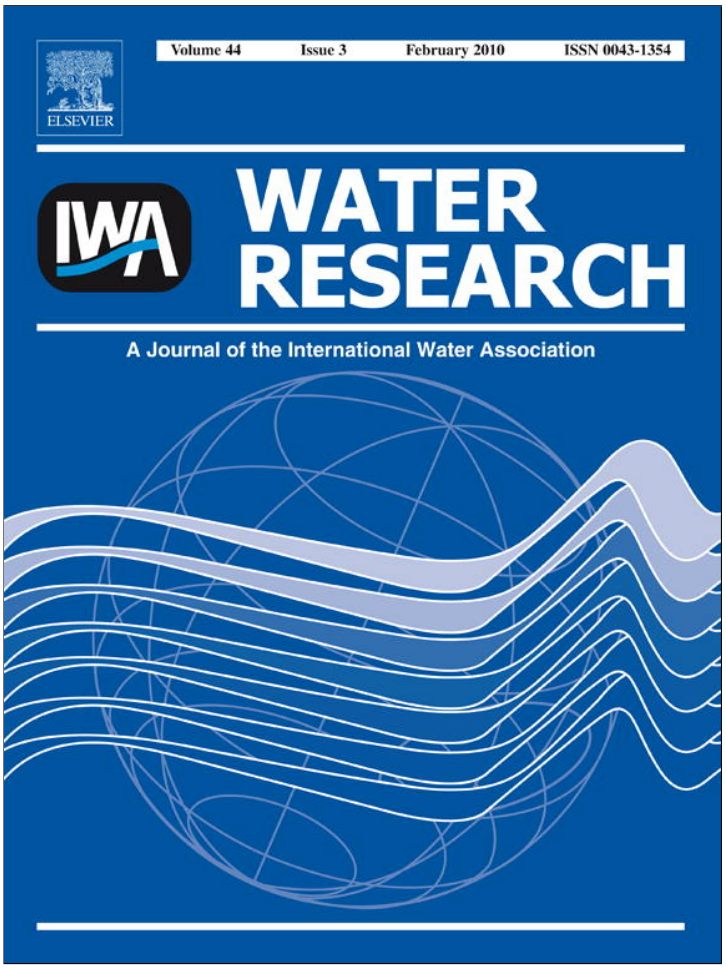

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Sorption of the pharmaceuticals carbamazepine and naproxen to dissolved organic matter: Role of structural fractions

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ABSTRACT

Pharmaceutical compounds and dissolved organic matter (DOM) are co-introduced into the environment by irrigation with reclaimed wastewater and/or application of biosolids. In this study, we evaluate the role and mechanism of interaction of the pharmaceuticals naproxen and carbamazepine with structural fractions of biosolids-derived DOM. Sorption interactions were estimated from dialysis-bag experiments at different pHs.

Sorption of naproxen and carbamazepine by the hydrophobic acid fraction exhibited strong pH-dependence. With both pharmaceuticals, the highest sorption coefficients (K_{DOC}) were at pH 4. With the hydrophobic neutral fraction, pH affected only naproxen sorption (decreasing with increasing pH). Among the hydrophilic DOM fractions, the hydrophilic acid fraction exhibited the highest K_{DOC} value for carbamazepine, probably due to their bipolar character. In the hydrophilic acid fraction-naproxen system, significant anionic repulsion was observed with increasing pH. The hydrophilic base fraction contains positively charged functional groups. Therefore with increasing ionization of naproxen (with increasing pH), K_{DOC} to this fraction increased. The hydrophilic neutral fraction exhibited the lowest K_{DOC} with both studied pharmaceuticals.

The K_{DOC} value of carbamazepine with the bulk DOM sample was higher than the calculated K_{DOC} value based on sorption by the individual isolated fractions. The opposite trend was observed with naproxen at pH 8: the calculated K_{DOC} value was higher than the value obtained for the bulk DOM. These results demonstrate that DOM fractions interact with each other and do not act as separate sorption domains.

1. Introduction

Due to the shortage of fresh water in semiarid and arid zones, reclaimed wastewater is becoming an important source of irrigation. The influx of dissolved organic matter (DOM) originating from reclaimed wastewater and/or from sludge application into the soil can affect the behavior of organic pollutants. Due to their colloidal properties, DOM can enhance the apparent solubility of hydrophobic organic pollutants and reduce their sorption to solid matrixes in soil and sediments (Chiou et al., 1986; Chin and Gschwend, 1992; Chin et al., 1997; Schwarzenbach et al., 2003; Marschner et al., 2005). Therefore, interactions with DOM may influence the potential mobility and bioavailability of organic pollutants in soils (Raber et al., 1998; Totsche and Kogel-Knabner, 2004; Cox et al., 2007).

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DOM is a highly heterogeneous mixture of compounds varying in size, shape, composition and physicochemical properties (Kalbitz et al., 2000; Imai et al., 2001; Her et al., 2003; Schwarzenbach et al., 2003; Polubesova et al., 2007). Therefore, the interactions and reactivity of DOM in an aqueous system are based on both the DOM concentration and properties. DOM can be fractionated based on the hydrophobic-hydrophilic characteristics of its materials (Leenheer, 1981). This fractionation scheme has proven useful in providing fundamental and mechanistic information on the interaction of DOM in the environment and with organic pollutants (Han and Thompson, 1999; Ilani et al., 2005; Polubesova et al., 2007; Polubesova et al., 2008). Ilani et al. (2005) reported that sorption of triazine herbicides by DOM is mainly governed by the relative content of the hydrophobic acid and neutral fractions of the DOM. Therefore, they concluded that an evaluation of the mobility of organic pollutants under wastewater irrigation requires an assessment of not only the total dissolved organic carbon (DOC) concentration but also, more importantly, the contents of the hydrophobic fractions.

The objective of this study was to evaluate the interactions of the pharmaceutical compounds (PCs) carbamazepine and naproxen (Table 1) with DOM structural components. Carbamazepine is a drug used for the treatment of epilepsy, trigeminal neuralgia, bipolar affective disorder and acute mania (Zerrouk et al., 2001). It is considered an environmentally recalcitrant compound which exhibits only limited removal efficiency in municipal wastewater-treatment plants (Ternes, 1998; Zhang et al., 2008). Carbamazepine has been detected in groundwater, surface water and reclaimed wastewater (Tixier et al., 2003; Clara et al., 2004). Naproxen is a nonsteroidal anti-inflammatory drug which has also been detected in wastewater effluents (Stumpf et al., 1999; Metcalfe et al., 2003; Tixier et al., 2003; Chefetz et al., 2008). The novelty of the current research lies in the investigation of the interactions of major DOM fractions with environmentally relevant PCs. The current research is of high importance due to extensive irrigation with reclaimed wastewater and the application of biosolids (containing both active PCs and DOM) to agricultural soils in semiarid and arid zones.

2. Materials and methods

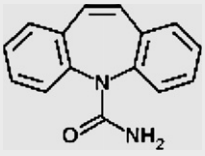
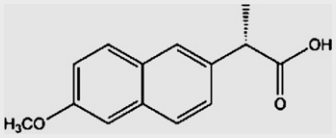
2.1. DOM: extraction, fractionation, purification and characterization

Commercially available, anaerobically digested sewage sludge (biosolids) was sampled from a municipal wastewater-treatment plant in Netanya, Israel. DOM was obtained from aqueous sludge extract, which was prepared by shaking (200 rpm) the sludge with distilled water for 2 h. The sludge-to-water ratio was 1:10 based on sludge dry weight. The suspension was centrifuged (15,000 *g* for 30 min) and filtered (0.45 μm) to obtain the bulk DOM solution. DOM was fractionated as described in detail by Leenheer (1981) and Chefetz et al. (1998). In brief, the DOM solution was acidified to pH 2.0 with 6 M HCl and loaded onto a glass column containing Supelite™ DAX-8 resin (Supelco, Bellefonte, PA, USA). The hydrophobic acid (HoA) fraction was displaced from the resin with 0.1 M NaOH; then the hydrophobic neutral (HoN) fraction was desorbed from the DAX-8 resin by Soxhlet extraction (24 h) with methanol. The DOM solution containing the hydrophilic fractions (not adsorbed to the DAX-8 resin) was loaded onto cation- and anion-exchange resins (Amberlyst® 15 and Amberlyst® A21, respectively) to obtain the hydrophilic acid and base fractions (HiA and HiB, respectively). The hydrophilic neutral fraction (HiN) was not adsorbed to any of the resins. All purified fractions were freeze-dried and stored in a desiccator. The freeze-dried samples were analyzed in triplicate for C, H, N and O contents with FlashEA 1112 elemental analyzer (Thermo Fisher Scientific Inc., Milan, Italy). The total acidity of the samples was determined using a procedure described for humic substances by Swift (1996).

2.2. Dialysis-bag sorption experiments

Carbamazepine (5*H*-dibenzo[b,f]azepine-5-carboxamide, 98%) and naproxen (2-naphthaleneacetic acid, 6-methoxy-alpha-methyl, >98%) were purchased from Sigma–Aldrich, Rehovot,

Table 1 – Selected chemical and physical properties of the studied pharmaceutical compounds.

	Carbamazepine	Naproxen
Chemical formula	$C_{15}H_{12}N_2O$	$C_{14}H_{14}O_3$
Structure		
Molecular weight (g mol^{-1})	236.27	230.27
Aqueous solubility (mg L^{-1})	125.0 ± 2	60.1 ± 2
Log K_{ow}	2.45[a]	3.18[b]
pKa	–	4.15[b]

a Hanna et al. (1998).
b Avdeef et al. (2000).

Israel. The sorption coefficients were measured using dialysis-bag sorption experiments (Seol and Lee, 2000; Ilani et al., 2005). Spectra/Por 6 dialysis bags (Spectrum Laboratories, Rancho Dominguez, CA, USA) with a molecular-weight cutoff of 1000 Da were washed with distilled water, 1 M Na_2CO_3, 1 M $NaHCO_3$, and again in distilled water before use. DOM solutions at a concentration of 1000 mg L^{-1} were prepared by dissolving the freeze-dried samples in diluted alkaline solution. The solutions were stirred overnight and then the pH was adjusted. Before use, the solutions were refiltered (0.45 μm) and if necessary, the pH was readjusted. Aliquots (10 mL) of the solutions were placed in the dialysis bags. Prior to the sorption experiments, the bags were dialyzed overnight against background solution (100 mg L^{-1} NaN_3 and 5 mM $CaCl_2$) to remove the <1000 Da fraction. Dialysis was performed until the DOC level was below detection limit. This step was essential to ensuring that during the sorption experiments, only the >1000 Da DOM fraction would be used.

The dialysis bags containing the predialyzed DOM were placed in 40 mL glass tubes containing 25 mL of background solution with carbamazepine or naproxen at concentrations ranging from 0 to 10 mg L^{-1}. The tubes (in triplicate for each analyte concentration) were agitated in the dark on a platform shaker at 90 rpm for 72 h at 25 °C. Data obtained from preliminary experiments indicated that 48 h is sufficient time for sorbate-sorbent equilibrium. Two types of blanks were measured for the sorption experiments: blank tubes in the absence of DOM to verify that PC concentrations inside and outside the dialysis bag are equal; and blank tubes with DOM without PCs for measurement of DOC. Sorption of the tested PCs to the dialysis bag was found to be negligible. PC concentrations inside and outside the dialysis tubes were determined using L-7100 LaChrom HPLC (Merck-Hitachi, Darmstadt, Germany) equipped with an Ascentis® RP-Amide (Supelco) column (25 cm × 4.6 mm, 5 μm). Carbamazepine and naproxen were eluted at a flow rate of 1 mL min^{-1} using isocratic conditions of 60/40 and 55/45 acetonitrile/0.1% formic acid, respectively. Carbamazepine was detected with a photodiode array detector at an absorbance of 286 nm; naproxen was detected with a fluorescence detector using 230 and 365 nm as excitation and emission wavelengths, respectively. Both compounds were quantified using external standards. The sorbed amounts were quantified as the difference between PC concentrations inside and outside the dialysis bag.

Sorption parameters were calculated using the Freundlich equation, $q = K_F \times C_e^N$, where q is the sorbed amount (mg kg^{-1} DOC), C_e is the equilibrium concentration, K_F [(mg kg^{-1} DOC)·(mg L^{-1})$^{-N}$] is the Freundlich sorption coefficient, and N describes the isotherm curvature. Since the K_F value depends on the N value, it is not possible to compare K_F values for isotherms with different N values. Thus, single-point carbon-normalized distribution coefficients (K_{OC}) were calculated for a C_e of 0.1 mg L^{-1} using the equation $K_{OC} = K_F \times C_e^{(N-1)}$. Statistical analysis was performed by JMPIN software, version 4.0.4. (SAS Institute Inc., Cary, NC, USA).

3. Results and discussion

The sludge-derived DOM was composed of 35 ± 7% (on a DOC basis) hydrophobic matter (HoA and HoN fractions) and 65 ± 7% hydrophilic matter (HiA, HiB and HiN fractions). The proportion of the hydrophilic fractions in our studied sludge-derived DOM was higher than that reported for DOM isolated from wastewater (Ilani et al., 2005; Zhang et al., 2009) and composted sludge (Zhou and Wong, 2001; Polubesova et al., 2007). The DOM composition and the relative proportion of the DOM fractions have been reported to vary in DOM samples based on their origin, maturity level, storage time and concentration (Chefetz et al., 1998; Imai et al., 2002; Ilani et al., 2005; Polubesova et al., 2007; Zhang et al., 2008). In our study, the HoA and HoN fractions made up 86 ± 8% and 16 ± 7%, respectively, of the hydrophobic matter. The HiA, HiB and HiN fractions made up 44 ± 2%, 24 ± 4%, and 33 ± 3%, respectively, of the hydrophilic matter. The >1000 Da hydrophobic fractions were 30 and 16% on a DOC basis of the bulk HoA and HoN fractions, respectively. The >1000 Da hydrophilic samples were 45, 5 and 30% on DOC basis of the bulk HiA, HiB and HiN fractions, respectively. These findings suggest that the weight-averaged molecular weight of the bulk DOM samples was relatively low, similar to other reports for DOM samples (Zhou et al., 2000; Imai et al., 2002; Mei et al., 2009).

Elemental analysis demonstrated relatively high values of H/C ratios for all isolated fractions (Table 2), suggesting their highly aliphatic nature. In accordance with the isolation procedure, the hydrophobic fractions (HoA and HoN) exhibited the low polarity values (i.e., (O + N)/C ratio). The HiB fraction, which is probably rich in peptide-containing compounds, exhibited high N content and a low C/N ratio. The HiA fraction exhibited the highest amount of carboxyl groups and the highest total acidity.

Table 2 – Selected chemical characterization of the DOM fractions: hydrophobic acid (HoA), hydrophobic neutral (HoN), hydrophilic acid (HiA), hydrophilic base (HiB), and hydrophilic neutral (HiN).

	(%)				(atomic ratio)			(mmol g^{-1})		
	C	N	H	O	C/N	H/C	(O + N)/C	Carboxyl	Phenol	Total acidity
HoA	43.50	7.08	6.26	25.58	7.17	1.73	0.58	2.1	1.2	3.4
HoN	38.20	5.53	5.71	22.75	8.06	1.79	0.57	1.4	0.3	1.7
HiA	26.20	3.30	3.70	22.84	9.26	1.69	0.76	3.8	2.7	6.5
HiB	41.10	10.30	6.10	22.85	4.66	1.78	0.63	1.8	1.7	3.5
HiN	43.50	8.50	6.90	27.53	5.97	1.90	0.64	0.8	0.9	1.7

DOM exhibits a large amount of acidic and polar functionalities and therefore, depending on its physicochemical properties, changes in pH may influence the nature of the sorption domains. Similarly, weak organic acids (e.g., naproxen) may be partially or fully ionized depending on their pKa values. Here we investigated the sorption of naproxen, a weak acid (pKa of 4.15) having greater solubility in alkaline than in acidic media (Avdeef et al., 2000), and carbamazepine, which is a neutral compound (Table 1). Therefore, the solution pH was expected to influence both the sorbent (i.e., DOM) and the sorbate in the naproxen-DOM system, and only the sorbent in the carbamazepine-DOM system.

Sorption coefficients (K_{DOC}, L kg^{-1}) of the studied PCs at an equilibrium concentration of 0.6–0.7 mg L^{-1} versus pH are presented in Fig. 1. Sorption isotherms (Fig. 2) were obtained at pH 4 (close to the pH of maximum sorption of the studied PCs with the DOM fractions) and 8 (close to the pH value of sewage sludge and reclaimed wastewater). Sorption parameters are listed in Tables 3 and 4.

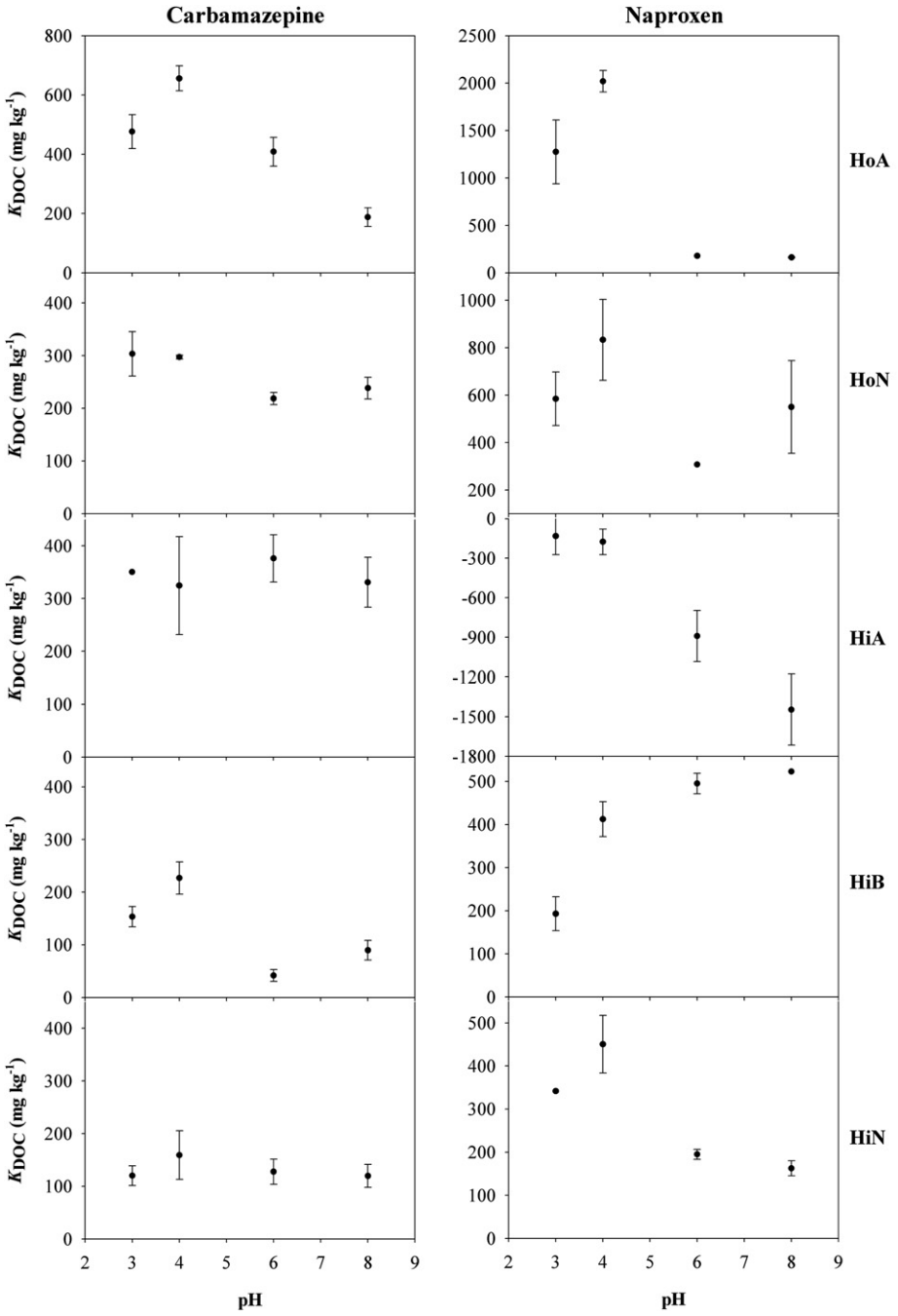


Fig. 1 – Sorption coefficients (K_{DOC}) of carbamazepine (left column) and naproxen (right column) with the isolated DOM fractions as a function of pH. HoA, hydrophobic acid; HoN, hydrophobic neutral; HiA, hydrophilic acid; HiB, hydrophilic base; HiN, hydrophilic neutral. K_{DOC} values were calculated at an equilibrium concentration of 0.6–0.7 mg L^{-1} (mean values and standard deviation bars are presented).

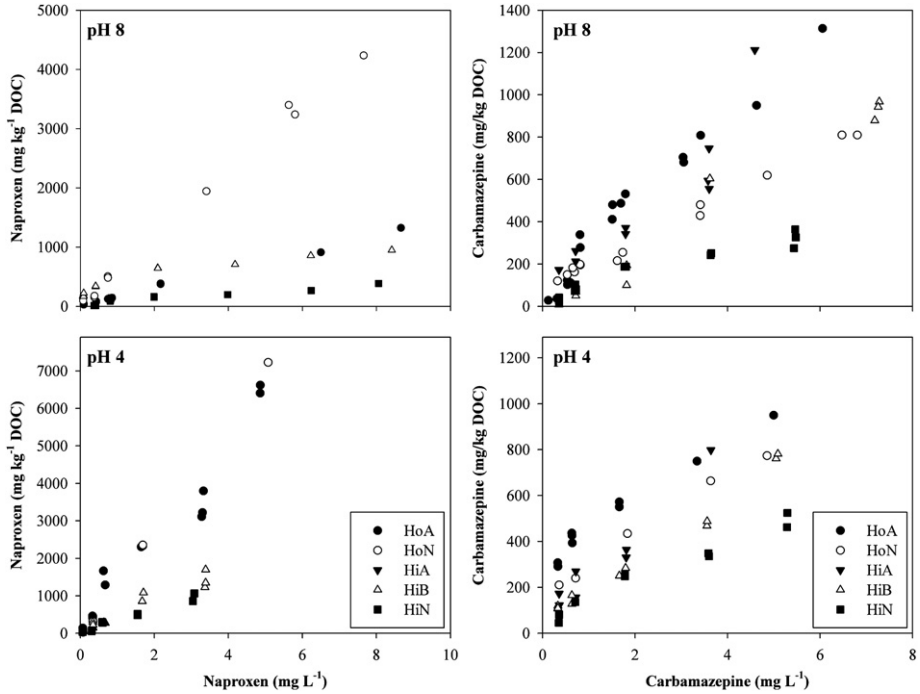


Fig. 2 – Sorption isotherms for naproxen (left) and carbamazepine (right) with the isolated DOM fractions at pH 8 (top) and pH 4 (bottom). HoA, hydrophobic acid; HoN, hydrophobic neutral; HiA, hydrophilic acid; HiB, hydrophilic base; HiN, hydrophilic neutral.

Sorption of hydrophobic compounds by DOM is typically viewed as a partitioning process in which the DOM structure is considered a rubbery type of organic matter (Kopinke et al., 2000). This type of interaction yields linear isotherms. In our study, most of the sorption isotherms for naproxen at pH 4 were linear with *N* values close to unity. At pH 8, the naproxen isotherms were nonlinear, especially with HiB and HiN (Table 3). Carbamazepine exhibited nonlinear isotherms with the hydrophobic fractions (HoA and HoN) at both pHs; with the hydrophilic fractions, higher isotherm nonlinearity was obtained at pH 8. The nonlinear type of isotherms obtained for the studied PCs with the DOM fractions suggests that partitioning cannot be considered the sole sorption mechanism for relatively small, polar and in some cases ionized compounds (such as the studied PCs) to DOM. Moreover, the structure and composition of the sorbent (i.e., DOM) strongly affects the sorption ability and mechanism. This is less pronounced for larger sorbents such as dissolved humic materials and highly hydrophobic materials (Kopinke et al., 2000).

In general, the Freundlich sorption coefficients (K_F) and the calculated K_{DOC} values were higher for both PCs at pH 4. Moreover, sorption of naproxen was higher than that of carbamazepine. This is in contrast to the sorption affinities of these compounds to soils (Chefetz et al., 2008), probably due to the higher polarity of the DOM as compared to matured and humified natural organic matter in soil.

3.1. *Sorption by the hydrophobic acid fraction (HoA)*

Sorption of naproxen and carbamazepine to HoA exhibited strong pH-dependence between pH 3 and 9 (Fig. 1). In both systems, the highest K_{DOC} values were at pH 4 (Table 4). Below this pH, the carboxyl groups of the HoA are protonated and naproxen is present as an uncharged compound. Above this pH, both the sorbent and the sorbate become progressively deprotonated and therefore, the sorption coefficients of naproxen declined sharply. For carbamazepine, the deprotonation of the HoA resulted in a reduction in the sorption coefficient. This trend is similar to the decrease in sorption of hydrophobic compounds with increasing sorbent polarity (Kang and Xing, 2005). HoA can considered a model low-molecular-size fulvic acid (Chefetz et al., 1998) and it is therefore expected to be strongly influenced by the pH of the system, as observed for dissolved humic materials. The conformation of humic materials has been reported to be affected by pH (Martin-Neto et al., 2001; Ferreira et al., 2002). At lower pH, protonation of carboxylic groups is promoted; this facilitates intra- and intermolecular interactions, forming a more condensed structure which can provide better sorption sites for hydrophobic compounds. Due to its smaller molecular size, HoA aggregation is expected to be less influenced by pH than that of humic materials. The sorption coefficients of carbamazepine with HoA therefore did not decline sharply with increasing pH as is expected with humic materials.

Our data suggest that polar interactions (H-bonding) played a major role in the sorption of both PCs (but mainly naproxen) to HoA, since sorption decreased with increasing pH. This trend is similar to the H-bonding ability of carboxylic acid groups of both naproxen and DOM which declines as these moieties become deprotonated with increasing pH (Gu et al., 2007). Van der Waals forces and probably π–π interactions between the aromatic moiety of naproxen and aromatic moieties of the HoA

Table 3 – Freundlich sorption parameters ($q = K_F \times C^N$) of naproxen and carbamazepine with dissolved organic matter (DOM) samples (HoA, hydrophobic acid; HoN, hydrophobic neutral; HiA, hydrophilic acid; HiB, hydrophilic base; HiN, hydrophilic neutral). Average values ± standard deviation data are presented.

	Naproxen						Carbamazepine					
	pH 4			pH 8			pH 4			pH 8		
	K_F[a]	N	r^2	K_F	N	r^2	K_F	N	r^2	K_F	N	r^2
HoA	1250 ± 213	0.99 ± 0.12	0.944	170 ± 9	0.93 ± 0.02	0.995	480 ± 11	0.41 ± 0.02	0.983	290 ± 18	0.82 ± 0.05	0.974
HoN	1330 ± 80	1.0 ± 0.04	0.999	640 ± 56	0.93 ± 0.05	0.997	320 ± 18	0.56 ± 0.05	0.986	200 ± 18	0.75 ± 0.05	0.962
HiA[b]							250 ± 32	0.86 ± 0.12	0.923	195 ± 68	1.05 ± 0.02	0.943
HiB	480 ± 51	0.97 ± 0.07	0.982	460 ± 11	0.34 ± 0.01	0.989	180 ± 19	0.86 ± 0.07	0.970	110 ± 30	1.08 ± 0.14	0.969
HiN	350 ± 31	0.89 ± 0.09	0.968	99 ± 14	0.61 ± 0.09	0.882	160 ± 14	0.67 ± 0.06	0.971	110 ± 10	0.66 ± 0.06	0.949

a $\frac{(\text{mg kg}^{-1}\text{DOC})}{(\text{mg L}^{-1})^N}$

b Sorption of naproxen to HiA was negligible and therefore parameters were not calculated.

are suggested to govern the interactions between HoA and naproxen at high pH. Although sorption decreased with increasing pH (Figs. 1 and 2), HoA was still a relatively efficient sorbent at the pH of natural soil and water systems.

3.2. Sorption by the hydrophobic neutral fraction (HoN)

In contrast to HoA, the HoN fraction is less polar and pH has only a limited effect on its properties. Therefore, with carbamazepine, pH did not affect the sorption to HoN. With naproxen, sorption at high pH (8) was expected to be lower than at pH 4 due to the predominance of anionic species, but this was not observed in Fig. 1. However, based on the sorption isotherms (Fig. 2), we calculated K_{DOC} values for naproxen at an equilibrium concentration of 0.1 mg L^{-1}. These values decreased by 37% (from pH 4–8; Table 4). The relative decrease in K_{DOC} with increasing pH was significantly lower than that observed for HoA with naproxen. This suggests that the hydrophobic interactions of naproxen with HoN governs the sorption over this pH range (3–8), as has been observed for nonionic chemicals (Burkhard, 2000). At both pHs, carbamazepine exhibited lower K_{DOC} values than naproxen with HoN. This might be related to the planar structure of the naphthalene moiety of naproxen, whereas the two benzene rings in the carbamazepine structure are nonplanar (Adam et al., 2003; Cruz Cabeza et al., 2006). In our previous publications (Ilani et al., 2005; Polubesova et al., 2007), HoN was reported to be a better sorption domain than HoA for both nonpolar solutes, such as pyrene, and polar triazine herbicides. It was concluded that HoN promotes hydrophobic interactions with all solutes. Here we investigated the sorption of smaller-sized and more polar compounds (PCs) which interact mainly with DOM via polar functionalities; therefore, in most cases, the less polar sorption domain (i.e., HoN) exhibited lower sorption capabilities than the polar one (i.e., HoA).

3.3. Sorption by the hydrophilic acid fraction (HiA)

HiA exhibited the highest level of carboxylic moieties among the studied DOM samples and therefore at pH values higher than 4, it is expected to carry a negative charge. With carbamazepine (a nonionic compound), increasing the pH of the system resulted in a decrease in K_{DOC} values (Table 4). With naproxen (ionized at pH > 4.15), significant anionic repulsion was observed with increasing pH (Fig. 1). As pH increased, a higher proportion of both HiA and naproxen were negatively charged and therefore a higher concentration of naproxen was measured outside the dialysis tube (HiA was placed inside the dialysis bag), resulting in negative calculated K_{DOC} values. This suggests that although the HiA fraction can be considered a sorption domain for nonionic compounds such as carbamazepine, for acidic drugs in neutral pH systems, HiA contributes negatively to the overall sorption capability of the DOM. Due to this anionic repulsion, sorption isotherms of naproxen with HiA were not obtained (Fig. 2).

3.4. Sorption by the hydrophilic base fraction (HiB)

HiB is a DOM fraction with positively charged functional groups. Therefore, with increasing ionization of naproxen (with increasing pH), sorption coefficients to HiB increased (Fig. 1). These observations are similar to the pH-dependence curve for the sorption of macrolide (a cationic antibiotic) to dissolved humic acid (Sibley and Pedersen, 2008). Those authors suggested that electrostatic interactions between the positively charged tertiary amine (sorbate) and deprotonated acid groups of humic acid (sorbent) govern sorption. In our experiments, the sorbent (HiB) was positively charged and the sorbate (naproxen) was anionic. It is interesting to note that at pH 4, HiB-naproxen sorption isotherms were linear (Freundlich N values of 0.97); however at pH 8, the sorption isotherm was curved with a Freundlich N value of 0.34. This supports the hypothesis that naproxen sorption to HiB is governed by electrostatic interactions. The calculated sorption capacity of HiB for naproxen was 909 ± 54 mg kg^{-1} DOC. At an equilibrium concentration of 0.1 mg L^{-1} at pH 8, the K_{DOC} value of naproxen was the highest obtained for all DOM fractions (Table 4). Mura et al. (2003) reported that the amino acids arginine and lysine significantly enhance the solubility of naproxen. Even higher solubility of naproxen was observed when the two amino acids were used in the presence of cyclodextrin. This was due to the strong cationic properties of the amino acids and the anionic nature of naproxen. Enhanced solubility of naproxen with bovine serum albumin

Table 4 – Sorption coefficient values (K_{DOC}) and weight-adjusted K_{DOC} values of naproxen and carbamazepine with the investigated DOM fractions. K_{DOC} values were calculated at equilibrium concentration of 0.1 mg L^{-1}; Weight-adjusted K_{DOC} values were calculated based on Eq. (1).

	pH 8					pH 4				
	HoA	HoN	HiA	HiB	HiN	HoA	HoN	HiA	HiB	HiN
Naproxen										
K_{DOC} at 0.1 ppm	200 ± 10	750 ± 50		2130 ± 10	250 ± 15	1290 ± 210	1200 ± 80		520 ± 50	460 ± 30
Relative level of >1000 Da fraction in the > 1000 Da DOM (f)	32%	3%	45%	3%	18%	32%	3%	45%	3%	18%
Weight-adjusted K_{DOC}	65	25		55	45	410	40		15	80
Carbamazepine										
K_{DOC} at 0.1 ppm	440 ± 20	350 ± 20	170 ± 10	90 ± 30	230 ± 10	550 ± 10	870 ± 20	340 ± 30	250 ± 50	330 ± 10
Relative level of >1000 Da fraction in the > 1000 Da DOM (f)	32%	3%	45%	3%	18%	32%	3%	45%	3%	18%
Weight-adjusted K_{DOC}	140	10	80	3	40	170	30	150	6	60

(a protein) was also observed (Banerjee et al., 2006). A reduction in the sorption affinity of naproxen to bovine serum albumin with increasing ionic strength was also reported. This suggests prevailing electrostatic interactions in the complexation process. We believe that these interactions between proteins and amino acids are similar to our observed interactions with HiB.

Carbamazepine sorption to HiB decreased slightly with increasing pH (Fig. 1; Table 4). The HiB-carbamazepine isotherms were more linear than the HiB-naproxen isotherms, suggesting a preponderance of hydrophobic interactions in the sorption of carbamazepine, as observed with the drug amitriptyline which has a similar structure (Banerjee et al., 2006).

3.5. Sorption by the hydrophilic neutral fraction (HiN)

HiN has neutral properties, and thus pH is expected to influence the sorption of organic molecules only via its effects on the sorbate. Therefore, sorption of carbamazepine to HiN was not significantly affected by pH. In the HiN-naproxen system, lower K_{DOC} values were obtained at high pH. It appears that the highly polar nature of this DOM fraction does not facilitate high-affinity interactions with the studied PCs. This suggests that the H-bonding ability of this fraction was low and with increasing pH, it decreased even further due to deprotonation of the carboxyl groups. Our data suggest that HiN consists mainly of polysaccharides (Chefetz et al., 1998) which are poor sorption domains.

In contrast to our findings, solubility enhancement of naproxen has been reported with cyclodextrin (an oligomer of glucose). It was suggested that naproxen interacts with the hydrophobic inner cavity of the dextrin (Mura et al., 2002). In another study (Zerrouk et al., 2001), polyethylene glycol (PEG) 6000 was reported to efficiently enhance the solubility of carbamazepine. With both polymers, solubility enhancement increased with increasing level of the polymer. The HiN fraction may contain cyclodextrin- and PEG-like compounds. However, the relative concentrations of the pure polymers used in the abovementioned studies were much higher than the concentration of HiN used in our study, and the HiN sorption properties were therefore lower here.

3.6. Sorption by the bulk dissolved organic matter (DOM)

Sorption of naproxen and carbamazepine to bulk >1000 Da DOM (i.e., the nonfractionated DOM sample) was measured at pH 8. The obtained K_{DOC} value for the bulk DOM (K_{DOM}) was compared with the K_{DOM} calculated based on the K_{DOC} values of each fraction adjusted for its relative amount in the DOM (Eq. (1)). This calculation is based on the assumption that the bulk DOM is a mixture of the isolated fractions which do not interact with each other at a molecular level. Thus the DOM sorption properties can be described by independent sorption compartments according to the relative level of each fraction.

$$K_{DOM} = K_{HoA}\cdot f_{HoA} + K_{HoN}\cdot f_{HoN} + K_{HiA}\cdot f_{HiA} + K_{HiB}\cdot f_{HiB} + K_{HiN}\cdot f_{HiN} \quad (1)$$

K_{HoA}, K_{HoN}, K_{HiA}, K_{HiB}, K_{HiN} are the measured K_{DOC} of naproxen or carbamazepine with HoA, HoN, HiA, HiB and HiN fractions, respectively. f_{HoA}, f_{HoN}, f_{HiA}, f_{HiB}, f_{HiN} are the relative levels of each >1000 Da fraction (HoA, HoN, HiA, HiB and HiN) in the nonfractionated >1000 Da DOM, respectively. K_{DOC} and f values are presented in Table 4.

For naproxen at pH 4, HoA was the dominant sorption domain and accounted for 76% of the K_{DOM}. At pH 8, the weight-adjusted K_{DOC} values of HoA and HiB were close, each accounting for 34–30% of the total K_{DOM} value, respectively. HoN exhibited relatively high sorption coefficients for naproxen, but due to its lower level in the >1000 Da DOM, its relative contribution to the calculated K_{DOM} value was low. For carbamazepine at pH 4, HoA and HiA exhibited the highest weight-adjusted K_{DOC} values. The weight-adjusted K_{DOC} values of HiB were significantly lower than all other fractions, except for naproxen at pH 8. At this pH, the HiB-naproxen interaction was favorable due to electrostatic attractions.

If the bulk DOM is a physical mixture (the isolated fractions do not interact with each other), then the calculated K_{DOM} (Eq. (1)) should be similar to the measured K_{DOM}. The K_{DOM} value of carbamazepine with the bulk >1000 Da DOM sample was 440 L kg^{-1} (measured at pH 8), whereas the K_{DOM} value of carbamazepine calculated using Eq. (1) was 270 L kg^{-1} (for the same pH). In contrast, while the calculated K_{DOM} value of naproxen at pH 8 was 190 L kg^{-1}, sorption with the >1000 Da

nonfractionated DOM was negligible. Therefore, the assumption of DOM fractions being completely separate sorption domains in the DOM overestimates the sorption potential of the mixture (DOM) in the case of naproxen, and underestimates its sorption capacity in the case of carbamazepine.

4. Conclusions

Our data demonstrate that the hydrophobic DOM fractions were more efficient at sorbing naproxen and carbamazepine, and probably other pharmaceutical compounds, than the more polar hydrophilic fractions at a pH near the pKa of the analytes. At the pH of natural semiarid water and soil systems, including that of reclaimed wastewater and biosolids, the role of the hydrophobic fractions as sorption domains is less important than the contribution of the hydrophilic fractions. It is important to note that although the hydrophilic base (HiB) fraction exhibited the highest sorption affinity with naproxen at pH 8, the overall contribution of this fraction to the sorption of anionic pharmaceutical compounds to DOM is limited to its small proportion in the studied DOM and in DOM from wastewater effluents (Imai et al., 2002; Zhang et al., 2008, 2009).

The calculated K_{DOM} values for the bulk DOM (Eq. (1)) were not similar to the measured K_{DOM} values. Therefore we hypothesize that the DOM fractions interact with each other at the molecular level and do not act as independent sorption domains. Moreover, accessibility and availability of the sorption sites are also important. We assume that the hydrophobic fractions (hydrophobic acid and hydrophobic neutral) in the studied DOM are probably coated by the hydrophilic fractions and/or they interact with each other to form the bulk DOM structure. This physical arrangement reduces the sorption potential of the hydrophobic core of the DOM. This study also demonstrates that the sorption abilities of the DOM fractions can also significantly affect the mobility of pharmaceutical compounds in soils influenced by intensive irrigation with treated wastewater or amended with biosolids.

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