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Desorption kinetics of antipsychotic drugs from sandy sediments by diffusive gradients in thin-films technique

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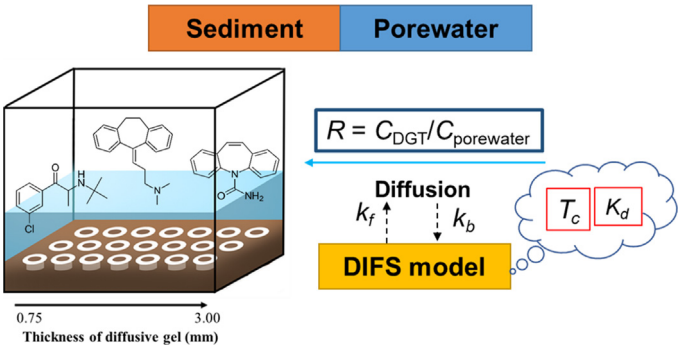
HIGHLIGHTS

- Dynamic processes of antipsychotics in sandy sediments were determined by diffusive gradients in thin-films (DGT) technique.
- Continuous removal of antipsychotics induced a flux to DGT devices.
- Lamotrigine and carbamazepine had the largest labile size to resupply from solid phase to solution in spiked sediment.
- *In situ* DGT-DIFS model from field sediments showed the resupply is not only depended on the labile pool size.

GRAPHICAL ABSTRACT



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ABSTRACT

Dynamic processes of organic contaminants in sediments can have important toxicological implications in aquatic systems. The current study used diffusive gradients in thin-films (DGT) devices in sandy sediments spiked with nine antipsychotics and in field sandy sediments. Samplers were deployed for 1 to 30 days to determine the flux of these compounds to DGT devices and the exchange rates between the porewater and sediment solid phase. The results showed a continuous removal of antipsychotics to a binding gel and induced a mobile flux from the DGT device to the adjacent sediment solution. A dynamic model, DGT-induced fluxes in soils and sediments, was used to derive rate constants of resupply of antipsychotics from solid phase to aqueous phase (response time, T_c) and distribution coefficients for labile antipsychotics. The largest labile pool was found for lamotrigine and carbamazepine in spiked sediments. Carbamazepine, clozapine, citalopram, and lamotrigine were resupplied rapidly by sediments with T_c (25–30 min). T_c values of bupropion and amitriptyline were the longest (≈5 h), which exhibited slow desorption rates in sediments. In field sediments, high resupply was found for carbamazepine and lamotrigine, which did not show higher labile pool. The T_c values were obviously higher in the filed sediments (52–171 h). Although the adsorption process is dominant for most studied antipsychotics in both spiked sediments and field sediments, the kinetic resupply of antipsychotic compounds may not be accurately estimated by laboratory-controlled incubation experiments. More studies are needed to explore the mechanisms of desorption kinetics by using *in situ* DGT technique in the field.

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1. Introduction

Due to the treatment of aging-related, chronic, and emerging diseases, as well as alterations of clinical practice, the consumption of pharmaceutical drugs continues to increase globally (Kümmerer, 2008). Global use of human pharmaceutical drugs was estimated to be approximately 100,000 metric tons annually (Kümmerer, 2008). In particular, consumption of antipsychotic drugs to treat or manage, *e.g.*, schizophrenia, severe depression, and autism, continues to increase globally (Kuroda et al., 2019; López-García et al., 2018). Drugs excreted from our bodies enter wastewater treatment plants through municipal sewage. Common technologies applied for treating domestic sewage are not designed to remove these pharmaceutical compounds or their metabolites, which results in the occurrence of pharmaceuticals in the environment (Escudero et al., 2021). For instance, the occurrence of several antipsychotic drugs, *e.g.*, venlafaxine (0.526–1.115 μg L^{-1}), citalopram (0.136–0.223 μg L^{-1}), fluoxetine (0.020–0.091 μg L^{-1}), and bupropion (0.070–0.191 μg L^{-1}) was observed in Canadian untreated wastewater with ~40% removal rate in the outlet (Metcalfe et al., 2010). Additionally, various psychoactive drugs and their metabolites have been detected in surface and drinking water (Caldas et al., 2016; Nannou et al., 2015; Silveira et al., 2013), wastewater (Bollmann et al., 2016; Reichert et al., 2019), offshore seawater (Alygizakis et al., 2016), river sediment (Nunes et al., 2019), and fish (Kalichak et al., 2017). These compounds have the potential to cause effects in aquatic ecosystems. For example, exposure to venlafaxine and citalopram could cause significant foot detachment from the substrate for two freshwater snails (*Leptoxis carinata* and *Stagnicola elodes*) (Fong and Hoy, 2012). Fluoxetine was found to significantly affect mating behavior of male fathead minnow (*Pimephales promelas*) at relatively small concentrations (1 μg L^{-1}) (Weinberger and Klaper, 2014).

After entering aquatic environments, these bioactive compounds can be dissolved in the aqueous phase or sorbed to organic material and particles, where they can settle in sediments (Stein et al., 2008). However, sorption of organic compounds onto sediments is influenced by various factors, including chemical structure, ionization state, and sorbent properties. Extensive H-bond interactions between sorbents and antipsychotic compounds are possible, given the polarity of these compounds (Stein et al., 2008). Therefore, cationic species of antipsychotic compounds are likely to interact electrostatically with negatively charged sorption sites of sorbents. Strong sorption caused by electrostatics was observed for some polar pharmaceuticals, such as sulfonamides and trimethoprim to soils (Chen et al., 2015), and ciprofloxacin to biosolid (D'Angelo and Starnes, 2016). Results of previous studies are consistent and indicate that most cationic species of antipsychotic compounds will bind to negatively charged sorption sites on/in the surfaces of clay and silt minerals, sediment organic matter, and clay mineral-humic complexes (Azuma, 2018; Gao and Pedersen, 2005; Nunes et al., 2019; Stein et al., 2008; Styszko, 2016). However, to date, the dynamics of these compounds have been studied mostly in batch or dynamic column experiments, and the kinetic exchange of antipsychotics has received less attention. Kinetic controls of antipsychotic resupply in the sediment environment can affect the mobility of these compounds in the water-sediment continuum and the availability of these compounds to aquatic organisms.

A passive sampling technology, DGT (diffusive gradients in thin-films) for organics, was initially designed for sampling from water (Chen et al., 2012) but has been recently used for *in-situ* measurement of desorption kinetics of antibiotics in soils (Chen et al., 2015; Chen et al., 2014; Ren et al., 2020) and biosolids (D'Angelo and Starnes, 2016; D'Angelo and Martin, 2018). Information on distributions of contaminants between solution and sediment is essential for understanding their environmental behaviors, which is usually expressed as the sediment-water distribution coefficient (K_d) (Martín et al., 2012; Nunes et al., 2019). However, most traditional methods cannot measure the dynamics of compounds while minimally disturbing the sediments. A dynamic model (DGT-Induced Fluxes in Sediments and Soils, DIFS) can be used to describe the release of solutes in sediments and offer better insights into the labile pool size and kinetics of solute resupply from the solid phase (Harper et al., 1998). DGTs are limited in their ability to provide quantitative results, primarily due to issues with knowledge of their sampling rate (Yao et al., 2019). Pseudo-first-order models work well because the slowest kinetic process is generally near-surface diffusion, which is by definition first-order and generally rate-limiting (Noh et al., 2019). If more accurate information is available for the kinetics of diffusion and if the duration of exposure is known, then rates of sampling can be calibrated for various compounds, and quantitative estimates of the available fraction and concentrations can be determined (Dunn et al., 2003). Only one study used DGT and DIFS model for the remobilization of organic pollutants (pesticide atrazine) in an intact sediment core for *in situ* fine scale (Li et al., 2021). The hypothesis of this study is that DIFS model can quantitatively estimate the dynamic processes of antipsychotics in either spiked sediment system or *in situ* field sediments.

Here, the DIFS model was adapted to describe the dynamics of antipsychotics in sediments in two different environments with quantitative parameters to describe kinetics and partitioning. The DGT samplers were deployed both in spiked sediments, which were well-equilibrated with nine representative and environmentally relevant antipsychotics (amitriptyline, bupropion, carbamazepine, citalopram, clozapine, duloxetine, fluoxetine, lamotrigine, and venlafaxine), and *in situ* surficial sediments from a natural river for various time periods up to 30 days. The concentrations accumulated in DGT samplers over time were fitted to the DIFS models to estimate desorption rate constants and labile pool sizes of antipsychotics in the solid phase of sediments.

2. Materials and methods

2.1. Standards, reagents, and chemicals

Nine high purity (>98%) antipsychotics (amitriptyline, bupropion, carbamazepine, citalopram, clozapine, duloxetine, fluoxetine, lamotrigine, and venlafaxine) and the corresponding nine mass-labelled internal standards (amitriptyline-d_6, bupropion-d_9, carbamazepine-d_{10}, citalopram-d_6, clozapine-d_4, duloxetine-d_7, fluoxetine-d_5, lamotrigine-[^{13}C;$^{15}N_4$], and venlafaxine-d_6) were used. The details on standards, reagents, and chemicals are shown in Text S1 and Table S1 (Supplementary material).

2.2. Theory of DGT and DIFS model in sediments

The DGT sampler for organics is composed of a binding layer, a diffusive layer, and a filter membrane for protection (Challis et al., 2016; Chen et al., 2012). External analyte diffuses through the diffusion layer with a certain diffusion coefficient (D) and is promptly bound by the adsorbent in the binding layer. After an initial period needed to reach steady-state diffusion dynamics, a constant concentration gradient is maintained in the diffusion layer (Fig. S1).

DGT *in situ* passive sampling is based on Fick's first law of diffusion (Davison and Zhang, 1994). After an initial period that is needed to reach steady-state diffusion dynamics, a constant concentration gradient is maintained in the diffusion layer. This gradient is determined by the thickness of the diffusion gel (Δg) and the interfacial concentration of labile analytes between DGT device and sediments (C_i). The flux of antipsychotics (F, mol cm^{-2} s^{-1}) through the diffusion phase to the binding phase can be calculated based on Fick's first law (Eq. (1)). As deployment time increases, the compound concentrations in the sediment solution are gradually depleted from increasingly further distances from the interface between sediments and the DGT sampler. This can induce a resupply of compounds through diffusive transport from the particle phase (Harper et al., 2000). Since the binding gel functions as an infinite sink that is consistently adsorbing compounds from sediment solution during deployment, the total mass of bound compounds can be determined after retrieval of the device. Meanwhile, the flux of compounds can be expressed as Eq. (2).

$$F(x,t) = \varepsilon D \frac{C_i(x,t)}{\Delta g}, 0 < t < T, x \in (-r, r) \quad (1)$$

$$m = \frac{\varepsilon D}{\Delta g}\int_{-r}^{r}\int_{0}^{T} C_i(x,t)dtdx \quad (2)$$

where ε is the porosity of the agarose diffusion gel, D ($cm^2\ s^{-1}$) is the diffusion coefficient of each analyte in the diffusion layer, t (s) is the deployment time, r represents the radius of the circular exposure window, and m (mg) is the accumulated mass of compounds in the binding gel. Porosity of the gel ($\varepsilon = 1 - \varnothing$, $\varnothing$ is the volume fraction of fibers) can be defined as an estimate of the pore size determined by using a hydrodynamic model that links permeability to the structural properties of the fibril-matrix (Levick, 1987). The Carman Kozeny equation (Carman, 1937) offers the relation between permeability, average hydraulic radius (r_H), and hydrodynamic screening distance (κ), explained as Eq. (3).

$$\kappa = \varepsilon\cdot\frac{r^2{}_H}{k} \quad (3)$$

where k represents the Kozeny factor, depending on the channel shape and tortuosity. Pluen et al. (1999) used this model for 2% agarose gel with results of $\varepsilon = 0.9805$, $\varnothing = 0.0195$, which were also used in our study.

The time-averaged interfacial concentration (C_{DGT}) of targeted solutes accumulated on the binding gel can be determined according to m shown as Eq. (4) (Lehto et al., 2008).

$$C_{DGT} = \frac{\int_{-r}^{r}\int_{0}^{T} C_i(x,t)d_t d_x}{T} = \frac{m\Delta g}{\varepsilon ADT} \quad (4)$$

where A is the area of exposure surface (2.54 cm^2). m can be determined with HPLC-Orbitrap MS after extraction of antipsychotics from the binding gel.

A ratio (R) between C_{DGT} and the independently measured initial concentration ($C_{porewater}$) in interstitial water (porewater) of sediment can explain the extent of depletion of concentrations at the interface of the DGT device (Eq. (5)) (Ernstberger et al., 2002).

$$R = \frac{C_{DGT}}{C_{porewater}} \quad (5)$$

The magnitude of the value of R depends on kinetics of adsorption-desorption in sediments. Kinetic parameters can be derived from inputting R to the DIFS model. The one-dimensional DIFS model is used for describing processes in only the sediment solution, while the two-dimensional DIFS model is used for simulating the DGT behavior within sediments (Lehto et al., 2008). In the sediment system, the flux from the solid phase to solution induced by DGT (F_{ss}) might not be equivalent to the maximum potential flux from the solid phase to the solution (F_{pm}), which depends on DGT characteristics and the sediment properties. There are three possibilities for the relationship between F_{ss} and F_{pm} (Fig. S1): (*i*) fully supplied-compounds adsorbed by the DGT device from sediment solutions can be replenished instantly from the solid phase supplied by a labile pool size, which efficiently maintains a constant concentration in the solution; (*ii*) diffusion only-no resupply from solid phase to the sediment solution ($F_{ss} \approx 0$). Concentrations of compounds in porewater at the interface of the device will gradually decrease, with this decline of concentration progressively extending to the sediments situated further away from the interface of the DGT device; (*iii*) there is partial resupply of compounds from the solid phase to sediment porewater whereas this supply is not enough to maintain the initial concentration in the porewater that can be taken up by the DGT device ($F_{ss} \approx F_{pm}$). Generally, the most probable condition for most organic compounds in sediments is case (*iii*) due to the supplies of organic compounds from the solid phase to solution through the release of several forces, *e.g.*, surface complexation, electrostatic interaction, and hydrogen bonding (Delle Site, 2001).

Values of R can be used to differentiate the three cases stated above. When $R \geq 0.95$, the compounds in porewater are completely replenished from the solid phase. When $0.1 < R < 0.95$ and $R < 0.1$, indicates scenarios of partially supplied and diffusion only, respectively. In general, larger values of R indicate larger sizes of labile pools and more rapid rates of replenishment. Another approach that does not rely on measurements of R to identify these cases is by simultaneously deploying DGT samplers with different thicknesses of diffusive layers (different Δg), that can be used to plot F against $1/\Delta g$. If there is a linear increase of fluxes with $1/\Delta g$ or time, it would be fully supplied, whereas the curved increase would be partially supplied or diffusion only.

The DIFS model can describe quantitatively the distribution ratio (K_{dl}, $cm^3\ g^{-1}$) between concentrations of labile compounds associated with the solid phase (C_s) to concentrations in sediment porewater ($C_{porewater}$) at steady state (Harper et al., 2000) (Eq. (6)) and the exchange rate of the sediment response time, T_c (s), which is the characteristic time in the disturbed system (after DGT deployment) to approach 63% of its steady-state (Eq. (7)) (Jannasch et al., 1988).

$$k_{dl} = \frac{C_s}{C_{porewater}} = \frac{k_f}{P_c k_b} \quad (6)$$

$$T_c = \frac{1}{k_f + k_b} = \frac{1}{k_b + (k_{dl}P_c + 1)} \quad (7)$$

where k_f and k_b represent adsorption and desorption rate constant (s^{-1}), and P_c is the particle concentration ($P_c = M/V$, g cm^{-3}, where M represents the gross mass of the solid particles and V represents the volume of porewater of the gross volume of sediment). Key parameters required by the DIFS model are listed in Table S2, hypothesizing a particle density of 2.56 g cm^{-3} (Chen et al., 2014). In the present study, DGT samplers with different diffusion layer thicknesses were deployed for different times. In each interval, C_{DGT} was calculated with Eq. (4) and $C_{porewater}$ was directly measured, and the corresponding R value was calculated (Eq. (5)). K_{dl} and T_c values were derived from the best-fit model of a plot of R *versus* t. Finally, k_b and k_f were derived from K_{dl} and T_c (Eqs. (6) and (7)).

2.3. Sediment preparation and spiking

Sediment for spiking was collected from an urban area of the South Saskatchewan River (52°09′22.8″N 106°38′08.2″W), in Saskatoon, Canada (Fig. S2), upstream of Saskatoon's wastewater treatment plant. Surface sandy-loam sediments (<5 cm) were sampled with a shovel and stored in a PVC bucket that was previously rinsed with river water, then immediately transferred to a thermostatic chamber (4 ± 1 °C) in the dark for 1 day. Afterward, the sediments were transferred to a freezer (−20 °C) before lyophilization (Dura-Dry MP FD2085, Stone Ridge, NY). The dried sediments were passed through a 2-mm sieve to remove large fragments and roots before the spiking experiment and determination of sediment physicochemical properties. The pH of sediment was potentiometrically measured in a 1:2.4 sediment-liquid mixture containing either ultrapure water or 0.01 M $CaCl_2$ solution. Maximum water holding capacity (MWHC) was determined by soaking the sediments in water and draining for 2 h (Priha and Smolander, 1999). Distributions of particle sizes, organic matter, and TOC (total organic carbon) were measured by hydrometer and federal standard method (MMFSPA Ch6 1991 m), respectively, which were conducted by Bureau Veritas Laboratory (Edmonton, AB). Characteristics of this sediment are: *p*H-H_2O 7.13, *p*H-$CaCl_2$ 6.69, MWHC 65%, sand 54%, silt 35%, clay 11%, organic matter 1%, and TOC 0.59%.

Before spiking, dried sediment was extracted and analyzed using high-performance liquid chromatography-Orbitrap™ mass spectrometry (HPLC-Orbitrap MS) (details in Section 2.8) to ensure that tested analytes did not pre-exist in our sediments. Approximately 2 mg of each antipsychotic compound was dissolved using a small volume of methanol (~2 mL), diluted in 50 mL ultrapure water, and added to 800 g of sediments (total in the tank). To do this, a small portion of the sediment was placed in a mortar, and the spiking solution was gradually added and mixed thoroughly to minimize solvent effects. Finally, all sediment portions were mixed and stirred together using an Omni Mixer Homogenizer (PerkinElmer, Waltham, MA) to reach a concentration of 2.5 mg kg^{-1} for each antipsychotic compound

in order to be adequate supply to sediment solution following a previous study (Chen et al., 2015). The well-mixed sediments were then placed in a glass tank (length: 12 cm, height: 7 cm, and width: 6 cm), and the overall weight (sediment + glass tank) was measured each day until the weight remained stable (±0.1 g) over three days at room temperature (21 ± 0.5 °C). Blank sediment was prepared using the same amount of methanol and ultrapure water without antipsychotic compounds following the same protocol. Afterward, the sediments were submerged under ~3.5 cm of ultrapure water and kept at the same water level for 24 h at room temperature before the deployment of DGT devices.

2.4. DGT preparation

Standard size of DGT devices (made from polytetrafluoroethylene) with 0.75 mm Sepra™ ZT (surface modified styrene divinylbenzene, Phenomenex, Torrance, CA) resin gels, 0.75 mm agarose diffusive gels, and 0.45 μm pore size polyethersulfone (PES) filter membranes (Sartorius Stedim Biotech GmbH, Gottingen, Germany) were prepared following the protocols of Challis et al. (2016). Additionally, DGT units were assembled with several thicknesses of diffusive gels (0.75, 1.0, 1.2, 1.5, 1.8, 2, and 3 mm). Briefly, a 2% dissolved agarose was cast between vertical glass sheets using the Mini-Protean® casting system (BioRad, Mississauga, ON). The gels were cut into corresponding disks and stored at room temperature in ultrapure water. The binding gels were cast horizontally to make the sorbent powder settle on one side of the gel. Eventually, cut gels contained ~25 mg of sorbent per gel disk. Both diffusive gels and binding gels were rinsed with ultrapure water before preparation of the DGT device. The binding gel was placed on the standard polytetrafluoroethylene DGT base (sorbent side pointed up), covered with the diffusive gel and PES filter membrane layered on top, and sealed with the DGT cap. To test the performance of DGT samplers, the potential adsorption of the targeted antipsychotics to the diffusive gel, DGT molding, and PES filter membrane, as well as the sorption efficiency of Sepra™ ZT binding gel were assessed (details in Text S2).

2.5. DGT deployment

2.5.1. Deployment in laboratory-controlled spiked sediments

DGT devices were assembled before deployment in sediments. DGT devices with various thicknesses of diffusive gels (triplicate) were then pressed firmly onto the sediment in order to achieve a close contact between sediment and DGT devices (Fig. 1). A digital thermometer was inserted into the tank water to ensure a constant temperature during the experiment. DGT devices were deployed for 1, 3, 5, 8, 11, 16, 20, 25, or 30 days in the laboratory at a water temperature of 21 ± 0.5 °C for obtaining the information about the extent of depletion of sediment solution concentrations of antipsychotics at the DGT interface.

2.5.2. Deployment in field

One DGT probe (length: 170 mm and width: 40 mm), constructed from acrylonitrile butadiene styrene (ABS) polymer and contained the same three layers as the DGT device, with different dimensions of binding gel (~250 mg per gel), diffusive gel, and PES membrane (length: 150.3 mm and width: 20.4 mm), and a temperature logger was attached in the bottom on a perforated stainless-steel profile (thickness: 3.18 cm, width: 3.18 cm, length: 183 cm). Three separate profiles with attached samplers were slowly inserted into sediments, with 2 cm of the probe board exposed out of sediments (15 cm was put into the sediment), and were supported by three cement blocks (height: 19 cm, width: 27 cm) for protection (Fig. S3). DGT setup for sediments was deployed from a natural area (Fred Heal Canoe Launch, 51°59′04.8″N 106°44′13.9″W) of the South Saskatchewan River, in Saskatoon, Canada (Fig. S2), downstream of Saskatoon's wastewater treatment plant. Characteristics of field sediment are: pH-H_2O 7.43, pH-$CaCl_2$ 6.21, MWHC 61%, sand 46%, silt 32%, clay 22%, organic matter 2%, and TOC 0.63%. The nine antipsychotic compounds were detected at this sampling site in previous investigation (unpublished data). Three extra DGT probes were brought to the field as the field blanks. DGT probes were deployed for 1, 3, 6, 9, 12, 15, and 21 days.

2.6. DGT retrieval, sediment sampling, and extraction

DGT devices/probes were retrieved after each duration of deployment in triplicate. Sediment attached to DGT devices was rinsed off using ultrapure water, and the devices were disassembled to remove the binding gel and transfer them into glass vials immediately. The cleaned DGT probes were covered by aluminum foil and delivered to the laboratory immediately. The procedure of extraction of binding gel and labile concentration is shown in Fig. 1. For binding gel disassembled from the DGT device, fifty microliters of 1 mg L^{-1} internal standards were added. Five milliliters of methanol were added into the vial for ultrasonic extraction for 10 min,

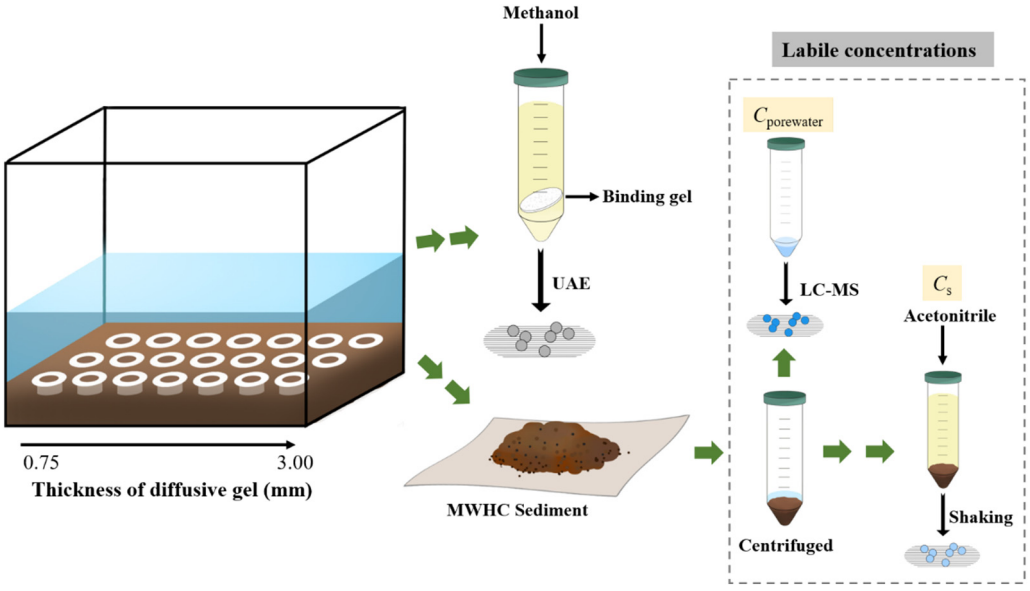

Fig. 1. Schematic representation of the deployment of DGT samplers with different diffusive gel thicknesses (0.75, 1.0, 1.2, 1.5, 1.8, 2.0, and 3.0 mm) in sediments. Three DGT devices in a row represent triplicate samplers, while the thickness of diffusive gels progressively increases. Additionally, the procedure used to obtain concentrations in the sediment porewater ($C_{porewater}$), and extract the labile concentration with the solid phase (C_s) as shown in Eq. (6), and the concentration of binding gel is depicted.

and the same procedure was repeated three times. Extracts were combined and reduced to near dryness with a gentle flow of nitrogen gas (purity >99%), reconstituted in 1 mL of methanol, and filtered through Target2™ 0.2 μm polytetrafluoroethylene syringe filters (Waltham, MA) into 2 mL LC vials.

Once DGT devices/probes were retrieved, approximately 5 g of wet sediment (adjacent to DGT probes in the field, depth: ~5 cm) was sampled and drained for 2 h (for maximum water-holding capacity) and then centrifuged at 1280 $\times g$ for 40 min to obtain sediment porewater. The sediments sampled from the field were stored in amber bottles which were covered by ice bags until delivering the laboratory. Fifty microliters of internal standards were added to 950 μL of this solution and filtered through a 0.2 μm polytetrafluoroethylene syringe filter into 2 mL LC vials for analysis of $C_{porewater}$. The remaining sediment was lyophilized, extracted twice with 5 mL of acetonitrile for 10 min on a shaker, fortified with internal standards, and then followed the same procedure above for analysis of C_s.

2.7. Agarose diffusion coefficient (D)

Diffusion coefficients of analytes were measured using a diaphragm diffusion cell in pseudo-steady-state mode (Fig. S4), which is the most accurate method to determine diffusion coefficients in agarose gel (Westrin et al., 1994; Zhang and Davison, 1999). Each cell (made of clear acrylic) held *ca.* 50 mL and had a 2.3 cm^2 circular connecting window. A diffusive gel was placed on the window (a spacer was made based on the gel thickness) between the two cells and gently sealed together with clamps. Each cell was full with 40 mL solution. To each cell, 20 mL of 10 mM NaCl was added, followed by a spike of the 9-analyte stock mixture (1000 μg L^{-1}) prepared in 5% methanol into the source cell at a target concentration of 500 μg L^{-1}. Meanwhile, 20 mL of 5% methanol spike was added into the receiving cell. Both cells were stirred gently on stir-plates. The water temperature was kept at 21 ± 0.5 °C during the experiment. Triplicate samples (195 μL) were taken from the receiving cell and source cell at ten different time points spread out over the experimental duration (5 to 140 min). Samples were pipetted directly into LC vials and spiked with 5 μL of 1000 μg L^{-1} internal standards before instrumental analysis.

The mass of analyte from the receiving cell was plotted as a function of time to acquire a slope (k) from the first-order diffusion rate constant, D can be calculated as Eq. (8).

$$D = \mathrm{k}\frac{g}{CA} \tag{8}$$

where Δg is the thickness of the agarose gel, C is concentrations of nine antipsychotics in the source cell, and A is the area of the window between two cells.

For D calculation for different temperatures, they were calculated from D values for 25 °C (D_{25}) using an empirical formula established by Yuan-Hui and Gregory (1974) (Eq. (9)):

$$\log\frac{D_{25}(273+T)}{298} = \log D_T - \frac{1.37023(T-25)+0.000836(T-25)^2}{109+T} \tag{9}$$

2.8. Instrumental analysis

Analysis of nine antipsychotic compounds from all samples was conducted using a Vanquish UHPLC and Q-Exactive™ HF Quadrupole-Orbitrap™ hybrid mass spectrometer (Thermo-Fisher, Mississauga, ON). LC separation was achieved with a Kinetex 1.7 μm XB-C_{18} LC column (100 × 2.1 mm) (Phenomenex, Torrance, CA) by gradient elution with 95% water + 5% methanol (A) and 100% methanol (B), both containing 0.1% formic acid (Optima MS grade) at a flow rate of 0.2 mL min^{-1} and a column temperature of 40 °C. The gradient method started at 10% B, ramping linearly to 100% B over 7 min, was held for 1.5 min, and returned to starting conditions for column re-equilibration between 8.5 and 11 min.

Samples were ionized using positive mode heated electrospray ionization (HESI). The Q-Exactive Orbitrap method used the following source parameters: sheath gas flow = 35; aux gas flow = 10; sweep gas flow = 1; aux gas heater = 400 °C; spray voltage = 3.8 kV; S-lens RF = 60; capillary temperature = 350 °C. A Full MS/parallel reaction monitoring (PRM) method was used with the following scan settings: 120,000/15,000 resolution, AGC target = $1 \times 10^6/2 \times 10^5$, max injection time = 50 ms/50 ms, full MS scan range of 80–500 m/z and PRM isolation window of 2.0 m/z and multiplexing count of 4.

Batch analyses of samples were conducted by running calibration standards at the beginning and end of each sample batch along with blanks run between replicate treatment sets and 50 μg L^{-1} single calibration standards after running calibration standards and every 20 samples as a QA/QC protocol. A nine-point calibration curve ranging from 0.01–950 μg L^{-1} and spiked with 50 μg L^{-1} IS was used for quantification by isotope dilution (linearity >0.99 for all analytes). All data acquisition and processing were conducted using Xcalibur v. 4.2 (Qual and Quan browser). The quantification of each analyte was according to precursor and product ions, and retention time (Table S3 and Fig. S5). The calibration curves (Table S4), method detection limits (MDL), limits of quantitation (LOQ), and limits of detection (LOD) are reported (Table S5). When the concentrations of analytes were below the detection limit, the substitution method (LOD/square root of 2) was used (Ganser and Hewett, 2010). MDL were calculated using the average blank DGT concentration plus three times the standard deviation (3σ). The extraction and processing procedures of DGT laboratory blanks were the same as described in the main text. The instrumental LOD and LOQ were regarded as the low concentration of analyte with a measured signal/noise (S/N) of 3 and 10, respectively (LOD = $3\sigma_{blank}$/slope, LOQ = $10\sigma_{blank}$/slope). Slopes were obtained from 9-points calibration curve.

2.9. Statistical analyses

Kolmogorov-Smirnov test and Shapiro-Wilk test were used to check the normality of datasets. Hartley's Fmax test was used for data homoscedasticity. Then, a one-way ANOVA with a Tukey's posthoc test was conducted to compare diffusion coefficients at various thicknesses of diffusive gels, and to compare concentrations measured by DGT and porewater concentrations directly analyzed by LC-MS. Significant differences were defined as $p \leq 0.05$. Statistical analysis was conducted using IBM SPSS 26.

3. Results and discussion

3.1. DGT performance and diffusion coefficient

3.1.1. Sorption to DGT materials

Sorption steady-state concentrations of the nine antipsychotics were quickly reached (<0.5 h) for DGT molding and diffusive gel. Concentrations remained consistent for 168 h with a negligible fraction (<0.01% total mass of the standard solution) adsorbed to DGT moldings and diffusive gels. This observation is consistent with tests for other organic compounds (*e.g.*, pharmaceuticals, hormones and pesticides) (Chen et al., 2018; Guan et al., 2018; Wang et al., 2019; Zhang et al., 2018; Zheng et al., 2015; Zou et al., 2018).

Concentrations of all compounds on the PES filter membrane increased within an hour and reached steady state sorption within 2 h (Fig. 2). Proportions of analytes sorbed were negligible (<1% of the total mass of the standard solution) for all durations. This result is consistent with results of previous studies, which confirms that PES filter membranes can support long deployment times, high sampling rates, and minimal adsorption of hydrophilic organic compounds (log K_{ow} < 3) (Alvarez et al., 2004; Zhang et al., 2018). Large amounts of sorption (>30% of the total mass of the standard solution) of some hydrophobic compounds (log K_{ow} = 3.7–5.1) by the PES filter membrane has been previously reported by Wang et al. (2019), which did not reach sorption equilibrium after as long as 6 h, thereby potentially resulting in a lag time for uptake into binding gels for short deployment periods. Among analytes studied here, log K_{ow} values of amitriptyline, bupropion, duloxetine, and fluoxetine were in a range similar to that of the

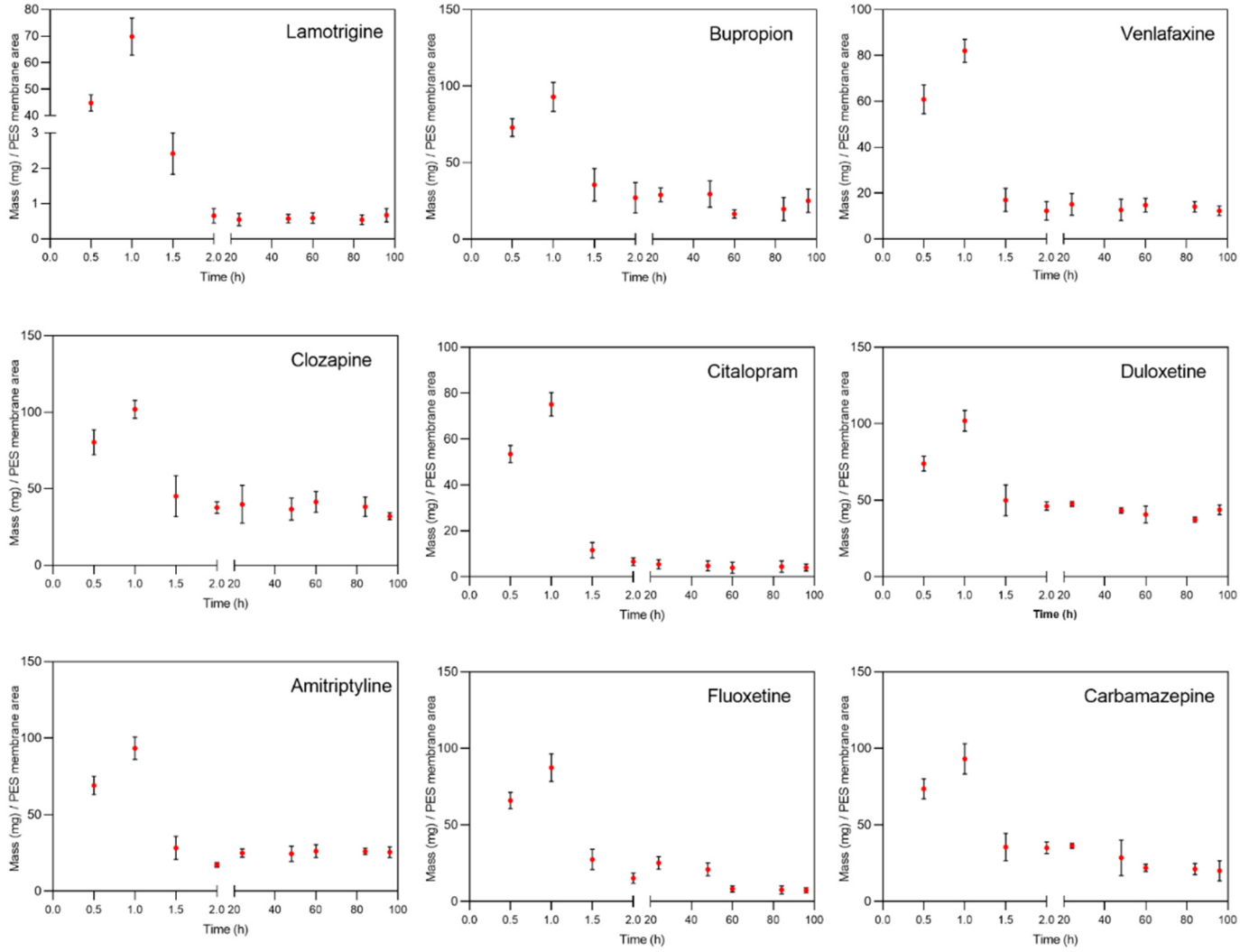

Fig. 2. Dependence of the mass of nine antipsychotics accumulated per the polyethersulfone (PES) filter membrane area (4.91 cm^2) was determined over time in a 250 μg L^{-1} standard solution at a water temperature of 21 ± 0.5 °C. Circles represent mean values, error bars the standard deviation of measurements from triplicate samples.

previous study by Wang et al. (2019) (3.85 to 4.95) but did not show similarly elevated sorption. By plotting equilibrium mass adsorbed *vs.* the final aqueous solution (Fig. 3), the adsorption trends did not follow log K_{ow} values.

3.1.2. Effect of contact time and adsorption capacity for binding gel

Adsorption of the nine antipsychotics to Sepra™ ZT binding gel was rapid, within 4 h, and became slower as it reached steady-state and the available surface binding sites became saturated (Fig. 4). To quantify adsorption capacity of a Sepra™ ZT binding gel for the analytes from a given solution, amounts of each analyte adsorbed by Sepra™ ZT binding gel *vs.* the original concentration of each analyte in the solution were plotted (Fig. 5). An increasing trend of the adsorption amount with solute concentration was observed for all nine compounds, ranging from 200 to 2000 μg L^{-1} without a significant deviation from linearity. At a solute concentration of 5000 μg L^{-1}, the amounts adsorbed were not significantly different from that at 2000 μg L^{-1}, which indicated that binding sites of the Sepra™ ZT adsorbents were saturated. Adsorption by Sepra™ ZT binding gel at a 2000 μg L^{-1} solute concentration was 0.23 μg mg^{-1} for lamotrigine, 0.06 μg mg^{-1} for bupropion, 0.15 μg mg^{-1} for venlafaxine, 0.25 μg mg^{-1} for clozapine, 0.07 μg mg^{-1} for citalopram, 0.10 μg mg^{-1} for duloxetine, 0.14 μg mg^{-1} for amitriptyline, 0.36 μg mg^{-1} for fluoxetine, and 0.30 μg mg^{-1} for carbamazepine. Taking 7 days as deployment time, the calculated time-average concentration is 58.19 μg L^{-1} for lamotrigine, 18.53 μg L^{-1} for bupropion, 58.80 μg L^{-1} for venlafaxine, 66.78 μg L^{-1} for clozapine, 14.47 μg L^{-1} for

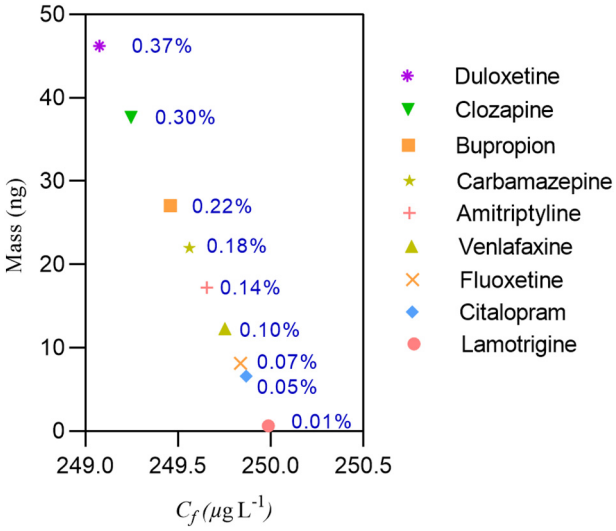

Fig. 3. The plot of the maximum equilibrium mass adsorbed by PES filter membrane *vs.* the final aqueous concentrations (C_f) for nine antipsychotic compounds. The blue numbers represent the adsorbed fraction (%, adsorbed mass by PES membrane/ total mass in the solution).

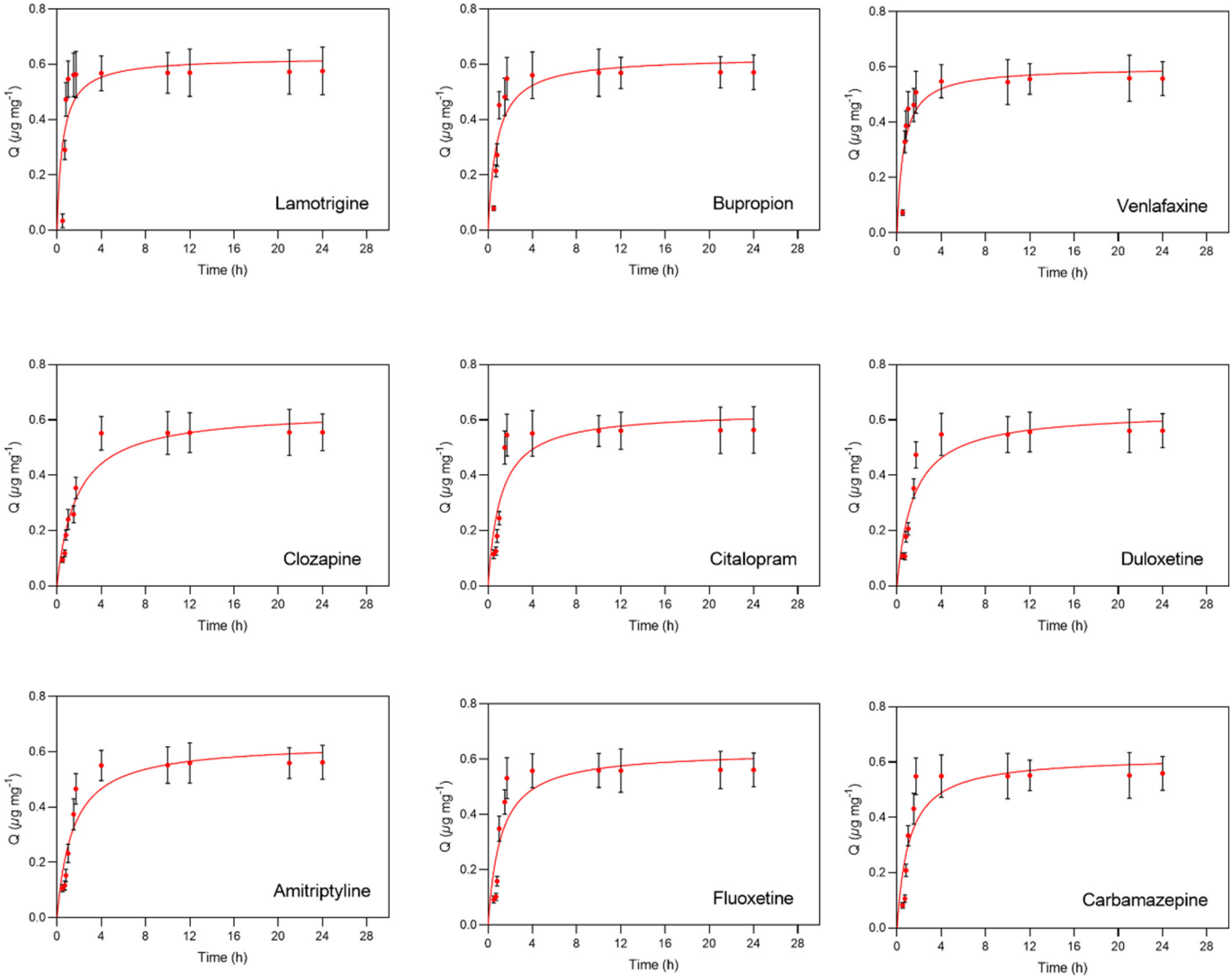

Fig. 4. Adsorption of nine antipsychotic compounds on Sepra™ ZT binding gel was observed at pH = 7 over 24 h at a temperature of 21 ± 0.5 °C. Circles represent mean values, and error bars are the standard deviation of measurements from triplicate samplers. The adsorption amount (Q, $\mu g\ mg^{-1}$) was calculated from $Q = \frac{(C_0 - C_i) \times V}{1000m}$. C_0 and C_i represent the initial concentration and concentration from each sampling time, respectively. V and m represent the volume of the standard solution (mL) and the mass of adsorbents in the binding gel (mg), respectively.

citalopram, 38.07 μg L^{-1} for duloxetine, 29.19 μg L^{-1} for amitriptyline, 105.69 μg L^{-1} for fluoxetine, and 74.99 μg L^{-1} for carbamazepine, which is adequate to detect concentrations in aquatic environment (<1 μg L^{-1}) (Metcalfe et al., 2010).

3.1.3. Diffusion coefficients

Diffusion coefficients (D) of nine antipsychotics were measured using the diaphragm diffusion cell are summarized in Table S6. Linear correlations (R^2 from 0.96 to 0.99) between diffused masses and deployment time were observed (Fig. S6). The concentration of amitriptyline in the source compartment was observed to be unstable due to its water solubility. Issues with low-aqueous-solubility chemicals were previously reported for similar diffusion cell systems (Wang et al., 2019). The exact comparison of diffusion properties for such analytes in hydrogel and water could be conducted to confirm the diffusion coefficients. However, D_w is difficult to measure and requires specialized equipment. Most studies to date have used either the Wike-Change equation (Wilke and Chang, 1955) or the Hayduk-Laudie equation (Hayduk and Laudie, 1974) to estimate D_w values rather than experimentally determining them.

The values of diffusion coefficients at 21 °C of 0.75-mm gels did not show a statistically significant difference compared to gels of other thicknesses (1–3 mm; $p > 0.05$). D values of 2 and 3-mm gels showed an overall slight decrease (1–2%) compared to those in 0.75 mm since the slope from plotting between the mass of analytes and time for thicker gels became smaller (Table S6). These results also demonstrated values of D that were not strictly dependent on molecular mass according to Archie's Law (Chen et al., 2013), which is consistent with previous results (Liu et al., 2020). The diffusion coefficients ($cm^2\ s^{-1}$) at 21 °C (0.75 mm) were 4.98×10^{-6} for carbamazepine, 4.03×10^{-6} for bupropion, 4.92×10^{-6} for lamotrigine, 5.97×10^{-6} for amitriptyline, 3.17×10^{-6} for venlafaxine, 3.27×10^{-6} for duloxetine, 4.24×10^{-6} for fluoxetine, 6.02×10^{-6} for citalopram, and 4.66×10^{-6} clozapine. Values for D determined in this study were similar to previously reported values for carbamazepine (5.01×10^{-6}) and fluoxetine (4.38×10^{-6}) at 25 °C (Challis et al., 2016), while D for bupropion was slightly lower than that determined in a previous study (5.21×10^{-6}) at 25 °C (Fang et al., 2019).

3.2. Distributions in spiked sediment and concentrations measured by DGT

Concentrations in sediment porewater ($C_{porewater}$) and solid phase (C_s) did not change ($p > 0.05$) after 11 days of aging (Table 1). Non-extractable fractions ranged from 75 to 87% for all compounds except

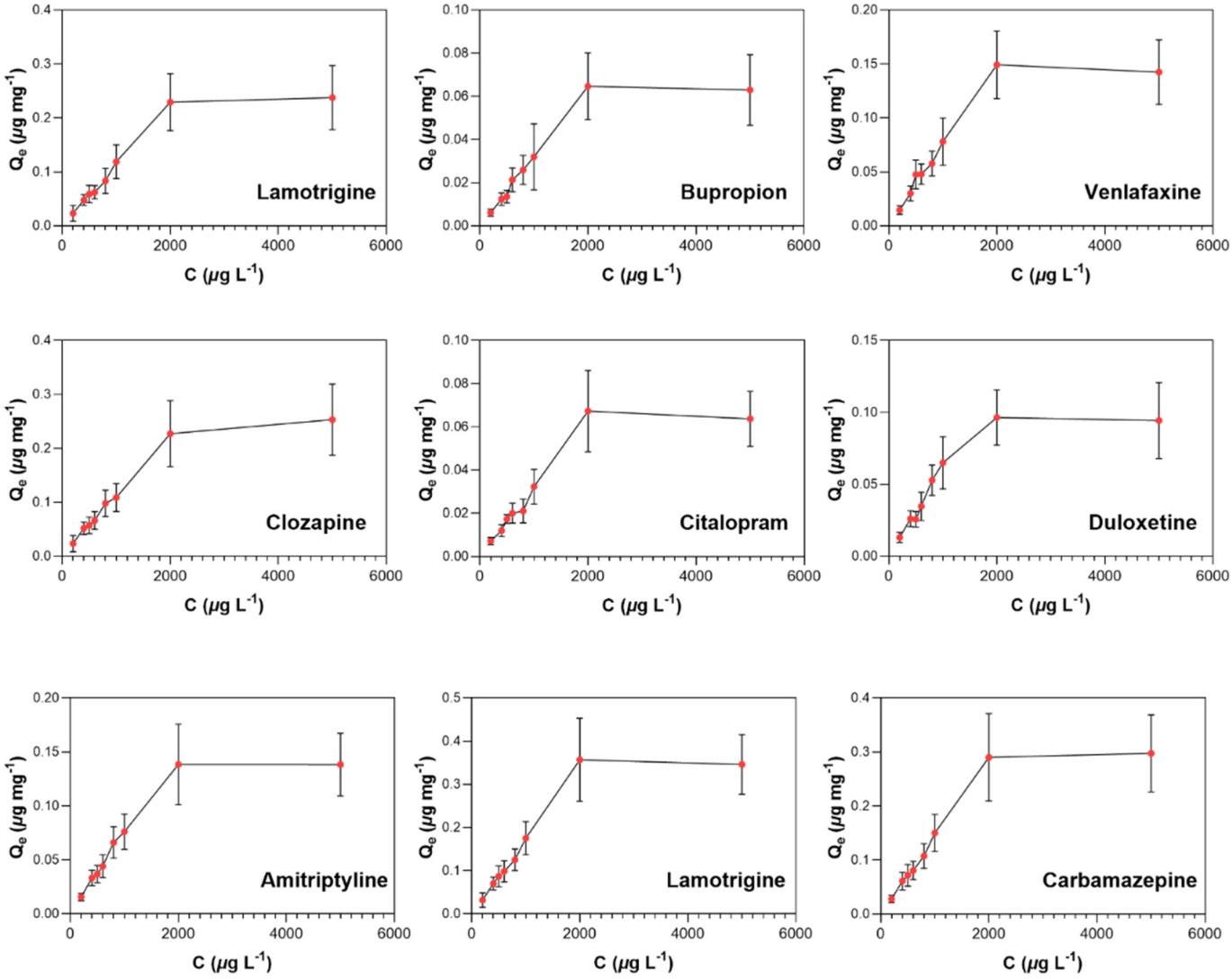

Fig. 5. Steady-state adsorption isotherms of nine antipsychotic compounds on Sepra™ ZT binding gel at pH 7 at 24 h and a temperature of 21 ± 0.5 °C. Circles represent mean values, error bars the standard deviation of measurements from triplicate samplers. C (μg L^{-1}) represents different concentrations of analyte standard solution. The steady-state adsorption amount (Q, $\mu g\ mg^{-1}$) was calculated from $Q_e = \frac{(C_0 - C_e) \times V}{1000m}$. C_0 and C_e represent the initial concentration and the reached steady-state concentration, respectively. V and m represent the volume of the standard solution (mL) and the mass of adsorbents in the binding gel (mg), respectively.

lamotrigine, for which it was 57%. This might be due to lesser organic carbon-water partitioning coefficients for lamotrigine (2.1) (Golovko et al., 2020) with small organic content of sediments (<0.6%). Decreasing concentrations of antipsychotics in sediment porewater were: carbamazepine > lamotrigine > bupropion > clozapine > amitriptyline > citalopram > duloxetine > venlafaxine > fluoxetine, which is dependent on kinetics of desorption from sediment.

Accumulated masses of antipsychotic compounds in DGT were directly proportional to the duration of deployment (Fig. 6). The nonlinear regression was obtained from curves of masses *vs.* duration (hyperbola equation)

Table 1
Concentrations (mean ± standard deviation, $n = 3$) of nine antipsychotic compounds in sediment porewater ($C_{porewater}$) and extracted by acetonitrile (C_s) at 0 day and at 11 day.

Compound	Day 0		Day 11	
	$C_{porewater}$ (μg L^{-1})	C_s (μg kg^{-1})	$C_{porewater}$ (μg L^{-1})	C_s (μg kg^{-1})
Amitriptyline	50.33 ± 6.14	365.09 ± 58.24	58.70 ± 8.93	375.90 ± 59.44
Bupropion	176.33 ± 25.52	330.65 ± 34.64	187.13 ± 28.21	341.40 ± 36.54
Carbamazepine	1160.32 ± 146	893.28 ± 113.77	1178.85 ± 127.56	907.23 ± 107.49
Citalopram	44.96 ± 5.48	301.62 ± 46.48	54.00 ± 7.57	309.76 ± 46.85
Clozapine	71.52 ± 7.84	601.19 ± 71.92	81.76 ± 11.88	613.61 ± 64.05
Duloxetine	39.16 ± 4.42	326.09 ± 44.66	47.24 ± 6.40	333.73 ± 34.44
Fluoxetine	31.34 ± 3.44	381.00 ± 39.00	38.35 ± 4.07	389.81 ± 46.30
Lamotrigine	595.15 ± 65.64	1063.83 ± 164.49	603.28 ± 71.46	1083.21 ± 148.19
Venlafaxine	39.71 ± 5.67	475.89 ± 65.82	45.96 ± 6.52	490.06 ± 65.86

No significant difference for $C_{porewater}$ and C_s at day 0 and day 11, respectively was found by Tukey's posthoc test.

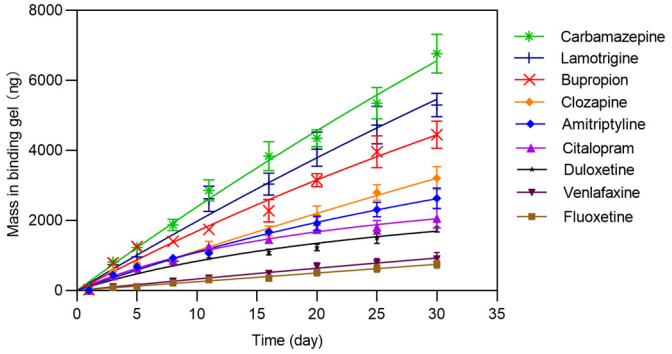

Fig. 6. The accumulated masses (mean values of triplicate samplers) of antipsychotics in the binding gel of DGT (0.75 mm diffusive gel) deployed in sediments with increasing deployment times.

indicated that the solid phase could not entirely supply porewater concentrations to sustain mass accumulation by DGT devices. Masses in DGT devices after all durations exhibited the same order of chemical accumulation as observed in sediment porewater. The fully sustained case with a theoretical straight line is related to the labile pool size and the desorption rate to resupply the sediment porewater (Lehto et al., 2008). Deviation of accumulated masses from the theoretical relationship can be explained by use of the DIFS model described below.

Deployment of DGT devices of various thicknesses of diffusive gels can provide further information on resupply kinetics. A plot of $1/\Delta g$ *vs.* measured fluxes (Fig. 7) indicated that concentrations of antipsychotic drugs were not fully replenished to sediment porewater through desorption from sediment particles. If the *R* ratio is equal to 1.0, there is no kinetic limitation in rates of replenishment of the aqueous phase from the solid phase. In this case, the theoretical slope of the *DC* (*D*: diffusion coefficient; *C*: a constant concentration gradient is maintained in the diffusion layer of DGT devices, adapted from Eq. (4)) is a straight line. However, concentrations of analytes could still not be efficiently resupplied from the solid phase since for all compounds, data fell below the $R = 1$ line. Duloxetine and fluoxetine exhibited <5% difference among thicknesses of diffusion layers, which indicated that, compared to the other antipsychotics, despite all values being lower than the theoretical slope, these two compounds had an extreme kinetic limitation of resupply from sediment particles. Fluxes to DGT devices with the smallest diffusion gel thicknesses were more limited through resupply from the solid phase. The largest values were observed for lamotrigine (0.42 pg cm^{-2} s^{-1}) and carbamazepine (0.83 pg cm^{-2} s^{-1}) for

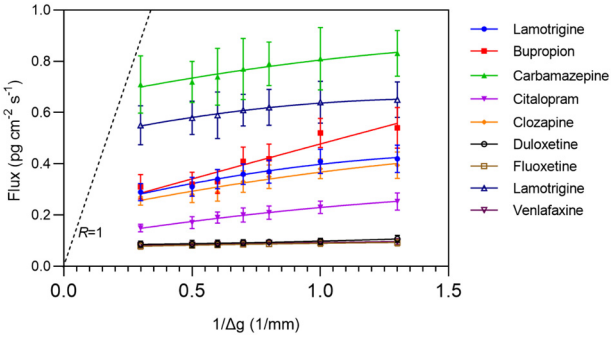

Fig. 7. The plot of DGT-induced fluxes of nine antipsychotics against the reciprocal of the diffusive layer thickness in the submerged sandy sediment. The fluxes of each antipsychotic compound to the DGT device were calculated from the measured mass in the binding gel *via* a defined exposure area during the deployment time. The hypothesis that steady-state flux from porewater to meet the demand of the DGT devices was not satisfied. The dashed line indicates the theoretical line based on Eq. (1). Symbols represent mean values, error bars the standard deviation of measured triplicate data.

the 0.75 mm diffusive gel, which represented approximately 55% and 77% of the potential fluxes (based on C_d), respectively.

3.3. Resupply from spiked sediment

Kinetics of desorption of antipsychotics from solid phases of sediments to interstitial porewater can be obtained by fitting experimental data to the DIFS model. The ratio *R*, plotted against duration of deployment, can provide information on rates of resupply of these compounds from sediment particles (Fig. 5). For lamotrigine, carbamazepine, venlafaxine, citalopram, bupropion, fluoxetine, and amitriptyline, there was an initially steep decrease in *R*, followed by either a less pronounced decrease. For clozapine and duloxetine, the ratio was constant. In theory, values of *R* increase during the initial phase of uptake while establishing a linear diffusion gradient within the diffusion layer. However, this process occurs very rapidly (<1 day), so it was not visible for longer durations. Thus, this could have led to a constant *R* value after the first rapid increase if there was a rapid resupply from the solid phase with a constant labile concentration of antipsychotics. During our study, since these compounds diffused into and were adsorbed by the DGT more rapidly than they could be resupplied by the solid phase of the sediments, the gradual decline for all nine antipsychotics resulted from the decreasing concentration in the porewater at the DGT interface. The decreasing order of values observed for *R* was lamotrigine > carbamazepine > venlafaxine > clozapine > citalopram > fluoxetine > bupropion > duloxetine ≈ amitriptyline, which reflects the same order of chemicals to resupply antipsychotics from sediments to sustain initial concentrations. Apparent values of *R* for bupropion, duloxetine, and amitriptyline indicated that $C_{porewater}$ remained at a small concentration during the entire duration of deployment. For clozapine, except for the first day, *R* values remained small, which indicated that the size of the labile pool of the compound was comparably small and not sufficient to resupply the soluble pool relative to the other antipsychotics.

The best fit of *R* values, plotted against duration of deployment for the 2D-DIFS model, was obtained by optimizing response times (T_c) and partition coefficients (K_{dl}) for each labile antipsychotic compound (Harper et al., 2000). Values of T_c and K_{dl} and derived parameters of dissociation and association rate constants are shown (Table 2). Comparisons of model simulations with empirical results were not ideal, with obvious deviations for all nine antipsychotics, especially when $T_c < 1$ day. Apart from potential experimental errors, this result indicated that the model does not accurately simulate all processes or compounds. Therefore, considering these limitations, parameters derived from the DIFS model should be used to estimate general kinetic information rather than detailed mechanisms, especially for various adsorption sites of various solid fractions.

Table 2
Parameters for nine antipsychotic compounds in sediment derived from the model fits using 2D-DIFS.

Compound	K_d* (mL g^{-1})	K_{dl}** (mL g^{-1})	T_c (s)	k_b (10^{-6} s^{-1})	k_f (10^{-5} s^{-1})
Amitriptyline	6.4	6.5	18984	3.58	4.91
Bupropion	1.8	30	12635	1.23	7.79
Carbamazepine	0.8	61	1498	5.14	66
Citalopram	5.7	53	1605	5.51	62
Clozapine	7.5	43	1515	7.16	65
Duloxetine	7.1	7.7	17184	3.38	5.48
Fluoxetine	10	44	9581	1.11	10
Lamotrigine	1.8	76	1844	3.38	54
Venlafaxine	11	49	2458	3.89	40

T_c is sediment response time (s) during the exchange.
k_f and k_b are adsorption rate constant (s^{-1}) and desorption rate constant (s_{-1}), respectively.
* Values of K_d were calculated using acetonitrile extract (the values are present in Table 1).
** Values of K_{dl} were calculated from DGT labile concentrations.

3.4. Size of the labile pool and kinetics of exchange in spiked sediments

Generally, K_{dl} is proportional to the size of the labile pool, which determines the magnitude of R during long-term deployments, and T_c is related to the rate of resupply from materials adsorbed to the solid phase, which influences values of R during shorter durations of deployment and is related to initial steepness of decline (Fig. 8) (Lehto et al., 2008). Values of K_{dl} were 4- to 42-fold greater than K_d ($p < 0.05$), except for duloxetine and amitriptyline, which exhibited comparable values. This implies that two approaches access different solid phase pools. It appeared that during short durations of deployment, duloxetine and amitriptyline could not dissociate from the sandy sediment used for the present study. Other antipsychotics could be more quickly released initially, which is in agreement with the expected ionic interactions of antipsychotics, such as lamotrigine and carbamazepine (Navon et al., 2011; Zhang et al., 2010), with various sediment components (*e.g.*, particles and minerals). Therefore, the labile fraction of antipsychotics cannot dissolve in acetonitrile, which also raises the issue that K_d of some compounds cannot be evaluated by extraction into acetonitrile. The fact that larger values of K_{dl} were observed for lamotrigine and carbamazepine implies that a large labile reservoir was available for resupplying these compounds to sediment porewater.

Values of T_c for these antipsychotics were in decreasing order: carbamazepine > clozapine > citalopram > lamotrigine > venlafaxine > fluoxetine > bupropion > duloxetine > amitriptyline. Carbamazepine, clozapine, citalopram, and lamotrigine could be supplied very quickly to sediment porewater (25–30 min). For lamotrigine and clozapine, the lesser values of T_c in the beginning resulted in an apparently greater resupply (R). However, increasing values of T_c resulted in a 10-fold lesser R for bupropion and amitriptyline, suggesting that the supply of these compounds was initially limited kinetically. In general, the more hydrophobic antipsychotics (fluoxetine, bupropion, duloxetine, and amitriptyline) appeared to be more difficult to supply from solid phase to porewater during short time periods. Given that our sediments had a comparably low organic carbon content, sediment mineral structure may be another factor that affects the release kinetics from the solid phase of these compounds. Kinetics of sorption of targeted antipsychotics have not previously been reported for sandy sediments. Values of k_f ranged from 7.79×10^{-5} to $66 \times 10^{-5}\ s^{-1}$, which is larger than k_b values (3.38×10^{-6} to 7.16×10^{-6}) in decreasing order of clozapine > citalopram > carbamazepine > venlafaxine > amitriptyline > duloxetine > lamotrigine > bupropion > fluoxetine, which indicated that adsorption, rather than desorption, dominated kinetics of sorption of all nine antipsychotics. The DIFS model can also be used to simulate the influence of kinetic factors on the transport of dissolved analytes (Fig. S6). Depletion of $C_{porewater}$ for carbamazepine, lamotrigine, and venlafaxine reached 2 cm while citalopram, fluoxetine, bupropion, duloxetine, and amitriptyline never went beyond 1 cm. Clozapine and citalopram displacement of 1.31 cm and 1.05 cm were observed from the DGT-sediment interface, respectively. This movement corresponds well with the respective K_{dl} values. Larger pools of labile carbamazepine, lamotrigine, and venlafaxine could still maintain the resupply from sediments to the solution until the maximum concentration within 2 cm was reached. This demonstrates that releases of these compounds in the long term are controlled by K_{dl} values. In contrast, duloxetine and amitriptyline were dominated by initial replenishment, a conclusion that is supported by the values

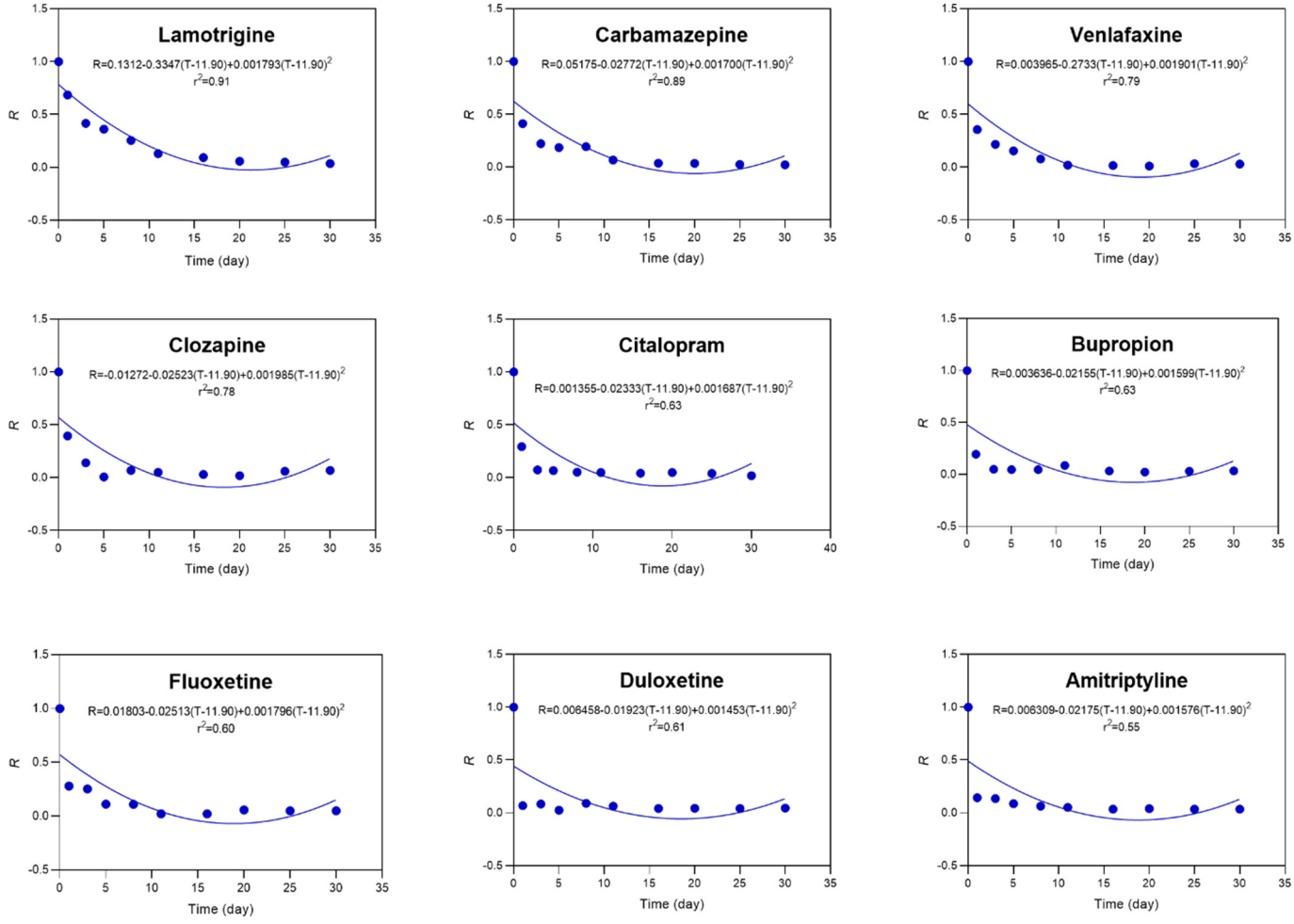

Fig. 8. The dependence of experimentally measured R ratios for nine antipsychotics with increasing deployment time. The blue lines represent the best fit lines of the 2D-DIFS model.

observed for T_c. However, the mechanism of interaction between sediment properties and these compounds to explain DIFS-derived parameters requires further dedicated studies.

3.5. Availability and resupply in field sediments

DIFS modeling is able to provide help information concerning interactions between solid phases and solutions in sediments. Therefore, application of DGT-DIFS can further understand *in situ* biogeochemical processes of antipsychotic drugs. The measured *R* for each antipsychotic compound was plotted against deployment time, showing an initial steep decline in *R* followed by a slower decrease, and finally reaching a stable value (Fig. 9), which is same trend as that in spiked sediments. Only venlafaxine showed a steeper decrease with longer deployment time (<15 day). This indicates that all antipsychotics experienced the gradual decline in sediment porewater at the probe interface, meaning these compounds are adsorbed by DGT binding gel more rapidly than they were supplied by diffusion and released from the sediment solid phase. The order of *R* values was followed: carbamazepine > fluoxetine > bupropion > lamotrigine ≈ clozapine ≈ citalopram > amitriptyline > duloxetine > venlafaxine. This implies that the capability of the sediments in field to remain initially the sediment porewater concentrations declined in the same order. However, this order is different from the results from spiked sediments. This may be due to non-constant sustaining source and dynamic sediment deposit rate to change the labile pool in the field.

Table 3
Parameters for nine antipsychotic compounds in the field sediment derived from the model fits using 2D-DIFS.

Compound	K_d (mL g^{-1})	K_{dl} (mL g^{-1})	T_c (s)	k_b (s^{-1})	k_f (s^{-1})
Amitriptyline	0.32	0.23	364919	6.19E−07	2.04E−06
Bupropion	8.42	0.14	261482	2.75E−06	8.45E−07
Carbamazepine	27.31	0.08	194191	4.26E−06	8.13E−07
Citalopram	4.62	0.13	372227	2.07E−06	6.51E−07
Clozapine	6.23	0.18	356254	1.83E−06	8.43E−07
Duloxetine	0.24	0.43	710013	9.20E−07	7.03E−07
Fluoxetine	10.24	0.06	332839	2.77E−06	3.42E−07
Lamotrigine	18.75	0.07	196907	2.45E−06	3.56E−07
Venlafaxine	0.03	0.009	145000	7.25E−07	1.74E−08

The annotations are followed as Table 2.

The best fits of R *versus* deployment time for antipsychotics were derived from DIFS model, showing that k_d and k_{dl} values of all antipsychotics were not close except for amitriptyline (Table 3). This implies that DGT and solvent extraction measurements access different solid phase pools, which is agreed to those obtained from spiked sediments (Table 2). T_c values for antipsychotics were in order of duloxetine > clozapine > citalopram > bupropion > amitriptyline > carbamazepine > lamotrigine > fluoxetine > venlafaxine. For venlafaxine, increasing T_c by an order of magnitude led to about 25% decrease in *R*. The results of T_c showed that the supply of antipsychotics in filed is partly limited kinetically in field sediments with

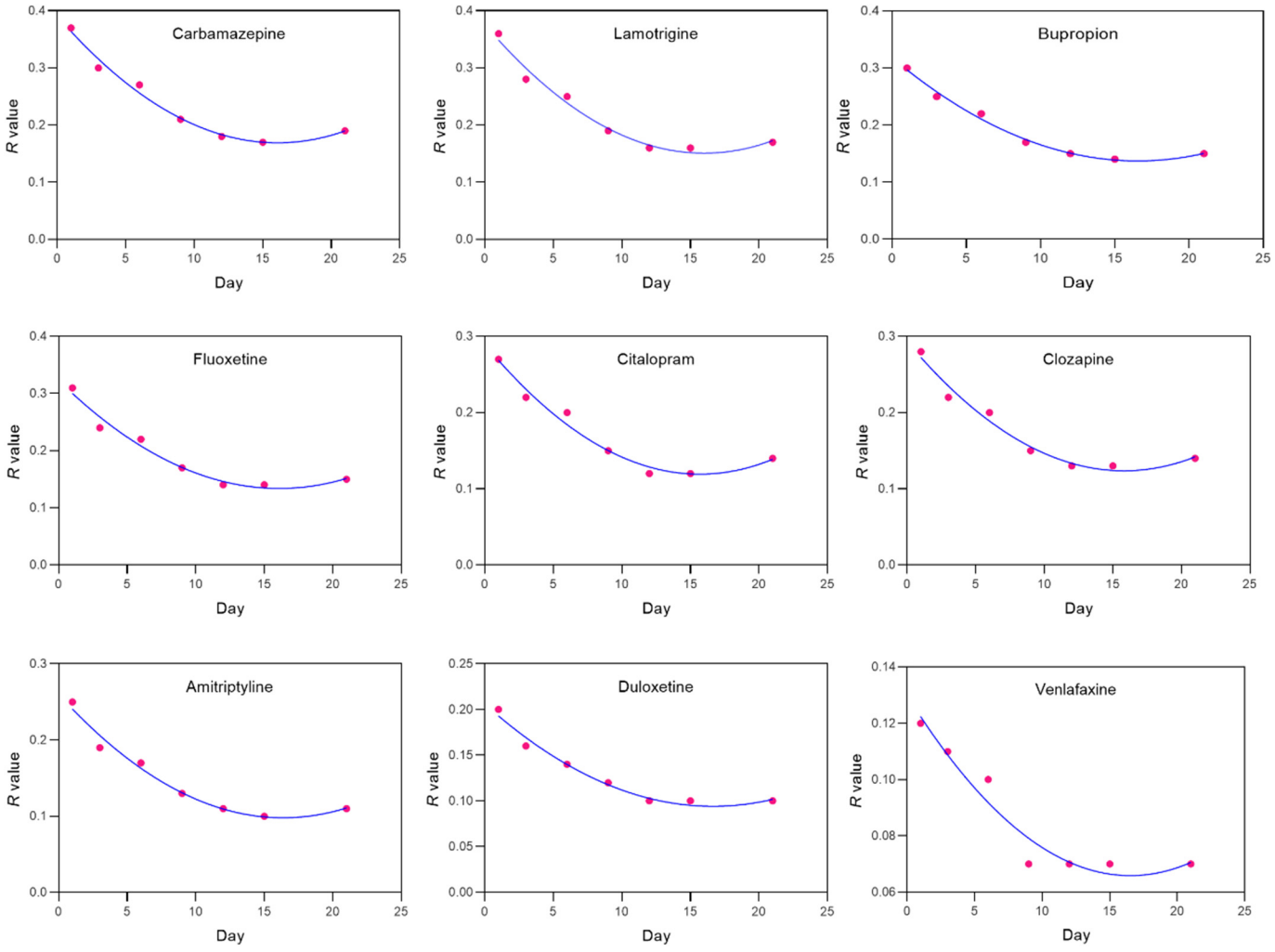

Fig. 9. The dependence of experimentally measured *R* ratios for nine antipsychotics with increasing deployment time from the field. The blue lines represent the best fit lines of the 2D-DIFS model.

increasing deployment time. From k_b and k_f values, the adsorption process was still dominant in field sediments for most antipsychotics whereas amitriptyline and duloxetine showed the predominant desorption process. This suggests that amitriptyline and duloxetine could be constantly released to the environment from sediments, which may be also ascribed to the small values observed for both k_d and k_{dl}.

4. Conclusion

Results of this study provide information related to the desorption kinetics of organic pollutants in sandy sediments with low organic matter content, which might be easily diffused and taken in by biota. Replenishment was most significant for lamotrigine and the least important for duloxetine and amitriptyline in spiked sediments, which could be explained by labile pool sizes for quick resupply over longer deployment times for lamotrigine and longer response time to supply the initial concentration in sediment porewater for duloxetine and amitriptyline. The difference in field sediments showed the most resupply from sediments to porewater was carbamazepine and lamotrigine, which is not highly depended on the labile pool size derived from DIFS model. The conventional experimental incubation DGT experiment may not represent the desorption process in natural sediments.

Although adsorption is still predominant in the studied both spiked and field sediments, the fluxes of DGT-induced gradient concentrations could be linked to their bioavailability. Fluxes measured by the use of DGTs have been indicated as an assessment/prediction tool for the potential of bio-uptake of metals (Bade et al., 2012; Degryse et al., 2006; Zhang et al., 2001). The DIFS model opens up the possibilities of quantitative measurements of sorption-desorption kinetic processes. Subsequently, these parameters can be linked to the processes by which sediment biota can absorb these compounds, which could enhance our understanding of the bioavailability of these compounds as a potential tool for risk assessment.

CRediT authorship contribution statement

Xiaowen Ji: conduct the whole experiment and wrote the manuscript.

Jonathan K. Challis: set up the LC-MS methods for nine antipsychotics and revised the manuscript.

Jenna Cantin: Running part of samples.

Ana S. Cardenas Perez: spiking the sediments.

Yufeng Gong: revised the manuscript.

John P. Giesy: revised the manuscript.

Markus Brinkmann: designed the experiment, secured funding, and revised the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.155104.

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Supplementary Material

Desorption kinetics of antipsychotic drugs from sandy sediments by diffusive gradients in thin-films technique

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Supplementary Caption

Text S1. Standards, reagents, and chemicals.

Table S1. Physical-chemical properties of targeted antipsychotic compounds.

Figure S1. Schematic diagram of sediment supplement type for organic compounds in a DGT configuration exposed to pore waters.

Table S2. Key parameters and values of DGT induced fluxes in sediments (DIFS) model.

Figure S2. Sampling site of sediment and site of DGT deployment in South Saskatchewan River, Saskatoon, Saskatchewan, Canada.

Text S2. Sorption experiments of DGT materials.

Figure S3. The setup for fixation of DGT sediment probes in the field.

Figure S4. The setup of the diffusion cell.

Table S3. Precursor and product ions ($[M+H]^+$), collision energy (HCD), and retention time of analytes.

Figure S5. Example chromatograms of nine antipsychotic compounds and their internal standards with scan filter of precursor ion (*m/z*) for a 500 ng mL^{-1} standard solution.

Table S4. Calibration curves (ranged from 0.01 to 950 μg L^{-1}) of the 9 antipsychotic compounds and R^2 ranges during the all samples run.

Table S5. LOD, LOQ, and MDL (μg L^{-1}) for all nine antipsychotic compounds.

Table S6. Diffusion coefficients (cm^2 s^{-1}) of nine antipsychotic compounds (average ± standard deviation) in different thicknesses of agarose diffusive gel measured by the two-compartment diffusion cell at 21 °C.

Figure S6. Diffused masses of nine antipsychotics in the receiving cell through 0.75 mm agarose gel at different times in a diffusion cell with 500 μg L^{-1} standard compounds in the source cell at an initial time.

Figure S7. DIFS model (1D) output for nine antipsychotics in the sandy sediment simulating concentration in porewater on the distance of DGT interface at 30 days.

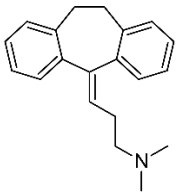
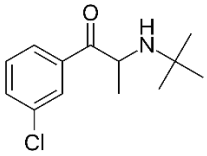
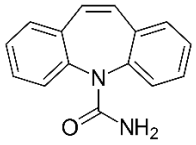
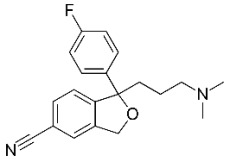
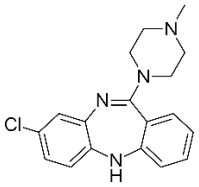
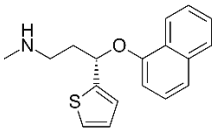
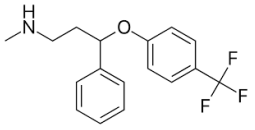
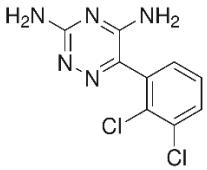
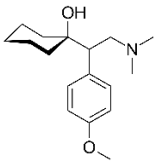
Text S1.

Standards, reagents, and chemicals

Nine high purity (> 98%) antipsychotics (amitriptyline[a], bupropion[b], carbamazepine[b], citalopram[a], clozapine[b], duloxetine[a], fluoxetine[c], lamotrigine[a], and venlafaxine[a]) and the corresponding nine mas-labelled internal standards (amitriptyline-d_6[b], bupropion-d_9[b], carbamazepine-d_{10}[b], citalopram-d_6[b], clozapine-d_4[b], duloxetine-d_7[b], fluoxetine-d_5[b], lamotrigine-[^{13}C;$^{15}N_4$][a], and venlafaxine-d_6[a]) were used. The standard compounds were purchased from: [a] Sigma-Aldrich (Oakville, ON), [b] Toronto Research Chemicals Inc. (North York, ON), and [c] Tokyo Chemical Industry Co., Ltd (Tokyo, Japan).

Antipsychotic stock solutions at 1 mg L^{-1} and internal standard (IS) mixture at 50 µg L^{-1} were dissolved in pure methanol. HPLC grade methanol, dichloromethane, and water purchased from Fisher Scientific (Ottawa, ON) were used for LC solvents, sample extraction, and chemical standards. Optima LC/MS grade formic acid was used as an additive of the LC mobile phase (Fisher Scientific). Agarose and potassium nitrate from Fisher Scientific were used for making gels and adjusting ionic strength, respectively. Milli-Q ultrapure water (EMD Milli-Pore Synergy® system, Etobicoke, ON) reaching resistivity of 18.2 MΩ.cm at 25 °C and total organic carbon (TOC) less than 5 ug/L (ppb) was used for making gels. All glassware was ashed at 450 °C for longer than 4 h and prewashed with methanol before use.

Table S1. Physical-chemical properties of targeted antipsychotic compounds.

Compound	Structure	CAS	MW	S_W (mg/L)	p$K_{a1,2}$	LogK_{ow}
Amitriptyline		50-48-6	277.4	0.8239	9.4	4.95
Bupropion		34911-55-2	239.74	140.2	8.22	3.85
Carbamazepine		298-46-4	236.27	17.66	13.9	2.25
Citalopram		59729-33-8	324.4	31.09	9.78	3.74
Clozapine		5786-21-0	326.8	11.84	7.5	3.35
Duloxetine		116539-59-4	297.4	10.00	9.7	4.68
Fluoxetine		54910-89-3	309.33	38.35	9.8	4.65
Lamotrigine		84057-84-1	256.09	3127	8.53	0.99
Venlafaxine		93413-69-5	277.4	266.7	10.09	3.28

Water solubilities (S_W) and *n*-octanol-water partitioning coefficients (LogK_{ow}) were predicted using US Environmental Protection Agency's EPISuite™.

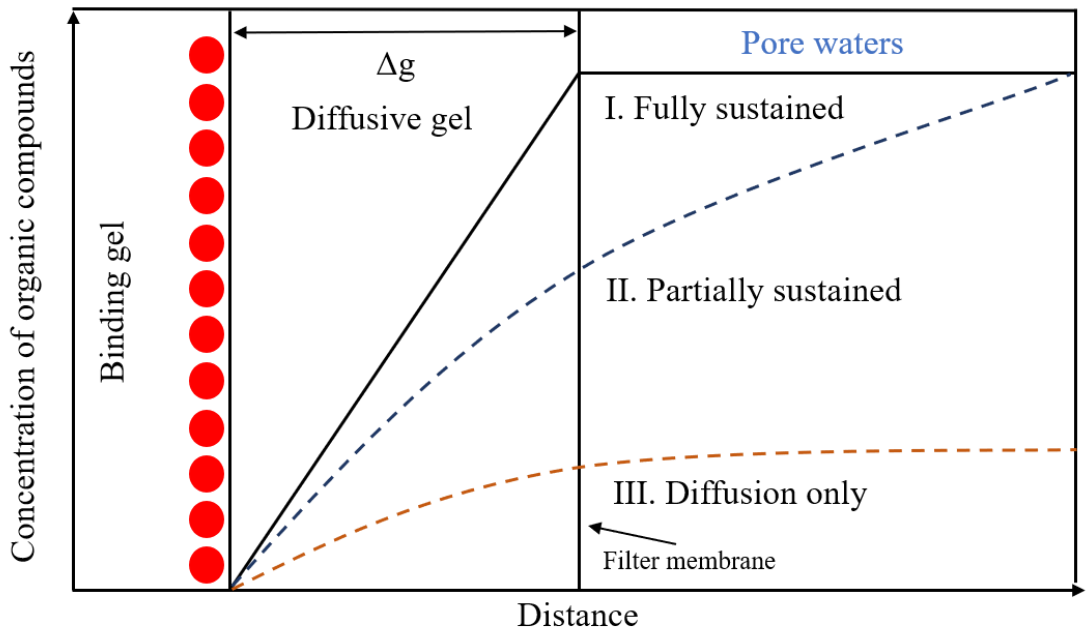


Figure S1. Schematic diagram of sediment supplement type for organic compounds in a DGT configuration exposed to pore waters where the concentration gradient resupplied from the solid phase is (*i*) fully sustained, (*ii*) partially sustained, or diffusion only (unsustained).

Table S2. Key parameters and values of DGT induced fluxes in sediments (DIFS) model.

Parameter	Description	Units	Default values
C	Dissolved concentration	mol cm^{-3}	Auto
C_s	Sorbed concentration (solid phase)	mol g^{-1}	Auto
D_s	Diffusion coefficient in sediment	cm^2 s^{-1}	Auto
D_d	Diffusion coefficient in diffusion layer	cm^2 s^{-1}	Input
T_c	Response time	s	Input/output
K_d	Distribution rate	cm^3 g^{-1}	Input/output
k_f	Adsorption rate	s^{-1}	Output
k_b	Desorption rate	s^{-1}	Output
Δg	Thickness of diffusion layer	mm	Input
m	Mass accumulated by unit area of resin	mol cm^{-2}	1
F	Flux from sediment solution to	mol cm^{-2} s^{-1}	1
R	Ratio of DGT estimated to solution concentration	Dimensionless	Input
t	Deployment time	h	Input
P_c	Particle concentration	g cm^{-3}	2.1
Φ_s	Porosity of sediment	Dimensionless	0.56
Φ_d	Porosity of diffusion gel	Dimensionless	0.98

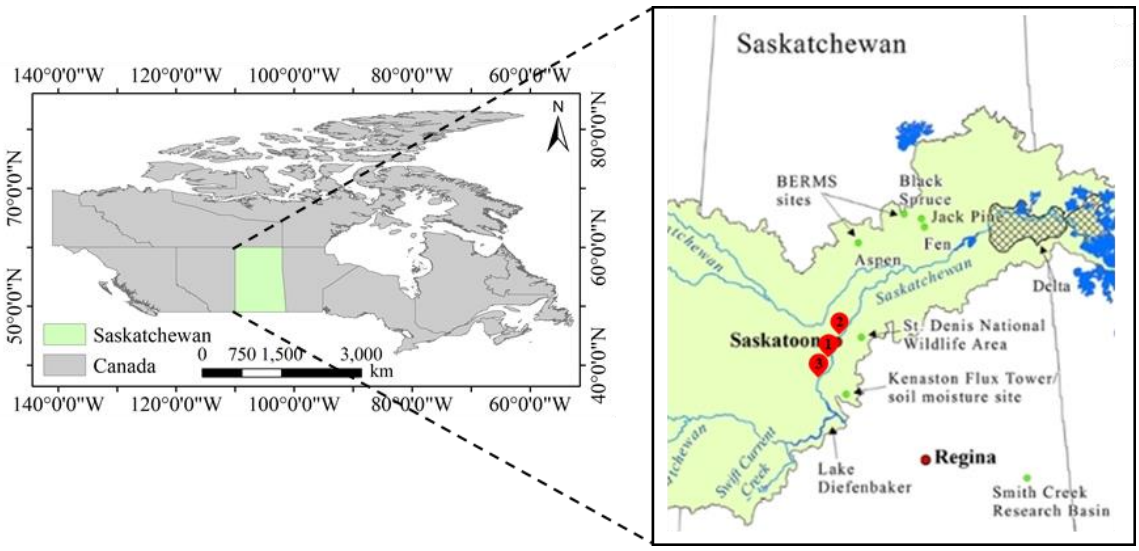


Figure S2. Sampling site of sediment and site of DGT deployment in South Saskatchewan River, Saskatoon, Saskatchewan, Canada. The number in map represents (1) Wastewater treatment plant, (2) the sampling site of sediment for spiking experiment, upstream of wastewater treatment plant, (3) in situ DGT deployment site in Fred heal Canoe Launch, downstream of wastewater treatment plant. The right graph is courtesy of the Global Institute for Water Security.

Text S2.

Sorption experiments of DGT materials

For testing of the potential adsorption of analytes in DGT, it is assumed that all DGT materials (molding, diffusive gel, and PES filter membrane) except for the binding gel do not have a significant affinity to adsorb analytes. A standard solution of the nine antipsychotic compounds at 250 μg L^{-1} was prepared in 1 mM KNO_3, and DGT materials were separately exposed to this solution as follows: All DGT materials were separately immersed in 50 mL of the standard solution that was placed in a 100 mL pre-ashed (450 °C in muffle furnace) glass beakers. A magnetic stir bar was added for agitation (4 rpm) at a water temperature of 21 ± 0.5 °C. In order to control for potential changes compared to initial concentrations, analytes in solution were quantified at various durations of 0.5, 1, 2, 48, 60, 72, 96 or 168 h. Samples of 190 μL were taken from the solution, transferred to LC vials, spiked with 10 μL of 1000 μg L^{-1} internal standards, and analyzed by LC-MS. DGT moldings, diffusive gels, and PES filter membrane were spiked with 50 ng internal standards, eluted with 5 mL of methanol, and sonicated three times for 10 min. Eluents were evaporated to near dryness by gentle nitrogen gas, reconstituted in 1 mL methanol, then filtered through a 0.2 μm polytetrafluoroethylene syringe filter into LC vials before quantification by use of LC-MS.

Adsorption experiment by binding gel

Efficient contact times were determined by placing a binding gel (25 mg Sepra^{TM} ZT sorbent) into a 50 mL glass beaker. Thirty milliliters of the standard solution (500 μg L^{-1}) were added to the beaker and magnetically stirred at a constant speed of 4 rpm at 21 ± 0.5 °C for 24 h. Triplicate samples of water were taken at 11 time intervals (0.5, 0.7, 0.8, 1, 1.5, 1.7, 4, 10, 12, 21 or 24 h), spiked with internal standards and then filtered through a 0.2 μm polytetrafluoroethylene syringe filter into LC vials before LC-MS analysis.

Capacities of Sepra^{TM} ZT binding gel to adsorb nine (9) antipsychotic compounds were conducted, using the same procedure as the determination for efficient contact time, but at different concentrations (200, 400, 500, 600, 800, 1000, 2000, and 5000 μg L^{-1}) at pH of 7 and 21 ± 0.5 °C. Amounts of analytes adsorbed (Q_e) were calculated according to the initial concentrations (C_0) and the steady state concentrations (C_e) as shown in Eq. (S1),

$$Q_e = \frac{(C_0 - C_e) \times V}{1000m} \qquad \text{(S1)}$$

where V and m represent the volume of the standard solution (mL) and the mass of adsorbent in the binding gel (mg), respectively.

Figure S3. The setup for fixation of DGT sediment probes in the field.

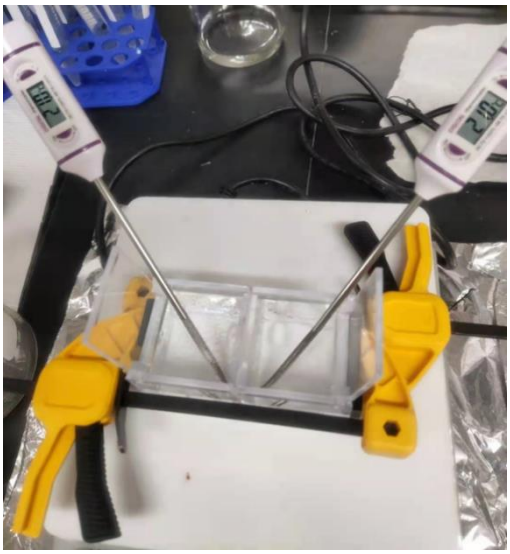


Figure S4. The setup of the diffusion cell.

Table S3. Precursor and product ions ([M+H]+), collision energy (HCD), and retention time of analytes using the full-scan parallel reaction monitoring (PRM) Orbitrap™ mass spectrometer method.

Compound	Precursor ion	Product ion	HCD	Retention time (min)
Amitriptyline	278.190	233.132	35	7.57
Amitriptyline-D_6	284.228	233.132	35	7.57
Bupropion	240.115	184.052	25	5.45
Bupropion-D_9	249.171	185.059	25	5.43
Carbamazepine	237.102	194.097	35	8.08
Carbamazepine-D_{10}	247.165	204.159	35	8.04
Citalopram	325.171	109.045	40	6.59
Citalopram-D_6	331.209	109.045	40	6.59
Clozapine	327.137	270.079	35	6.29
Clozapine-D_4	331.162	272.092	35	6.24
Duloxetine	298.126	183.081	30	7.53
Duloxetine-D_7	305.170	189.118	30	7.50
Fluoxetine	310.141	148.112	25	7.70
Fluoxetine-D5	315.173	153.144	25	7.70
Lamotrigine	256.015	210.983	70	4.57
Lamotrigine-[^{13}C;$^{15}N_4$]	261.007	213.980	70	4.57
Venlafaxine	278.211	260.201	25	6.10
Venlafaxine-D_6	284.249	266.239	25	6.09

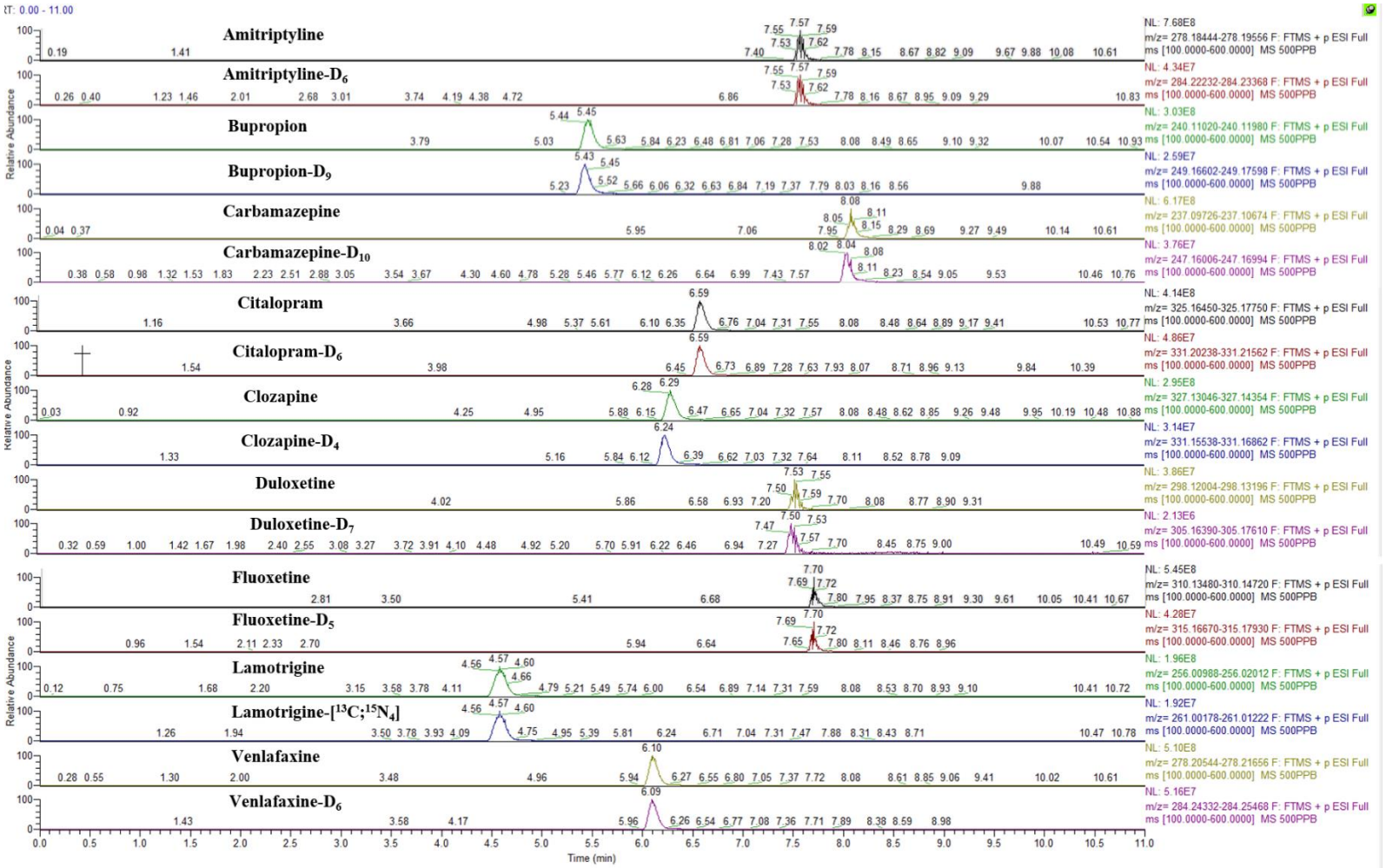


Figure S5. Example chromatograms of nine antipsychotic compounds and their internal standards with scan filter of precursor ion (*m/z*) for a 500 ng mL^{-1} standard solution.

Table S4. Calibration curves (ranged from 0.01 to 950 µg L^{-1}) of the 9 antipsychotic compounds and R^2 ranges during the all samples run.

Compound	*Calibration curve	*R^2	R^2 ranges
Venlafaxine	Y = -0.00293663+0.0283401 X	0.9973	0.9964–0.9974
Fluoxetine	Y = -0.00472171+0.0295973 X	0.9986	0.9986–0.9994
Clozapine	Y = -0.00252042+0.0224591 X	0.9912	0.9908–0.9915
Citalopram	Y = -0.047859+0.208303 X	0.9944	0.9940–0.9949
Duloxetine	Y = -0.00679154+0.0288166 X	0.9911	0.9905–0.9920
Amitriptyline	Y = -0.0593065+0.377414 X	0.9970	0.9965–0.9978
Bupropion	Y = -0.000962958+0.0205702 X	0.9917	0.9912–0.9918
Carbamazepine	Y = 5.21523e-006+0.0256232 X	0.9930	0.9926–0.9939
Lamotrigine	Y = -0.00576197+0.0252794 X	0.9928	0.9924–0.9934

*It should be noted that the calibration curves and R^2 values were taken from the test of standard curve solutions.

Table S5. LOD, LOQ, and MDL (μg L^{-1}) for all nine antipsychotic compounds.

Compound	LOD	LOQ	MDL
Venlafaxine	0.23	0.77	0.033
Fluoxetine	1.46	4.87	0.024
Clozapine	0.38	1.28	0.035
Citalopram	2.14	7.13	0.016
Duloxetine	0.21	0.69	0.124
Amitriptyline	1.81	6.03	0.059
Bupropion	0.35	1.17	0.030
Carbamazepine	1.25	4.17	0.016
Lamotrigine	0.20	0.67	0.025

Table S6. Diffusion coefficients ($cm^2\ s^{-1}$) of nine antipsychotic compounds (average ± standard deviation) in different thicknesses of agarose diffusive gel measured by the two-compartment diffusion cell at 21 °C.

Compound	0.75 mm	1 mm	2 mm	1.5 mm	1.8 mm	2 mm	3 mm
Carbamazepine	$4.98\times10^{-6}\pm6.25\times10^{-7}$	$4.88\times10^{-6}\pm6.66\times10^{-7}$	$4.95\times10^{-6}\pm1.17\times10^{-6}$	$4.90\times10^{-6}\pm7.13\times10^{-7}$	$4.96\times10^{-6}\pm1.23\times10^{-6}$	$4.79\times10^{-6}\pm9.06\times10^{-7}$	$4.72\times10^{-6}\pm7.47\times10^{-7}$
Bupropion	$4.03\times10^{-6}\pm4.61\times10^{-7}$	$3.95\times10^{-6}\pm1.01\times10^{-6}$	$3.98\times10^{-6}\pm5.5\times10^{-7}$	$4.02\times10^{-6}\pm9.19\times10^{-7}$	$4.01\times10^{-6}\pm5.68\times10^{-7}$	$3.87\times10^{-6}\pm8.58\times10^{-7}$	$3.85\times10^{-6}\pm4.98\times10^{-7}$
Lamotrigine	$4.92\times10^{-6}\pm2.83\times10^{-7}$	$4.99\times10^{-6}\pm3.4\times10^{-7}$	$4.98\times10^{-6}\pm2.91\times10^{-7}$	$5.00\times10^{-6}\pm3.13\times10^{-7}$	$5.01\times10^{-6}\pm3.48\times10^{-7}$	$4.94\times10^{-6}\pm3.50\times10^{-7}$	$4.97\times10^{-6}\pm4.36\times10^{-7}$
Amitriptyline	$5.97\times10^{-6}\pm1.24\times10^{-6}$	$5.86\times10^{-6}\pm8.44\times10^{-7}$	$5.86\times10^{-6}\pm6.92\times10^{-7}$	$5.96\times10^{-6}\pm6.37\times10^{-7}$	$5.88\times10^{-6}\pm1.03\times10^{-6}$	$5.78\times10^{-6}\pm1.03\times10^{-6}$	$5.66\times10^{-6}\pm7.91\times10^{-7}$
Venlafaxine	$3.17\times10^{-6}\pm5.09\times10^{-7}$	$3.12\times10^{-6}\pm7.16\times10^{-7}$	$3.12\times10^{-6}\pm7.22\times10^{-7}$	$3.14\times10^{-6}\pm5.62\times10^{-7}$	$3.13\times10^{-6}\pm3.66\times10^{-7}$	$3.07\times10^{-6}\pm7.93\times10^{-7}$	$2.98\times10^{-6}\pm3.09\times10^{-7}$
Duloxetine	$3.27\times10^{-6}\pm7.57\times10^{-7}$	$3.26\times10^{-6}\pm8.38\times10^{-7}$	$3.25\times10^{-6}\pm7.79\times10^{-7}$	$3.25\times10^{-6}\pm4.59\times10^{-7}$	$3.23\times10^{-6}\pm3.77\times10^{-7}$	$3.15\times10^{-6}\pm5.95\times10^{-7}$	$3.08\times10^{-6}\pm4.65\times10^{-7}$
Fluoxetine	$4.24\times10^{-6}\pm5.47\times10^{-7}$	$4.19\times10^{-6}\pm7.16\times10^{-7}$	$4.23\times10^{-6}\pm4.60\times10^{-7}$	$4.19\times10^{-6}\pm5.25\times10^{-7}$	$4.20\times10^{-6}\pm8.45\times10^{-7}$	$4.10\times10^{-6}\pm9.41\times10^{-7}$	$4.06\times10^{-6}\pm6.53\times10^{-7}$
Citalopram	$6.02\times10^{-6}\pm8.37\times10^{-7}$	$5.94\times10^{-6}\pm1.41\times10^{-6}$	$5.94\times10^{-6}\pm1.37\times10^{-6}$	$5.91\times10^{-6}\pm1.07\times10^{-6}$	$5.93\times10^{-6}\pm1.29\times10^{-6}$	$5.81\times10^{-6}\pm1.04\times10^{-6}$	$5.74\times10^{-6}\pm5.81\times10^{-7}$
Clozapine	$4.66\times10^{-6}\pm7.69\times10^{-7}$	$4.62\times10^{-6}\pm5.22\times10^{-7}$	$4.61\times10^{-6}\pm5.45\times10^{-7}$	$4.57\times10^{-6}\pm6.95\times10^{-7}$	$4.58\times10^{-6}\pm5.13\times10^{-7}$	$4.49\times10^{-6}\pm1.03\times10^{-6}$	$4.44\times10^{-6}\pm6.36\times10^{-7}$

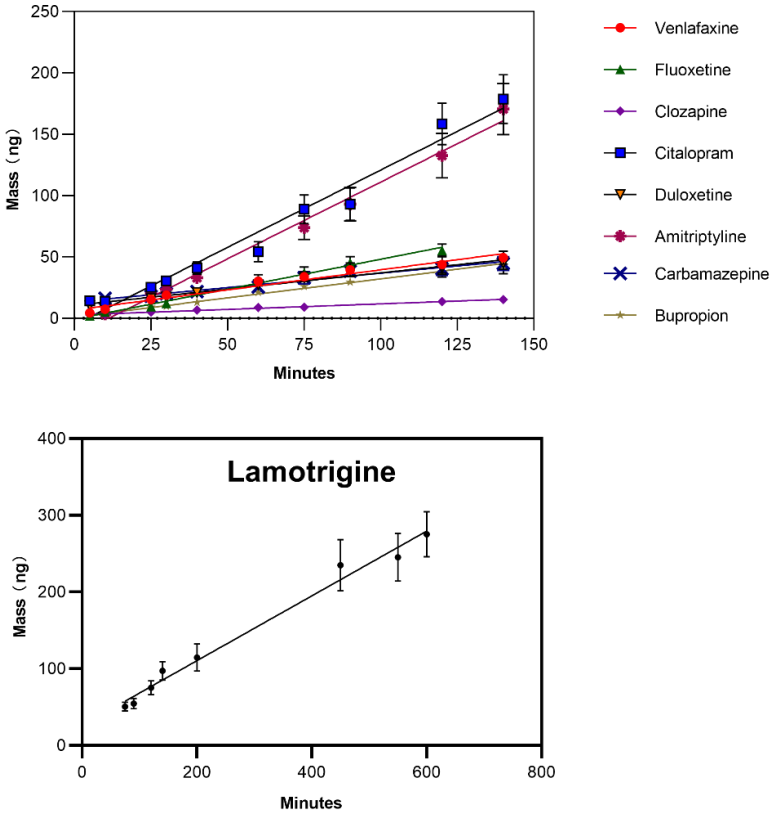


Figure S6. Diffused masses of bupropion, lamotrigine, amitriptyline, venlafaxine, duloxetine, fluoxetine, citalopram, and clozapine in the receiving cell through 0.75 mm agarose gel at different times in a diffusion cell with 500 μg L^{-1} standard compounds in the source cell at an initial time. The temperature was constant at 21 ± 0.5 °C, and ionic strength was 1 mM KNO_3. It should be noted that lamotrigine did not show a positive linear relationship with negligible mass detected before 75 mins. The symbols and errors bars represent the mean value calculated from mean values from three samples each time in triplicate parallel experiments.

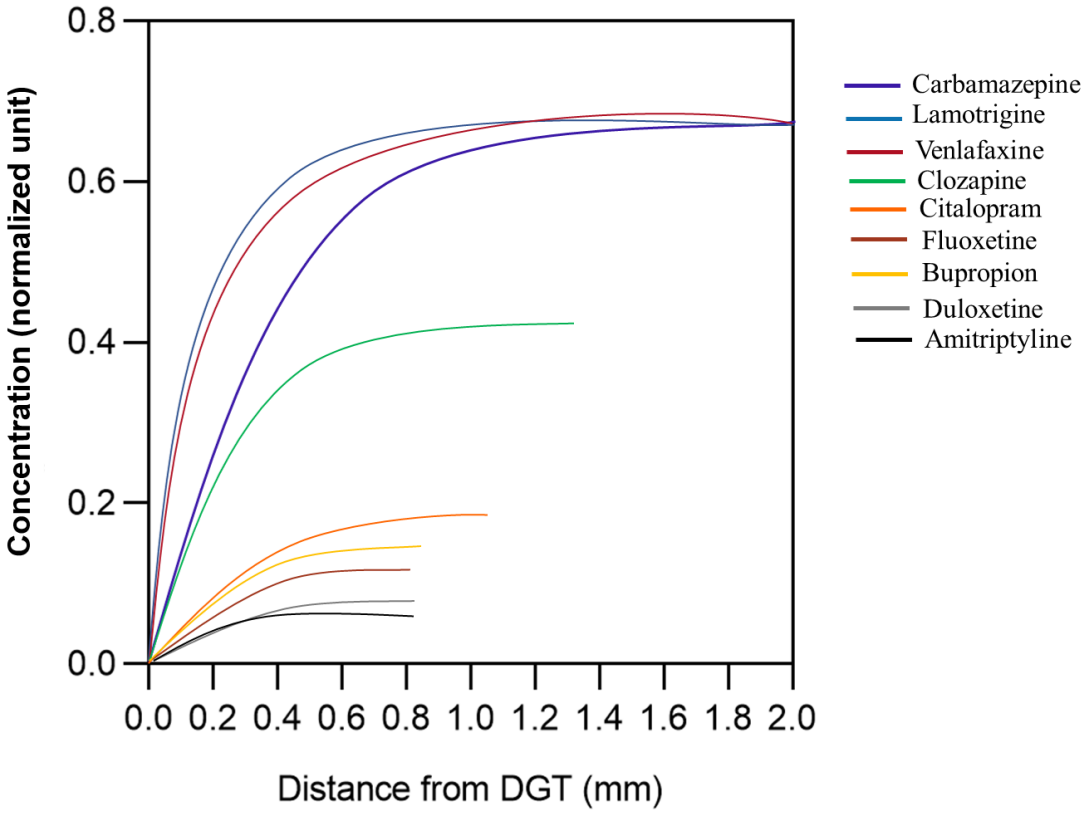


Figure S7. DIFS model (1D) output for nine antipsychotics in the sandy sediment simulating concentration in porewater on the distance of DGT interface at 30 days.

Supplementary Material

Desorption kinetics of antipsychotic drugs from sandy sediments by diffusive gradients in thin-films technique

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[c] *Toxicology Centre, University of Saskatchewan, Saskatoon, Canada*

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[e] *Department of Environmental Sciences, Baylor University, Waco, Texas, USA*

[f] *Centre for Hydrology, University of Saskatchewan, Saskatoon, Canada*

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Supplementary Caption

Text S1. Standards, reagents, and chemicals.

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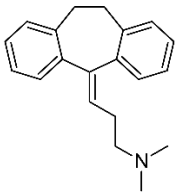
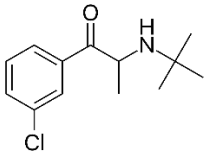
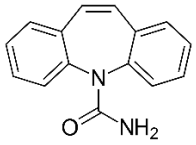
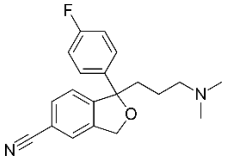
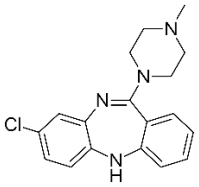
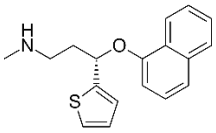
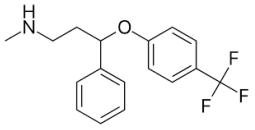
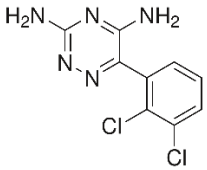
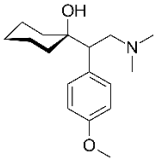
Text S1.

Standards, reagents, and chemicals

Nine high purity (> 98%) antipsychotics (amitriptyline[a], bupropion[b], carbamazepine[b], citalopram[a], clozapine[b], duloxetine[a], fluoxetine[c], lamotrigine[a], and venlafaxine[a]) and the corresponding nine mas-labelled internal standards (amitriptyline-d_6[b], bupropion-d_9[b], carbamazepine-d_{10}[b], citalopram-d_6[b], clozapine-d_4[b], duloxetine-d_7[b], fluoxetine-d_5[b], lamotrigine-[^{13}C;$^{15}N_4$][a], and venlafaxine-d_6[a]) were used. The standard compounds were purchased from: [a] Sigma-Aldrich (Oakville, ON), [b] Toronto Research Chemicals Inc. (North York, ON), and [c] Tokyo Chemical Industry Co., Ltd (Tokyo, Japan).

Antipsychotic stock solutions at 1 mg L^{-1} and internal standard (IS) mixture at 50 µg L^{-1} were dissolved in pure methanol. HPLC grade methanol, dichloromethane, and water purchased from Fisher Scientific (Ottawa, ON) were used for LC solvents, sample extraction, and chemical standards. Optima LC/MS grade formic acid was used as an additive of the LC mobile phase (Fisher Scientific). Agarose and potassium nitrate from Fisher Scientific were used for making gels and adjusting ionic strength, respectively. Milli-Q ultrapure water (EMD Milli-Pore Synergy® system, Etobicoke, ON) reaching resistivity of 18.2 MΩ.cm at 25 °C and total organic carbon (TOC) less than 5 ug/L (ppb) was used for making gels. All glassware was ashed at 450 °C for longer than 4 h and prewashed with methanol before use.

Table S1. Physical-chemical properties of targeted antipsychotic compounds.

Compound	Structure	CAS	MW	S_W (mg/L)	p$K_{a1,2}$	LogK_{ow}
Amitriptyline		50-48-6	277.4	0.8239	9.4	4.95
Bupropion		34911-55-2	239.74	140.2	8.22	3.85
Carbamazepine		298-46-4	236.27	17.66	13.9	2.25
Citalopram		59729-33-8	324.4	31.09	9.78	3.74
Clozapine		5786-21-0	326.8	11.84	7.5	3.35
Duloxetine		116539-59-4	297.4	10.00	9.7	4.68
Fluoxetine		54910-89-3	309.33	38.35	9.8	4.65
Lamotrigine		84057-84-1	256.09	3127	8.53	0.99
Venlafaxine		93413-69-5	277.4	266.7	10.09	3.28

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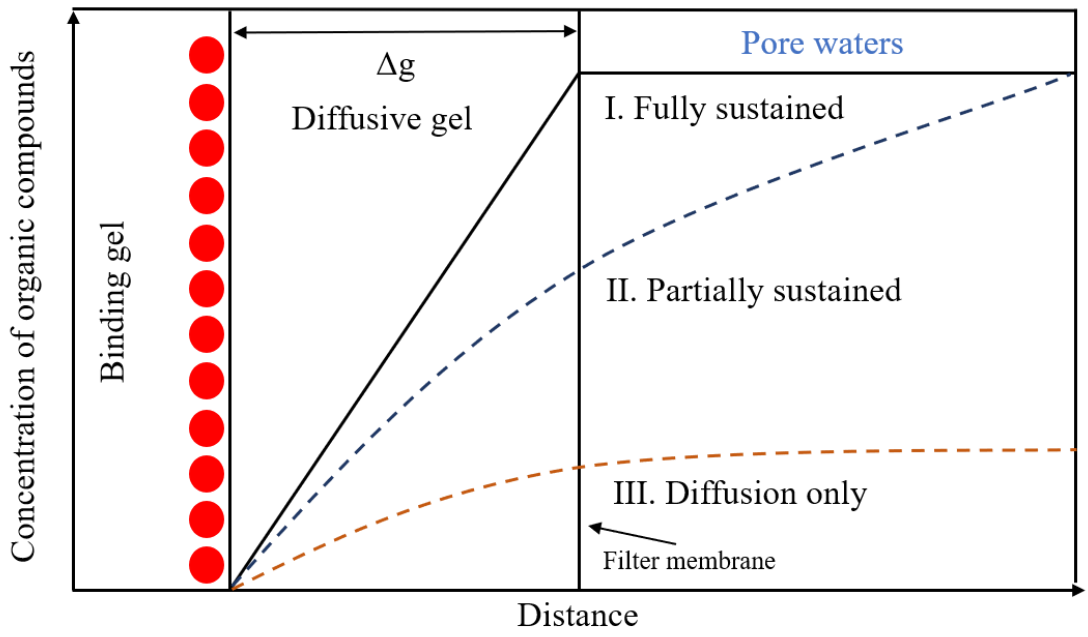

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D_s	Diffusion coefficient in sediment	cm^2 s^{-1}	Auto
D_d	Diffusion coefficient in diffusion layer	cm^2 s^{-1}	Input
T_c	Response time	s	Input/output
K_d	Distribution rate	cm^3 g^{-1}	Input/output
k_f	Adsorption rate	s^{-1}	Output
k_b	Desorption rate	s^{-1}	Output
Δg	Thickness of diffusion layer	mm	Input
m	Mass accumulated by unit area of resin	mol cm^{-2}	1
F	Flux from sediment solution to	mol cm^{-2} s^{-1}	1
R	Ratio of DGT estimated to solution concentration	Dimensionless	Input
t	Deployment time	h	Input
P_c	Particle concentration	g cm^{-3}	2.1
Φ_s	Porosity of sediment	Dimensionless	0.56
Φ_d	Porosity of diffusion gel	Dimensionless	0.98

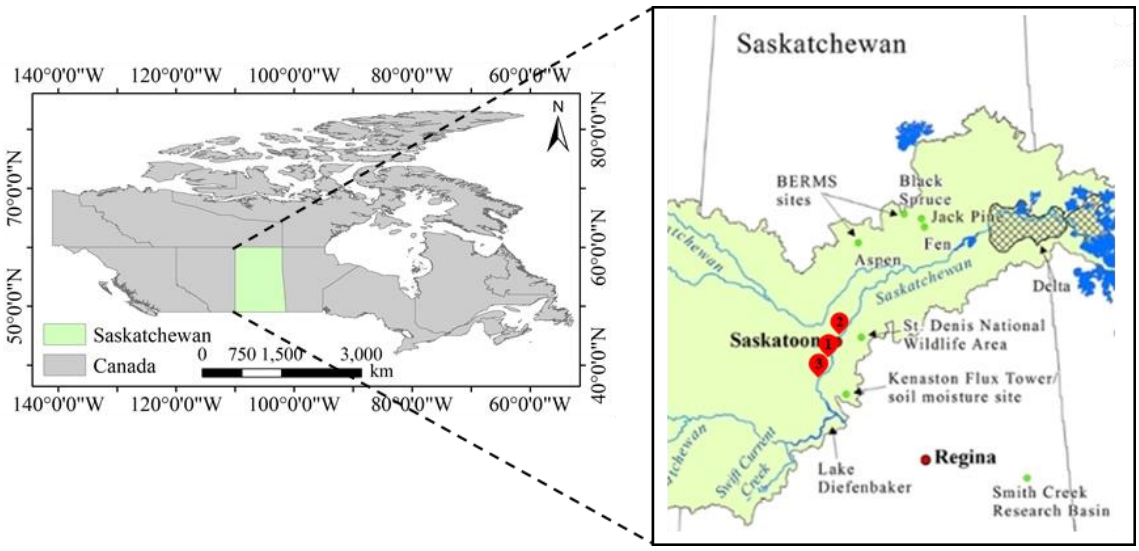

Figure S2. Sampling site of sediment and site of DGT deployment in South Saskatchewan River, Saskatoon, Saskatchewan, Canada. The number in map represents (1) Wastewater treatment plant, (2) the sampling site of sediment for spiking experiment, upstream of wastewater treatment plant, (3) in situ DGT deployment site in Fred heal Canoe Launch, downstream of wastewater treatment plant. The right graph is courtesy of the Global Institute for Water Security.

Text S2.

Sorption experiments of DGT materials

For testing of the potential adsorption of analytes in DGT, it is assumed that all DGT materials (molding, diffusive gel, and PES filter membrane) except for the binding gel do not have a significant affinity to adsorb analytes. A standard solution of the nine antipsychotic compounds at 250 μg L^{-1} was prepared in 1 mM KNO_3, and DGT materials were separately exposed to this solution as follows: All DGT materials were separately immersed in 50 mL of the standard solution that was placed in a 100 mL pre-ashed (450 °C in muffle furnace) glass beakers. A magnetic stir bar was added for agitation (4 rpm) at a water temperature of 21 $\pm$ 0.5 °C. In order to control for potential changes compared to initial concentrations, analytes in solution were quantified at various durations of 0.5, 1, 2, 48, 60, 72, 96 or 168 h. Samples of 190 μL were taken from the solution, transferred to LC vials, spiked with 10 μL of 1000 μg L^{-1} internal standards, and analyzed by LC-MS. DGT moldings, diffusive gels, and PES filter membrane were spiked with 50 ng internal standards, eluted with 5 mL of methanol, and sonicated three times for 10 min. Eluents were evaporated to near dryness by gentle nitrogen gas, reconstituted in 1 mL methanol, then filtered through a 0.2 μm polytetrafluoroethylene syringe filter into LC vials before quantification by use of LC-MS.

Adsorption experiment by binding gel

Efficient contact times were determined by placing a binding gel (25 mg Sepra^{TM} ZT sorbent) into a 50 mL glass beaker. Thirty milliliters of the standard solution (500 μg L^{-1}) were added to the beaker and magnetically stirred at a constant speed of 4 rpm at 21 $\pm$ 0.5 °C for 24 h. Triplicate samples of water were taken at 11 time intervals (0.5, 0.7, 0.8, 1, 1.5, 1.7, 4, 10, 12, 21 or 24 h), spiked with internal standards and then filtered through a 0.2 μm polytetrafluoroethylene syringe filter into LC vials before LC-MS analysis.

Capacities of Sepra^{TM} ZT binding gel to adsorb nine (9) antipsychotic compounds were conducted, using the same procedure as the determination for efficient contact time, but at different concentrations (200, 400, 500, 600, 800, 1000, 2000, and 5000 μg L^{-1}) at pH of 7 and 21 $\pm$ 0.5 °C. Amounts of analytes adsorbed (Q_e) were calculated according to the initial concentrations (C_0) and the steady state concentrations (C_e) as shown in Eq. (S1),

$$Q_e = \frac{(C_0 - C_e) \times V}{1000m} \qquad \text{(S1)}$$

where V and m represent the volume of the standard solution (mL) and the mass of adsorbent in the binding gel (mg), respectively.

Figure S3. The setup for fixation of DGT sediment probes in the field.

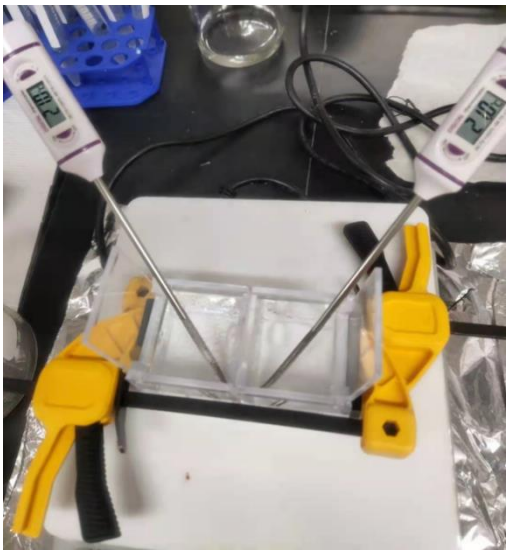

Figure S4. The setup of the diffusion cell.

Table S3. Precursor and product ions ([M+H]+), collision energy (HCD), and retention time of analytes using the full-scan parallel reaction monitoring (PRM) Orbitrap™ mass spectrometer method.

Compound	Precursor ion	Product ion	HCD	Retention time (min)
Amitriptyline	278.190	233.132	35	7.57
Amitriptyline-D_6	284.228	233.132	35	7.57
Bupropion	240.115	184.052	25	5.45
Bupropion-D_9	249.171	185.059	25	5.43
Carbamazepine	237.102	194.097	35	8.08
Carbamazepine-D_{10}	247.165	204.159	35	8.04
Citalopram	325.171	109.045	40	6.59
Citalopram-D_6	331.209	109.045	40	6.59
Clozapine	327.137	270.079	35	6.29
Clozapine-D_4	331.162	272.092	35	6.24
Duloxetine	298.126	183.081	30	7.53
Duloxetine-D_7	305.170	189.118	30	7.50
Fluoxetine	310.141	148.112	25	7.70
Fluoxetine-D5	315.173	153.144	25	7.70
Lamotrigine	256.015	210.983	70	4.57
Lamotrigine-[^{13}C;$^{15}N_4$]	261.007	213.980	70	4.57
Venlafaxine	278.211	260.201	25	6.10
Venlafaxine-D_6	284.249	266.239	25	6.09

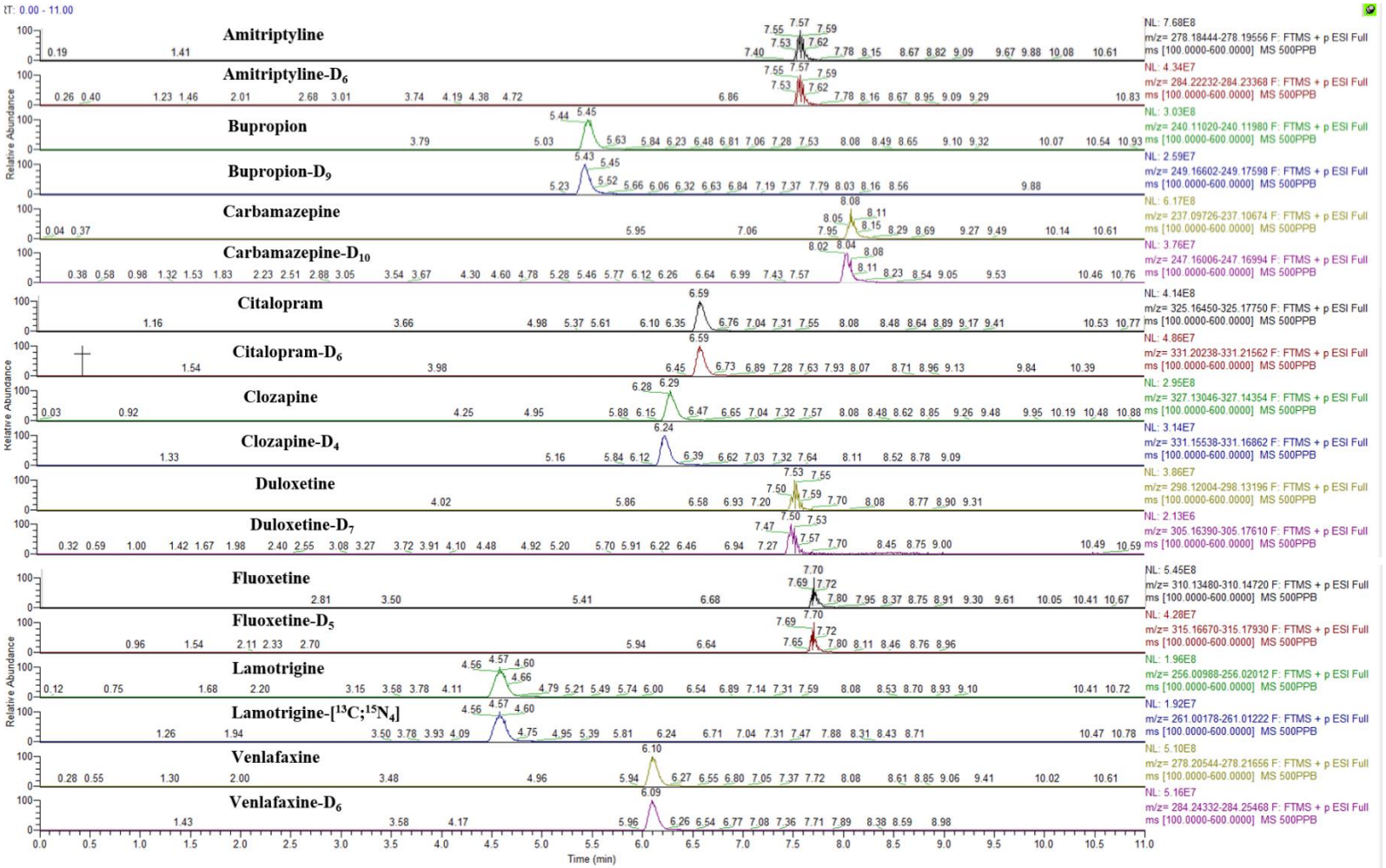

Figure S5. Example chromatograms of nine antipsychotic compounds and their internal standards with scan filter of precursor ion (*m/z*) for a 500 ng mL^{-1} standard solution.

Table S4. Calibration curves (ranged from 0.01 to 950 μg L^{-1}) of the 9 antipsychotic compounds and R^2 ranges during the all samples run.

Compound	*Calibration curve	*R^2	R^2 ranges
Venlafaxine	Y = -0.00293663+0.0283401 X	0.9973	0.9964–0.9974
Fluoxetine	Y = -0.00472171+0.0295973 X	0.9986	0.9986–0.9994
Clozapine	Y = -0.00252042+0.0224591 X	0.9912	0.9908–0.9915
Citalopram	Y = -0.047859+0.208303 X	0.9944	0.9940–0.9949
Duloxetine	Y = -0.00679154+0.0288166 X	0.9911	0.9905–0.9920
Amitriptyline	Y = -0.0593065+0.377414 X	0.9970	0.9965–0.9978
Bupropion	Y = -0.000962958+0.0205702 X	0.9917	0.9912–0.9918
Carbamazepine	Y = 5.21523e-006+0.0256232 X	0.9930	0.9926–0.9939
Lamotrigine	Y = -0.00576197+0.0252794 X	0.9928	0.9924–0.9934

*It should be noted that the calibration curves and R^2 values were taken from the test of standard curve solutions.

Table S5. LOD, LOQ, and MDL (μg L^{-1}) for all nine antipsychotic compounds.

Compound	LOD	LOQ	MDL
Venlafaxine	0.23	0.77	0.033
Fluoxetine	1.46	4.87	0.024
Clozapine	0.38	1.28	0.035
Citalopram	2.14	7.13	0.016
Duloxetine	0.21	0.69	0.124
Amitriptyline	1.81	6.03	0.059
Bupropion	0.35	1.17	0.030
Carbamazepine	1.25	4.17	0.016
Lamotrigine	0.20	0.67	0.025

Table S6. Diffusion coefficients ($cm^2\ s^{-1}$) of nine antipsychotic compounds (average ± standard deviation) in different thicknesses of agarose diffusive gel measured by the two-compartment diffusion cell at 21 °C.

Compound	0.75 mm	1 mm	2 mm	1.5 mm	1.8 mm	2 mm	3 mm
Carbamazepine	$4.98\times10^{-6}\pm6.25\times10^{-7}$	$4.88\times10^{-6}\pm6.66\times10^{-7}$	$4.95\times10^{-6}\pm1.17\times10^{-6}$	$4.90\times10^{-6}\pm7.13\times10^{-7}$	$4.96\times10^{-6}\pm1.23\times10^{-6}$	$4.79\times10^{-6}\pm9.06\times10^{-7}$	$4.72\times10^{-6}\pm7.47\times10^{-7}$
Bupropion	$4.03\times10^{-6}\pm4.61\times10^{-7}$	$3.95\times10^{-6}\pm1.01\times10^{-6}$	$3.98\times10^{-6}\pm5.5\times10^{-7}$	$4.02\times10^{-6}\pm9.19\times10^{-7}$	$4.01\times10^{-6}\pm5.68\times10^{-7}$	$3.87\times10^{-6}\pm8.58\times10^{-7}$	$3.85\times10^{-6}\pm4.98\times10^{-7}$
Lamotrigine	$4.92\times10^{-6}\pm2.83\times10^{-7}$	$4.99\times10^{-6}\pm3.4\times10^{-7}$	$4.98\times10^{-6}\pm2.91\times10^{-7}$	$5.00\times10^{-6}\pm3.13\times10^{-7}$	$5.01\times10^{-6}\pm3.48\times10^{-7}$	$4.94\times10^{-6}\pm3.50\times10^{-7}$	$4.97\times10^{-6}\pm4.36\times10^{-7}$
Amitriptyline	$5.97\times10^{-6}\pm1.24\times10^{-6}$	$5.86\times10^{-6}\pm8.44\times10^{-7}$	$5.86\times10^{-6}\pm6.92\times10^{-7}$	$5.96\times10^{-6}\pm6.37\times10^{-7}$	$5.88\times10^{-6}\pm1.03\times10^{-6}$	$5.78\times10^{-6}\pm1.03\times10^{-6}$	$5.66\times10^{-6}\pm7.91\times10^{-7}$
Venlafaxine	$3.17\times10^{-6}\pm5.09\times10^{-7}$	$3.12\times10^{-6}\pm7.16\times10^{-7}$	$3.12\times10^{-6}\pm7.22\times10^{-7}$	$3.14\times10^{-6}\pm5.62\times10^{-7}$	$3.13\times10^{-6}\pm3.66\times10^{-7}$	$3.07\times10^{-6}\pm7.93\times10^{-7}$	$2.98\times10^{-6}\pm3.09\times10^{-7}$
Duloxetine	$3.27\times10^{-6}\pm7.57\times10^{-7}$	$3.26\times10^{-6}\pm8.38\times10^{-7}$	$3.25\times10^{-6}\pm7.79\times10^{-7}$	$3.25\times10^{-6}\pm4.59\times10^{-7}$	$3.23\times10^{-6}\pm3.77\times10^{-7}$	$3.15\times10^{-6}\pm5.95\times10^{-7}$	$3.08\times10^{-6}\pm4.65\times10^{-7}$
Fluoxetine	$4.24\times10^{-6}\pm5.47\times10^{-7}$	$4.19\times10^{-6}\pm7.16\times10^{-7}$	$4.23\times10^{-6}\pm4.60\times10^{-7}$	$4.19\times10^{-6}\pm5.25\times10^{-7}$	$4.20\times10^{-6}\pm8.45\times10^{-7}$	$4.10\times10^{-6}\pm9.41\times10^{-7}$	$4.06\times10^{-6}\pm6.53\times10^{-7}$
Citalopram	$6.02\times10^{-6}\pm8.37\times10^{-7}$	$5.94\times10^{-6}\pm1.41\times10^{-6}$	$5.94\times10^{-6}\pm1.37\times10^{-6}$	$5.91\times10^{-6}\pm1.07\times10^{-6}$	$5.93\times10^{-6}\pm1.29\times10^{-6}$	$5.81\times10^{-6}\pm1.04\times10^{-6}$	$5.74\times10^{-6}\pm5.81\times10^{-7}$
Clozapine	$4.66\times10^{-6}\pm7.69\times10^{-7}$	$4.62\times10^{-6}\pm5.22\times10^{-7}$	$4.61\times10^{-6}\pm5.45\times10^{-7}$	$4.57\times10^{-6}\pm6.95\times10^{-7}$	$4.58\times10^{-6}\pm5.13\times10^{-7}$	$4.49\times10^{-6}\pm1.03\times10^{-6}$	$4.44\times10^{-6}\pm6.36\times10^{-7}$

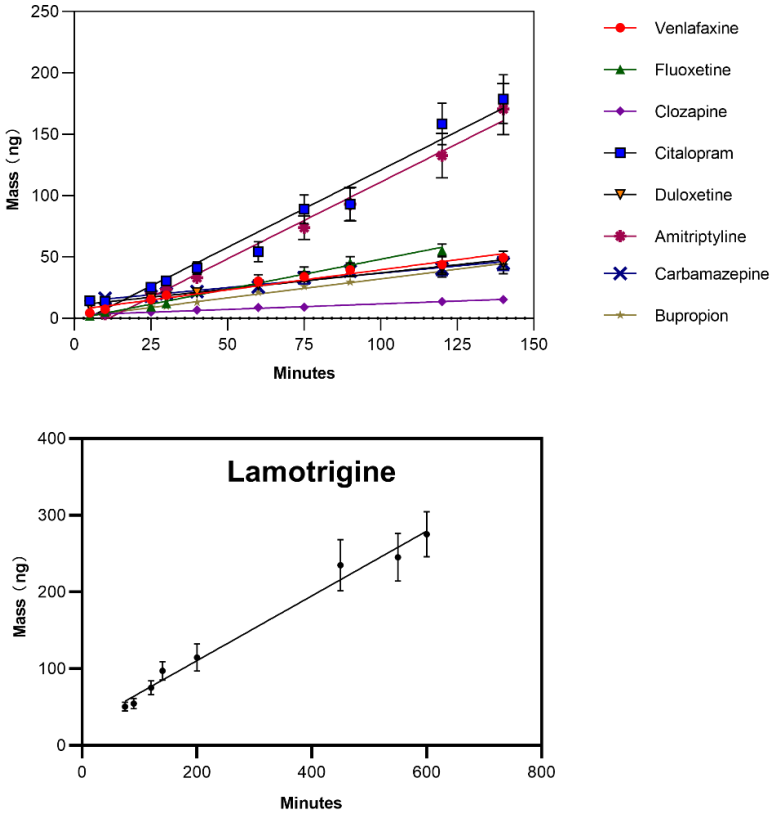

Figure S6. Diffused masses of bupropion, lamotrigine, amitriptyline, venlafaxine, duloxetine, fluoxetine, citalopram, and clozapine in the receiving cell through 0.75 mm agarose gel at different times in a diffusion cell with 500 μg L^{-1} standard compounds in the source cell at an initial time. The temperature was constant at 21 ± 0.5 ° C, and ionic strength was 1 mM KNO_3. It should be noted that lamotrigine did not show a positive linear relationship with negligible mass detected before 75 mins. The symbols and errors bars represent the mean value calculated from mean values from three samples each time in triplicate parallel experiments.

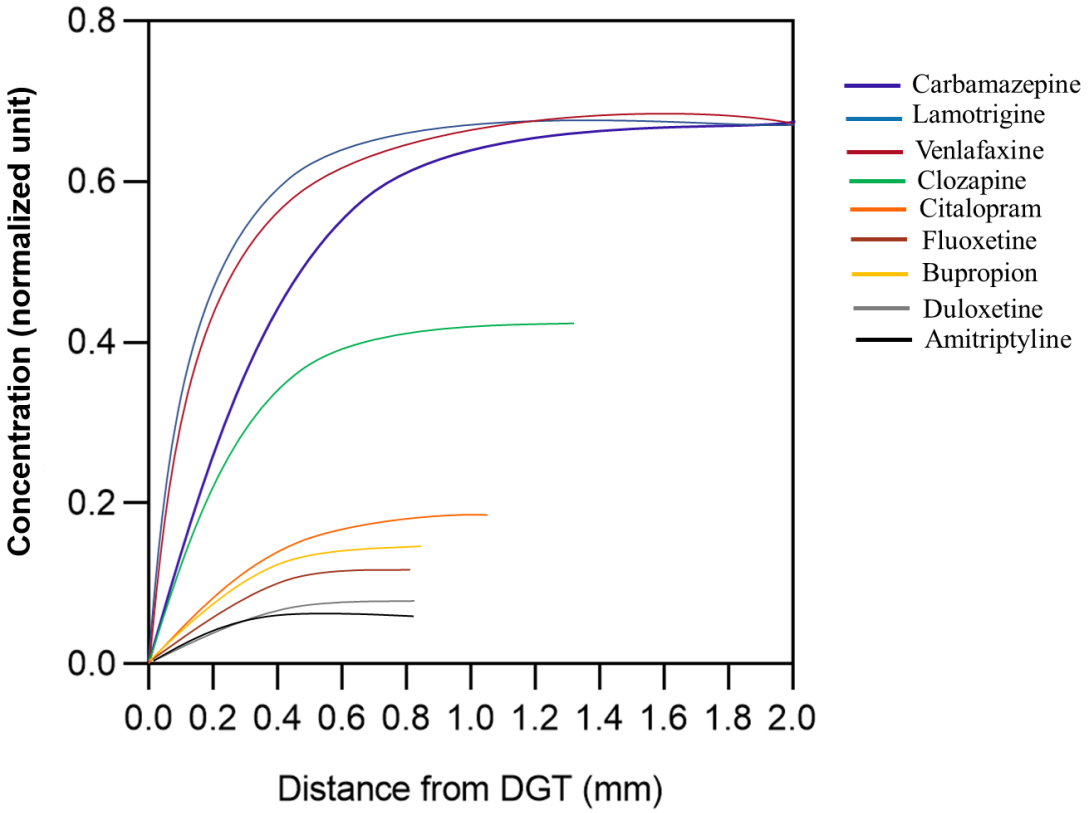

Figure S7. DIFS model (1D) output for nine antipsychotics in the sandy sediment simulating concentration in porewater on the distance of DGT interface at 30 days.