O.; Anumol, T.; Barlaz, M.; Snyder, S. A., Investigating landfill leachate as a source of trace organic pollutants. *Chemosphere* **2015**, 127, 269-275.
21. Eggen, T.; Moeder, M.; Arukwe, A., Municipal landfill leachates: A significant source for new and emerging pollutants. *Science of the Total Environment* **2010**, 408, 5147-5157.
22. Merel, S.; Snyder, S. A., Critical assessment of the ubiquitous occurrence and fate of the insect repellent N,N-diethyl-m-toluamide in water. *Environment International* **2016**, 96, 98-117.
23. Luo, H.; Zeng, Y.; Cheng, Y.; He, D.; Pan, X., Recent advances in municipal landfill leachate: A review focusing on its characteristics, treatment, and toxicity assessment. *Science of the Total Environment* **2020**, 703, 135468.
24. FOEN, Gewässerqualität: Revision der Gewässerschutzverordnung.
<https://www.bafu.admin.ch/bafu/fr/home/themes/formation/communiqués.msg-id-59323.html> **2017**.
25. Andrews, W. J.; Masoner, J.; Cozzarelli, I. M., Emerging contaminants at a closed and an operating landfill in Oklahoma. *Ground Water Monitoring & Remediation* **2012**, 30, 120-130.

26. Barnes, K. K.; Christenson, S. C.; Kolpin, D. W.; Focazio, M. J.; Furlong, E. T.; Zaugg, S. D.; Meyer, M. T.; Barber, B. L., Pharmaceutical and other organic waste water contaminants within a leachate plume downgradient of a municipal landfill. *Ground Water Monitoring & Remediation* **2004**, *24*, 119-126.
27. Velpandian, T.; Halder, N.; Nath, M.; Das, U.; Moksha, L.; Gowtham, L.; Batta, S. P., Un-segregated waste disposal: An alarming threat of antimicrobials in surface and ground water sources in Delhi. *Environmental Science and Pollution Research* **2018**, *25*, 29518-29528.
28. Buszka, P. M.; Yeskis, D. J.; Kolpin, D. W.; Furlong, E. T.; Zaugg, S. D.; Meyer, M. T., Waste-indicator and pharmaceutical compounds in landfill-leachate-affected ground water near Elkhart, Indiana, 2000-2002. *Bulletin of Environmental Contamination and Toxicology* **2009**, *82*, 653-659.
29. Holm, J. V.; Rugge, K.; Bjerg, P. L.; Christensen, T. H., Occurrence and distribution of pharmaceutical organic compounds in the groundwater downgradient of a landfill (Grindsted, Denmark). *Environmental Science & Technology* **1995**, *29*, 1415-1420.
30. Qi, C.; Huang, J.; Wang, B.; Deng, S.; Wang, Y.; Yu, G., Contaminants of emerging concern in landfill leachate in China: A review. *Emerging Contaminants* **2018**, *4*, 1-10.
31. Van Boeckel, T. P.; Brower, C.; Gilbert, M.; Grenfell, B. T.; Levin, S. A.; Robinson, T. P.; Teillant, A.; Laxminarayan, R., Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences of the United States of America* **2015**, *112*, 5649-5654.
32. Larson, C., Pharmaceuticals China's lakes of pig manure spawn antibiotic resistance. *Science* **2015**, *347*.
33. Kuppusamy, S.; Kakarla, D.; Venkateswarlu, K.; Megharaj, M.; Yoon, Y.-E.; Lee, Y. B., Veterinary antibiotics (VAs) contamination as a global agro-ecological issue: A critical view. *Agriculture, Ecosystems and Environment* **2018**, *257*, 47-59.
34. Luo, Y.; Guo, W.; Ngo, H. H.; Nghiem, L. D.; Hai, F. I.; Zhang, J.; Liang, S.; Wang, X. C., A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Science of The Total Environment* **2014**, *473-474*, 619-641.
35. Van Doorslaer, X.; Dewulf, J.; Van Langenhove, H.; Demeestere, K., Fluoroquinolone antibiotics: An emerging class of environmental micropollutants. *Science of the Total Environment* **2014**, *500-501*, 250-269.
36. Cheng, D.; Ngo, H. H.; Guo, W.; Chang, S. W.; Nguyen, D. D.; Liu, Y.; Wei, Q.; Wei, D., A critical review on antibiotics and hormones in swine wastewater: Water pollution problems and control approaches. *Journal of Hazardous Materials* **2020**, *387*, 121682.
37. Zhang, M.; Liu, Y. S.; Zhao, J. L.; Liu, W. R.; He, L. Y.; Zhang, J. N.; Chen, J.; He, L. K.; Zhang,

- 646 Q. Q.; Ying, G. G., Occurrence, fate and mass loadings of antibiotics in two swine wastewater
647 treatment systems. *Science of the Total Environment* **2018**, 639, 1421-1431.
- 648 38. Bengtsson-Palme, J.; Larsson, D. G. J., Concentrations of antibiotics predicted to select for
649 resistant bacteria: Proposed limits for environmental regulation. *Environment International* **2016**, 86,
650 140-149.
- 651 39. Wu, D.; Huang, Z.; Yang, K.; Graham, D.; Xie, B., Relationships between antibiotics and
652 antibiotic resistance gene levels in municipal solid waste leachates in Shanghai, China.
653 *Environmental Science & Technology* **2015**, 49, 4122-4128.
- 654 40. Su, Y.; Wang, J.; Huang, Z.; Xie, B., On-site removal of antibiotics and antibiotic resistance
655 genes from leachate by aged refuse bioreactor: Effects of microbial community and operational
656 parameters. *Chemosphere* **2017**, 178, 486-495.
- 657 41. Masoner, J. R.; Kolpin, D. W.; Furlong, E. T.; Cozzarelli, I. M.; Gray, J. L., Contaminants of
658 emerging concern in fresh leachate from landfills in the conterminous United States. *Environmental*
659 *Science: Process & Impacts* **2014**, 16, 2335-2354.
- 660 42. Schwarzbauer, J.; Heim, S.; Krooss, B.; Littke, R., Analysis of undisturbed layers of a waste
661 deposit landfill – Insights into the transformation and transport of organic contaminants. *Organic*
662 *Geochemistry* **2006**, 37, 2026-2045.
- 663 43. Ratola, N.; Cincinelli, A.; Alves, A.; Katsoyiannis, A., Occurrence of organic microcontaminants in
664 the wastewater treatment process. A mini review. *Journal of Hazardous Materials* **2012**, 239, 1-18.
- 665 44. Tran, N. H.; Reinhard, M.; Gin, K. Y.-H., Occurrence and fate of emerging contaminants in
666 municipal wastewater treatment plants from different geographical regions - A review. *Water*
667 *Research* **2018**, 133, 182-207.
- 668 45. Sim, W. J.; Lee, J. W.; Lee, E. S.; Shin, S. K.; Hwang, S. R.; Oh, J. E., Occurrence and
669 distribution of pharmaceuticals in wastewater from households, livestock farms, hospitals and
670 pharmaceutical manufactures. *Chemosphere* **2011**, 82, 179-86.
- 671 46. Zhang, X. H.; Xu, Y. B.; He, X. L.; Huang, L.; Ling, J. Y.; Zheng, L.; Du, Q. P., Occurrence of
672 antibiotic resistance genes in landfill leachate treatment plant and its effluent-receiving soil and
673 surface water. *Environmental Pollution* **2016**, 218, 1255-1261.
- 674 47. Sui, Q.; Zhao, W.; Cao, X.; Lu, S.; Qiu, Z.; Gu, X.; Yu, G., Pharmaceuticals and personal care
675 products in the leachates from a typical landfill reservoir of municipal solid waste in Shanghai, China:
676 Occurrence and removal by a full-scale membrane bioreactor. *Journal of Hazardous Materials* **2017**,
677 323, 99-108.
- 678 48. Cheng, D. L.; Ngo, H. H.; Guo, W. S.; Liu, Y. W.; Zhou, J. L.; Chang, S. W.; Nguyen, D. D.; Bui, X.

- T.; Zhang, X. B., Bioprocessing for elimination antibiotics and hormones from swine wastewater. *Science of the Total Environment* **2018**, 621, 1664-1682.
49. Peng, X.; Ou, W.; Wang, C.; Wang, Z.; Huang, Q.; Jin, J.; Tan, J., Occurrence and ecological potential of pharmaceuticals and personal care products in groundwater and reservoirs in the vicinity of municipal landfills in China. *Science of the Total Environment* **2014**, 490, 889-898.
50. Tran, N. H.; Chen, H.; Reinhard, M.; Mao, F.; Gin, K. Y., Occurrence and removal of multiple classes of antibiotics and antimicrobial agents in biological wastewater treatment processes. *Water Research* **2016**, 104, 461-472.
51. Zhang, Q. Q.; Ying, G. G.; Pan, C. G.; Liu, Y. S.; Zhao, J. L., Comprehensive evaluation of antibiotics emission and fate in the river basins of China: Source analysis, multimedia modeling, and linkage to bacterial resistance. *Environmental Science & Technology* **2015**, 49, 6772-6782.
52. Tasho, R. P.; Cho, J. Y., Veterinary antibiotics in animal waste, its distribution in soil and uptake by plants: A review. *Science of the Total Environment* **2016**, 563-564, 366-376.
53. Matošić, M.; Terzić, S.; Jakopović, K. K.; Mijatović, I.; Ahel, M., Treatment of a landfill leachate containing compounds of pharmaceutical origin. *Water Science & Technology* **2008**, 58, 597-602.
54. Wilkinson, J.; Hooda, P. S.; Barker, J.; Barton, S.; Swinden, J., Occurrence, fate and transformation of emerging contaminants in water: An overarching review of the field. *Environmental Pollution* **2017**, 231, 954-970.
55. Yin, L.; Wang, B.; Yuan, H.; Deng, S.; Huang, J.; Wang, Y.; Yu, G., Pay special attention to the transformation products of PPCPs in environment. *Emerging Contaminants* **2017**, 3, 69-75.
56. Inam, E.; Offiong, N. A.; Kang, S.; Yang, P.; Essien, J., Assessment of the occurrence and risks of emerging organic pollutants (EOPs) in Ikpa river basin freshwater ecosystem, Niger Delta-Nigeria. *Bulletin of Environmental Contamination and Toxicology* **2015**, 95, 624-631.
57. Benbow, T. J.; Frew, R. D.; Hayman, A. R., Validation of a rapid and simple method for the preparation of aqueous organic compounds prior to compound specific isotope analysis. *Organic Geochemistry* **2008**, 39, 1690-1702.
58. Masoner, J. R.; Kolpin, D. W.; Furlong, E. T.; Cozzarelli, I. M.; Gray, J. L., Landfill leachate as a mirror of today's disposable society: Pharmaceuticals and other contaminants of emerging concern in final leachate from landfills in the conterminous United States. *Environmental Toxicology and Chemistry* **2016**, 35, 906-918.
59. Liu, H. Q.; Lam, J. C. W.; Li, W. W.; Yu, H. Q.; Lam, P. K. S., Spatial distribution and removal performance of pharmaceuticals in municipal wastewater treatment plants in China. *Science of the Total Environment* **2017**, 586, 1162-1169.

60. Wang, Z.; Zhang, X. H.; Huang, Y.; Wang, H., Comprehensive evaluation of pharmaceuticals and personal care products (PPCPs) in typical highly urbanized regions across China. *Environmental Pollution* **2015**, *204*, 223-232.
61. Chung, S. S.; Zheng, J. S.; Burket, S. R.; Brooks, B. W., Select antibiotics in leachate from closed and active landfills exceed thresholds for antibiotic resistance development. *Environment International* **2018**, *115*, 89-96.
62. You, X.; Wu, D.; Wei, H.; Xie, B.; Lu, J., Fluoroquinolones and beta-lactam antibiotics and antibiotic resistance genes in autumn leachates of seven major municipal solid waste landfills in China. *Environment International* **2018**, *113*, 162-169.
63. Merel, S.; Nikiforov, A. I.; Snyder, S. A., Potential analytical interferences and seasonal variability in diethyltoluamide environmental monitoring programs. *Chemosphere* **2015**, *127*, 238-245.
64. Aronson, D.; Weeks, J.; Meylan, B.; Guiney, P. D.; Howard, P. H., Environmental release, environmental concentrations, and ecological risk of N,N-Diethyl-m-toluamide (DEET). *Integrated Environmental Assessment and Management* **2012**, *8*, 135-166.
65. Li, Y.; Zhang, L.; Liu, X.; Ding, J., Ranking and prioritizing pharmaceuticals in the aquatic environment of China. *Science of the Total Environment* **2019**, *658*, 333-342.
66. Sui, Q.; Wang, B.; Zhao, W.; Huang, J.; Yu, G.; Deng, S.; Qiu, Z.; Lu, S., Identification of priority pharmaceuticals in the water environment of China. *Chemosphere* **2012**, *89*, 280-286.
67. Acuna, V.; Ginebreda, A.; Mor, J. R.; Petrovic, M.; Sabater, S.; Sumpter, J.; Barcelo, D., Balancing the health benefits and environmental risks of pharmaceuticals: Diclofenac as an example. *Environment International* **2015**, *85*, 327-333.
68. Lu, M.-C.; Chen, Y. Y.; Chiou, M.-R.; Chen, M. Y.; Fan, H.-J., Occurrence and treatment efficiency of pharmaceuticals in landfill leachates. *Waste Management* **2016**, *55*, 257-264.
69. Yi, X.; Tran, N. H.; Yin, T.; He, Y.; Gin, K., Removal of selected PPCPs, EDCs, and antibiotic resistance genes in landfill leachate by a full-scale constructed wetlands system. *Water Research* **2017**, *121*, 46-60.
70. Wu, D.; Huang, X.-H.; Sun, J.-Z.; Graham, D. W.; Xie, B., Antibiotic resistance genes and associated microbial community conditions in aging landfill systems. *Environmental Science & Technology* **2017**, *51*, 12859-12867.
71. Yu, Z.; He, P.; Shao, L.; Zhang, H.; Lu, F., Co-occurrence of mobile genetic elements and antibiotic resistance genes in municipal solid waste landfill leachates: A preliminary insight into the role of landfill age. *Water Research* **2016**, *106*, 583-592.

72. Ngo, H. H.; Guo, W.; Xing, W., Applied technologies in municipal solid waste landfill leachate treatment. *Waste Water Treatment Technologies* **2008**, *11*, 199.
73. Renou, S.; Givaudan, J. G.; Poulain, S.; Dirassouyan, F.; Moulin, P., Landfill leachate treatment: Review and opportunity. *Journal of Hazardous Materials* **2008**, *150*, 468-493.
74. Sui, Q.; Gebhardt, W.; Schroder, H. F.; Zhao, W.; Lu, S.; Yu, G., Identification of new oxidation products of bezafibrate for better understanding of its toxicity evolution and oxidation mechanisms during ozonation. *Environmental Science & Technology* **2017**, *51*, 2262-2270.
75. Sui, Q.; Huang, J.; Deng, S.; Yu, G.; Fan, Q., Occurrence and removal of pharmaceuticals, caffeine and DEET in wastewater treatment plants of Beijing, China. *Water Research* **2010**, *44*, 417-426.
76. Sui, Q.; Huang, J.; Deng, S.; Chen, W.; Yu, G., Seasonal variation in the occurrence and removal of pharmaceuticals and personal care products in different biological wastewater treatment processes. *Environmental Science & Technology* **2011**, *45*, 3341-3348.
77. Blair, B.; Nikolaus, A.; Hedman, C.; Klaper, R.; Grundl, T., Evaluating the degradation, sorption, and negative mass balances of pharmaceuticals and personal care products during wastewater treatment. *Chemosphere* **2015**, *134*, 395-401.
78. Papageorgiou, M.; Kosma, C.; Lambropoulou, D., Seasonal occurrence, removal, mass loading and environmental risk assessment of 55 pharmaceuticals and personal care products in a municipal wastewater treatment plant in Central Greece. *Science of the Total Environment* **2016**, *543*, 547-569.
79. Li, W. L.; Zhang, Z. F.; Ma, W. L.; Liu, L. Y.; Song, W. W.; Li, Y. F., An evaluation on the intra-day dynamics, seasonal variations and removal of selected pharmaceuticals and personal care products from urban wastewater treatment plants. *Science of the Total Environment* **2018**, *640-641*, 1139-1147.
80. Sun, Q.; Li, M.; Ma, C.; Chen, X.; Xie, X.; Yu, C. P., 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* **2016**, *208*, 371-381.
81. Jia, A.; Wan, Y.; Xiao, Y.; Hu, J., Occurrence and fate of quinolone and fluoroquinolone antibiotics in a municipal sewage treatment plant. *Water Research* **2012**, *46*, 387-394.
82. Zhang, X.; Jing, R.; Feng, X.; Dai, Y.; Tao, R.; Vymazal, J.; Cai, N.; Yang, Y., Removal of acidic pharmaceuticals by small-scale constructed wetlands using different design configurations. *Science of The Total Environment* **2018**, *639*, 640-647.
83. Zhang, D.; Gersberg, R. M.; Ng, W. J.; Tan, S. K., Removal of pharmaceuticals and personal care products in aquatic plant-based systems: A review. *Environmental Pollution* **2014**, *184*, 620-639.

- 776 84. Cao, X.; Sui, Q.; Lyu, S.; Zhao, W.; Guo, Y.; Qiu, Z.; Gu, X.; Yu, G., Occurrence and removal of
777 pharmaceuticals and personal care products in leachates from a landfill site of municipal solid waste.
778 *China Environmental Science* **2016**, *36*, 2027-2034 (in Chinese).
- 779 85. Xiao, K.; Liang, S.; Wang, X.; Chen, C.; Huang, X., Current state and challenges of full-scale
780 membrane bioreactor applications: A critical review. *Bioresource Technology* **2019**, *271*, 473-481.
- 781 86. Zhao, W.; Sui, Q.; Mei, X.; Cheng, X., Efficient elimination of sulfonamides by an
782 anaerobic/anoxic/oxic-membrane bioreactor process: Performance and influence of redox condition.
783 *Science of the Total Environment* **2018**, *633*, 668-676.
- 784 87. Patel, M.; Kumar, R.; Kishor, K.; Mlsna, T.; Pittman, C. U., Jr.; Mohan, D., Pharmaceuticals of
785 emerging concern in aquatic systems: Chemistry, occurrence, effects, and removal methods.
786 *Chemical Reviews* **2019**, *119*, 3510-3673.
- 787 88. Lapworth, D. J.; Baran, N.; Stuart, M. E.; Ward, R. S., Emerging organic contaminants in
788 groundwater: A review of sources, fate and occurrence. *Environmental Pollution* **2012**, *163*, 287-303.
- 789 89. Erickson, M. L.; Langer, S. K.; Roth, J. L.; Kroening, S. E., Contaminants of Emerging Concern in
790 Ambient Groundwater in Urbanized Areas of Minnesota, 2009–12 (ver. 1.2, September 2014): U.S.
791 Geological Survey Scientific Investigations Report 2014–5096, 38 p., with appendix,
792 <http://dx.doi.org/10.3133/sir>. **2014**.
- 793 90. Gao, J.; Oloibiri, V.; Chys, M.; Audenaert, W.; Decostere, B.; He, Y.; Van Langenhove, H.;
794 Demeestere, K.; Van Hulle, S. W. H., The present status of landfill leachate treatment and its
795 development trend from a technological point of view. *Reviews in Environmental Science and*
796 *Bio/Technology* **2015**, *14*, 93-122.
- 797 91. Xu, Y.; Xue, X.; Dong, L.; Nai, C.; Liu, Y.; Huang, Q., Long-term dynamics of leachate production,
798 leakage from hazardous waste landfill sites and the impact on groundwater quality and human health.
799 *Waste Management* **2018**, *82*, 156-166.
- 800 92. Barnes, K. K.; Kolpin, D. W.; Furlong, E. T.; Zaugg, S. D.; Meyer, M. T.; Barber, L. B., A national
801 reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States -
802 I) Groundwater. *Science of the Total Environment* **2008**, *402*, 192-200.
- 803 93. Dai, G.; Xu, H.; Yang, Q., Pollution characteristics of antibiotics in water source of the
804 surrounding of health garbage's landfill, Bijie. *Environmental Science & Technology (China)* **2015**, *38*,
805 263-268 (in Chinese).
- 806 94. Schwarzbauer, J.; Heim, S.; Brinker, S.; Littke, R., Occurrence and alteration of organic
807 contaminants in seepage and leakage water from a waste deposit landfill. *Water Research* **2002**, *36*,
808 2275-2287.

95. Ahel, M.; Jeličić, I., Phenazone analgesics in soil and groundwater below a municipal solid waste landfill. In: Daughton, C.G., Jones-Lepp, T. (eds.), *Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues. Symposium Series, American Chemical Society, Washington DC 2001*, 791, 100-115.
96. Peng, X.; Wang, C.; Zhang, K.; Wang, Z.; Huang, Q.; Yu, Y.; Ou, W., Profile and behavior of antiviral drugs in aquatic environments of the Pearl River Delta, China. *Science of the Total Environment* **2014**, 466-467, 755-761.
97. Yu, X.; Sui, Q.; Lyu, S.; Zhao, W.; Cao, X.; Wang, J.; Yu, G., Do high levels of PPCPs in landfill leachates influence the water environment in the vicinity of landfills? A case study of the largest landfill in China. *Environment International* **2020**, 135, 105404.
98. Verlicchi, P.; Al Aukidy, M.; Zambello, E., Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after a secondary treatment - A review. *Science of the Total Environment* **2012**, 429, 123-155.
99. Xie, H.; Hao, H.; Xu, N.; Liang, X.; Gao, D.; Xu, Y.; Gao, Y.; Tao, H.; Wong, M., Pharmaceuticals and personal care products in water, sediments, aquatic organisms, and fish feeds in the Pearl River Delta: Occurrence, distribution, potential sources, and health risk assessment. *Science of the Total Environment* **2019**, 659, 230-239.
100. Focazio, M. J.; Kolpin, D. W.; Barnes, K. K.; Furlong, E. T.; Meyer, M. T.; Zaugg, S. D.; Barber, L. B.; Thurman, M. E., A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States - II) Untreated drinking water sources. *Science of the Total Environment* **2008**, 402, 201-216.
101. Hernando, M. D.; Mezcua, M.; Fernandez-Alba, A. R.; Barcelo, D., Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. *Talanta* **2006**, 69, 334-342.
102. Kortenkamp, A.; Faust, M.; Scholze, M.; Backhaus, T., Low-level exposure to multiple chemicals: Reason for human health concerns? *Environmental Health Perspectives* **2007**, 115 Supplement 1, 106-114.
103. USEPA, Risk Assessment Guidance for Superfund, vol I. Human Health Evaluation Manual (Part A). *Office of Emergency and Remedial Response U.S. Environmental Protection Agency Washington, D.C. 20450*. https://www.epa.gov/sites/production/files/2015-09/documents/rags_a.pdf **1989**.
104. Ma, X. Y.; Li, Q.; Wang, X. C.; Wang, Y.; Wang, D.; Ngo, H. H., Micropollutants removal and health risk reduction in a water reclamation and ecological reuse system. *Water Research* **2018**, 138, 272-281.

105. Metzger, J. W., Drugs in municipal landfills and landfill leachates. In: Kümmerer K. (eds) Pharmaceuticals in the Environment. Springer, Berlin, Heidelberg. **2004**.
106. Kapelewska, J.; Kotowska, U.; Karpińska, J.; Kowalczyk, D.; Arciszewska, A.; Świrydo, A., Occurrence, removal, mass loading and environmental risk assessment of emerging organic contaminants in leachates, groundwaters and wastewaters. *Microchemical Journal* **2018**, *137*, 292-301.
107. Rodriguez-Navas, C.; Bjorklund, E.; Bak, S. A.; Hansen, M.; Krogh, K. A.; Maya, F.; Forteza, R.; Cerda, V. c., Pollution pathways of pharmaceutical residues in the aquatic environment on the island of Mallorca, Spain. *Archives of Environmental Contamination and Toxicology* **2013**, *65*, 56-66.
108. Kapelewska, J.; Kotowska, U.; Wisniewska, K., Determination of personal care products and hormones in leachate and groundwater from Polish MSW landfills by ultrasound-assisted emulsification microextraction and GC-MS. *Environmental Science and Pollution Research* **2016**, *23*, 1642-1652.
109. Schaidler, L. A.; Ackerman, J. M.; Rudel, R. A., Septic systems as sources of organic wastewater compounds in domestic drinking water wells in a shallow sand and gravel aquifer. *Science of the Total Environment* **2016**, *547*, 470-481.