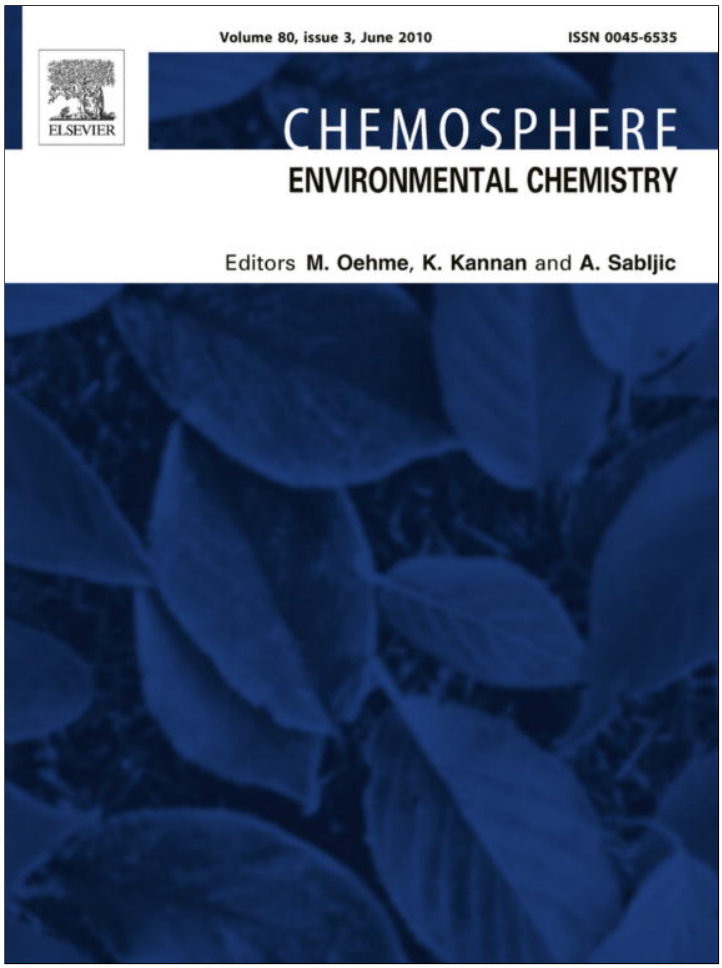

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Sorption of benzimidazole anthelmintics to dissolved organic matter surrogates and sewage sludge

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ABSTRACT

The sorption coefficients of four rarely studied zwitterionic pharmaceuticals (benzimidazoles: fenbendazole, albendazole, thiabendazole and flubendazole) and four metabolites of fenbendazole to various dissolved organic matter surrogates (humic acid, sodium dodecyl sulfate micelle, hydroxypropyl-β-cyclodextrin and liposomes made of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), and sewage sludge) were measured to extend the available sorption coefficients and eventually to evaluate their environmental fate in soil and water environment. For the entire range of dissolved organic matters, the more hydrophobic fenbendazole and albendazole had higher sorption coefficients than thiabendazole and flubendazole, indicating that the traditional hypothesis of hydrophobic interaction holds for zwitterionic benzimidazole anthelmintics. However, the sorption coefficients of a given benzimidazole to selected dissolved organic matters (DOMs) varied within an order of magnitude. The measured K_{oc} values decreased in the order of fenbendazole, albendazole, thiabendazole and flubendazole for sewage sludge and hydroxypropyl-β-cyclodextrin whereas the orders were different for the other DOM surrogates, implying the hydrophilic nature of sewage sludge. This was also supported by the (N + O)/C elemental ratio of the sewage sludge sample used in this study. The correlations between $\log K_{oc}$ and $\log K_{ow}$ were weak (r^2 = 0.28–0.64) and the magnitude of the sorption coefficients to the hydrophilic organic matters (hydroxypropyl-β-cyclodextrin and sewage sludge) were similar to or slightly smaller than those for the hydrophobic organic matters (humic acids and liposome). This suggests that specific hydrophilic interactions also play a significant role in the sorption of moderately hydrophobic benzimidazoles to organic matters.

1. Introduction

The fate of human and animal pharmaceuticals in the environment has attracted great attention from the public and scientific community (e.g., Calisto and Esteves, 2009; Kümmerer, 2009a,b) since their occurrence was identified in aqueous samples from wastewater treatment plants (e.g., Ternes, 1998; Carballa et al., 2004; Castiglioni et al., 2006; Suárez et al., 2008), surface waters (e.g., Kolpin et al., 2002), and even treated tap waters (e.g., Hernando et al., 2006; Loos et al., 2007). Among various physical, chemical and biological processes, sorption to organic matters is one of the dominant processes determining the fate of micropollutants including veterinary pharmaceuticals in the environment. Their removal efficiency in conventional sewage treatment plants varies with the degree of their sorption to the sludge (Heidler and Halden, 2008; Zhang et al., 2008; Carballa et al., 2008b; Matamoros et al., 2009) and their retardation in farmland soil is also strongly governed by their sorption to soil organic matters (Kreuzig et al., 2007; Lorphensri et al., 2007; Chefetz et al., 2008).

Many researchers have investigated the sorption coefficients of various pharmaceuticals to organic matters and their retardation in soil both in the laboratory and on field scales (e.g., Golet et al., 2003; Göbel et al., 2005; Carballa et al., 2008a). However, the measured sorption coefficients of veterinary pharmaceuticals with various polar functional groups deviated from the typical relationships derived under the earlier assumption that hydrophobic interactions between chemicals and organic matters dominate (Karickhoff et al., 1979; Sabljic et al., 1995). The organic carbon–water partition coefficient (K_{oc}) were often underestimated by typical relationships that use the 1-octanol–water partition coefficient (K_{ow}) (Tolls, 2001; Deng et al., 2006; Kwon and Armbrust, 2008; Qiao et al., 2008). The disparity was more significant for relatively polar compounds with $\log K_{ow}$ less than 3.0 (Rabølle and Spliid,

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2000; Cunningham et al., 2004; Carballa et al., 2008a; Heidler and Halden, 2008; Kim et al., 2009). For example, the partition coefficient of paroxetine between water and sewage solids estimated using log K_{ow} was two orders of magnitude lower than those determined experimentally (Cunningham et al., 2004). Researchers have proposed that the sorption of compounds to organic matters may be explained by various polar interactions, including cation exchange, surface complexation and hydrogen bonding (Tolls, 2001; Cunningham et al., 2004). Nonetheless, the compilation of experimental data for such pharmaceuticals is currently insufficient for understanding the mechanistic behavior of the sorption or to derive reliable relationships for the estimation of their sorption coefficients (Pan et al., 2009).

Benzimidazole anthelmintics have recently caught attentions due to their high production volumes and potential adverse effects on non-target ecological receptors (Svendsen et al., 2005; Oh et al., 2006; Kreuzig et al., 2007; Escher et al., 2008). For example, annual sales amount and production of fenbendazole in Korea was reported 356 (Kim et al., 2006) and 220 tons (Oh et al., 2006), respectively. Because benzimidazoles are not readily degraded in the environment (Kreuzig et al., 2007), their sorption to soil and sewage sludge is very important in assessing their predicted environmental concentration (PEC) in the environmental risk assessment. Although benzimidazoles have not been extensively monitored, the concentration of flubendazole in seepage water after sprinkler irrigation of a manured area was reported as high as 25–56 $\mu g\,L^{-1}$ (Weiss et al., 2008), which was comparable to the EC_{50} values of selected benzimidazoles to *Daphnia magna*, 10–100 $\mu g\,L^{-1}$ (Oh et al., 2006). Escher et al. (2008) reported the baseline toxicity of albendazole, together with lipid membrane-water partitioning and membrane permeability, to provide basic experimental data for a higher level environmental risk assessment. Unlike the evaluation of ecotoxicity, sorption phenomena in aqueous and soil environments have rarely been investigated for benzimidazole anthelmintics. The mobility and the metabolic fate of flubendazole and fenbendazole have only recently been evaluated in manure and manured soil under laboratory and field conditions (Kreuzig et al., 2007), which lead to the conclusion, based on their relatively high soil/water distribution coefficient, that their leaching into groundwater was unlikely despite their refractory nature in soil. However, experimental data are still far too limited to evaluate their potential environmental risks or fully account for their environmental fate in soil and water. Because benzimidazole anthelmintics are zwitterionic chemicals with their log K_{ow} between 1.5 and 4, reliable experimental sorption coefficients are required to assess their fate in soil and water environments. Because of the expected diversity of molecular interactions involved in sorption processes for benzimidazoles, use of well-characterized surrogate organic matters can be advantageous in this purpose.

Consequently, the sorption coefficients of selected benzimidazoles to surrogate dissolved organic matters, i.e., humic acids, sodium dodecyl sulfate micelle, hydroxypropyl-β-cyclodextrin, liposomes made of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), and sewage sludge were evaluated. Four widely used benzimidazoles, fenbendazole, albendazole, thiabendazole and flubendazole, were chosen for the evaluation of sorption. In addition, four metabolites of fenbendazole were also chosen because the annual production of fenbendazole is the highest in Korea. The sorption coefficients to the dissolved organic matters were measured using the changes in the concentration in a third phase, poly(dimethylsiloxane) (PDMS) to extend the available dataset for rarely studied benzimidazoles which will eventually contribute to mechanistic understanding of the sorption to organic matters of different nature. The measured sorption coefficients for the tested organic matters were compared and simple quantitative relationships using K_{ow} are presented to evaluate the contribution of non-specific hydrophobic interactions in the sorption processes.

2. Materials and methods

2.1. Materials

Albendazole (ABZ), thiabendazole (TBZ) and flubendazole (FLBZ) were purchased from Sigma–Aldrich (St. Louis, MO, USA). Fenbendazole (FBZ) and its four metabolites, oxfendazole (FBZSO), fenbendazole sulfone (FBZSO2), *p*-hydroxyfenbendazole (FBZOH) and amino-fenbendazole (FBZNH2), were kindly provided by Dr. Sung-Hwa Yoon (Ajou University, Suwon, Republic of Korea). The purities of all the benzimidazoles and the metabolites were higher than 99%, as determined by either the suppliers or our HPLC analyses.

Aldrich humic acid (sodium salt, CAS RN 68131-04-4), hydroxypropyl-β-cyclodextrin (CAS RN 128446-35-5), and sodium dodecyl sulfate (CAS RN 151-21-3) were purchased from Sigma–Aldrich. Chloroform solution, containing 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC, C16:0, C18:0), was purchased from Avanti Polar Lipids (Alabaster, AL, USA). The sewage sludge sample used for the ready-biodegradability test under good laboratory practice was kindly provided by the Environmental Chemistry Laboratory of the Korea Institute of Toxicology (Daejeon, Republic of Korea). Sodium azide (10 mM) was added to inhibit microbial activities for the sorption experiment.

Medical grade PDMS sheet (1 mm thick, density = 1170 $kg\,m^{-3}$) was obtained from Specialty Silicone Products, Inc. (Ballston Spa, NY, USA). This sheet was cut into disks with 3 and 6 mm diameters before use. The PDMS disks were cleaned for 3 h in a Soxhlet extractor, using *n*-hexane and methanol, and then stored in methanol until use.

2.2. Preparation of palmytoyl-oleoyl-phosphatidylcholine (POPC) liposome suspension

Large unilamella vesicles of POPC were prepared using a thin-film hydration technique (Mueller et al., 1983), followed by rapid extrusion processes (Hope et al., 1985; Kwon et al., 2006). The chloroform dissolving POPC was completely evaporated under a gentle nitrogen stream, and the resulting thin residue film was dissolved in the deionized water to produce a POPC liposome suspension. The suspension was extruded through a polycarbonate membrane filter (0.8 μm) 11 times at room temperature, above the main transition temperature of POPC (Jain, 1988). The extruded suspension was stored at 4 °C until use.

2.3. Instrumental analyses

Benzimidazoles and the metabolites of fenbendazole were analyzed using an HPLC system equipped with a Water 600E multi solvent delivery system and a 717+ autosampler (Waters Corp., Milford, MA, USA). Deionized water, methanol and potassium phosphate buffer (40 mM, pH 7) were used as the mobile phase in an isocratic mode. The solvent composition was varied depending on the analytes. Chemicals were separated on a Waters Symmetry C18 column (150 mm × 4.6 mm, 5 μm, Waters) at 35 °C, and detected using a Waters 2998 photodiode array detector (Waters). Concentrations of the analytes were measured at 295 nm, except for FLBZ, which was measured at 250 nm.

The total organic carbon content of the liposome and the sewage sludge was measured using Sievers 5310C TOC analyzer (GE Analytical Instruments, Boulder, CO, USA). The elemental composition of the sludge sample was analyzed using a Thermo-Finnigan

elemental analyzer (Fisons Instrument Co., Milano, Italy), after freeze-drying at −40 °C and 5 torr. The C, H, N and S contents were measured using WO_3/Cu catalysis, with 2,5-bis(5-tert-butylbenzoxazole-2-yl)thiophene as the standard. The oxygen content was measured using Ni catalysis, with sulfanilamide as the standard.

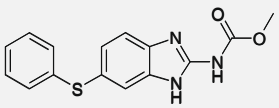
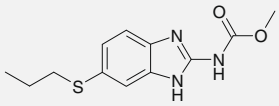
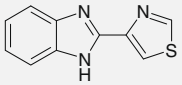
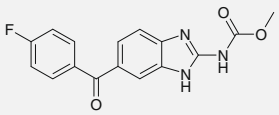
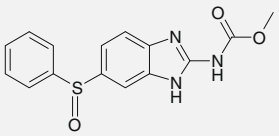
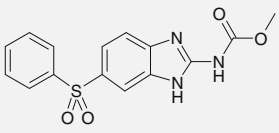
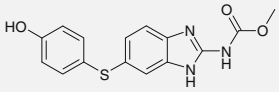
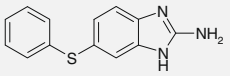
2.4. Determination of partition coefficients between PDMS and buffer

The partition coefficient between PDMS and the buffer (K_{PDMSw}) was determined using a conventional shaking method (Kwon et al., 2007). A pre-cleaned PDMS disk was placed in a 2 mL amber vial, containing buffer solution spiked with methanol and the test chemical species. The fraction of spiked methanol did not exceed 0.2% of the total solution. Vials were shaken at 150 rpm for 96 h at 25 ± 1 °C. Preliminary experiments, using fenbendazole, which has the highest K_{ow} and molecular weight of the selected chemicals, confirmed that 96 h was sufficiently long to attain equilibrium between PDMS and the buffer solution. After equilibrium had been obtained, the aqueous solution was directly injected into the HPLC system to measure the aqueous concentrations of the analytes. Chemicals dissolved in the PDMS disks were extracted using methanol by shaking for 2 h prior to HPLC quantification. Preliminary experiments showed that over 98% of the analytes were extracted in the first extraction. The volume of buffer (V_w) to PDMS (V_{PDMS}) was carefully designed to ensure that the analyte was evenly distributed between both phases. The range of aqueous solution of benzimidazoles was between 0.1 and 25 μmol L^{-1}, sufficiently lower than their aqueous solubilities. Partitioning experiments were conducted at least three different initial concentration in the buffer solution and the K_{PDMSw} was calculated from the slope of the linear regression using the measured chemical concentrations in PDMS and buffer.

2.5. Determination of sorption coefficients to dissolved organic matter surrogates

The sorption coefficients to the dissolved organic carbons (K_{DOCw}) were determined using a PDMS depletion method (Ter Laak et al., 2005; Kwon et al., 2009). K_{DOCw} values were measured at pH 7.0 because benzimidazoles except for amino-fenbendazole are electrically neutral in a wide range of pH based on their p*K*a values (Table 1). Test chemicals were loaded into a pre-cleaned PDMS disk, with an initial concentration of approximately 1 μmol L^{-1}. After apparent equilibrium between PDMS and DOC

Table 1
Selected benzimidazoles and their physico-chemical properties.

Compounds	Chemical structure	CAS reg no.	Molecular weight (g mol^{-1})	Water solubility (mg L^{-1})	log K_{ow}	p*K*a
Fenbendazole (FBZ)		43210-67-9	299.4	0.01–0.04[a]	3.85[b]	5.12, 12.72[c]
Albendazole (ABZ)		54965-21-8	265.3	46.4[d]	3.14[b]	3.37, 9.93[e]
Thiabendazole (TBZ)		148-79-8	201.3	30[f]	2.47[g]	4.7, 12.0[f]
Flubendazole (FLBZ)		31430-15-6	313.3	194.3[d]	2.91[d]	3.6, 9.6[h]
Oxfendazole (FBZSO)		20559-55-1	315.4	407.2[d]	1.63[b]	4.13, 11.79[c]
Fenbendazole sulfone ($FBZSO_2$)		54029-20-8	331.4	113.1[d]	2.17[d]	3.41, 11.12[c]
p-Hydroxyfenbendazole (FBZOH)		72447-64-4	315.4	285.5[d]	3.37[d]	5.49, 9.48, 11.38[i]
Amino-fenbendazole ($FBZNH_2$)		53065-28-4	241.3	51.4[d]	3.17[d]	6.94, 10.65[i]

[a] American Hoechst Corp. (1983).
[b] Tomasz et al. (2010).
[c] Danaher et al. (2007).
[d] EPISuite 4.00 (US EPA, 2008).
[e] Takacs-Novak et al. (1995).
[f] European Commission (2001).
[g] Sabljic et al. (1995).
[h] Weiss et al. (2008).
[i] Estimated using ACD/p*K*a v8.02 (Advanced Chemistry Development, 2009).

solution was attained (96 h), the PDMS disks were extracted using methanol, as described previously. The methanol solution was injected into the HPLC system to obtain the equilibrium concentration in PDMS in the presence of the DOC solution. Assuming a 100% mass balance, the equilibrium concentration in the PDMS (C_{PDMS}) over the initial PDMS concentration ($C_{PDMS,0}$) is given by (Kwon et al., 2009):

$$\frac{C_{PDMS}}{C_{PDMS,0}} = \frac{1}{1 + \frac{V_{DOC\ solution}/V_{PDMS}}{K_{PDMS/DOC}}} \quad (1)$$

where $V_{DOC\ solution}$ and V_{PDMS} are the volumes of the DOC solution and the PDMS (m^3) and $K_{PDMS/DOC}$ is a dimensionless partition coefficient between PDMS and the DOC solution. The $K_{PDMS/DOC}$ values were obtained by a non-linear regression using Eq. (1) from at least six different volume ratios and from at least three replicates. The equilibrium sorption coefficients to DOC were calculated by:

$$K_{DOCw} = \frac{\frac{K_{PDMSw}}{K_{PDMS/DOC}} - 1}{C_{DOC}} \times 10^6 \quad (2)$$

where C_{DOC} is the concentration of DOC in the solution (mg C L^{-1}). The C_{DOC} values were 5000–15 000 mg L^{-1} for humic acid, 20 000 mg L^{-1} for hydroxypropyl-β-cyclodextrin, 480–1700 mg C L^{-1} for POPC liposome, 10 000–25 000 mg L^{-1} for sodium dodecyl sulfate and 310–610 mg C L^{-1} for the sewage sludge.

3. Results and discussion

3.1. Partitioning of benzimidazoles between PDMS and buffer

The partition coefficients between PDMS and the buffer solution (K_{PDMSw}) for all selected chemicals are listed in Table 2. The K_{PDMSw} values for the parent benzimidazoles ranged between 32 and 104, whereas those for the metabolites were less than 11. For oxfendazole, the K_{PDMSw} was less than unity, indicating that the solubility of oxfendazole in PDMS is even lower than that in water. Fig. 1 shows the relationship between the log K_{PDMSw} measured in this study and log K_{ow} values (Sabljic et al., 1995; US EPA, 2008; Tomasz et al., 2010). The long and short dashed lines represent the linear relationships obtained for 40 polar and non-polar chemicals, with log K_{ow} values ranging from 1 to 7 (Kwon et al., 2007), and for highly hydrophobic chemicals with log K_{ow} values between 4.5 and 7.5 (Mayer et al., 2000). If all substances were included, the linear correlation between the two quantities was weak ($r^2 = 0.35$) in the present work compared to the earlier water pollutants studies (Mayer et al., 2000; Kwon et al., 2007), although there is possibility for uncertainties in the estimated log K_{ow} values for flubendazole and three of metabolites of fenbendazole (Table 1). The phenolic

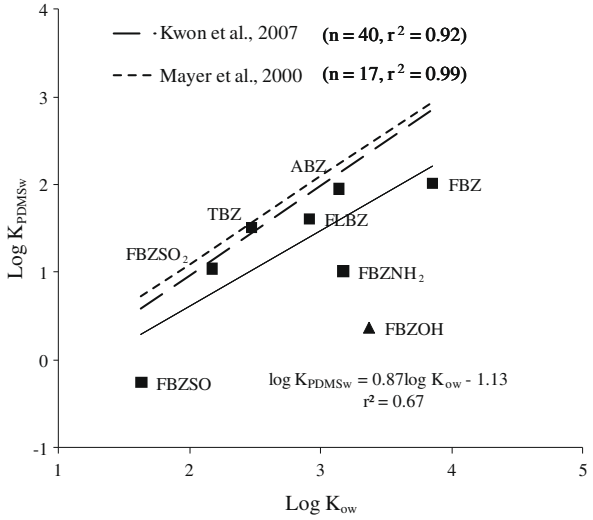


Fig. 1. Relationship between log K_{PDMSw} and log K_{ow}. The solid line shows a quantitative relationship excluding *p*-hydroxyfenbendazole. The short and long dashed lines represent the best-fit lines reported in the literature.

metabolite of fenbendazole, FBZOH, showed the greatest deviation from the quantitative relationship, and the r^2 value increased to 0.67 in its absence. A low K_{PDMSw} value for a phenolic compound would be due to the contribution of hydrogen bonding of the phenolic OH with the surrounding medium being much weaker in PDMS than in 1-octanol. This is consistent with the orders of magnitude lower K_{PDMSw} values obtained for chlorinated phenols under acidic pH using the general predictive equation (Kwon et al., 2007).

The relatively high K_{PDMSw} values of benzimidazole anthelmintics compared with other pharmaceuticals suggest that PDMS can be used as a passive sampling material for benzimidazole anthelmintics in aqueous phases for time-integrative monitoring purposes due to their high affinity to PDMS. However, non-polar polymers, such as PDMS, are unlikely to accumulate more polar metabolites, as shown for the four metabolites of fenbendazole. Thus, the use of PDMS poses an analytical challenge for simultaneous time-integrative passive sampling of benzimidazoles and their metabolites.

3.2. Sorption of benzimidazoles to surrogate dissolved organic matters and sewage sludge

As described previously, the K_{DOCw} values were obtained by measuring the decrease in the chemical concentrations in PDMS

Table 2
Summary of K_{PDMSw} and K_{DOCw} values of the selected benzimidazoles using Aldrich humic acid (K_{HAw}), hydroxypropyl-β-cyclodextrin (K_{CDw}), POPC liposome (K_{LIPw}), sodium dodecyl sulfate (K_{SDSw}), and sewage sludge ($K_{sludgew}$).

Chemicals	K_{PDMSw} (L kg^{-1})	K_{HAw} (L kg^{-1})	K_{CDw} (L kg^{-1})	K_{LIPw} (L kg^{-1})	K_{SDSw} (L kg^{-1})	$K_{sludgew}$ (L kg^{-1})
FBZ	103 ± 3	1170 ± 150	1790 ± 240	1690 ± 160	841 ± 120	4100 ± 840
FBZSO	0.555 ± 0.017					
$FBZSO_2$	11.0 ± 1.0					
FBZOH	2.35 ± 0.12					
$FBZNH_2$	10.3 ± 0.2					
ABZ	89.6 ± 0.2	3330 ± 420	918 ± 137	5840 ± 290	1040 ± 180	1870 ± 320
TBZ	32.0 ± 1.4	383 ± 42	243 ± 49	n.d.[a]	220 ± 36	103 ± 168
FLBZ	41.0 ± 0.4	400 ± 73	120 ± 41	n.d.[a]	110 ± 26	n.d.[a]

Abbreviations: FBZ (fenbendazole), FBZSO (oxfendazole), FBZSO2 (fenbendazole sulfone), FBZOH (*p*-hydroxyfenbendazole), $FBZNH_2$ (amino-fenbendazole), ABZ (albendazole), TBZ (thiabendazole), FLBZ (flubendazole), HA (humic acid), CD (hydroxypropyl-β-cyclodextrin), LIP (liposome), SDS (sodium dodecyl sulfate).
All sorption coefficients were normalized by the organic carbon content. Experimental K_{PDMSw} values in the table represent the mean ± standard deviation; the other sorption coefficients to dissolved organic carbons represent the mean ± standard error. Values left blanks were not determined.
[a] n.d.: not detectable at the DOM concentrations used.

in the presence of DOC solution. Fig. 2 shows an example plot of $C_{PDMS}/C_{PDMS,0}$ versus $V_{DOC\ solution}/V_{PDMS}$ for the determination of K_{DOCw} for albendazole between sewage sludge and the buffer solution using Eqs. (1) and (2). The measured K_{DOCw} values are summarized in Table 2. To our best knowledge, sorption coefficients of benzimidazoles to DOC have not previously been reported in the literature, with the exception of the liposome–water partition coefficient for albendazole using POPC unilamella vesicles, which was $10^{3.47}$ L kg_{lipid}^{-1} at pH 7 using equilibrium dialysis (Escher et al., 2008). This value is very close to $10^{3.77}$ L kg_C^{-1} obtained in this study, considering that the carbon content of POPC is 0.537. Of all DOCs studied in this work, FBZ and ABZ had higher sorption coefficients than TBZ and FLBZ, which is consistent with their values of K_{ow} (Table 1) that has been widely used to account for the traditional hydrophobic interactions.

K_{oc} values for flubendazole and fenbendazole in a field soil were reported to be greater than 8800 and 1500 L kg^{-1}, respectively (Kreuzig et al., 2007). Their K_{oc} for fenbendazole is close to those obtained using surrogate organic matters in this study, whereas that for flubendazole was at least an order of magnitude lower in our study. Since Kreuzig et al. (2007) measured soil/water distribution coefficient, K_d, and converted it to K_{oc} dividing it by the fraction of organic carbon, their K_{oc} might be overestimated if there are sufficient interactions between flubendazole and inorganic components of soils.

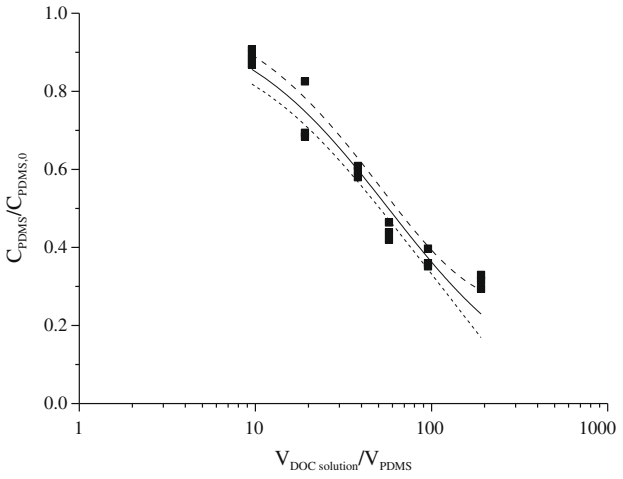


Fig. 2. Determination of K_{DOCw} using a PDMS depletion method for albendazole in sewage sludge as an example. Solid line represents the best-fit of the experimental data with Eq. (1). Dashed lines denote 95% confidence limits of the regression.

The K_{DOCw} values for a compound varied within an order of magnitude. Albendazole had relatively high K_{DOCw} values in liposomes and humic acids whereas those for fenbendazole were relatively high in hydroxypropyl-β-cyclodextrin and the sludge, even though their chemical structures are very close except for the propyl group bound to the sulfur atom in albendazole and the phenyl group in fenbendazole. Due to their molecular dipole moments, they are likely to enter the parallel region of the lipid bilayers, anchoring the hydrophilic zwitterionic imidazole moiety with the hydrophilic head region of the bilayers. The free energy required for the creation of a cavity in the parallel region of the bilayer would be higher for fenbendazole because phenyl group of fenbendazole bound to the sulfur atom is likely to require more space in the lipid bilayer than the propyl chain of albendazole.

Interestingly, the measured $K_{sludgew}$ and K_{CDw} values decreased in the order: FBZ, ABZ, TBZ and FLBZ, but the orders were different for the other DOM surrogates (Table 2). This tendency may be explained by the elemental composition of organic matters. The elemental composition of the sewage sludge was 15.9% C, 3.2% H, 19.8% O, 6.5% N, and 0.0% S. Thus, (N + O)/C molar ratio, often used for an indication of the polarity of sorbing phases (De Paolis and Kukkonen, 1997; Yamamoto et al., 2003), was 1.28. Theoretical (N + O)/C molar ratios of HA, SDS, POPC liposome, and CD were calculated from their chemical formula to be 0.44, 0.33, 0.21, and 0.67, respectively. Although K_{DOCw} values generally decreased with increasing (N + O)/C ratio (De Paolis and Kukkonen, 1997), this tendency was not shown for benzimidazoles in this study. Many functional groups in sewage sludge are able to be involved in specific polar interactions with benzimidazoles, including hydrogen bonding. This suggests that both hydrophobic interactions and specific hydrophilic interactions are likely to be important in the sorption of benzimidazoles to dissolved organic matters and sewage sludge.

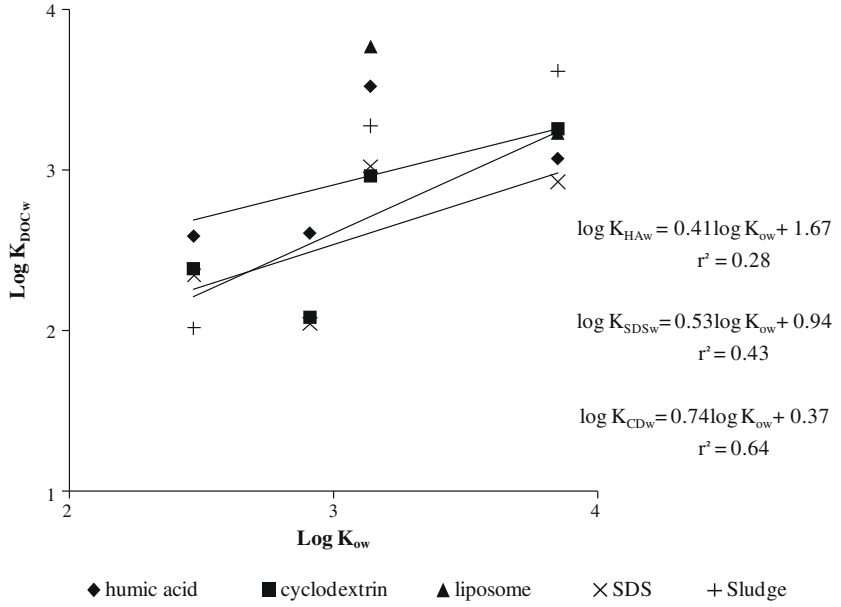


Fig. 3. Relationships between log K_{DOCw} and log K_{ow} with linear correlation equations. K_{HAw}, K_{SDSw}, and K_{CDw} are organic carbon normalized sorption coefficients to Aldrich humic acid, sodium dodecyl sulfate, and hydroxypropyl-β-cyclodextrin, respectively.

Sorption coefficients can be better predicted from multi-parameter quantitative structure–activity relationships after the accumulation of experimental data for benzimidazoles and other pharmaceutically active compounds.

Fig. 3 shows the relationship between log K_{DOCw} and log K_{ow}, where the trend lines show HA, SDS and CD. The r^2 values were between 0.28 and 0.64, with slopes of the regressions between 0.41 and 0.74, indicating that the K_{ow} is not a precise descriptor for estimating the K_{DOCw} of benzimidazoles, although the number of data is limited. This low sensitivity of K_{DOCw} with respect to K_{ow} is consistent with previous findings for phenolic estrogens (Yamamoto et al., 2003) and pharmaceuticals (Carballa et al., 2008a; Kwon and Armbrust, 2008).

3.3. Significance of the research

Predictive models using log K_{ow} (Karickhoff et al., 1979; Sabljic et al., 1995) or the molecular connectivity index (Sabljic, 1987; Meylan et al., 1992) are still limited to predict measured K_{DOCw} values to accurately assess the fate and transport of many pharmaceuticals. This, in part, could be due to the variations in the properties of organic matters, as shown in this study. Although the size of the dataset generated in this study is limited, the accumulation of K_{DOCw} for pharmaceuticals with various polar functional groups will eventually contribute the improvement of the predictive models.

When livestocks are raised intensively in a small area, wastewaters generated in livestock farm are often treated in a sewage treatment plant as is the case in Korea. As suggested by many researchers, hydrophobic contaminants are likely to be removed during conventional activated sludge treatment processes due to their great affinity to the suspended sludge particles. In a conventional sewage treatment plant, compounds with log K_{oc} greater than 4.0, over 90% are predicted to be removed during sludge removal while compounds with log K_{oc} values less than 2.0 are not removed unless they are biologically degraded (Kim et al., 2009). Benzimidazoles chosen in this study showed log K_{oc} values ranging from 2 to 4 (Table 2), indicating the efficiencies of their removals in an STP would be difficult to predict. Further investigation is necessary to evaluate the distribution of benzimidazoles between dissolved and sorbed forms in an STP treating animal wastewaters.

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