Adsorption of a diverse range of pharmaceuticals to polyethylene microplastics in wastewater and their desorption in environmental matrices.

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Adsorption of a diverse range of pharmaceuticals to polyethylene microplastics in wastewater and their desorption in environmental matrices

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Abstract

It is proposed that microplastics discharged from wastewater treatment plants act as a vector of pharmaceuticals. In this study, adsorption of pharmaceuticals to polyethylene microplastics was investigated in municipal wastewater. Pharmaceuticals for study were selected to represent different speciation (anionic, cationic, and neutral) and a range of pH dependant octanol-water distribution coefficients (log D_{OW}). Findings revealed adsorption favoured those in cationic form with the greatest hydrophobicity (e.g., fluoxetine log D_{OW} 2.0 at pH 7.8). Adsorption of anionic pharmaceuticals was restricted due to repulsion with the microplastic's negatively charged surface. Only atorvastatin had any appreciable adsorption due to its comparatively high log D_{OW} value (2.9). Those pharmaceuticals predominantly in neutral form (carbamazepine and ketamine) with log D_{OW} values ≥2.4 had similar adsorption. Freundlich K_F values were 3400, 386, 284, 259 and 218 (mg kg^{-1})(mg L^{-1})$^{1/n}$ for fluoxetine, propranolol, atorvastatin, ketamine, and carbamazepine, respectively. All pharmaceuticals with log D_{OW} values <1.0 (atenolol, gliclazide, bezafibrate, and ifosfamide) did not adsorb to microplastics, irrespective of their speciation. Changing composition of wastewater (pH, dilution with stormwater and NaCl addition) within the range expected for municipal wastewater had limited influence on adsorption. Pharmaceutical desorption from microplastics was assessed in river water and simulated gastric and intestinal fluids. Solution pH was considered the most important factor for pharmaceutical desorption, influencing both pharmaceutical speciation and microplastic surface charge. Greatest desorption was observed for the cationic pharmaceuticals in gastric fluids due to a reduced surface charge of the microplastics under low pH conditions. Up to 50 % desorption of fluoxetine occurred in gastric fluid at 37 °C. These findings show that pharmaceuticals adsorbed to microplastics are 'bioavailable'. However,

this is often overlooked as an exposure route to aquatic organisms because water samples are normally pre-filtered prior to chemical analysis.

Keywords: water pollution; emerging contaminant; drug; sewage; microplastic; sorption

1. Introduction

Microplastics are plastic pieces smaller than 5 mm in all dimensions and those smaller than 1,000 nm are termed nanoplastics (Gigault et al., 2018; Guo et al., 2019). Microplastics are ubiquitous in the environment and can be present in the form they were manufactured (i.e., primary microplastics) or from the breakdown of larger plastics (i.e., secondary microplastics) (Issac and Kandasubramanian, 2021). A common pathway for microplastics to enter the environment is the discharge of treated effluents from wastewater treatment plants (WTPs) or combined sewer overflows (CSOs) following heavy rainfall (Sun et al., 2019; Polanco et al., 2020). The most common polymer types of microplastics found in wastewater include polyethylene, polyamide, and polyethylene terephthalate (Sun et al., 2019). Treated effluents contain up to 447 particles L^{-1} whilst untreated wastewater can contain up to >10,000 particles L^{-1} (particles retained on a 10 μm steel filter) (Simon et al., 2018).

Research has found that other pollutants including persistent organic pollutants, pharmaceuticals, pesticides, and personal care product ingredients can adsorb to the surface of microplastics (Wu et al., 2016; Zhao et al., 2020; Mo et al., 2021). There are concerns that the refractory nature of microplastics will result in the transport of these adsorbed pollutants for considerable distances from their source. Furthermore, organisms can ingest microplastics resulting in their exposure to the adsorbed pollutants. Microplastics have been found in the gastrointestinal tract or tissues of a variety of organisms including birds, fish, macroinvertebrate, marine turtles, and seals (Duncan et al., 2019; Windsor et al., 2019; Zhu et al., 2019; Wang et al., 2021; Weitzel et al., 2021).

Pharmaceuticals also enter the environment in wastewater and CSO discharges, with more than 200 individual pharmaceuticals previously detected in the environment (Hughes et al., 2013). Little research has been undertaken on the adsorption of pharmaceuticals to microplastics in wastewater despite this being a pathway for both pollutant types entering the environment. Wastewater is a heterogeneous

matrix containing comparatively high concentrations of other dissolved organic species. Previous research has shown that other dissolved organics (e.g., humic acid) can enhance or reduce pharmaceutical adsorption to microplastics (Xu et al., 2018a; Zhang et al., 2018). Other properties of wastewater that vary (and can influence pharmaceutical adsorption) are pH, salinity, and temperature (Elizalde-Velázquez et al., 2020; Lin et al., 2020; Puckowski et al., 2021).

Microplastics are typically negatively charged at the pH of municipal wastewater and electrostatic interactions are important for understanding the adsorption of charged species to their surface (Tourinho et al., 2019). Previous research found that cationic pharmaceuticals that are more hydrophobic in nature adsorb to polyamide microplastics in wastewater under a range of conditions (Wagstaff et al., 2021). However, pharmaceuticals are a diverse group of pollutants encompassing a broad range of physicochemical properties. Research conducted in simple solutions (e.g., 0.01 M calcium chloride – $CaCl_2$) have found that anti-inflammatories present in anionic form have little interaction with microplastics at pH 6.9 (Elizalde-Velázquez et al., 2020). It has been concluded that the negative charge of microplastics results in charge repulsion with the similarly charged pharmaceuticals. Further studies have found that other anionic pharmaceuticals such as atorvastatin adsorb to microplastics (Liu et al., 2020a), possibly due to its higher octanol-water partition coefficient. The pH dependent octanol-water partition coefficient (log D_{ow}) which accounts for hydrophobicity and speciation has been used to indicate the likely environmental fate of pharmaceuticals (Zhang et al., 2012; Li et al., 2019). However, there is a lack of studies which investigate the adsorption of a range of pharmaceuticals (cationic, anionic, and neutral species) to microplastics under the same experimental conditions.

It is also important to consider the desorption of pharmaceuticals from microplastics in the variety of environments they can enter. This is essential for those ionisable pharmaceuticals because the gastrointestinal tract of exposed organisms has a range of pH environments. Other than pharmaceutical speciation, the surface charge of microplastics change with pH (Xu et al., 2018b). It has been proposed that changes to microplastic charge under low pH conditions of gastric fluids resulted in the release of cationic pharmaceuticals from their surface (Wagstaff et al., 2021). However, only a few studies have investigated the desorption of pharmaceuticals from microplastics under gastric or intestinal conditions

(Razanajatovo et al., 2018; Lin et al., 2020; Liu et al., 2020b). Further studies are now needed on pharmaceuticals representing a range of properties to better understand their desorption from microplastics in various environments.

The aim of this study was to investigate how a diverse range of pharmaceuticals interact with microplastics in wastewater and to what extent they desorb in different environments. The objectives of the study were to *(i)* investigate the adsorption of cationic, anionic, and neutral pharmaceuticals, with a range of log D_{OW} values, to polyethylene microplastics in wastewater, *(ii)* determine the influence of pH, salinity, stormwater dilution and temperature on their adsorption, and *(iii)* evaluate the desorption of adsorbed pharmaceuticals in river water, gastric fluid, and intestinal fluid conditions. Polyethylene microplastics were selected for study due to their prevalence in wastewater (Sun et al., 2019). The cationic drugs atenolol, propranolol and fluoxetine, the anionic drugs gliclazide, bezafibrate and atorvastatin, and the non-ionised drugs ifosfamide, carbamazepine and ketamine in wastewater (pH 7.8) were investigated (Figure 1, Table S1). These pharmaceuticals represent a range of log D_{OW} values and are often found in municipal wastewater (Petrie et al., 2016).

2. Materials and methods

2.1. Materials

Pharmaceutical reference standards of atenolol, atorvastatin calcium trihydrate, bezafibrate, carbamazepine, codeine (as internal standard), fluoxetine hydrochloride, gliclazide, ifosfamide, ketamine hydrochloride and propranolol hydrochloride were purchased from Sigma Aldrich (Gillingham, UK). Sodium azide (NaN_3), sodium chloride (NaCl), sodium taurocholate (98 %), bovine serum albumin (>98 %) and pepsin A (≥500 U mg^{-1}) were also obtained from Sigma Aldrich. Methanol, ammonium formate and formic acid of high-performance liquid chromatography (HPLC) grade as well as GF/F glass fibre filter papers, 4 mm PVDF 0.45 µm syringe filters, hydrochloric acid (HCl) and sodium hydroxide (NaOH) were obtained from Fisher Scientific (Loughborough, UK). Ultrapure water was 18.2 MΩ cm^{-1} quality. Ultra-high molecular weight polyethylene microplastics (mean size 150 µm) were purchased from Goodfellow Cambridge Limited (Huntingdon, UK; Table 1). Municipal wastewater (50 L) was collected from a septic tank in North-East Scotland during May 2021 and frozen

107 at -20 °C. The wastewater did not contain detectable levels of any of the studied pharmaceuticals.
108 Stormwater (road runoff, 5 L) and river water (5 L) was also collected and frozen at -20 °C.

109 **2.2. Adsorption experiments**

110 Wastewater was defrosted overnight, filtered through GF/F filters and 0.2 g L^{-1} sodium azide added to
111 limit microbial activity. Wastewater volumes of 20 mL had 10 mg of polyethylene microplastic (0.5 g
112 L^{-1}) added in 20 mL borosilicate bottles with screw top caps lined with aluminium. These were kept in
113 the dark at 20 °C and mixed using a flask shaker (Cole-Palmer, Staffordshire, UK) at 500 oscillations
114 (osc) min^{-1}. A pharmaceutical concentration of 0.5 mg L^{-1} was used to establish uptake kinetics and
115 equilibrium time. Samples were collected at 0, 0.5, 1, 2, 3, 4, 6 and 24 hours. The uptake kinetics were
116 fitted using the pseudo-second order model (eq. 1):

117 $$\frac{t}{q_e} = \frac{1}{K_2 q_e^2} + \frac{1}{q_e} t \quad (1)$$

118 q_e (mg kg^{-1}) is the adsorbed pharmaceutical concentration, t (hours) is the mixing time and K_2 (kg mg^{-1}
119 h^{-1}) is the equilibrium rate constant.

120 Pharmaceutical concentrations of 0.1, 0.2, 0.3, 0.4, 0.5, 0.75, 1 and 2 mg L^{-1} in wastewater were used
121 to determine adsorption isotherms. The linear (eq. 2), Freundlich (eq. 3) and Langmuir isotherms (eq.
122 4) were used to model the data:

123 $$q_e = K_d C_e \quad (2)$$

124 $$q_e = K_F {C_e}^{1/n} \quad (3)$$

125 $$q_e = \frac{q_{max} K_L C_e}{1 + K_L C_e} \quad (4)$$

126 C_e (mg L^{-1}) is the remaining pharmaceutical concentrations in wastewater, K_d (L kg^{-1}) is the distribution
127 coefficient between the microplastic and wastewater, K_F [(mg kg^{-1})(mg L^{-1})$^{1/n}$] and n are the Freundlich
128 constants. Q_{max} (mg kg^{-1}) is the estimated maximum adsorption capacity and K_L (L mg^{-1}) is the Langmuir
129 constant.

Pharmaceutical adsorption was investigated at pH 3, 6, 7, 8 and 11. To investigate the influence of stormwater dilution on pharmaceutical adsorption varying compositions of wastewater:stormwater (100:0, 75:25, 50:50, 25:75 and 0:100) were prepared. Salinities of 0, 2.5, 5, 7.5 and 10 g L^{-1} NaCl in 50:50 wastewater:stormwater were also investigated. To assess the influence of temperature on pharmaceutical adsorption, experiments were conducted in wastewater at 5 °C and 20 °C. All samples were collected following 6 hours of mixing. Equivalent experiments without microplastic were utilised to evaluate any pharmaceutical losses to glassware for all experiments. All experiments were performed in triplicate. Samples were passed through 0.45 µm PVDF filters and spiked with 1 mg L^{-1} of the appropriate internal standard and analysed within 24 hours (see Table S2, Wagstaff et al., 2021).

2.3. Desorption experiments

Adsorption of pharmaceuticals at 2 mg L^{-1} was undertaken to ensure adequate adsorbed concentrations for desorption studies. Following adsorption, samples were filtered through GF/F filters and the retained microplastics transferred to a flask containing 20 mL desorption medium. The desorption media investigated were filtered river water (20 °C), simulated intestinal fluids (20 °C and 37 °C) and simulated gastric fluids (20 °C and 37 °C). Intestinal fluids and gastric fluids were prepared as described in Lui et al (2020). Intestinal fluid comprised of 5 g L^{-1} bovine serum albumin and 10 mM sodium taurocholate in 100 mM NaCl (pH 7) and gastric fluid 3.2 g L^{-1} pepsin A in 100 mM NaCl (pH 2) (Liu et al., 2020). Samples were prepared in triplicate and collected at 1, 2, 3, 4 and 24 hours. They were prepared for analysis as described in Section 2.2.

2.4. Analytical methods

Analysis was performed with an Agilent 1260 Infinity Series HPLC coupled to a 6420 triple quadrupole mass spectrometer. Separation was performed on a 100 x 2.1 mm Kinetex 5 µm C18 column (Phenomenex, Cheshire, UK) using a gradient elution at 0.3 mL min^{-1} of water and methanol, with both containing 10 mM ammonium formate and 0.1 % formic acid (see Table S3 for details). The column temperature was 25 °C and the injection volume was 2 µL. All samples were analysed against a calibration curve prepared in wastewater ranging from 0.01 to 2.5 mg L^{-1}, with 1 mg L^{-1} internal standard. Preparing the calibration curve in matrix compensated for any matrix effects. Details of MRM

transitions are outlined (Table S2). Wastewater spiked with known concentrations of pharmaceuticals were used as quality control samples. Procedural blanks (non-spiked wastewater) were also prepared and analysed. Zeta potential measurements were made using a Zetasizer Nano ZS (Malvern Panalytical, Malvern, UK).

2.5. Statistical analysis

The effect of pH, dilution of wastewater with stormwater, and NaCl addition on pharmaceutical adsorption to polyethylene microplastics were analysed using one-way ANOVA followed by Tukey's multiple comparison tests. The effect of temperature was analysed by unpaired t-tests followed by Welch's correction. Differences in desorption at different exposure times was assessed by one-way ANOVA. The statistical analysis was performed using Prism v.9.0.1 (GraphPad Software, USA). A *p*-value of <0.05 was considered significant.

3. Results and discussion

3.1. Adsorption of pharmaceuticals to polyethylene microplastics in wastewater

The adsorption of pharmaceuticals to polyethylene microplastics was assessed during 24 hours of mixing. A flask shaker was used to ensure complete mixing of the polyethylene microplastic in wastewater. The common approach of mixing microplastics (including polyethylene) in water for adsorption studies is to use an orbital or reciprocal shaker (e.g., see Razanajatovo et al., 2018; Xu et al., 2018b; Elizalde-Velázquez et al., 2020). However, it was found that the polyethylene floated, with half of its surface not exposed to the wastewater, irrespective of mixing speed or the length of time mixing took place. Therefore, more vigorous shaking was achieved using a flask shaker at 500 osc min^{-1}. This ensured adequate mixing to replicate the turbulent nature of wastewater as it is transported through pipes and sewers to the WTP.

Five of the studied pharmaceuticals had sufficient adsorption such that a measurable difference was possible between the wastewater which did not have microplastic added (control), and the wastewater with microplastics removed by filtration following mixing. These were propranolol, fluoxetine, atorvastatin, carbamazepine, and ketamine. Fluoxetine had the greatest adsorption (~ 360 mg kg^{-1}),

followed by propranolol (~ 190 mg kg^{-1}) and then atorvastatin, carbamazepine, and ketamine (all ~70-80 mg kg^{-1}). Their adsorption fitted the pseudo-second order kinetic model with coefficient of determination (r^2) values ≥0.997 (Table 2). As can be observed in Figure 2 and Table 2, both the calculated and experimental values of q_e compare well. Previous research has found that the adsorption of pharmaceuticals to polyethylene microplastics fits the pseudo-second order model (Razanajatovo et al., 2018; Xu et al., 2018b). The remaining pharmaceuticals atenolol, gliclazide, bezafibrate and ifosfamide had no appreciable adsorption to the polyethylene microplastics. Adsorption equilibrium for all pharmaceuticals was achieved within the first few hours of mixing (Figure 2). Therefore, for future studies all samples were collected following 6 hours mixing to ensure equilibrium was reached. Typical sewer residence times of wastewater during dry weather conditions are up to 24 hours (Petrie et al., 2019).

The equilibrium time was comparatively faster than the previous study with polyamide microplastics in wastewater despite studying some of the same pharmaceuticals (e.g., propranolol and fluoxetine) (Wagstaff et al., 2021). However, this is due to using a higher pharmaceutical to microplastic ratio in the present study which results in faster equilibration (Atugoda et al., 2021). The microplastic concentration in wastewater was 0.5 g L^{-1} instead of 2.5 g L^{-1} used previously (Wagstaff et al., 2021). Short adsorption equilibration times have also been found for ciprofloxacin (3 hours) and triclosan (0.5 hours) to polyethylene microplastics (Atugoda et al., 2020; Chen et al., 2021).

The data fitted to the linear isotherm across the pharmaceutical concentration range studied (0.1-2 mg L^{-1}) with r^2 values ranging from 0.800 for carbamazepine to 0.998 for fluoxetine (Table 2). The determined partition coefficients (K_d) values were 440, 3350, 227, 182 and 216 L kg^{-1} for propranolol, fluoxetine, atorvastatin, carbamazepine, and ketamine, respectively. The adsorption data was also fitted to the Freundlich and Langmuir isotherms with r^2 values in the range 0.821-0.997 (Table 2, Figure S1). The pharmaceuticals had similar or greater r^2 values when fitted to the Freundlich isotherm compared to the Langmuir isotherm (Table 2). Fitting to the Freundlich isotherm indicates heterogeneous multilayer adsorption to the polyethylene surface (Guo et al., 2019). The Freundlich isotherm has been

used numerous times to model the adsorption of pharmaceuticals to microplastics (Razanajatovo et al., 2018; Zhang et al., 2018; Guo et al., 2019).

The pharmaceuticals studied were selected to represent a range of speciation (positively charged, negatively charged and non-ionised or neutral form) and log D_{OW} values at the pH of the studied wastewater. It should be noted that at pH 7.8 ketamine was present in both non-ionised (81 %) and cationic form (19 %) while all other drugs were present as a single species (≥99 %) (Figure 1). The adsorption of pharmaceuticals to polyethylene microplastics followed fluoxetine > propranolol > atorvastatin > ketamine > carbamazepine (Table 2). Adsorption favoured those in cationic form (e.g., fluoxetine and propranolol). This is unsurprising considering polyethylene holds a negative surface charge at pH 7.8 (Table 1). Several studies report that electrostatic interactions are important for the adsorption of pharmaceuticals to microplastics (Seidensticker et al., 2018; Tourinho et al., 2019; Puckowski et al., 2021). However, despite being positively charged in wastewater no appreciable adsorption of atenolol occurred. Atenolol has a low log D_{OW} value (-1.7) compared to fluoxetine (2.0) and propranolol (1.8) at pH 7.8 demonstrating that charge alone cannot be used to describe their adsorption to polyethylene microplastics, and hydrophobicity is also important for cationic pharmaceuticals. Hydrophobic interactions are the attraction of non-polar or slightly polar molecules to the non-polar microplastic surface (Tourinho et al., 2019). Polyethylene is considered non-polar due to the C-C and C-H bonds of the repeating monomer (Table 1).

There was no adsorption of the anionic pharmaceuticals gliclazide (log D_{OW} -1.1) and bezafibrate (log D_{OW} 0.0) due to charge repulsion with the microplastic and their low hydrophobicity. On the other hand, the negative charge of atorvastatin was compensated for by its greater hydrophobicity (log D_{OW} 2.9). However, atorvastatin adsorption was significantly lower than both propranolol and fluoxetine despite its higher log D_{OW} value (Table 2). Both ketamine (log D_{OW} 3.0) and carbamazepine (log D_{OW} 2.4) also had substantially lower adsorption than fluoxetine and propranolol, but similar adsorption (and log D_{OW} values) to atorvastatin. Whereas ifosfamide had a log D_{OW} value of 0.9 but no appreciable adsorption. Puckowski et al (2021) previously showed greater adsorption of propranolol over anionic and neutral pharmaceuticals with similar log D_{OW} values. Therefore, pharmaceutical speciation is essential for

236 understanding their adsorption to polyethylene microplastics, but this needs consideration with their
237 hydrophobicity.

238 ### 3.2. Influence of wastewater characteristics to pharmaceutical adsorption

239 The influence of pH, stormwater dilution, NaCl addition and temperature on pharmaceutical adsorption
240 to polyethylene microplastics in wastewater was investigated. Adsorption was studied at pH 3, 6, 7, 8
241 and 11 to encompass typical wastewater pH values (6-8) and acidic and basic conditions (pH 3 and 11)
242 to better understand the dominant adsorption interactions. Propranolol and fluoxetine showed a similar
243 trend whereby greatest adsorption occurred at pH 7 and 8 (Figure 3). Reduced adsorption was observed
244 at pH 3 despite both pharmaceuticals still being in the cationic form (Figure 1). At pH 3 the microplastic
245 had reduced surface charge as demonstrated by the zeta potential measurements (Table 1), resulting in
246 reduced interactions with these pharmaceuticals. These results agree with previous studies on
247 propranolol (Puckowski et al., 2021; Wagstaff et al., 2021) and fluoxetine (Wagstaff et al., 2021).
248 However, at pH 11 their adsorption was lower in comparison to pH 7 and 8 (Figure 3). At pH 11
249 propranolol and fluoxetine are present in non-ionised form demonstrating the significance of charged
250 interactions on the adsorption of these drugs to the polyethylene surface. Interestingly, previous
251 research found augmented adsorption of propranolol to polyamide in wastewater at pH 11 (Wagstaff et
252 al., 2021), and to polyethylene in 0.01 M $CaCl_2$ at pH 12 (Puckowski et al., 2021). This suggests that
253 the interactions between pharmaceuticals and microplastics are different between polymer types, but
254 also with the same microplastic polymer in different background solutions.

255 On the other hand, atorvastatin adsorption increased when present in the non-ionic form. The K_d value
256 was 1354 L kg^{-1} at pH 3 and between 158 and 368 L kg^{-1} when in anionic form at pH values 6, 7, 8 and
257 11 (Figure 3). This is like data obtained on naproxen, ibuprofen and diclofenac which have similar
258 speciation at different pH values (Elizalde-Velázquez et al., 2020). It should be noted that when present
259 in the non-ionised form atorvastatin has the greatest log D_{OW} value of all the studied pharmaceuticals
260 (Figure 1). Furthermore, both gliclazide (216 L kg^{-1}) and bezafibrate (267 L kg^{-1}) adsorbed to the
261 polyethylene microplastics at pH 3 and not under any other condition studied. Wastewater pH did not
262 affect carbamazepine adsorption which is in neutral form across the pH range studied (Figure 1, Figure

263 3). This agrees with a previous study which showed little influence of solution pH on carbamazepine
264 adsorption to polyethylene microplastics (Seidensticker et al., 2018). Ketamine showed a similar trend
265 to propranolol and fluoxetine with respect to speciation and adsorption. Greatest adsorption was
266 observed at pH 6 when present in the cationic form (Figure 1, Figure 3). Lower adsorption at pH 3 was
267 due to the reduced surface charge of the microplastics and low adsorption at pH values ≥7 when present
268 in non-ionic form (Figure 3).

269 Pharmaceutical adsorption to polyethylene microplastics was investigated in wastewater diluted with
270 increasing amounts of stormwater. Dilution had little influence on adsorption with only fluoxetine
271 showing a significant reduction (ANOVA, $p<0.05$) between undiluted wastewater and 100 %
272 stormwater (Figure 3). Previous research has found that bulk organics such as humic acid can act as a
273 bridge for cations and zwitterions to adsorb to some microplastics (Zhang et al., 2018). Indeed, greater
274 adsorption of cationic pharmaceuticals to polyamide microplastics was found in undiluted wastewater
275 compared to diluted wastewater (Wagstaff et al., 2021). Previous studies report that due to the
276 hydrophilic properties of humic acid it has little interaction with polyethylene (Wu et al., 2016).
277 However, humic acid has been found to adsorb to polyamide (Zhang and Bai, 2002). Polyamide has
278 polar functional groups within its structure which could facilitate interactions with hydrophilic organics
279 such as humic acid. Nevertheless, pharmaceutical adsorption to polyethylene microplastics in
280 wastewater was largely unaffected by stormwater dilution expected during storm events that lead to
281 CSO discharges.

282 Salt applied to roads during winter months is mainly comprised of NaCl (>97 %) (Prosser et al., 2017).
283 These enter wastewater from road run-off into combined sewers. Run-off following de-icing has been
284 found to contain ~1 g L^{-1} Na^+ (Barbier et al., 2018), although concentrations could be considerably
285 higher. Therefore, the influence of salinity (up to 10 g L^{-1} NaCl) on pharmaceutical adsorption in
286 wastewater was investigated. Only fluoxetine demonstrated reduced adsorption in the presence of
287 additional NaCl (Figure 3). The Na^+ ion can result in a charge shielding effect on the microplastic
288 surface (Lu et al., 2018). If this was the case it may be expected that increased adsorption of atorvastatin
289 may be observed due to reduced repulsion between the anionic species of the pharmaceutical and the

290 microplastic surface. However, no trend in the data between atorvastatin adsorption and NaCl
291 concentration was observed (Figure 3). Previous research showed that NaCl addition has no influence
292 on the adsorption of sulfamethoxazole present as the anionic species (Xu et al., 2018b), however other
293 research has shown that the influence of NaCl on sulfamethoxazole adsorption is less clear (Guo et al.,
294 2019). The addition of NaCl did not affect carbamazepine or ketamine adsorption to polyethylene
295 (Figure 3). Similar observations have been made for carbamazepine up to a NaCl concentration of 3.5
296 g L^{-1} (Wu et al., 2016).

297 The influence of wastewater temperature on pharmaceutical adsorption was assessed at 5 °C and 20 °C.
298 The data suggested a species dependent effect on adsorption whereby only the cationic pharmaceuticals
299 showed a significant change. Both propranolol and fluoxetine had significantly reduced adsorption in
300 wastewater at 5 °C (Figure 3). This has also been observed for the adsorption of propranolol, fluoxetine,
301 and amitriptyline to polyamide microplastics (Wagstaff et al., 2021). Tetracycline adsorption to
302 polyamide microplastics has also been found to increase with increasing temperature (Lin et al., 2020).
303 Endothermic adsorption processes see an increase in adsorption with increased temperature (Xu et al.,
304 2021). However, it should be noted that wastewater temperatures are only likely to reach 5 °C in
305 treatment processes with long retention times (e.g., lagoons) during winter months (Delatolla et al.,
306 2019).

307 ### 3.3. Pharmaceutical desorption from polyethylene microplastics in river water, gastric fluid
308 ### and intestinal fluids

309 The desorption of propranolol, fluoxetine, atorvastatin, carbamazepine, and ketamine was investigated
310 in river water (pH 7.4), gastric fluid at 20 °C and 37 °C (pH 2) and intestinal fluid at 20 °C and 37 °C
311 (pH 7). Gastric and intestinal fluids were maintained at both 20 °C and 37 °C to represent temperatures
312 of cold- and warm-blooded organisms (Liu et al., 2020; Wagstaff et al., 2021). Desorption occurred
313 rapidly for all pharmaceuticals in the studied matrices (Figure 4). There was little difference in
314 desorption between 1, 2, 3, 4 and 24 hours exposure in any of the matrices. Only atorvastatin in river
315 water and gastric fluid, and fluoxetine in intestinal fluid at 20 °C showed significant differences between

different exposure times. Liu et al. (2020) previously reported a fast desorption phase for atorvastatin and amlodipine from polystyrene microplastics.

Propranolol had 11-12 % desorption in river water (Figure 4). This was increased to 23-26 % in gastric fluid and 21-23 % in intestinal fluid at 20 °C (Figure 4). Previous research has found similar desorption of propranolol from polyamide microplastics in river water and gastric fluid at 20 °C (Wagstaff et al., 2021). Razanajatovo et al. (2018) reported ~8 % desorption from polyethylene microplastics in intestinal fluid. Enhanced desorption was observed in both gastric and intestinal fluids at warm-blooded over cold-blooded organism temperatures. At 37 °C the desorption was 32-33 % in gastric fluid and 24-29 % in intestinal fluids (Figure 4). Higher desorption of pharmaceuticals at 37 °C over 18 °C has been observed in gastric and intestinal fluids (Liu et al., 2020), and in intestinal fluid at 37 °C over 27 °C (Lin et al., 2020). However, >50 % desorption for propranolol from polyamide microplastics has been observed in gastric fluids at 37 °C previously (Wagstaff et al., 2021).

Fluoxetine showed a similar trend to propranolol albeit greater desorption was observed across the matrices studied; 9-13 % in river water, 34-40 % in gastric fluid at 20 °C and 46-50 % at 37 °C, and 20-28 % in intestinal fluid at 20 °C and 19-21 % at 37 °C (Figure 4). The desorption observed in river water and gastric fluid is like equivalent studies using polyamide microplastics (Wagstaff et al., 2021). In contrast, desorption of atorvastatin from polyethylene followed intestinal fluid > river water > gastric fluid (Figure 4). Furthermore, there was no appreciable difference in desorption between cold- and warm-blooded temperatures of gastric and intestinal fluids. Desorption was ~20 % in intestinal fluids. Previous research has found >50 % desorption is possible from polystyrene microplastics in intestinal fluids (Liu et al., 2020). On the other hand, little difference in desorption was observed for carbamazepine or ketamine between the different matrices (and temperatures) studied. Carbamazepine desorption was in the range 13-19 % and ketamine 9-11 % for all individual time points and desorption matrices.

Our findings suggest that the pH of the matrix has the greatest influence on desorption of pharmaceuticals from polyethylene microplastics. Enhanced desorption of the cationic pharmaceuticals reflects their reduced adsorption in the low pH adsorption studies due to a lower surface charge of the

343 microplastic at this pH and less electrostatic attraction (Figure 3; Table 2). Atorvastatin also showed
344 increased adsorption (Figure 3) and reduced desorption at low pH (Figure 4). In this case it is the change
345 in pharmaceutical speciation from anionic to non-ionised form that is considered to account for the low
346 desorption observed in gastric fluid (shifting from predominantly electrostatic attraction to stronger
347 hydrophobic interactions). Furthermore, as pH did not influence adsorption of carbamazepine and
348 ketamine between low pH conditions and pH 7 (Figure 3), there was no change to their desorption
349 between matrices with different pH. Gastric and intestinal components (pepsin, bovine serum albumin
350 and sodium taurocholate) may also contribute to desorption for some pharmaceuticals. Liu et al. (2020)
351 reported they can increase desorption of atorvastatin and amlodipine (cationic speciation at neutral pH)
352 from polystyrene through increased solubilisation of the drugs and competition for adsorption sites on
353 the microplastic. However, in our study lower desorption of atorvastatin was observed in gastric fluid
354 compared to river water, and there was no difference in desorption for carbamazepine or ketamine
355 between river water and gastric or intestinal fluids.

356 **3.4. Environmental significance**

357 The study revealed that a diverse range of pharmaceuticals can adsorb to polyethylene microplastics in
358 wastewater. Changing wastewater characteristics (pH, dilution with stormwater, salinity) within
359 expected ranges of municipal wastewater have little effect on pharmaceutical adsorption. Only
360 fluoxetine adsorption was significantly impacted by NaCl addition to wastewater, and ketamine
361 adsorption in the pH range 6-8 (Figure 3). However, adsorption of ionised pharmaceuticals will be
362 significantly influenced by changes to pH out with expected values of municipal wastewater (pH 6-8).
363 Those pharmaceuticals present as cationic species had the greatest adsorption to polyethylene
364 microplastics. Exposure of microplastics to river water revealed pharmaceuticals had low desorption in
365 the range 10-20 % (Figure 4). This suggests that most of the adsorbed pharmaceutical concentration can
366 remain on the microplastic once discharged into the environment. Considerable desorption was
367 observed for the cationic pharmaceuticals in gastric fluid with up to 50 % desorption observed for
368 fluoxetine at 37 °C (Figure 3). This is significant as it demonstrates that microplastic bound
369 pharmaceuticals are 'bioavailable' if consumed and enter the gastrointestinal tract. However, a common

approach of assessing the risk posed by pharmaceuticals in wastewater effluents or river water is to compare predicted no effect concentrations (PNECs) or environmental quality standards with pre-filtered environmental samples (e.g., Singh and Suthar, 2021; An et al., 2022; Ofrydopoulou et al., 2022). Therefore, the contribution of particle bound pharmaceuticals released in wastewater effluents are not considered.

As a 'worst-case scenario', the amount of fluoxetine in river water associated with polyethylene microplastics from WTP effluents ($Fluoxetine_{MP}$, mg L^{-1}) was estimated using eq. 5.

$$Fluoxetine_{MP} = \frac{MP_{eff} \times q_e}{DF} \times \frac{(100 - des)}{100} \quad (5)$$

Where MP_{eff} is the concentration of polyethylene microplastics in wastewater effluent (kg L^{-1}). This is the median concentration of microplastics in effluent taken from Ngo et al. (2019) and assuming 50 % of the microplastic concentration is polyethylene (2.5 x 10^{-7} kg L^{-1}), q_e is the adsorbed fluoxetine concentration calculated using eq. 2 (4.4 mg kg^{-1}). This was calculated using the highest reported fluoxetine concentration in influent wastewater (Bean et al., 2017, 1.3 x 10^{-3} mg L^{-1}) and the K_d value from Table 2. *DF* is a default dilution factor of 10 for wastewater effluents in river water (European Medicines Agency, 2006), and *des* is the average desorption in river water from Figure 4 (10 %). Using this information, the concentration of fluoxetine adsorbed to polyethylene microplastics in the mixing zone of the river is equivalent to 1.0 x 10^{-7} mg L^{-1}. This represents 5 % and 4 % of the fluoxetine PNEC compiled by Pereira et al. (2020) for invertebrate and fish, respectively. This seems small compared to the PNEC, however this is just one exposure route of bioavailable fluoxetine for organisms in the environment. There will also be exposure to free or 'dissolved' fluoxetine as well as fluoxetine adsorbed to other microplastics and particulates discharged from WTPs. Although the approach taken here has considerable uncertainties, it demonstrates that pharmaceuticals adsorbed to microplastics needs to be considered as an exposure route to organisms in the environment, and not accounting for these adsorbed pollutants can underestimate exposure and risk.

4. Conclusion

A range of pharmaceuticals including those in cationic, anionic, and neutral form adsorb to polyethylene microplastics in wastewater. Both pharmaceutical speciation and hydrophobicity are important for adsorption with those cationic and more hydrophobic in nature having the greatest adsorption. Changing composition of wastewater (pH, dilution with stormwater and NaCl addition) typically expected for municipal wastewater had little effect to pharmaceutical adsorption. However, changes to pH out with the typical range of municipal wastewater (pH 6-8) had a significant influence on those ionisable pharmaceuticals. Adsorbed pharmaceuticals had low desorption (≤19 %) in river water. Up to 50 % desorption of fluoxetine was found in gastric fluids at 37 °C. Findings suggest that despite low amounts of pharmaceuticals entering the environment adsorbed to polyethylene microplastics they are still an important exposure route for aquatic organisms. Further research is needed to understand the risks posed by the cocktail of pharmaceuticals adsorbed to the surface of microplastics and released into the environment from WTPs.

Acknowledgements

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References

An, W., Duan, L., Zhang, Y., Zhou, Y., Wang, B., Yu, G., 2022. Pollution characterization of pharmaceutically active compounds (PhACs) in the northwest of Tai Lake Basin, China: Occurrence, temporal changes, riverine flux and risk assessment. J. Hazard. Mater., 422, 126889. DOI: 10.1016/j.jhazmat.2021.126889

Atugoda, T., Vithanage, M., Wijesekara, H., Bolan, N., Sarmah, A.K., Bank, M.S., You, S., Ok, Y.S., 2021. Interactions between microplastics, pharmaceuticals and personal care products: Implications for vector transport. Environ. Int., 149, 106367. DOI: 10.1016/j.envint.2020.106367

Atugoda, T., Wijesekara, H., Werellagama, D.R.I.B., Jinadasa, K.B.S.N., Bolan, N.S., Vithanage, M., 2020. Adsorptive interaction of antibiotic ciprofloxacin on polyethylene microplastics: Implications for vector transport in water. Environ. Technol. Innov., 19, 100971. DOI: 10.1016/j.eti.2020.100971

Barbier, L., Suaire, R., Durickovic, I., Laurent, J., Simonnot, M.-O., 2018. Is a Road Stormwater Retention Pond Able to Intercept Deicing Salt? Water Air Soil Pollut., 229 (8), 251. DOI: 10.1007/s11270-018-3908-9

Bean, T.G., Arnold, K.E., Lane, J.M., Bergström, E., Thomas-Oates, J., Rattner, B.A., Boxall, A.B.A., 2017. Predictive framework for estimating exposure of birds to pharmaceuticals. Environ. Toxicol. Chem., 36 (9), 2335-2344. DOI: 10.1002/etc.3771

ChemAxon, 2021. Calculator Plugins were used for structure property prediction and calculation, Marvin 20.16.0, http://www.chemaxon.com Accessed 15/02/21.

Chen, X., Gu, X., Bao, L., Ma, S., Mu, Y., 2021. Comparison of adsorption and desorption of triclosan between microplastics and soil particles. Chemosphere, 263, art. no. 127947. DOI: 10.1016/j.chemosphere.2020.127947

Delatolla, R., Tufenkji, N., Comeau, Y., Gadbois, A., Lamarre, D., Berk, D., 2019. Kinetic analysis of attached growth nitrification in cold climates. Water Sci. Technol. 60 (5), 1173-1184. DOI: 10.2166/wst.2009.419

Duncan, E.M., Broderick, A.C., Fuller, W.J., Galloway, T.S., Godfrey, M.H., Hamann, M., Limpus, C.J., Lindeque, P.K., Mayes, A.G., Omeyer, L.C.M., Santillo, D., Snape, R.T.E., Godley, B.J., 2019. Microplastic ingestion ubiquitous in marine turtles. Glob. Change Biol., 25 (2), 744-752. DOI: 10.1111/gcb.14519

Elizalde-Velázquez, A., Subbiah, S., Anderson, T.A., Green, M.J., Zhao, X., Cañas-Carrell, J.E., 2020. Sorption of three common nonsteroidal anti-inflammatory drugs (NSAIDs) to microplastics. Sci. Total Environ. 715, 136974. DOI: 10.1016/j.scitotenv.2020.136974

European Medicines Agency, Amsterdam, 2006. Environmental risk assessment of medicinal products for human use. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-environmental-risk-assessment-medicinal-products-human-use-first-version_en.pdf Accessed 06/10/21

Gigault, J., Halle, A.T., Baudrimont, M., Pascal, P.-Y., Gauffre, F., Phi, T.-L., El Hadri, H., Grassl, B., Reynaud, S., 2018. Current opinion: What is a nanoplastic? Environ. Pollut., 235, 1030-1034. DOI: 10.1016/j.envpol.2018.01.024

Guo, X., Chen, C., Wang, J., 2019. Sorption of sulfamethoxazole onto six types of microplastics. Chemosphere 228, 300-308. DOI: 10.1016/j.chemosphere.2019.04.155

Hughes, S.R., Kay, P., Brown, L.E., 2013. Global synthesis and critical evaluation of pharmaceutical data sets collected from river systems. Environ. Sci. Technol., 47 (2), 661-677. DOI: 10.1021/es3030148

Issac, M.N., Kandasubramanian, B., 2021. Effect of microplastics in water and aquatic systems. Environ. Sci. Pollut. Res., 28 (16), 19544-19562. DOI: 10.1007/s11356-021-13184-2

Li, Y., Sallach, J.B., Zhang, W., Boyd, S.A., Li, H., 2019. Insight into the distribution of pharmaceuticals in soil-water-plant systems. Water Res., 152, 38-46. DOI: 10.1016/j.watres.2018.12.039

Lin, L., Tang, S., Wang, X.S., Sun, X., Han, Z., Chen, Y., 2020. Accumulation mechanism of tetracycline hydrochloride from aqueous solutions by nylon microplastics. Environ. Technol. Innov. 18, 100750. DOI: 10.1016/j.eti.2020.100750

Liu, P., Lu, K., Li, J., Wu, X., Qian, L., Wang, M., Gao, S., 2020a. Effect of aging on adsorption behavior of polystyrene microplastics for pharmaceuticals: Adsorption mechanism and role of aging intermediates. J. Hazard. Mater., 384, 121193. DOI: 10.1016/j.jhazmat.2019.121193

Liu, P., Wu, X., Liu, H., Wang, H., Lu, K., Gao, S., 2020b. Desorption of pharmaceuticals from pristine and aged polystyrene microplastics under simulated gastrointestinal conditions. J. Hazard. Mater. 392, 122346. DOI: 10.1016/j.jhazmat.2020.122346

Lu, S., Zhu, K., Song, W., Song, G., Chen, D., Hayat, T., Alharbi, N.S., Chen, C., Sun, Y., 2018. Impact of water chemistry on surface charge and aggregation of polystyrene microspheres suspensions. Sci. Total Environ. 630, 951-959. DOI: 10.1016/j.scitotenv.2018.02.296

Mo, Q., Yang, X., Wang, J., Xu, H., Li, W., Fan, Q., Gao, S., Yang, W., Gao, C., Liao, D., Li, Y., Zhang, Y., 2021. Adsorption mechanism of two pesticides on polyethylene and polypropylene microplastics: DFT calculations and particle size effects. Environ. Pollut., 291, 118120. DOI: 10.1016/j.envpol.2021.118120

476 Ngo, P.L., Pramanik, B.K., Shah, K., Roychand, R., 2019. Pathway, classification and removal
477 efficiency of microplastics in wastewater treatment plants. Environ. Pollut., 255, 113326. DOI:
478 10.1016/j.envpol.2019.113326

479 Ofrydopoulou, A., Nannou, C., Evgenidou, E., Christodoulou, A., Lambropoulou, D., 2022.
480 Assessment of a wide array of organic micropollutants of emerging concern in wastewater
481 treatment plants in Greece: Occurrence, removals, mass loading and potential risks. Sci. Total
482 Environ., 802, 149860. DOI: 10.1016/j.scitotenv.2021.149860

483 Pereira, A., Silva, L., Laranjeiro, C., Lino, C., Pena, A., 2020. Selected pharmaceuticals in different
484 aquatic compartments: Part II-Toxicity and environmental risk assessment. Molecules, 25 (8),
485 25081796. DOI: 10.3390/molecules25081796

486 Petrie, B., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2016. Multi-residue analysis of 90 emerging
487 contaminants in liquid and solid environmental matrices by ultra-high-performance liquid
488 chromatography tandem mass spectrometry. J. Chromatogr. A, 1431, 64-78. DOI:
489 10.1016/j.chroma.2015.12.036

490 Petrie, B., Lopardo, L., Proctor, K., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2019. Assessment
491 of bisphenol-A in the urban water cycle. Sci. Total Environ. 650, 900-907. DOI:
492 10.1016/j.scitotenv.2018.09.011

493 Polanco, H., Hayes, S., Roble, C., Krupitsky, M., Branco, B., 2020. The presence and significance of
494 microplastics in surface water in the Lower Hudson River Estuary 2016–2019: A research note.
495 Mar. Pollut. Bull., 161, 111702. DOI: 10.1016/j.marpolbul.2020.111702

496 Prosser, R.S., Rochfort, Q., McInnis, R., Exall, K., Gillis, P.L., 2017. Assessing the toxicity and risk of
497 salt-impacted winter road runoff to the early life stages of freshwater mussels in the Canadian
498 province of Ontario. Environ. Pollut., 230, 589-597. DOI: 10.1016/j.envpol.2017.07.001

499 Pubchem, Maryland, USA, 2021. National Institutes of Health https://pubchem.ncbi.nlm.nih.gov.
500 Accessed 05/01/21.

501 Puckowski, A., Cwięk, W., Mioduszewska, K., Stepnowski, P., Białk-Bielińska, A., 2021. Sorption of
502 pharmaceuticals on the surface of microplastics. Chemosphere 263, 127976. DOI:
503 10.1016/j.chemosphere.2020.127976

504 Razanajatovo, R.M., Ding, J., Zhang, S., Jiang, H., Zou, H., 2018. Sorption and desorption of selected
505 pharmaceuticals by polyethylene microplastics. Mar. Pollut. Bull. 136, 516-523. DOI:
506 10.1016/j.marpolbul.2018.09.048

507 Seidensticker, S., Grathwohl, P., Lamprecht, J., Zarfl, C., 2018. A combined experimental and modeling
508 study to evaluate pH-dependent sorption of polar and non-polar compounds to polyethylene and
509 polystyrene microplastics. Environ. Sci. Eur., 30 (1), DOI: 10.1186/s12302-018-0155-z

510 Simon, M., van Alst, N., Vollertsen, J., 2018. Quantification of microplastic mass and removal rates at
511 wastewater treatment plants applying Focal Plane Array (FPA)-based Fourier Transform Infrared
512 (FT-IR) imaging. Water Res. 142, 1-9. DOI: 10.1016/j.watres.2018.05.019

513 Singh, V., Suthar, S., 2021. Occurrence, seasonal variations, and ecological risk of pharmaceuticals and
514 personal care products in River Ganges at two holy cities of India. Chemosphere, 268, 129331.
515 DOI: 10.1016/j.chemosphere.2020.129331

516 Sun, J., Dai, X., Wang, X., van Loosdrecht, M.C.M., Ni, B.-J., 2019. Microplastics in wastewater
517 treatment plants: Detection, occurrence and removal. Water Res. 152, 21-37. DOI:
518 10.1016/j.watres.2018.12.050

519 Tourinho, P.S., Kočí, V., Loureiro, S., van Gestel, C.A.M., 2019. Partitioning of chemical contaminants
520 to microplastics: Sorption mechanisms, environmental distribution and effects on toxicity and
521 bioaccumulation. Environ. Pollut. 252, 1246-1256. DOI: 10.1016/j.envpol.2019.06.030

Wagstaff, A., Lawton, L.A., Petrie, B., 2021. Polyamide microplastics in wastewater as vectors of cationic pharmaceutical drugs. Chemosphere, 132578. DOI: 10.1016/j.chemosphere.2021.132578

Wang, F., Yu, Y., Wu, H., Wu, W., Wang, L., An, L., Cai, W., 2021. Microplastics in spotted seal cubs (Phoca largha): Digestion after ingestion? Sci. Total Environ., 785, 147426. DOI: 10.1016/j.scitotenv.2021.147426

Weitzel, S.L., Feura, J.M., Rush, S.A., Iglay, R.B., Woodrey, M.S., 2021. Availability and assessment of microplastic ingestion by marsh birds in Mississippi Gulf Coast tidal marshes. Marine Pollut. Bull., 166, 112187. DOI: 10.1016/j.marpolbul.2021.112187

Windsor, F.M., Tilley, R.M., Tyler, C.R., Ormerod, S.J., 2019. Microplastic ingestion by riverine macroinvertebrates. Sci. Total Environ., 646, 68-74. DOI: 10.1016/j.scitotenv.2018.07.271

Wu, C., Zhang, K., Huang, X., Liu, J., 2016. Sorption of pharmaceuticals and personal care products to polyethylene debris. Environ. Sci. Pollut. Res. 23 (9), 8819-8826. DOI: 10.1007/s11356-016-6121-7

Xu, B., Liu, F., Brookes, P.C., Xu, J., 2018a. Microplastics play a minor role in tetracycline sorption in the presence of dissolved organic matter. Environ. Pollut., 240, 87-94. DOI: 10.1016/j.envpol.2018.04.113

Xu, B., Liu, F., Brookes, P.C., Xu, J., 2018b. The sorption kinetics and isotherms of sulfamethoxazole with polyethylene microplastics. Marine Pollut. Bull., 131, 191-196. DOI: 10.1016/j.marpolbul.2018.04.027

Xu, Y., Yu, X., Xu, B., Peng, D., Guo, X., 2021. Sorption of pharmaceuticals and personal care products on soil and soil components: Influencing factors and mechanisms. Sci. Total Environ., 753, 141891. DOI: 10.1016/j.scitotenv.2020.141891

Zhang, X., Bai, R., 2002. Adsorption behavior of humic acid onto polypyrrole-coated nylon 6,6 granules. J. Mater. Chem., 12 (9), 2733-2739. DOI: 10.1039/b201364a

Zhang, D.Q., Gersberg, R.M., Zhu, J., Hua, T., Jinadasa, K.B.S.N., Tan, S.K., 2012. Batch versus continuous feeding strategies for pharmaceutical removal by subsurface flow constructed wetland. Environ. Pollut., 167, 124-131. DOI: 10.1016/j.envpol.2012.04.004

Zhang, H., Wang, J., Zhou, B., Zhou, Y., Dai, Z., Zhou, Q., Chriestie, P., Luo, Y., 2018. Enhanced adsorption of oxytetracycline to weathered microplastic polystyrene: Kinetics, isotherms and influencing factors. Environ. Pollut., 243, 1550-1557. DOI: 10.1016/j.envpol.2018.09.122

Zhao, L., Rong, L., Xu, J., Lian, J., Wang, L., Sun, H., 2020. Sorption of five organic compounds by polar and nonpolar microplastics. Chemosphere, 257, 127206. DOI: 10.1016/j.chemosphere.2020.127206

Zhu, L., Wang, H., Chen, B., Sun, X., Qu, K., Xia, B., 2019. Microplastic ingestion in deep-sea fish from the South China Sea. Sci. Total Environ., 677, 493-501. DOI: 10.1016/j.scitotenv.2019.04.380

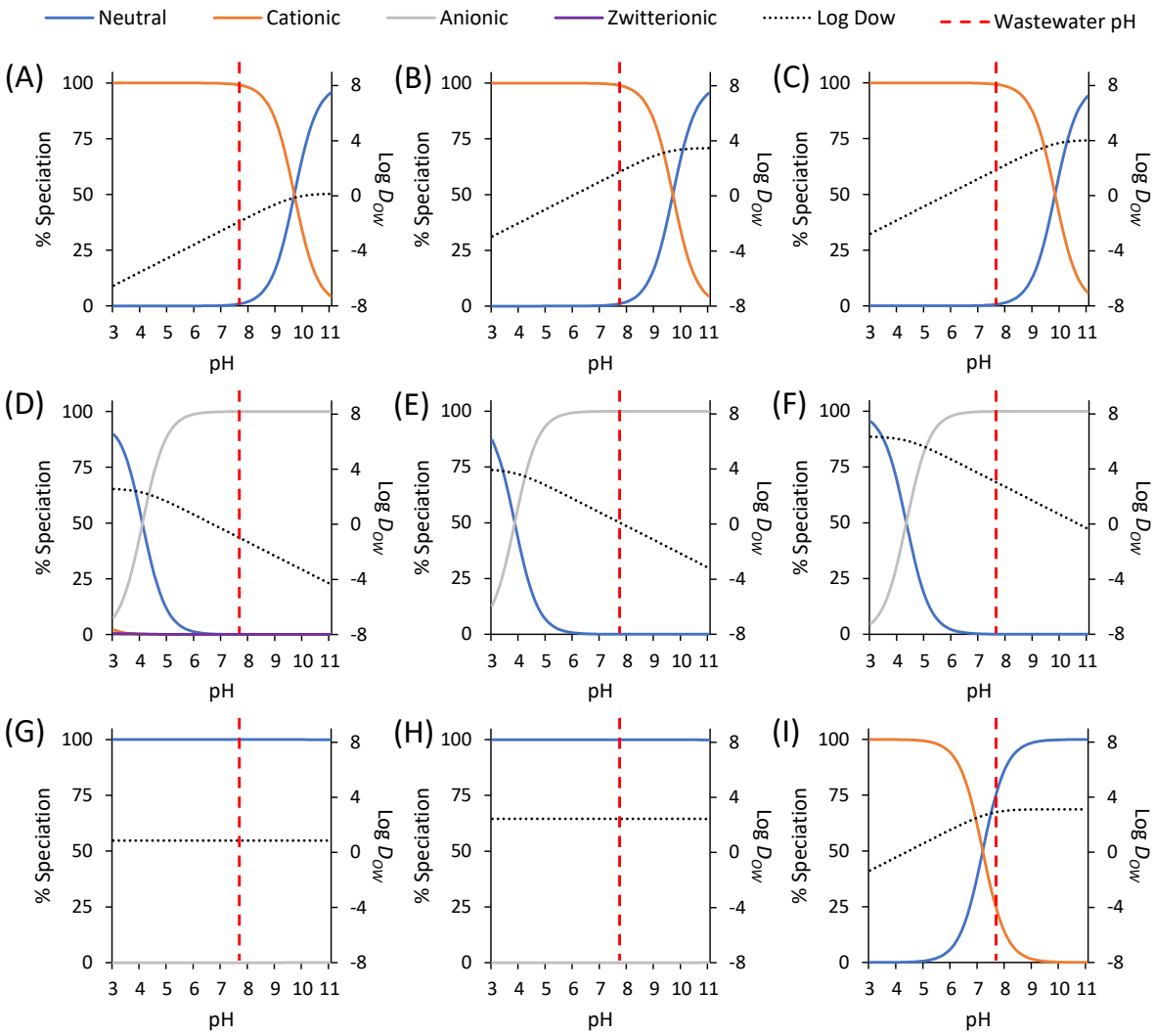
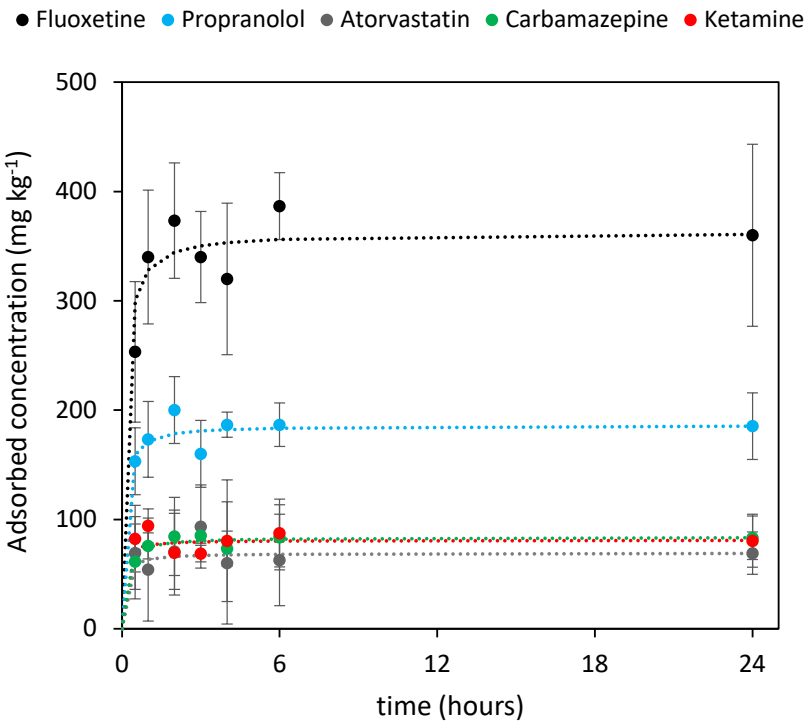


Figure 1. Speciation of studied pharmaceuticals at different pH values. Pharmaceuticals are grouped based on their dominant species at the pH of the studied wastewater (7.8) - cationic (A, atenolol; B, propranolol; C, fluoxetine), anionic (D, gliclazide; E, bezafibrate; F, atorvastatin) and neutral or predominantly non-ionised (G, ifosfamide; H, carbamazepine; I, ketamine). The pH dependant octanol-water partition coefficient (log D_{OW}) is presented on the secondary axis. Data obtained from ChemAxon, 2021 and PubChem, 2021. The log D_{OW} = log K_{OW} for ifosfamide and carbamazepine.



571
572 Figure 2. Adsorbed concentration of fluoxetine, propranolol, ketamine, atorvastatin, and
573 carbamazepine to polyethylene microplastics in wastewater over 24 hours. The dashed line represents
574 the data fitted to the pseudo-second order model.
575

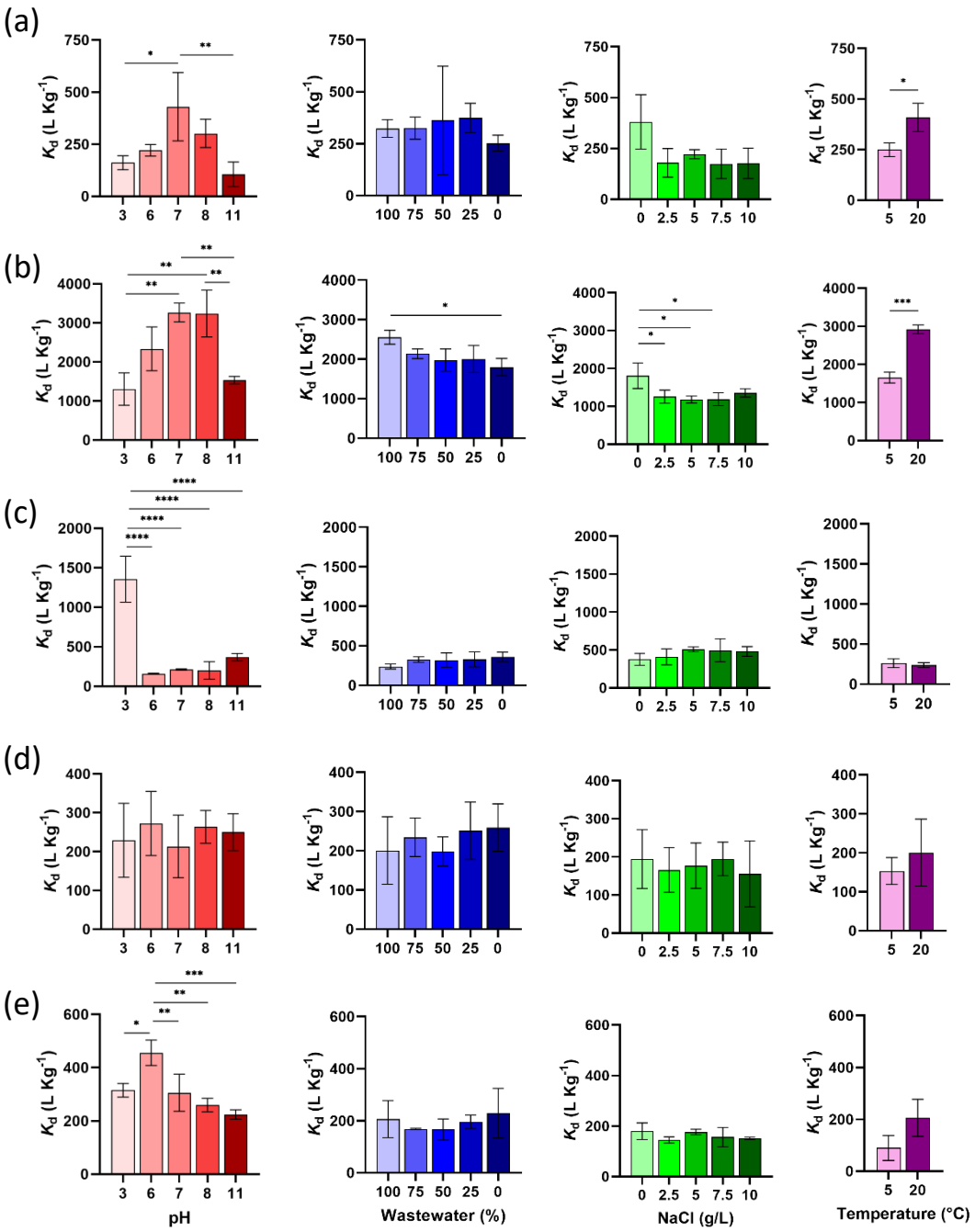


Figure 3. Influence of pH (red bars), wastewater-stormwater composition (blue bars), addition of NaCl (green bars) and temperature (lilac bars) on pharmaceutical adsorption to polyethylene microplastics. The different pharmaceuticals studied were propranolol (a), fluoxetine (b), atorvastatin (c), carbamazepine (d) and ketamine (e). The y-axis scale is different for each pharmaceutical. The asterisks represent statistical significance whereby *p<0.05, ** p<0.01, *** p<0.001, and **** p<0.0001 based on one-way ANOVA for pH, wastewater % and NaCl and on unpaired t-tests for wastewater temperature.

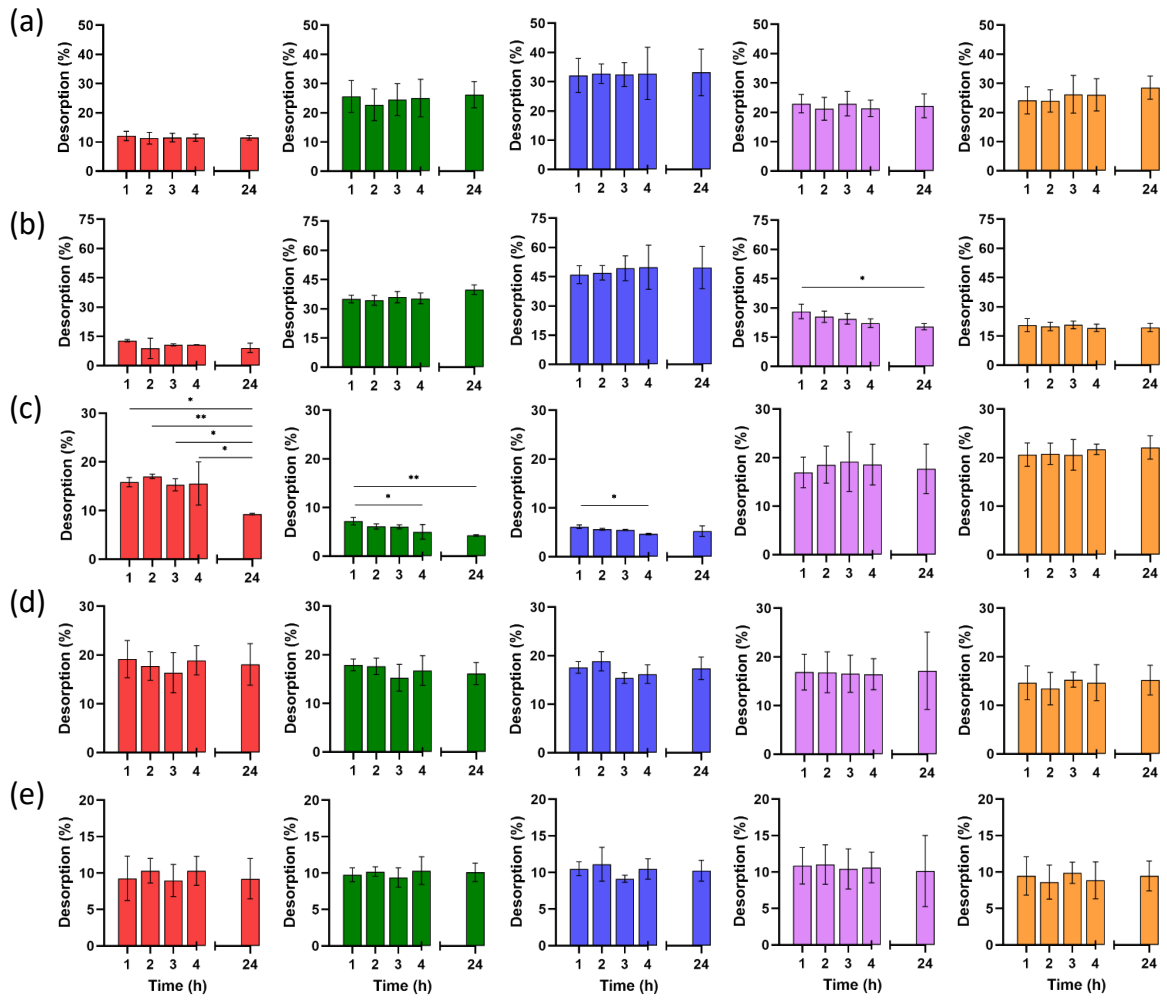
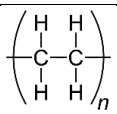
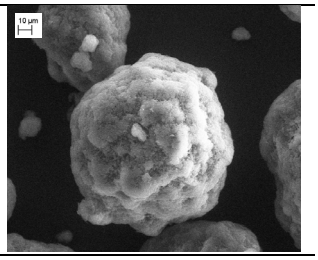


Figure 4. Desorption of pharmaceuticals from polyethylene microplastics in river water at 20 °C (red bars), gastric fluid at 20 °C (green bars), gastric fluid at 37 °C (blue bars), intestinal fluid at 20 °C (lilac bars) and intestinal fluids at 37 °C (orange bars). The different pharmaceuticals studied were propranolol (a), fluoxetine (b), atorvastatin (c), carbamazepine (d) and ketamine (e). The y-axis scale is different for each pharmaceutical. The asterisks represent statistical significance whereby *p<0.05 and ** p<0.01 based on one-way ANOVA.

601 Table 1. Properties of the ultra-high molecular weight polyethylene microplastics

Monomer	Molecular weight (g mol^{-1})[a]	Mean size (µm)[a]	Density (g cm^{-3})[a]	Zeta potential (mV)	SEM image[b]
	~5 x 10^6	150	0.94	-10.5 (pH 3) -19.5 (pH 6) -21.1 (pH 7) -26.8 (pH 8) -28.9 (pH 11)	

602 [a]As detailed by the manufacturer [b]1,000 x magnification
603 Key: SEM, scanning electron microscopy
604
605

606 Table 2. Kinetics and isotherm data for pharmaceuticals and polyethylene microplastics in wastewater

Model	Type	Parameter	Pharmaceutical drug				
			Propranolol	**Fluoxetine**	**Atorvastatin**	**Carbamazepine**	**Ketamine**
Kinetics	Pseudo-second order	q_e (mg kg^{-1})	186	362	69.1	83.7	80.9
		K_2 (kg mg^{-1} h^{-1})	6.34 x 10^{-2}	2.67 x 10^{-2}	0.165	9.60 x 10^{-2}	0.226
		r^2	0.999	0.999	0.997	0.999	0.999
Isotherm	Linear	K_d (L kg^{-1})	440	3.35 x 10^3	227	182	216
		r^2	0.978	0.998	0.921	0.800	0.877
	Freundlich	K_F [(mg kg^{-1})(mg L^{-1})$^{1/n}$]	386	3.40 x 10^3	284	218	259
		n	0.793	0.937	1.44	1.38	1.32
		r^2	0.984	0.997	0.964	0.821	0.900
	Langmuir	q_{max} (mg kg^{-1})	1.52 x 10^5	4.70 x 10^5	1.29 x 10^5	631	922
		K_L (L mg^{-1})	2.55 x 10^{-3}	6.82 x 10^{-3}	2.15 x 10^{-3}	0.549	0.412
		r^2	0.955	0.994	0.843	0.822	0.907

607

608

Electronic supplementary material

Adsorption of a diverse range of pharmaceuticals to polyethylene microplastics in wastewater and their desorption in environmental matrices

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The electronic supplementary information contains one figure and three tables showing adsorption isotherms, properties of studied pharmaceuticals, the mobile phase gradient and MS/MS parameters.

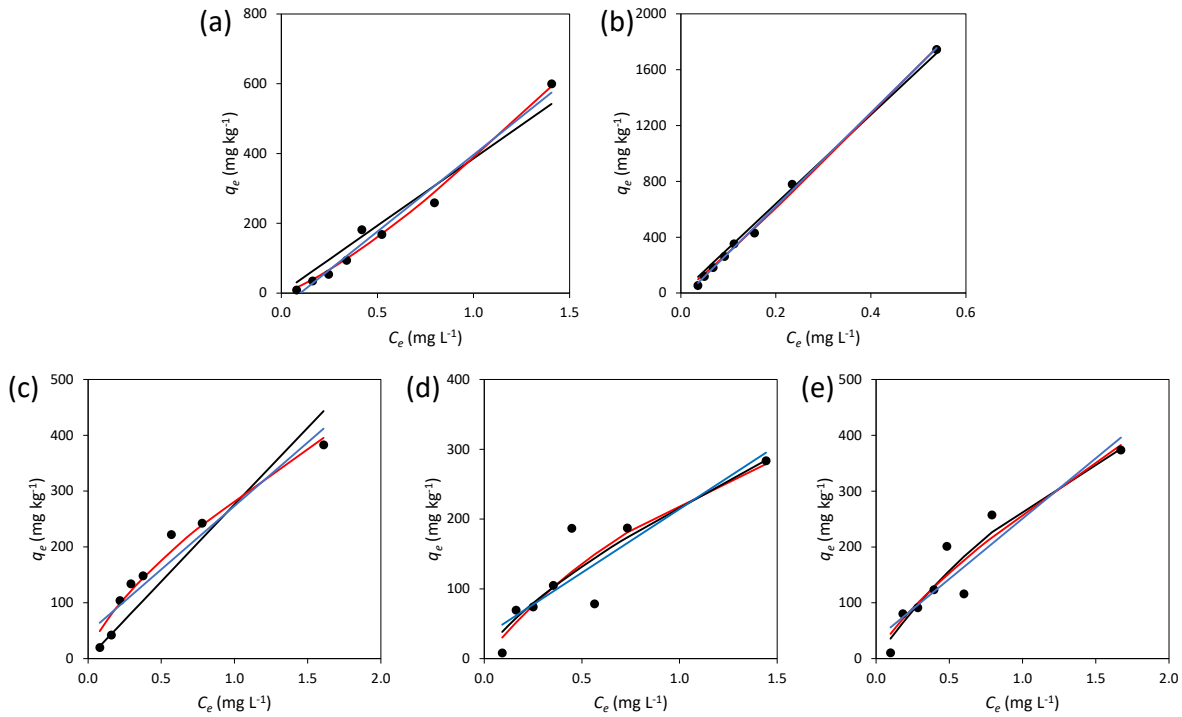

Figure S1. Linear (blue), Langmuir (black), Freundlich (red) isotherms of propranolol (a), fluoxetine (b), atorvastatin (c), carbamazepine (d), and ketamine (e) adsorption to polyethylene microplastics in wastewater. Circles show the experimental data.

Table S1. Properties of the studied pharmaceuticals (ChemAxon, 2021; Pubchem 2021)

Dominant species at pH 7.6	**Pharmaceutical**	**Therapeutic group**	**Molecular mass (g mol^{-1})**	***pK$_a$***	**Log *K$_{OW}$*[a]**
Cationic	Atenolol	Betablocker	266.34	9.67	0.16
	Propranolol	Betablocker	259.34	9.42	3.48
	Fluoxetine	Antidepressant	309.33	9.80	4.05
Anionic	Gliclazide	Antidiabetes	323.41	4.07	2.60
	Bezafibrate	Lipid-lowering	361.82	3.83	3.99
	Atorvastatin	Lipid-lowering	558.64	4.31	6.36
Neutral	Ifosfamide	Chemotherapeutic	261.08	14.64	0.86
	Carbamazepine	Anti-epilepsy	236.27	15.96	2.45
	Ketamine	Anaesthetic	237.73	7.45	3.12

[a]octanol-water partition coefficient

Table S2. MS/MS parameters of all pharmaceuticals and internal standards determined in positive ionisation mode

Pharmaceutical	**R_t (minutes)**	**Precursor (m/z)**	**Fragmentor (V)**	**Product 1 (m/z)**	**CE (eV)**	**Product 2 (m/z)**	**CE (eV)**	**Internal standard**
Atenolol	3.4	266.9	110	189.9	20	145.0	30	Codeine
Propranolol	10.6	259.9	110	182.9	10	115.9	10	Carbamazepine
Fluoxetine	12.4	309.8	90	147.7	2	44.0	10	Carbamazepine
Gliclazide	12.5	324.0	100	110.0	20	91.0	40	Carbamazepine
Bezafibrate	13.1	362.0	100	316.1	10	139.0	30	Carbamazepine
Atorvastatin	13.8	559.2	100	440.1	20	250.0	40	Carbamazepine
Ifosfamide	9.5	260.8	100	92.0	30	153.9	20	Propranolol
Carbamazepine	11.5	236.8	130	193.9	20	178.9	40	Propranolol
Ketamine	7.9	238.1	100	125.0	10	220.0	30	Propranolol
Codeine[a]	4.8	300.0	100	214.9	20	-	-	-

Key: R_t, retention time; CE, collision energy

[a]Internal standard only

Table S3. Mobile phase gradient used for the determination of pharmaceuticals

Time (minutes)	**10 mM ammonium formate and 0.1 % formic acid in water (%)**	**10 mM ammonium formate and 0.1 % formic acid in methanol (%)**
0.0	90	10
0.5	90	10
10.0	20	80
14.5	20	80
14.6	90	10
21.0	90	10

References

ChemAxon, 2021. Calculator Plugins were used for structure property prediction and calculation, Marvin 20.16.0, http://www.chemaxon.com Accessed 15/02/21.

Pubchem, Maryland, USA, 2021. National Institutes of Health https://pubchem.ncbi.nlm.nih.gov. Accessed 05/01/21.