ENVIRONMENTAL ENGINEERING SCIENCE
Volume 35, Number 9, 2018

DOI: 10.1089/ees.2017.0499

Adsorption and Thermodynamics of Pharmaceuticals, Acyclovir and Fluconazole, onto Quartz Sand Under Static and Dynamic Conditions

Theodosia V. Fountouli and Constantinos V. Chrysikopoulos*

School of Environmental Engineering, Technical University of Crete, Chania, Greece.

Received: November 29, 2017 *Accepted in revised form: February 6, 2018*

Abstract

Pharmaceuticals are characterized as emerging contaminants. Their fate and transport in environmental systems are of substantial importance and should be thoroughly understood. This study investigated the interaction of two pharmaceuticals (acyclovir and fluconazole) with quartz sand. Acyclovir is an antiviral drug, often used for the treatment of herpes infections; whereas fluconazole is an azole fungicide that is widely used as an active ingredient in a variety of pharmaceutical and personal care products (PPCPs) for the treatment of fungal infections. Adsorption behavior of acyclovir and fluconazole onto quartz sand at three different temperatures (4°C, 10°C, and 22°C) under static and dynamic conditions was examined. Kinetic adsorption data were described successfully with a pseudo-second-order model. Furthermore, adsorption equilibrium data were quantified with a linear adsorption isotherm. Results at three different temperatures indicated that PPCPs were weakly adsorbed onto quartz sand. Adsorption of acyclovir and fluconazole is slightly higher under dynamic than static conditions. Although no significant differences were observed between the three different temperatures employed in this study, adsorption of acyclovir and fluconazole increased slightly with increasing temperature.

Keywords: acyclovir; adsorption; fluconazole; pharmaceuticals; quartz sand; thermodynamics

Introduction

Pharmaceutical and personal care products (PPCPs) include a wide range of chemicals, such as human and veterinary drugs, nutraceuticals (e.g., vitamins, herbal remedies, and amino acids), and sunscreen agents. Some of these chemicals can cause adverse impacts on wildlife and humans, and they are characterized as emerging organic contaminants (Daughton and Ternes, 1999). Numerous pharmaceuticals are extensively used in large quantities. Furthermore, several pharmaceuticals are incompletely absorbed and metabolized by the human organism. The scientific interest in pharmaceutical occurrence in the environment arises largely from concern over possible toxicological risks and implications stemming from human exposure through drinking water (Schulman *et al.*, 2002; Schwab *et al.*, 2005; Wang *et al.*, 2016) and aquatic organism exposure (Jones *et al.*, 2001).

After application, the unutilized portion of pharmaceuticals can be removed from the body by washing or through urinary excretion, which are the main entry pathways of pharmaceuticals to municipal wastewater (Hirsch *et al.*, 1999; Gros *et al.*, 2010; Prasse *et al.*, 2010; Kosma *et al.*, 2014). The incomplete removal of pharmaceuticals during wastewater treatment may be the origin of their presence in the effluent and sewage sludge of wastewater treatment plants (WWTPs) (Jelic *et al.*, 2011; Garcia-Valcarcel and Tadeo, 2012; Funke *et al.*, 2016). As a result, pharmaceuticals have been observed repeatedly in the aquatic environment worldwide (Heberer, 2002; Tixier *et al.*, 2003; Gros *et al.*, 2010; Prasse *et al.*, 2010; Bu *et al.*, 2013; Liu and Wong, 2013; Peng *et al.*, 2014; Richardson and Ternes, 2014; Fisher *et al.*, 2016). The sludge of WWTPs is often used as fertilizer in agriculture in many countries (Scheytt *et al.*, 2006; Garcia-Valcarcel and Tadeo, 2012). When the sludge is dispersed on a field, the PPCPs present in the sludge may be leached and threaten the groundwater (Diaz-Cruz *et al.*, 2003).

Knowledge of the fate of pharmaceuticals in soils or sediments is important for estimation of environmental exposure and risk assessment (Pan *et al.*, 2009). Sorption is one of the key factors controlling the input, transport, and transformation of pharmaceuticals in the aquatic environment and in the subsurface (Scheytt *et al.*, 2005). Highly mobile pharmaceuticals have the potential to leach into groundwater, whereas strongly adsorbing pharmaceuticals can accumulate in the topsoil layer, affect the soil microbial community, and may be taken up by plants (Thiele-Bruhn, 2003). The adsorption of pharmaceuticals onto soils is influenced by solution chemistry, type of mineral, and organic sorbents (Tolls, 2001; Boxall

**Corresponding author:* School of Environmental Engineering, Technical University of Crete, Environmental Engineering Laboratory, Chania 73132, Greece. *Phone:* +30 28210 37797; *Fax:* +30 28210 37847; *E-mail:* cvc@enveng.tuc.gr

et al., 2002; Drillia *et al.*, 2005; Hari *et al.*, 2005; Loffler *et al.*, 2005; Williams *et al.*, 2006; Blackwell *et al.*, 2007; Chefetz *et al.*, 2008).

Acyclovir and fluconazole are two pharmaceuticals with wide production and use around the world (Prasse *et al.*, 2011; Yu *et al.*, 2012; Loos *et al.*, 2013), which may find their way to the environment if they are not effectively eliminated during wastewater treatment. Acyclovir is the most commonly used oral antiviral agent because of its selectivity and low cytotoxicity. It is employed for the treatment and prophylaxis of initial and recurrent episodes of genital and labial herpes, as well as for the acute treatment of herpes zoster and varicella (chickenpox) in immunocompetent individuals. It can be administered in very high doses (from 200 to 1,000 mg three to four times daily). Fluconazole is an azole fungicide that is widely used as an active ingredient in a variety of PPCPs to treat fungal infections by blocking sterol biosynthesis (Zarn *et al.*, 2003; Correa and Salgado, 2011). Fluconazole is administered topically and orally. Due to its low cost and few side effects, fluconazole has become one of the most commonly prescribed drugs (Yang *et al.*, 2012).

Several studies have reported the occurrence of acyclovir in wastewater, landfill leachate, river water, reservoir water, and well water worldwide at tens of ng/L to low μg/L levels (Prasse *et al.*, 2010; Yu *et al.*, 2012; Peng *et al.*, 2014). Prasse *et al.* (2011) revealed rapid biotransformation of acyclovir in activated sludge, whereas the transformation product, carboxy-acyclovir, was found to be persistent and was detected in drinking water, groundwater, and surface water. The biodegradation half-life of acyclovir was reported as only 5.3 h, indicating rapid degradation during conventional sewage treatment. In addition, an ozonation product of acyclovir was detected in treated drinking water (Prasse *et al.*, 2012).

Fluconazole has been detected in surface waters (Kahle *et al.*, 2008; Kim *et al.*, 2009; Peng *et al.*, 2012). In addition, fluconazole is known to have low removal rates in conventional WWTPs (Wishart *et al.*, 2008). Kahle *et al.* (2008) reported practically identical fluconazole concentrations in the influent and effluent streams of WWTPs, whereas other azoles (e.g., clotrimazole) were removed by adsorption onto sludge. Garcia-Valcarcel and Tadeo (2012) reported that fluconazole previously adsorbed onto soil, under certain conditions, can be desorbed and may contribute to contamination of surface and ground waters.

The aim of this study was to determine the adsorption behavior of acyclovir and fluconazole onto quartz sand under static and dynamic conditions and to examine if the adsorption process is temperature dependent. To our knowledge, no previous study has explored the adsorption behavior of acyclovir and fluconazole onto quartz sand at different temperatures.

Materials and Methods

Pharmaceuticals

Pharmaceuticals examined in this study are acyclovir and fluconazole and their molecular structures are shown in Fig. 1. Acyclovir [9-((2-hydroxyethoxy)methyl)guanine] has the empirical formula $C_8H_{11}N_5O_3$, molecular weight 225.2 g/mol, is relatively soluble in water (water solubility 1.62–2.00 g/L), hydrophilic ($\log K_{ow} = -1.56$), and nonvolatile

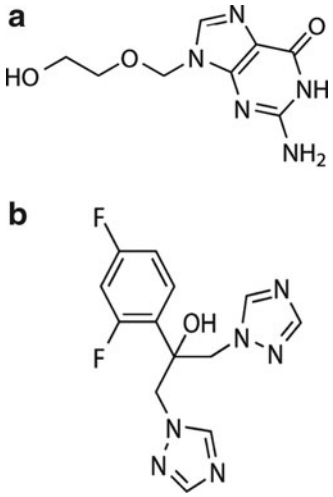

FIG. 1. Molecular structure of **(a)** acyclovir and **(b)** fluconazole.

(Garcia-Valcarcel and Tadeo, 2012; Bruni *et al.*, 2013). Fluconazole [2-(2,4-difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)-2-propanol] has the empirical formula $C_{13}H_{12}F_2N_6O$, molecular weight 306.27 g/mol (Wishart *et al.*, 2008), is slightly soluble in water (water solubility $\sim$1 g/L), slightly hydrophobic ($\log K_{ow}$ in the range 0.25 – 0.4), nonvolatile (Garcia-Valcarcel and Tadeo, 2012), and with good stability in aqueous solutions (stable for more than 15 days) (Dentinger and Swenson, 2009; Correa and Salgado, 2011). The pharmaceuticals were purchased from Sigma and used as received. All stock solutions were prepared with ultrapure water (EASYpureRF; Barnstead/Thermolyne). Subsequently, all desired acyclovir and fluconazole concentrations were made by appropriate dilution of stock solutions with ultrapure water.

Although the concentrations of pharmaceuticals in environmental systems are mostly in the ng/L range (Prasse *et al.*, 2010; Yu *et al.*, 2012; Loos *et al.*, 2013; Kosma *et al.*, 2014), in this work, we used relatively high concentrations of acyclovir and fluconazole (3, 7, and 10 mg/L) to elucidate their interactions with quartz sand, which is a common practice in studies examining the fate and transport of pharmaceuticals (Unold *et al.*, 2010; Chen *et al.*, 2011, 2015; Dong *et al.*, 2016).

Quartz sand

Quartz sand was employed in this study as in many other studies, focusing on adsorption and mobility of pharmaceuticals in porous media (Chen *et al.*, 2011, 2015; Dong *et al.*, 2016), because quartz is the most common mineral found on the surface of the earth (Chrysikopoulos and Aravantinou, 2014). The grain diameter of quartz sand used in this study was in the range of 0.425–0.600 mm (sieve no. 30/40), obtained with procedures reported by Chrysikopoulos and Aravantinou (2014). The chemical composition of quartz sand was 96.2% SiO_2, 1.75% Al_2O_3, 0.78% K_2O, 0.46% Fe_2O_3, 0.15% Na_2O, 0.11% CaO, 0.06% SO_3, 0.03% P_2O_5, 0.02% BaO, 0.02% MgO, 0.01% Mn_3O_4, and 0.28% loss on ignition, as reported by the manufacturer (Filcom, The Netherlands). The quartz sand were cleaned with 0.1 M HNO_3 (70%) for a period of 3 h, rinsed with distilled

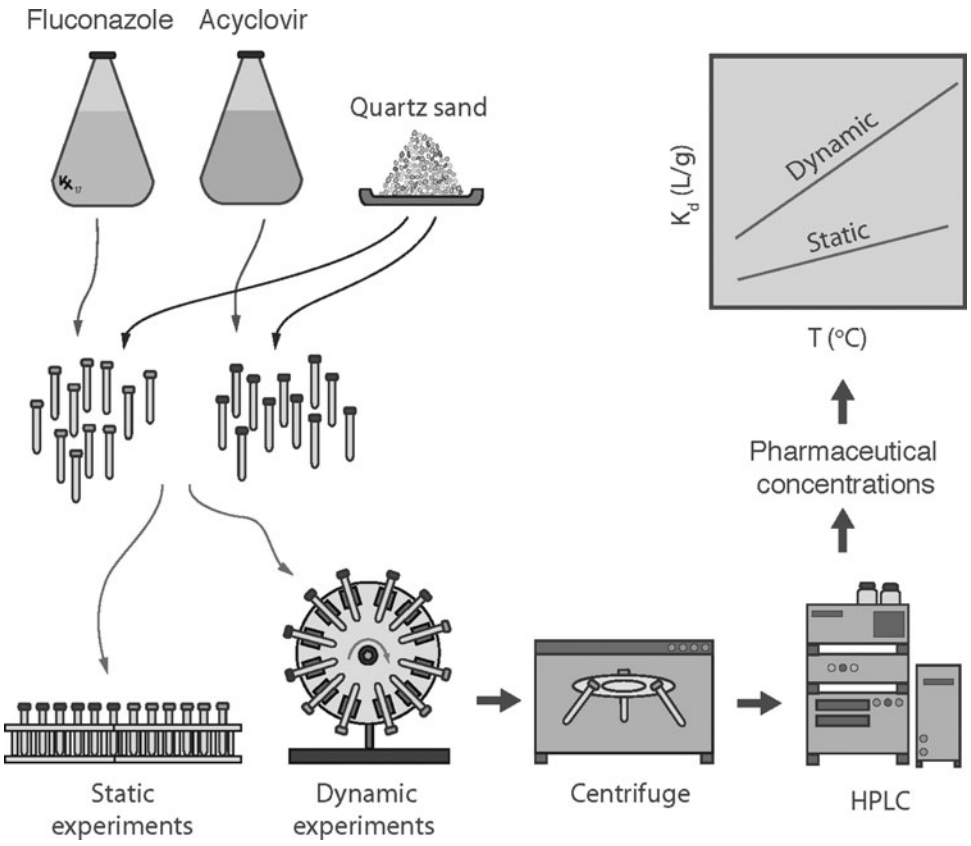

FIG. 2. Schematic illustration of experimental procedure.

deionized water (ddH_2O), soaked in 0.1 M NaOH for 3 h, and subsequently rinsed again with ddH_2O (Syngouna and Chrysikopoulos, 2010; Chrysikopoulos and Aravantinou, 2012; Chrysikopoulos *et al.*, 2012). Finally, the sand was dried and sterilized at 80°C.

Batch experiments

Static and dynamic batch experiments were performed individually under controlled conditions for three different initial concentrations ($C_0 = 3$, 7, and 10 mg/L) at 22°C and at three different temperatures (4°C, 10°C, and 22°C) with an initial concentration of $C_0 = 10$ mg/L. All batch experiments were performed in 20-mL Pyrex glass screw-cap tubes (Fisher Scientific). The tubes were washed with detergent, rinsed in ddH_2O, autoclave sterilized, and dried in an oven at 80°C.

For each experiment, 11 glass tubes were employed. The glass tubes contained 14 mL of fluconazole solution with 14 g of sand. All glass tubes were filled to the top. The experiments at 4 and 10°C were conducted in an incubator. For the dynamic batch experiments, the tubes were attached to a tube rotator (Selecta; Agitador Orbit), which was operated at 12 rpm, to allow the sand to mix within either the fluconazole or the acyclovir solution. One tube was removed from the rotator randomly at preselected time intervals (1 h, 2 h, 3 h, 6 h, 12 h, 24 h, 2 days, 3 days, 5 days, 7 days, and 10 days). This 10-day time period was shown to be adequate for the acyclovir– and fluconazole–sand systems to reach equilibrium.

Collected samples were centrifuged at 13,200 rpm for 15 min in a microcentrifuge to remove soil particles. Modified high-performance liquid chromatography (HPLC; Agilent 1100 series HPLC) with a Supelco C-18 column (5 μm, 280 × 4.6 mm) was used for the determination of pharmaceuticals. A diode array detector was used to detect acyclovir (3.5 min) and fluconazole (5.9 min) at a wavelength of 252 and 210 nm, respectively. A 50/50 water/methanol mixture was used as the mobile phase, with a low flow rate of 0.8 mL/min, at a constant temperature of 40°C. A schematic illustration of the experimental procedure employed in this work is presented in Fig. 2.

Theoretical Considerations

Equilibrium and kinetic adsorption

Concentrations of pharmaceuticals adsorbed onto quartz sand (C^*_t [M_p/M_s]) were determined by the following equation (in units of mg pharmaceutical/g sand):

$$C_t^* = \frac{(C_0 - C_t)\ V}{W} \tag{1}$$

where C_0 [M_p/L^3] is the initial liquid-phase concentration (in units of mg pharmaceutical/L), C_t [M_p/L^3] is the liquid-phase concentration at time t (in units of mg pharmaceutical/L), V [L^3] is the solution volume, and W [M_s] is the dry mass of the adsorbent (in units of g sand). Note that M_p represents the mass of pharmaceuticals and M_s the mass of quartz sand.

Kinetic adsorption experimental data were fit by the following pseudo-second-order expression (Tsai *et al.*, 2003; Ho, 2006):

$$\frac{dC^*}{dt} = k_{p2}\left(C^*_{eq} - C^*_t\right)^2 \quad (2)$$

where t [t] is time, C^*_t [M_p/M_s] is the concentration of the pharmaceutical adsorbed onto the quartz sand at time t, and k_{p2} [$M_s/(M_p \cdot t)$] is the rate constant of the pseudo-second-order adsorption model. Separation of variables and integration of time from 0 to t and C* from 0 to C^*_t yield the following:

$$C^*_t = \frac{\left(C^*_{eq}\right)^2 k_{p2} t}{1 + C^*_{eq} k_{p2} t} \quad (3)$$

which can also be rearranged in the following linear form:

$$\frac{t}{C^*_t} = \frac{1}{k_{p2}\left(C^*_{eq}\right)^2} + \frac{t}{C^*_{eq}} \quad (4)$$

It is worthy to note that the pseudo-second-order kinetic adsorption model has been employed in numerous adsorption studies of environmental interest (Upadhyayula *et al.*, 2009; Vasiliadou and Chrysikopoulos, 2011; Sotirelis and Chrysikopoulos, 2015, 2017).

The relationship between the pharmaceutical concentrations in solution and those adsorbed onto quartz sand at equilibrium, which is known as the adsorption isotherm (Scheytt *et al.*, 2005), was determined from the classical adsorption isotherm plots of the amount of the pharmaceutical retained per unit mass of quartz sand versus the equilibrium concentration of the pharmaceutical in the liquid phase at constant temperature. There are several equilibrium adsorption models available in the literature. The most commonly used adsorption isotherm models are linear, Freundlich, and Langmuir. In this study, the equilibrium adsorption of acyclovir and fluconazole onto quartz sand was quantified by a linear adsorption isotherm:

$$C^*_{eq} = K_d C_{eq} \quad (5)$$

where C_{eq} [M_p/L^3] is the concentration of the pharmaceutical at equilibrium (in units of mg pharmaceutical/L), C^*_{eq} [M_p/M_s] is the concentration of the pharmaceutical adsorbed onto sand at equilibrium (in units of mg pharmaceutical/g sand), and K_d [L^3/M_s] is the distribution coefficient (in units of L/g sand). The experimental data were fitted with a pseudo-second-order adsorption model [Eq. (3)] using the autonomous multipurpose fitting software, ColloidFit (Katzourakis and Chrysikopoulos, 2017).

Thermodynamic considerations

Thermodynamic behavior of acyclovir and fluconazole adsorption onto quartz sand was investigated by estimating the following thermodynamic quantities: Gibbs free energy change (ΔG° [kJ/mol]), enthalpy change (ΔH° [kJ/mol]), and entropy change (ΔS° [J/mol · K]). These thermodynamic quantities give insights of the adsorption process and were calculated using the following equations:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad (6)$$

$$\Delta G^\circ = -R_a T \ln K_0 \quad (7)$$

where $R_a = 8.3145$ J/(mol/K) is the universal gas constant, T [K] is the absolute temperature, and K_0 [L^3/M] is the thermodynamic distribution coefficient (ten Hulscher and Cornelissen, 1996; He *et al.*, 2010). Note that ΔG° characterizes the spontaneity of the adsorption process (e.g., for ΔG <0, the adsorption process is spontaneous).

The thermodynamic parameter, Gibb's free energy change, ΔG°, was calculated using K_d obtained from the linear isotherm [Eq. (5)]. In view of Equation (6), the enthalpy change, ΔH°, and the entropy change, ΔS°, were obtained from the intercept and slope of the plot of Gibb's free energy change ΔG° versus temperature T.

Results and Discussion

Experimental data from the kinetic batch experiments of fluconazole and acyclovir adsorption onto quartz sand at 22°C for three different initial concentrations ($C_0 = 3$, 7, and 10 mg/L), under both static and dynamic conditions, are presented in Figs. 3 and 4, respectively. The fitted model simulations are presented together with the experimental data (Figs. 3 and 4). Furthermore, the experimental data from the kinetic batch experiments of fluconazole and acyclovir adsorption onto quartz sand at three different temperatures (4°C, 10°C, and 22°C) with initial concentrations of $C_0 = 10$ mg/L, under both static and dynamic conditions, together with the fitted model simulations are presented in Figs. 5 and 6, respectively.

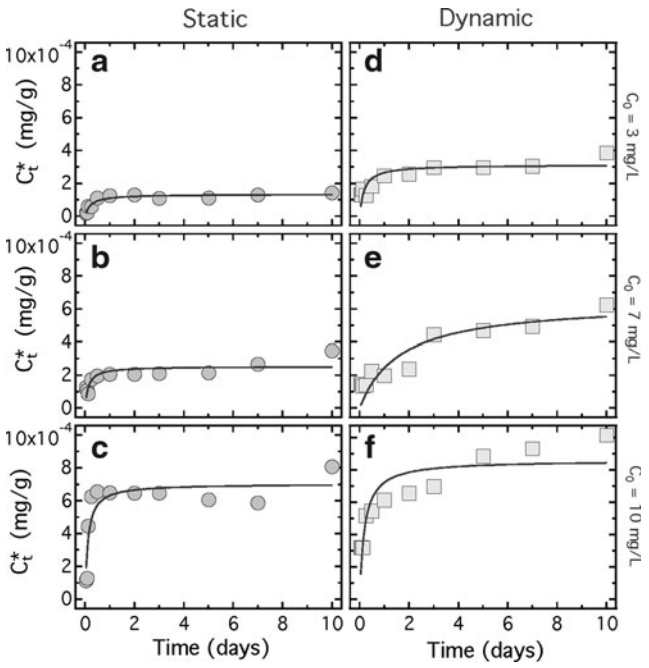

FIG. 3. Kinetic data of fluconazole adsorption onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) for three different initial concentrations at 22°C. The solid curves correspond to the fitted model simulations.

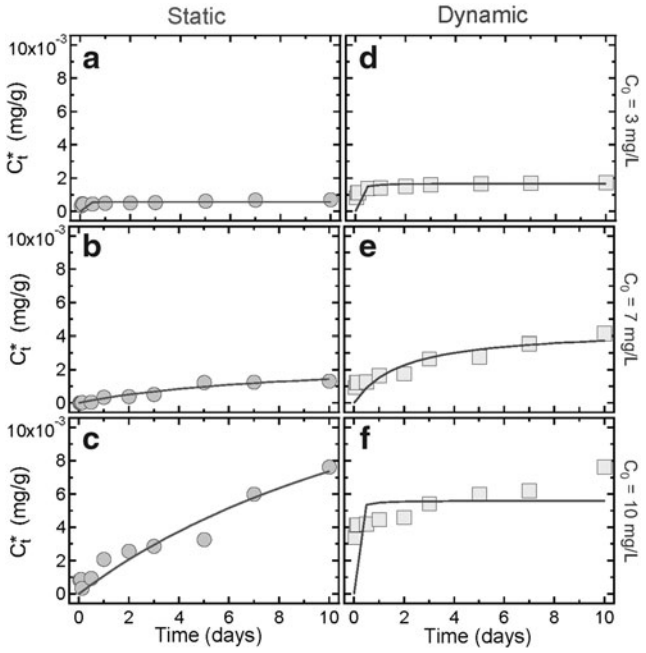

FIG. 4. Kinetic data of acyclovir adsorption onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) for three different initial concentrations at 22°C. The solid curves correspond to the fitted model simulations.

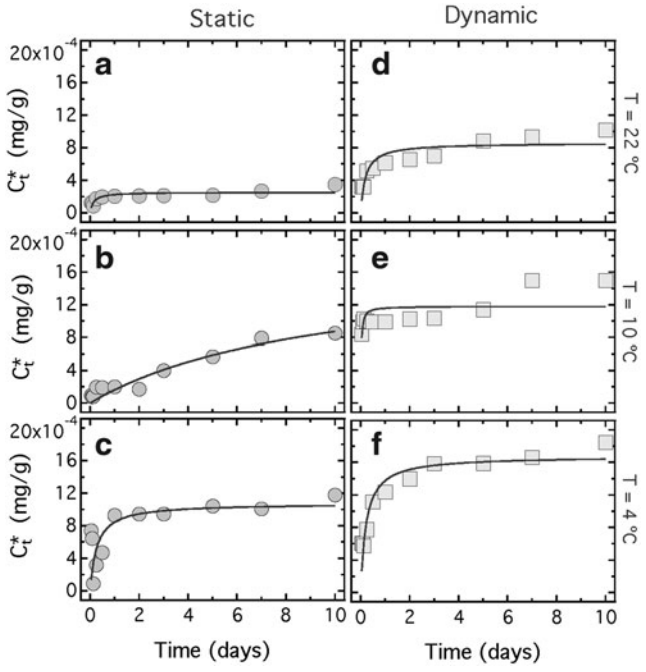

FIG. 5. Kinetic data of fluconazole adsorption onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) at three different temperatures for $C_0 = 10$ mg/L. The solid curves correspond to the fitted model simulations.

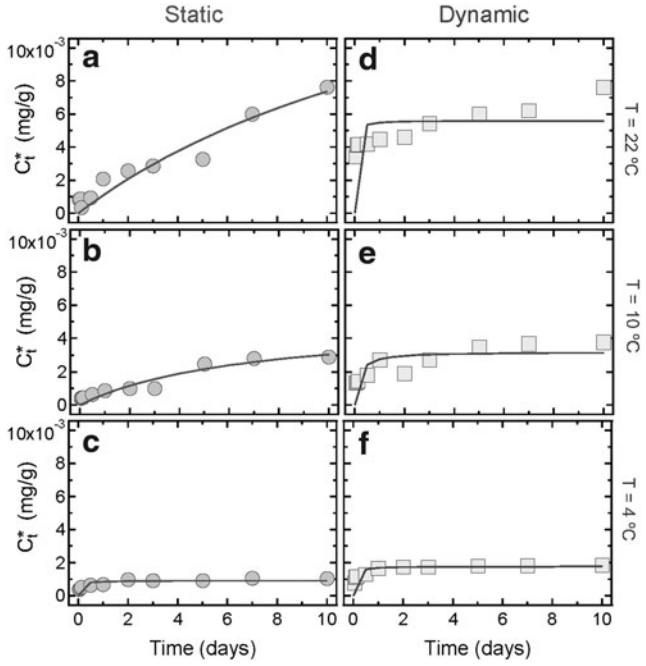

FIG. 6. Kinetic data of acyclovir adsorption onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) at three different temperatures for $C_0 = 10$ mg/L. The solid curves correspond to the fitted model simulations.

Kinetic batch experimental data collected in this study (Figs. 3–6) suggested that the adsorption of both fluconazole and acyclovir onto quartz sand increased with increasing temperature for all initial concentrations considered in this study. It is worthy to note that the effect of temperature was slightly more pronounced under dynamic than static conditions. Based on our kinetic experimental data (Figs. 3–6), it was evident that by increasing the initial concentrations, the adsorption rate decreased. In addition, by increasing the temperature, the adsorption rate decreased. Therefore, the adsorption rate was shown to decrease with either increasing the initial concentration of fluconazole and acyclovir or by increasing the temperature.

Experimental data from the equilibrium adsorption experiments of fluconazole and acyclovir onto quartz sand at three different temperatures (4°C, 10°C, and 22°C) under both static and dynamic conditions are shown in Figs. 7 and 8, respectively. The equilibrium adsorption data were fitted with the linear isotherm [Eq. (5)] using ColloidFit (Katzourakis and Chrysikopoulos, 2017). The fitted parameter values together with the corresponding coefficients of determination, R^2, which ranged between 0.811 and 0.976, are listed in Table 1. The equilibrium adsorption data suggested that in general, the sorption of acyclovir and fluconazole onto quartz sand, under both static and dynamic conditions, increased slightly with increasing temperature. Note that in agreement with the kinetic batch experiments, the equilibrium adsorption of both acyclovir and fluconazole onto quartz sand was slightly higher under dynamic than static conditions. This was attributed to agitation, which improves the contact of quartz sand particles with the liquid and decreases the resistance to mass transfer (Moore *et al.*, 1981;

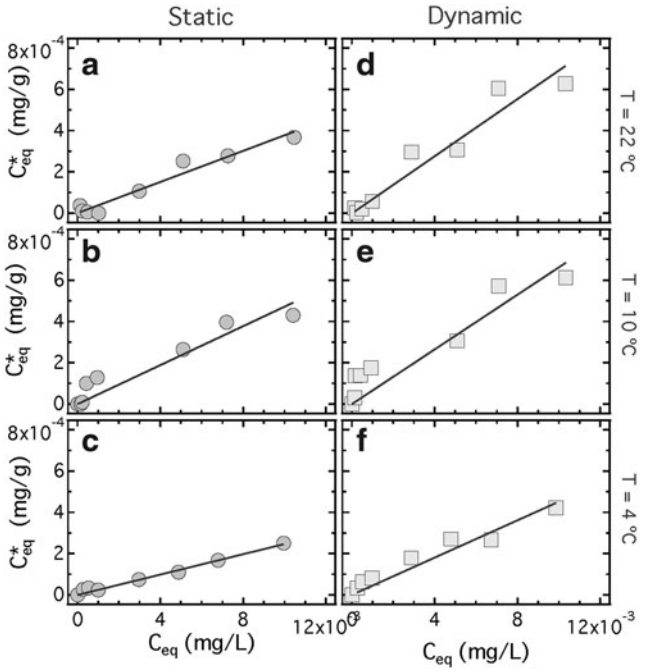

FIG. 7. Equilibrium adsorption data (isotherms) of fluconazole onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) at three different temperatures. The *solid lines* correspond to the fitted linear isotherm with the slope equal to K_d. Here, R^2 is in the range 0.811–0.976.

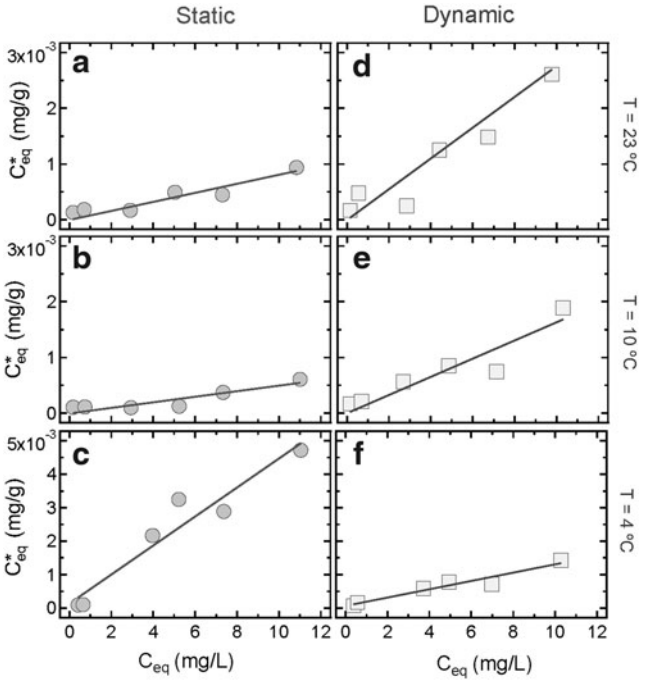

FIG. 8. Equilibrium adsorption data (isotherms) of acyclovir onto quartz sand under **(a–c)** static conditions (*circles*) and **(d–f)** dynamic conditions (*squares*) at three different temperatures. The *solid lines* correspond to the fitted linear isotherm with the slope equal to K_d. Here, R^2 is in the range 0.821–0.926.

TABLE 1. FITTED K_D VALUES AND 95% CONFIDENCE INTERVALS FOR FLUCONAZOLE AND ACYCLOVIR LINEAR ADSORPTION ISOTHERMS

	Fluconazole		*Acyclovir*	
T (°C)	$K_d \times 10^3$ (L/g)	R^2	$K_d \times 10^3$ (L/g)	R^2
Static				
4	0.025 ± 0.004	0.976	0.05 ± 0.001	0.926
10	0.038 ± 0.003	0.886	0.05 ± 0.003	0.821
22	0.047 ± 0.005	0.953	0.08 ± 0.008	0.862
Dynamic				
4	0.045 ± 0.001	0.906	0.10 ± 0.010	0.928
10	0.066 ± 0.002	0.811	0.20 ± 0.011	0.864
22	0.069 ± 0.005	0.931	0.20 ± 0.007	0.899

Chrysikopoulos and Aravantinou, 2012). However, the K_d values determined for fluconazole and acyclovir under static and dynamic conditions, for all three different temperatures examined in this study, are relatively low (Table 1) and suggest that both pharmaceuticals are weakly adsorbed onto quartz sand. This result is consistent with previous studies reported in the literature (Garcia-Valcarcel and Tadeo, 2012). Furthermore, the two PPCPs examined in this study have low vapor pressure (Garcia-Valcarcel and Tadeo, 2012) and negligible dissipation by volatilization. Therefore, fluconazole and acyclovir with relatively low affinity for soils are expected to be mobile in environmental systems and to migrate substantial distances in the subsurface. However, given that the K_d value for both fluconazole and acyclovir increases with temperature, the corresponding retardation factor also increases. Note that for linear instantaneous adsorption, the dimensionless retardation factor, $R \geq 1$, is expressed as $R = 1 + (\rho_b/\theta)K_d$ [where ρ_b (M/L^3) is the bulk density of the solid matrix and θ (–) is the porosity] and represents the ratio of the interstitial fluid velocity to the velocity of the pharmaceutical (fluconazole or acyclovir) in the aqueous phase within the porous medium (Chrysikopoulos *et al.*, 1990). Therefore, migration of both fluconazole and acyclovir is expected to become progressively more restrictive with increasing temperature.

Thermodynamic parameter values for fluconazole and acyclovir adsorption onto quartz sand under static and dynamic conditions are listed in Table 2, and the Gibbs free energy values are presented in Fig. 9. It should be noted that the value of K_0 was shown to increase with temperature, suggesting that the adsorption process was endothermic for both pharmaceuticals examined. The adsorption process was nonspontaneous and endothermic because all $\Delta G°$ and $\Delta H°$ values were positive, respectively. Nonspontaneous and endothermic adsorption is associated with structural changes of the sand surfaces due to chemisorption (Sotirelis and Chrysikopoulos, 2015). Finally, the value of $\Delta S°$ for both static and dynamic experiments was negative, indicating that the adsorption process was enthalpy driven.

Conclusions

Based on the experimental results of this study, it can be presumed that acyclovir and fluconazole are weakly adsorbed

Table 2. Thermodynamic Parameters for Adsorption of Fluconazole and Acyclovir onto Quartz Sand

	Fluconazole				*Acyclovir*			
T (°C)	$K_0 \times 10^3$ *(L/g)*	$\Delta G°$ *(kJ/mol)*	$\Delta H°$ *(kJ/mol)*	$\Delta S°$ *(J/[mol · K])*	$K_0 \times 10^3$ *(L/g)*	$\Delta G°$ *(kJ/mol)*	$\Delta H°$ *(kJ/mol)*	$\Delta S°$ *(J/[mol · K])*
Static								
4	0.025	24.4	21.2	–0.011	0.05	22.8	18.3	–0.0169
10	0.038	24.0			0.05	23.3		
22	0.047	24.5			0.08	23.2		
Dynamic								
4	0.045	23.1	13.1	–0.035	0.1	20.54	20.5	–0.0001
10	0.066	22.6			0.2	20.53		
22	0.069	23.6			0.2	20.52		

onto quartz sand. However, adsorption of the two pharmaceuticals was slightly higher under dynamic than static conditions at the three temperatures examined in this study. The adsorption rate was shown to decrease by either increasing the initial concentration of fluconazole and acyclovir or by increasing the temperature. The adsorption of fluconazole and acyclovir onto quartz sand was characterized as nonspontaneous, endothermic, and enthalpy driven. Consequently, it is anticipated that these pharmaceuticals will be considerably mobile in sandy subsurface formations and can be potentially transported to the aquatic environment with possible negative effects on living organisms and human health. However, migration of both fluconazole and acyclovir in subsurface porous media is expected to become progressively more restrictive with increasing temperature because the K_d values and, in turn, the retardation factor were shown to increase with temperature. Experiments of acyclovir and fluconazole transport through columns packed with quartz sand are highly recommended as an extension to this study.

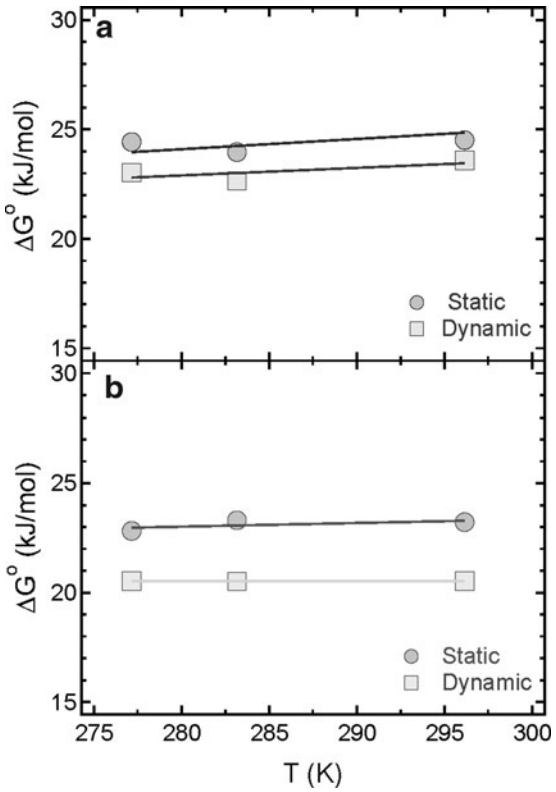

FIG. 9. Plot of Gibbs free energy change versus temperature for **(a)** fluconazole and **(b)** acyclovir.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors are thankful to R. Sarika and N. Xekoukoulotakis for valuable laboratory assistance.

Author Disclosure Statement

No competing financial interests exist.

References

Blackwell, P.A., Kay, P., and Boxall, A.B. (2007). The dissipation and transport of veterinary antibiotics in a sandy loam soil. *Chemosphere* 67, 292.

Boxall, A.B., Blackwell, P., Cavallo, R., Kay, P., and Tolls, J. (2002). The sorption and transport of a sulphonamide antibiotic in soil systems. *Toxicol. Lett.* 131, 19.

Bruni, G., Maietta, M., Maggi, L., Mustarelli, P., Ferrara, C., Berbenni, V., Milanese, C., Girella, A., and Marini, A. (2013). Preparation and physicochemical characterization of acyclovir cocrystals with improved dissolution properties. *J. Pharm. Sci.* 102, 4079.

Bu, Q., Wang, B., Huang, J., Deng, S., and Yu, G. (2013). Pharmaceuticals and personal care products in the aquatic environment in China: A review. *J. Hazard. Mater.* 262, 189.

Chefetz, B., Mualem, T., and Ben-Ari, J. (2008). Sorption and mobility of pharmaceutical compounds in soil irrigated with reclaimed wastewater. *Chemosphere* 73, 1335.

Chen, H., Gao, B., Li, H., and Ma, L.Q. (2011). Effects of pH and ionic strength on sulfamethoxazole and ciprofloxacin transport in saturated porous media. *J. Contam. Hydrol.* 126, 29.

Chen, H., Gao, B., Yang, L.Y., and Ma, L.Q. (2015). Montmorillonite enhanced ciprofloxacin transport in saturated porous media with sorbed ciprofloxacin showing antibiotic activity. *J. Contam. Hydrol.* 173, 1.

Chrysikopoulos, C.V., and Aravantinou, A.F. (2012). Virus inactivation in the presence of quartz sand under static and dynamic batch conditions at different temperatures. *J. Hazard. Mater.* 233, 148.

Chrysikopoulos, C.V., and Aravantinou, A.F. (2014). Virus attachment onto quartz sand: Role of grain size and temperature. *J. Environ. Chem. Eng.* 2, 796.

Chrysikopoulos, C.V., Roberts, P.V., and Kitanidis, P.K. (1990). One-dimensional solute transport in porous media with partial well-to-well recirculation: Application to field experiments. *Water Resour. Res.* 26, 1189.

Chrysikopoulos, C.V., Syngouna, V.I., Vasiliadou, I.A., and Katzourakis, V.E. (2012). Transport of *Pseudomonas putida* in a three-dimensional bench scale experimental aquifer. *Transport Porous Med.* 94, 617.

Correa, J.C.R., and Salgado, H.R.N. (2011). Review of fluconazole properties and analytical methods for its determination. *Crit. Rev. Anal. Chem.* 41, 124.

Daughton, C.G., and Ternes, T.A. (1999). Pharmaceuticals and personal care products in the environment: Agents of subtle change. *Environ. Health Perspect.* 107, 907.

Dentinger, P.J., and Swenson, C.F. (2009). Stability of reconstituted fluconazole oral suspension in plastic bottles and oral syringes. *Ann. Pharmacother.* 43, 485.

Diaz-Cruz, M.S., de Alda, M.J.L., and Barceló, D. (2003). Environmental behavior and analysis of veterinary and human drugs in soils, sediments and sludge. *Trends Anal. Chem.* 22, 340.

Dong, S., Gao, B., Sun, Y., Shi, X., Xu, H., Wu, J., and Wu, J. (2016). Transport of sulfacetamide and levofloxacin in granular porous media under various conditions: Experimental observations and model simulations. *Sci. Total Environ.* 573, 1630.

Drillia, P., Stamatelatou, K., and Lyberatos, G. (2005). Fate and mobility of pharmaceuticals in solid matrices. *Chemosphere* 60, 1034.

Fisher, I.J., Phillips, P.J., Colella, K.M., Fisher, S.C., Tagliaferri, T., Foreman, W.T., and Furlong, E.T. (2016). The impact of onsite wastewater disposal systems on groundwater in areas inundated by Hurricane Sandy in New York and New Jersey. *Mar. Pollut. Bull.* 107, 509.

Funke, J., Prasse, C., and Ternes, T.A. (2016). Identification of transformation products of antiviral drugs formed during biological wastewater treatment and their occurrence in the urban water cycle. *Water Res.* 98, 75.

Garcia-Valcarcel, A., and Tadeo, J.L. (2012). Influence of moisture on the availability and persistence of clotrimazole and fluconazole in sludge-amended soil. *Environ. Toxicol. Chem.* 31, 501.

Gros, M., Petrović, M., Ginebreda, A., and Barceló, D. (2010). Removal of pharmaceuticals during wastewater treatment and environmental risk assessment using hazard indexes. *Environ. Int.* 36, 15.

Hari, A.C., Paruchuri, R.A., Sabatini, D.A., and Kibbey, T.C. (2005). Effects of pH and cationic and nonionic surfactants on the adsorption of pharmaceuticals to a natural aquifer material. *Environ. Sci. Technol.* 39, 2592.

He, J., Hong, S., Zhang, L., Gan, F., and Ho, Y. (2010). Equilibrium and thermodynamic parameters of adsorption of methylene blue onto rectorite. *Fresenius Environ. Bull.* 19, 2651.

Heberer, T. (2002). Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: A review of recent research data. *Toxicol. Lett.* 131, 5.

Hirsch, R., Ternes, T., Haberer, K., and Kratz, K.L. (1999). Occurence of antibiotics in the aquatic environment. *Sci. Total Environ.* 225, 109.

Ho, Y.-S. (2006). Review of second-order models for adsorption systems. *J. Hazard. Mater.* 136, 681.

Jelic, A., Gros, M., Ginebreda, A., Cespedes-Sánchez, R., Ventura, F., Petrovic, M., and Barcelo, D. (2011). Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment. *Water Res.* 45, 1165.

Jones, O.A., Voulvoulis, N., and Lester, J.N. (2001). Human pharmaceuticals in the aquatic environment—a review. *Environ. Technol.* 22, 1383.

Kahle, M., Buerge, I.J., Hauser, A., Muller, M.D., and Poiger, T. (2008). Azole fungicides: Occurrence and fate in wastewater and surface waters. *Environ. Sci. Technol.* 42, 7193.

Katzourakis, V.E., and Chrysikopoulos, C.V. (2017). Fitting the transport and attachment of dense biocolloids in one-dimensional porous media: ColloidFit. *Groundwater* 55, 156.

Kim, J.W., Jang, H.S., Kim, J.G., Ishibashi, H., Hirano, M., Nasu, K., Ichikawa, N., Takao, Y., Shinohara, R., and Arizono, K. (2009). Occurrence of pharmaceutical and personal care products (PPCPs) in surface water from Mankyung River, South Korea. *J. Health Sci.* 55, 249.

Kosma, C.I., Lambropoulou, D.A., and Albanis, T.A. (2014). Investigation of PPCPs in wastewater treatment plants in Greece: Occurrence, removal and environmental risk assessment. *Sci. Total Environ.* 466, 421.

Liu, J.L., and Wong, M.H. (2013). Pharmaceuticals and personal care products (PPCPs): A review on environmental contamination in China. *Environ. Int.* 59, 208.

Loffler, D., Rombke, J., Meller, M., and Ternes, T.A. (2005). Environmental fate of pharmaceuticals in water/sediment systems. *Environ. Sci. Technol.* 39, 5209.

Loos, R., Carvalho, R., António, D.C., Comero, S., Locoro, G., Tavazzi, S., Paracchini, B., Ghiani, M., Lettieri, T., Blaha, L., Jarosova, B., Voorspoels, S., Servaes, K., Haglund, P., Fick, J., Lindberg, R.H., Schwesig, D., and Gawlik, BM. (2013). EU-wide monitoring survey on emerging polar organic contaminants in wastewater treatment plant effluents. *Water Res.* 47, 6475.

Moore, R.S., Taylor, D.H., Sturman, L.S., Reddy, M.M., and Fuhs, G.W. (1981). Poliovirus adsorption by 34 minerals and soils. *Appl. Environ. Microbiol.* 42, 963.

Pan, B., Ning, P., and Xing, B. (2009). Part V—sorption of pharmaceuticals and personal care products. *Environ. Sci. Pollut. Res. Int.* 16, 106.

Peng, X., Wang, C., Zhang, K., Wang, Z., Huang, Q., Yu, Y., and Ou, W. (2014). Profile and behavior of antiviral drugs in aquatic environments of the Pearl River Delta, China. *Sci. Total Environ.* 466, 755.

Peng, X.Z., Huang, Q.X., Zhang, K., Yu, Y.Y., Wang, Z.F., and Wang, C.W. (2012). Distribution, behavior and fate of azole antifungals during mechanical, biological, and chemical treatments in sewage treatment plants in China. *Sci. Total Environ.* 426, 311.

Prasse, C., Schlüsener, P.M., Schulz, R., and Ternes, A.T. (2010). Antiviral drugs in wastewater and surface waters: A new pharmaceutical class of environmental relevance? *Environ. Sci. Technol.* 44, 1728.

Prasse, C., Wagner, M., Schulz, R., and Ternes, A.T. (2011). Biotransformation of the antiviral drugs acyclovir and penciclovir in activated sludge treatment. *Environ. Sci. Technol.* 45, 2761.

Prasse, C., Wagner, M., Schulz, R., and Ternes, A.T. (2012). Oxidation of the antiviral drug acyclovir and its biodegradation product carboxy-acyclovir with ozone: Kinetics and identification of oxidation products. *Environ. Sci. Technol.* 46, 2169.

Richardson, S.D., and Ternes, T.A. (2014). Water analysis: Emerging contaminants and current issues. *Anal. Chem.* 86, 2813.

Scheytt, T.J., Mersmann, P., and Heberer, T. (2006). Mobility of pharmaceuticals carbamazepine, diclofenac, ibuprofen, and propyphenazone in miscible-displacement experiments. *J. Contam. Hydrol.* 83, 53.

Scheytt, T., Mersmann, P., Lindstädt, R., and Heberer, T. (2005). Determination of sorption coefficients of pharmaceutically active substances carbamazepine, diclofenac, and ibuprofen, in sandy sediments. *Chemosphere* 60, 245.

Schulman, L.J., Sargent, E.V., Naumann, B.D., Faria, E.C., Dolan, D.G., and Wargo, J.P. (2002). A human health risk assessment of pharmaceuticals in the aquatic environment. *Hum. Ecol. Risk Assess.* 8, 657.

Schwab, B.W., Hayes, E.P., Fiori, J.M., Mastrocco, F.J., Roden, N.M., Cragin, D., Meyerhoff, R.D., D'Aco, V.J., and Anderson, P.D. (2005). Human pharmaceuticals in US surface waters: A human health risk assessment. *Regul. Toxicol. Pharmacol.* 42, 296.

Sotirelis, N.P., and Chrysikopoulos, C.V. (2015). Interaction between graphene oxide nanoparticles and quartz sand. *Environ. Sci. Technol.* 49, 13413.

Sotirelis, N.P., and Chrysikopoulos, C.V. (2017). Interaction between graphene oxide nanoparticles and kaolinite colloids. *Sci. Total Environ.* 579, 736.

Syngouna, V.I., and Chrysikopoulos, C.V. (2010). Interaction between viruses and clays in static and dynamic batch systems. *Environ. Sci. Technol.* 44, 4539.

ten Hulscher, Th.E.M., and Cornelissen, G. (1996). Effect of temperature on sorption equilibrium and sorption kinetics of organic micropollutants—a review. *Chemosphere* 32, 609.

Thiele-Bruhn, S. (2003). Pharmaceutical antibiotic compounds in soils–a review. *J. Plant Nutr. Soil Sci.* 166, 145.

Tixier, C., Singer, H.P., Oellers, S., and Müller, S.R. (2003). Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters. *Environ. Sci. Technol.* 37, 1061.

Tolls, J. (2001). Sorption of veterinary pharmaceuticals in soils: A review. *Environ. Sci. Technol.* 35, 3397.

Tsai, W.T., Lai, C.W., and Hsien, K.J. (2003). The effects of pH and salinity on the kinetics of paraquat dorption on activated clay. *Colloids Surf. A Physicochem. Eng. Asp.* 224, 99.

Unold, M., Kasteel, R., Groeneweg, J., and Vereecken, H. (2010). Transport of sulfadiazine in undisturbed soil columns: Effects of flow rate, input concentration and pulse duration. *J. Environ. Qual.* 39, 2147.

Upadhyayula, V.K.K., Deng, S., Smith, G.B., and Mitchell, M.C., (2009). Adsorption of *Bacillus subtilis* on single-walled carbon nanotube aggregates, activated carbon and NanoCeram. *Water Res.* 43, 148–156.

Vasiliadou, I.A., and Chrysikopoulos, C.V. (2011). Cotransport of *Pseudomonas putida* and kaolinite particles through water saturated columns packed with glass beads. *Water Resour. Res.* 47, W02543.

Wang, L., Zhang, J., Sun, H., and Zhou, Q. (2016). Widespread occurrence of benzotriazoles and benzothiazoles in tap water: Influencing factors and contribution to human exposure. *Environ. Sci. Technol.* 50, 2709.

Williams, C.F., Williams, C.F., and Adamsen, F.J. (2006). Sorption–desorption of carbamazepine from irrigated soils. *J. Environ. Qual.* 35, 1779.

Wishart, D.S., Knox, C., Guo, A.C., Cheng, D., Shrivastava, S., Tzur, D., Gautam, B., and Hassanali, M. (2008). DrugBank: A knowledgebase for drugs, drug actions and drug targets. *Nucleic Acids Res.* 36, D901–D906.

Yang, Y.L., Lin, C.C., Chang, T.P., Lauderdale, T.L., Chen, H.T., Lee, C.F., Hsieh, C.W., Chen, P.C., and Lo, H.J. (2012). Comparison of human and soil *Candida tropicalis* isolates with reduced susceptibility to fluconazole. *PLoS One* 7, e34609.

Yu, K., Li, B., and Zhang, T. (2012). Direct rapid analysis of multiple PPCPs in municipal wastewater using ultrahigh performance liquid chromatography-tandem mass spectrometry without SPE pre-concentration. *Anal. Chim. Acta* 738, 59.

Zarn, J.A., Bruschweiler, B.J., and Schlatter, J.R. (2003). Azole fungicides affect mammalian steroidogenesis by inhibiting sterol 14a-demethylase and aromatase. *Environ. Health Perspect.* 111, 255.