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Impacts of compound properties and sediment characteristics on the sorption behaviour of pharmaceuticals in aquatic systems

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Abstract

Sorption is a key factor in determining the persistence, attenuation and bioavailability of sediment-associated contaminants. However, our understanding of the sorption behaviour of pharmaceuticals in sediments is poor. In this study, we investigated the sorption behaviour of a diverse set of pharmaceuticals in a range sediment types. Sorption affinity of pharmaceuticals for all sediments was found to increase in the order mefenamic acid < cimetidine < atenolol < amitriptyline < diltiazem. Comparison of the experimental observations with predictions from an existing model for estimating sorption revealed the model worked poorly for the study pharmaceuticals. Multiple linear regression analysis was therefore used to develop new models for estimating sorption of individual pharmaceuticals based on sediment properties. The analyses indicated that sorption is related to properties such as Log Dow of a compound in the the sediment (lipophilicity corrected for the sediment pH), cation exchange capacity, clay%, organic carbon content and exchangeable Ca^{2+}, although, with the exception of atenolol, robust relationships between sediment properties and sorption were not obtained. Overall, the results demonstrate how complex the processes are that drive the sorption of pharmaceuticals in sediments and highlight the need for generation of further experimental data and further model development work.

KEYWORDS: Pharmaceuticals, Sediment characteristics, Sorption isotherms, Distribution coefficient (Kd), Modelling.

1. Introduction

Concerns over pharmaceuticals as environmental contaminants have increased in recent years [1-5]. Due to their continuous use by society, these substances are emitted into the environment continuously [6,7]. Consequently, pharmaceuticals have been detected in surface waters, wastewaters, soils, sludges and sediments across the globe [5, 8-11]. While the concentrations of these substances in the environment are low and therefore are unlikely to cause acute effects on organisms, it is possible that chronic and subtle effects could occur [12,13]. A range of chronic and subtle effects, including feminization of male fish and effects on wildlife behaviour, have been observed under laboratory conditions with effect concentrations being similar to those measured in the environment, [14-16]. Pharmaceuticals have also been shown to be accumulated by plants and to occur in drinking water supplies [17,18].

Once pharmaceuticals are introduced into surface water, they may undergo biodegradation, hydrolysis or photodegradation, as well as partition to natural solid matter such as suspended solids and bed sediments [19,20]. The fate of a pharmaceutical is thought to depend on factors such as the compounds lipophilicity, water solubility, chemical functionality as well as the ambient conditions of the receiving environment [21-23]. Sorption is one of the major factors determining the persistence and attenuation of pharmaceuticals in the natural environment [24,25]. Unlike neutral organic compounds, where differences in partitioning typically occurs through van der Waals interactions with soil organic carbon and is correlated to the hydrophobicity of the chemical (e.g. the octanol–water partitioning coefficients (Kow)), the sorption of pharmaceuticals, which are typically ionisable compounds, to environmental solids is thought to be through a combination of interactions e.g. hydrogen bonds, electrostatic interactions, ionic exchange and hydrophobic interactions [26-30]. Moreover, while the organic carbon content (OC) of sediments is known to be important in explaining the differences in the sorption behaviour of a neutral organic chemical across different soil or sediment types, factors such as the solid phase component (clay and metal content), surface exchangeable cations and pH probably play an important role in determining sorption of ionisable compounds [30-32].

While research into the sorption of pharmaceuticals in water-sediment systems has recently increased [13,20,27,33-36] data are still only available for a few active ingredients so our understanding of the factors and processes affecting sorption of pharmaceuticals is limited. A number of studies have also proposed predictive models for estimating the sorption behaviour of pharmaceuticals in sewage sludge and soil [37,38]. For example, Franco and Trapp [37] showed that predictors such as log Kow and pKa could be used successfully to predict the sorption of cationic dissociating groups to organic content in soils while failing to predict sorption for anionic groups. In sludge–water and soil–water systems, Barron et al. [38] used a non-linear correlation modelling techniques (artificial

neural networks) to predict the value of the distribution coefficient (Kd) in sewage sludge and found good agreement between the model predictions and experimental observations (R=0.88). Log Kow was found to be the largest contributor to Kd with approximately 11% deviation while pKa was the second most important descriptor. However, models for predicting sorption behaviour of pharmaceuticals in the sediment compartment are still lacking. The development of these models would be invaluable in supporting the assessment of environmental risks of pharmaceuticals released to surface waters and, in particular, characterizing likely impacts on benthic organisms.

The objective of this study was therefore to develop a better understanding of the sorption behaviour of pharmaceuticals in sediment-water systems and of how sediment and pharmaceutical physico-chemical properties influence this behaviour. The specific objectives were to: 1) explore the effects of sediment type on the sorption behaviour of a range pharmaceuticals with different properties; 2) evaluate the suitability of existing predictive models for ionsible compounds for use on pharmaceuticals in sediments; and 3) develop improved models for estimating the sorption behaviour of pharmaceuticals in different sediment types. The study was performed using five pharmaceuticals chosen based on a risk-based screening studies in aquatic and terrestrial systems that was performed by our group to identify the pharmaceuticals of most concern in environment in the UK [64] and Iraq [65]. The compounds varied in their physicochemical properties. Ten sediments, with different characteristics, collected from UK and Iraq were used in the studies.

2. Materials and methods

2.1 Chemicals and solvents

Amitriptyline hydrochloride (≥98% purity), atenolol (≥98%), cimetidine (≥98%), diltiazem hydrochloride (≥99%) and mefenamic acid (≥98%) were all purchased from Sigma-Aldrich (UK), (Table 1). The solvents used, including methanol (high performance liquid chromatography (HPLC) gradient grade), acetonitrile (gradient grade) and HPLC grade water were purchased from Fisher scientific (UK). Calcium chloride, hydrogen peroxide, potassium dihydrogen orthophosphate, nitric acid and hydrochloric acid were purchased from Fisher scientific (UK); formic acid was obtained from Sigma-Aldrich (UK).

2.2 Sediment collection and characterization

Eight surface sediment samples (0-5 cm) were collected from various rivers and streams around England and two were collected from Iraq (Table 2). Sediments from England were collected from Buttercrambe, Bishop Wilton,

Millington, German beck, Helmsley and North Yorkshire Moors National Park, all in North Yorkshire; and Harborough and Skeffington in Leicestershire. The sediments from Iraq were collected from the Tigris River in Baghdad and the Alhussainya River in Karbala city which branches from the Euphrates River. After sampling, the sediments were immediately taken to the laboratory. Sediments were wet sieved through a 2mm sieve and transferred into pre-cleaned glass jars and stored at 5± 1°C until use. Plant residues and debris were removed manually. Sorption studies were performed within three months of sediment collection. The pH of the sediments was measured in 0.01 M $CaCl_2$ (Thermo Orion pH meter, USA) according to the ISO 10390 protocol. The organic carbon content (OC) in the sediments was measured using a total carbon content analyser (Viro Macro Elemental (CN) Analyser, Germany) after drying and fine grinding (ISO10694). Sediment texture (clay (<2 μm), silt (2-50 μm) and sand (50-2000 μm)) was analysed using a Malvern laser granulometer (Hydro 2000MU, UK). Hydrogen peroxide was used to degrade the organic matter in sediments with organic content >3.5% prior to particles size measurements. Total metal ion contents of acid digested sediments were measured quantitatively using inductively coupled plasma atomic emission spectrophotometry (ICP-AES) using an iCAP 7000 Series instrument (Thermo Scientific, UK) following the ISO11466 protocol. Cation exchange capacity and exchangeable metals were measured by Forest Research UK following the ISO 11260 & 14254 protocols using a dual view ICP-OES (Thermo iCAP 6500 duo).

2.3 Sorption studies

Sorption studies were conducted based on the OECD test guideline 'Adsorption-Desoprtion Using a Batch Equilibrium Method' [39]. The study was performed in two phases. Initial experiments were done to identify the optimum sediment:solution ratio for each pharmaceutical. A definitive study was then done to develop the sorption isotherm. In the initial experiments, 1 g of sediment (dry weight equivalent) was weighed into 50 ml centrifuge tubes (centrifugation tube, Fisher scientific, Mexico) and mixed with either 10, 25 or 30 ml of 0.01 M $CaCl_2$ over 24 h prior to spiking of the test pharmaceuticals. Triplicate tubes were prepared for each sediment:solution ratio, time point and pharmaceutical. Aluminium foil was used to wrap the centrifuge tubes to prevent photochemical reactions during mixing. The pharmaceuticals were then spiked into the aqueous phase to give a concentration of 100 mg L^{-1}. Tubes were then agitated at 120 oscillation min^{-1} at room temperature (20±2^{o}C) for 2, 4, 6, 8 and 24 h. At the end of mixing, samples were centrifuged at 4500 rpm for 10 min and the supernatant solution was filtered through a 0.22 μm nylon filter to remove the suspended solids and particulate matter. Finally, 2 ml of the supernatant was taken for

determination of pharmaceuticals concentrations. A control treatment with the same test conditions but without sediment was set up to determine possible degradation or adsorption of the pharmaceuticals to vessels.

In the main study, a sediment to solution ratio of 1:10 was used for atenolol, cimetidine and mefenamic acid while ratios of 1:25 and 1:30 were used for diltiazem and amitriptyline respectively (as determined in the preliminary experiments). In order to create sorption isotherms, pharmaceuticals were spiked into vessels to give concentrations of 20, 40, 60, 80 and 100 mgL^{-1}.

2.4 Analytical method

Concentrations of the study compounds in supernatant from the sorption experiments were determined using analytical methods developed by our group using an HPLC (Perkin Elmer, Flexar) coupled with photodiode array detection and equipped with an automated injection system. An isocratic elution method was used for all compounds. Separation was achieved using a Supelco 516 C-18-DB reverse-phase column (5µm, 4.6×150 mm). For atenolol and cimetidine, the mobile phase comprised 1% formic acid [v/v], pH 2.7(± 0.05) and acetonitrile (65:35 v/v), the column was kept at 30^{o}C and the detection wavelength was 227 nm. The flow rate of the mobile phase was 1.0 ml min^{-1} into which 10µL of sample was injected. For amitriptyline and diltiazem, the mobile phase comprised 30 mM potassium dihydrogen orthophosphate (KH_2PO_4) and acetonitrile (35:65 v/v), pH 3.65 (±0.05). The flow rate was 1ml min^{-1}, the injection volume was 20 µL and the detection wavelength was 210nm. The column was kept at 35^{o}C. For mefenamic acid, the mobile phase consisted of 0.05% formic acid in HPLC water [v/v], pH 2.7 (± 0.05) and methanol (20:80 v/v) and the flow rate was 1ml/min. The sample injection volume was 20 µL and the detection wavelength was 227 nm. The column temperature was 30^{o}C. Analytical method details are shown in Table S1 and Figure S1 (supporting information).

2.5 Sorption isotherms modeling

The mass difference between the initial (C_i) and residual concentration (C_e) were used to determine the sorbed amount (Qe) in the sediment [mg kg^{-1}], Equation 1.

$$Q_e=(C_i-C_e)\ xV_w/m_s \qquad \text{Eqn. 1}$$

Where, V_w is the solute volume [L]; and m_s is the sediment mass [kg], respectively. Sorption isotherms were then modelled using the linear, Freundlich, and Langmuir isotherm models and Kd, Kf and KL values were derived.

Sorption modelling was done by SigmaPlot 12.0, Systat Software, Inc. The organic carbon-normalised sorption coefficient was then estimated from the Kd value and the total organic carbon content of the soil Equation 2.

$$K_{OC}=Kd/\int_{oc} *100 \qquad \text{Eqn. 2}$$

Statistical analyses were conducted on the resulting sorption coefficients, using the SPSS 22.0 statistical software package, to evaluate differences in a compounds behaviour across sediment types. One-way ANOVA was performed to explore the effect of sediment type on sorption of individual pharmaceuticals . Post Hoc ANOVA test was used to show the difference of sorption from one sediment to another. Kruskal Wallis non parametric analysis of varience was used when normality test failed.

2.6 Evaluation of existing models for estimating the sorption behaviour of pharmaceuticals

Koc values were calculated for each pharmaceutical and each sediment type using models proposed by Franco and Trapp [38] for acidic (Equation 3) and basic electrolytes (Equation 4).

$$\text{Log Koc}=\log(\phi_n.\ 10^{0.54\cdot \log Kow+1.11}+\phi_{ion}.10^{0.11\cdot \log Kow+1.54}) \qquad \text{Eqn. 3}$$

$$\text{Log Koc}= \log(\phi_n\ .\ 10^{0.37\cdot \log Kow+1.70}+\phi_{ion}\ .10^{pKa\hat{}_{0.65}\cdot f\hat{}0.14}) \qquad \text{Eqn. 4}$$

Where: Kow is the octanol-water partition coefficient; pKa is the acid dissociation constant; *f* is a parameter expresses a diffusion limiting factor and equal to Kow/(Kow+ 1). While, ϕ_n and ϕ_i are neutral and ion fractions respectively and were determined using Equations 5 and 6.

$$\phi_n=1/1+10^{a\ (pH-pKa)} \qquad \text{Eqn. 5}$$

$$\phi_{ion}=1-\phi_n \qquad \text{Eqn. 6}$$

Where a = 1 for acids and -1 for bases.

Estimates of Koc were then compared to measured values to assess the performance of the models.

2.7 Development of new models for estimating the sorption behaviour of the study pharmaceuticals across sediment types

The stepwise multiple-linear regression function in SPSS 22.0 was employed to try to develop relationships between Kd as the dependent variable and combinations of sediment physical-chemical property parameters as the explanatory variables. The Dow, which is a measure of the pH-corrected hydrophobicity of an ionisable compound in a particular environment was also estimated (using Equations 7 and 8) and used in the analyses as this parameter has previously been shown to explain differences in the sorption behaviour of ionisable compounds [24,40]. The Pearson correlation coefficient (R and P-value) was used to show the degree of linear relationship between Kd and single sediment or pharmaceutical properties (table S2).

$$LogDow_{acid} = \log Kow - \log (1+10^{(pH-pKa)}) \quad \text{Eqn. 7}$$

$$LogDow_{base} = \log Kow - \log (1+10^{(pKa-pH)}) \quad \text{Eqn. 8}$$

3. Results and discussion

3.1 Partitioning of pharmaceuticals between water and sediment

In the control treatments, for all pharmaceuticals, at least 95% of the initial concentrations remained after 24 h suggesting no significant degradation or adsorption onto centrifuge tubes. The linear (R^2 0.540-0.999), Freundlich (R^2 0.571-0.999) and Langmuir (R^2 0.283-0.998) models all appropriately described the sorption of the investigated pharmaceuticals over the range of test concentrations (see Supporting Information, table S2). The sorption coefficients obtained using the linear model were selected for use in the model evaluation and development studies and are discussed more fully below. Linear sorption isotherms for the five study compounds across the ten sediment types are shown in Figure 1.

Sorption coefficients for the compounds increased in the order mefenamic acid (Kd 1.83-1.19.04; Koc 75.86-331.13) < cimetidine (Kd 2.28-15.88; Koc 102.33-426.78) < atenolol (Kd 2.22-20.56; Koc 85.11-489.78) < amitriptyline (Kd 8.79-247.97320.8; Koc 912.01-12589.25) < diltiazem (Kd 22.03-1022.6; Koc 799.24-13182.57) (Figure 2; Table S2). Variability in pharmaceuticals sorption behaviour is likely due to several factors including total organic content, sediment texture, pH, salinity, the duration of incubation, particle size, degree of sediment–water interactions or the heterigenicity of the organic carbon in the sediments [25,26,43,51-54,68].

The patterns of sorption across the different test sediments were different for each study pharmaceutical. For amitriptyline, greatest sorption was seen for the BW sediment which had a high organic carbon content and CEC (9.9%, 35.58 cmol+/kg) while the lowest Kd value was obtained for the HLM sediment which had a low organic carbon content and CEC (0.98%, 5.85 cmol+/kg). Based on the hydrophobicity of amitriptyline (log Kow 4.92), a higher sorption was expected than seen in the current study. No previous data are available on sorption of amitriptyline in sediments but our Kd values are at the lower end of the range of Kd values reported for soils and sludge for this compound [37,43]. Significant differences in sorption across sediment types were also seen for atenolol (excluding MIL and SKF; $p<0.05$), cimetidine (excluding MIL and SKF and BW and BTC sediments; $p<0.01$), diltiazem (excluding GER and HUS; $p<0.05$), and mefenamic acid (excluding HUS and SKF and HLM and SKF sediments; $p<0.001$). For atenolol, the highest and lowest Kd values were seen for BW and HLM sediments respectively. Diltiazem sorption was the most variable amongst the studied pharmaceuticals across the sediment types with Kd values ranging from 22.03 to 1022.6 LKg^{-1} with the greatest sorption being seen in the BW sediment and lowest sorption being observed in the HLM sediment. For mefanamic acid, the greatest Kd was obtained for BW sediment whereas the lowest Kd was for sediment HUS from Iraq. For cimetidine, highest sorption was seen in the SKF (OC% 7.92, clay % 36.52) sediment and lowest in the HAB (OC% 1.12, clay %1.12) sediment. For atenolol, diltiazem and mefenamic acid where sediment sorption data are available in the literature, Kd ranges that we observed are not dissimilar from literature values (Table 3).

3.2 Evaluation of existing predictive model for sorption

Generally, for each study pharmaceutical, the variability in predicted Koc across sediments, obtained using the model of Franco and Trapp [38] was lower than the variability observed in the experiments (Table 3). The model tended to over-predict the sorption of the basic compounds and under-predict the sorption of the acids. No correlation between predicted and measured Koc was observed except for cimetidine (Figure 3). This result is not unsurprising as the properties of the sediments investigated in this study fall outside the applicability domain specified by Franco and Trapp for their model in terms of the relationship between soil organic carbon content and %clay. It is important to also recognize that this is a model for soils so may not be directly transferrable to sediments [66]. Therefore, sorption model that consider specific properties of the sorbate and sorbent are probably needed to describe the partitioning of ionisable chemicals in the environment [67].

3.3 Multiple linear regressions for Kd prediction

As the Franco and Tapp model did not perform well for the study pharmaceuticals and sediment systems being investigated, studies were done to explore whether it is possible to model the sorption behavior of each study pharmaceutical based on sediment properties. This approach has been used for other ionisable compounds in different environmental matrices [40,59]. Multiple linear regression analysis was performed to explore relationships between sediment and chemical properties and sorption coefficients (Kd) for each individual pharmaceuticals. The best performing regression models for each study compound are shown in Table 4. Combinations of only significantly correlated properties (sediment and pharmaceutical) were selected by the software package. In the case of cimitedine (clay %, OC %) and diltiazem (log Dow, Ex.Ca^{2+}), a combination of properties resulted in the best prediction of Kd with R^2 values of 0.922 ($p<0.001$) and 0.956 ($p<0.001$), respectively. The regression equations for amitriptyline, atenolol and mefenamic acid only included a single descriptor with Log D being found to be one of the strongest predictors of sorption behaviour chosen by the software.

To evaluate the developed regression equations, we applied them to sediment types that have been used for the study compounds elsewhere in the literature (Figure 4). For cimetidine and mefenamic acid, there were limited data in the literature for this evaluation. For atenolol, there was enough data to allow comparison, while amitriptyline has no previous adsorption study in sediment and exchangeable calcium cation (EX Ca^{2+}) in sediment have not been listed in literature when sorption of diltiazem was studied. The equation based on CEC for atenolol sorption resulted in a close match to Kd values for atenolol reported by Yamamoto et al. [20], Martínez-Hernández et al. [29] and Schaffer et al. [41] on (R^2=0.72, $p<0.001$). For mefenamic acid and cimetidine, the regression equation failed to predict the literature Kd values for both compounds with (R^2=0.07, $p<0.05$) and (R^2= 0.3, $p<0.05$). The wider applicability of some of the regression equations is therefore limited and further explerimental data is probably needed before strong conclusions can be made as to the predictive power of the relationships.

3.4 Suggested mechanisms of interaction

Potential Mechanisms for the adsorption of selected pharmaceuticals and how they are influenced by properties of the compound and the sediment are shown in Table 5. For amitriptyline, the only property extrapolated from multiple regression model to best explain the variability in sorption across sediment types was the log Dow. This suggests that the hydrophobic interaction of the non-ionised form of this cationic pharmaceutical is the dominant sorption mechanism for amitriptyline. Sorption was also correlated with CEC and selected sediments cations (Table S3); so these properties may also be contributing to sorption and additional mechanism such as electrostatic interactions between sorbent and substance is also possible [42,43].

The sorption of mefenamic acid and atenolol across sediment types appeared to be dependent on OC% and CEC respectively. Mefenamic acid is highly dissociated at natural pH values; and when the carboxylic group deprotonates, the negatively charged sepcies become dominant [44]. This may lead to electrostatic repulsion between mefenamic acid molecules and the negatively charged sediments which might explain why this compound is not highly adsorbed by sediments [45]. The bonding mechanism seems to be much more complex than simple hydrophobicity and hydrogen bonding and suggesting another interaction mechanism such as bridging between –COOH group and exchangeable cations on clay or organic matter [26,46-48]. The extent and strength of this coordination depends on the nature of the cation that saturated the clays [69].

With a pKa of 9.6, atenolol is predominantly positively charged at environmental pH values. The main suggested sorption mechanisms of atenolol in the literature are electrochemical interaction and ion exchange [29,41, 49,50] and could be via charge transfer interaction due to the structure of the molecule, with its electron donor atoms (two nitrogen atoms and one oxygen form OH group) or hydrogen bonding interaction [49,56]. Schaffer et al. [41] found that 99% of the total sorption of atenolol was by cation exchange interaction. On the other hand, Williams et al. [28] found that atenolol sorption is concentration dependent due to 1/n value <1 which is similar to the adsorption behaviour on sediments in this study except for HAB sediment. Despite the significant correlation to different sediment properties, CEC in this study seem to have a noticeable effect.

For diltiazem, sorption was found to depend on log Dow and sediment exchangeable Ca^{2+}. The relationships with Dow is likely explained by hydrophobic interactions of the neutral species with sediment organic matter [43,57]. Additionally, higher concentration of exchangeable divalent cations (e.g. Ca^{2+}) adhering to the surface of sorbent increase the sorption of pharmaceuticals greater than monovalent ctions (K^{+}) via ion-exchange interaction [26,47,48].

The Kd of cimetidine is positively impacted by clay% and OC%. Hydrophobic interaction with organic matter and hydrogen bonding probably play a greater role in the sorption process due to the presence of a greater neutral form fraction. In addition, basic ionisable compounds are known to interact to clay fraction via electrostatic interaction to surface particles [40,58]. However, the high surface area of clay leads to an increase in the number of available sorption sites [59].

4. Conclusion

This study investigated the sorption of five pharmaceuticals with different physico–chemical properties onto ten different sediments. The study showed that organic carbon content is not the only predominant factor controlling the

sorption behaviour in sediments with high variability in CEC and texture content. Multiple linear regressions showed that the Kd prediction using proposed models depended on a combination of OC% and clay% in the case of cimetidine and Log Dow and exchangeable cations (Ca^{2+}) for diltiazem. Single predictors were chosen to predict the sorption of amitriptyline, atenolol and mefenamic acid respectively across sediment types. The validity of the proposed regression equations was tested using independent data and gave good results for atenolol. The model evaluation indicated that the models performed poorly for mefenamic acid and cimetidine.

Overall, the results demonstrate how complex the processes driving the sorption of pharmaceuticals in sediments are. Much more work of this type is needed before we can fully understand the interplays between pharmaceutical and sediment properties and sorption. In the future, we recommend that work is done using a wide range of pharmaceuticals and sediments that are well characterized in terms of the properties of the sediment solids and pore water chemistry. Such work could lead to the development of new models that would allow the prediction of partitioning of a wide range of pharmaceuticals at high spatial resolutions. These models will be invaluable for better characterizing the environmental risks of pharmaceuticals in natural systems.

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Table 1. Structure, therapeutic class and physicochemical properties of pharmaceuticals used in the sediment sorption studies

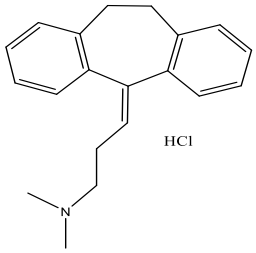
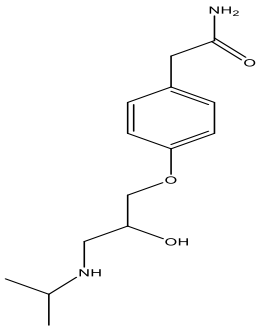
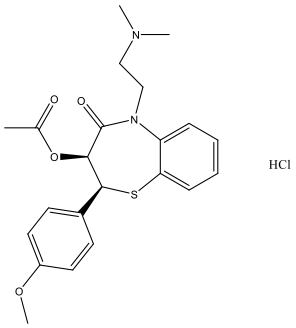
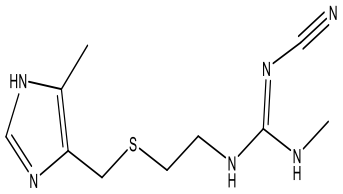
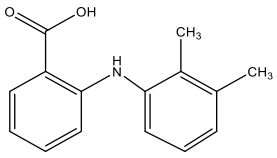
Compound Formula CAS-RN	Therapeutic class	Structure	Molecular weight Mwt. g/mol	pKa	Water solubility mg/L	Log Kow
Amitriptyline Hydrochloride $C_{20}H_{24Cl}N$ 549-18-8	Anti-depressant		313.86	9.4	9.71	4.92
Atenolol $C_{14}H_{22}N_2O_3$ 29122-68-7	β- Blocker		266.34	9.6	1.33E+4	0.16/1.37
Diltiazem Hydrochloride $C_{22}H_{27}ClN_2O_4S$ 33286-22-5	Calcium channel blocker		450.98	8.06	465	2.8
Cimetidine $C_{10}H_{16}N_6S$ 51481-61-9	Anti-histamine		252.34	6.8	9380	0.40
Mefenamic acid $C_{15}H_{15}NO_2$ 61-68-7	non-steroidal anti-inflammatory drug (NSAID)		241.29	3.73[a]	20	2.42

Table 2. Measured properties of the study sediments used in the sorption studies with the pharmaceuticals

Sediment	Coordinate	Texture	Silt %	Clay %	Sand%	OC %	pH $CaCl_2$	CEC cmol+/kg	Total AL^{3+} mg/Kg	Total Fe^{2+} mg/Kg	Total Ca^{2+} mg/Kg	Total K^{+} mg/Kg	Total Mg^{2+} mg/Kg	Total Na^{+} mg/Kg
									Ex. AL^{3+} (cmol+/kg)	Ex. Fe^{2+} (cmol+/kg)	Ex. Ca^{2+} (cmol+/kg)	Ex. K^{+} (cmol+/kg)	Ex. Mg^{2+} (cmol+/kg)	Ex. Na^{+} (cmol+/kg)
Buttercrambe (BTC), YO, UK	54.017012, -0.881074	Sandy loam	35.48	34.25	62.92	2.83	6.88	13.45	405.7	697.3	423.6	44.1	86.5	0.07
									0.016	0.001	12.72	0.140	0.413	0.112
Bishop Wilton (BW), YO, UK	53.982712, -0.790092	Loam	45.92	4.73	49.35	9.9	8.1	35.58	979.2	1130.4	2227.4	196.8	662.9	10.7
									0.025	0.001	32.49	0.658	1.847	0.200
Millington (MIL), YO, UK	53.964920, -0.719305	Sandy clay	0.88	37.25	61.87	8.02	7.15	37.08	972.1	1400.6	975.3	88.6	134.2	3.0
									0.026	0.002	34.53	0.379	1.592	0.376
German beck (GER),YO, UK	53.935850, -1.054470	Sandy clay loam	1.22	30.97	67.81	5.69	7.1	24.26	635.3	1252.0	825.6	86.3	306.9	8.4
									0.020	0.002	19.90	0.283	2.446	0.336
Helmsley (HLM), YO, UK	54.242978, -1.055166	Sandy	10.08	0.12	89.8	0.98	6.65	5.85	299.6	1307.5	215.2	27.1	40.7	0.0
									0.013	0.001	5.05	0.079	0.303	0.067
Moors (MOR), YO, UK	54.371324, -0.965524	Loamy sand	21.05	0.35	78.6	3.52	6.35	11.26	510.5	1367.6	490.1	32.5	101.2	2.2
									0.017	0.002	8.89	0.173	1.181	0.160
Harborough (HAB), LT, UK	52.626226, -0.890155	Loamy sand	26.7	1.12	72.18	1.12	7.45	11.34	753.9	3706.1	682.1	62.9	116.3	1.9
									0.015	0.001	10.58	0.170	0.422	0.146
Skeffington (SKF), LT, UK	52.620847, -0.905779	Sandy clay loam	0.38	36.52	63.1	7.92	7.02	28.39	662.8	827.3	2113.5	79.2	365.9	5.2
									0.123	0.021	27.18	0.195	0.595	0.123
Tigris River (BGD), Baghdad, Iraq	33.361904, 44.370943	Silt loam	58.15	2.04	39.81	3.42	7.1	12.99	973.5	1204.1	2374.4	94.3	923.4	9.7
									0.015	0.001	10.34	0.262	2.006	0.355
Alhussainya River (HUS), Karbala, Iraq	32.623024, 44.027632	Silt loam	71.15	2.91	25.94	3.51	7.3	19.07	1270.3	1884.5	2245.5	116.8	1170.6	34.5
									0.018	0.001	13.46	0.430	3.768	1.389

Table 3.Comparison of Kd and Koc values measured for pharmaceuticals in sediments in the current study with predictions using the model of Franco and Trapp (2008) and other experimental data on sorption to environmental matrices reported in the literature

Compound	Measured		Predicted [a]		Literature		Matrix	Reference
	Kd	Koc	Kd	Koc	Kd	Koc		
Amitriptyline	147.9 (8.79-247.97)	2818.38 (912.01-12589.25)	905.71 191.13-1857.02	19382.42 18757.7-19517.3	2343±292-5694±684	6025.6-11481.5	sludge	[42]
					346.7-1318.3	1621.8	sludge	[43]
					138	3630.8	soil	[37]
					1049	3388.4	sludge	[37]
					4100, 2800	-		[70]
					2600-26000	-	sludge	[71]
Atenolol	9.31 (2.22-20.56)	197.51 (85.11-489.78)	1040.03 219.08-2148.2	22249.68 21699.05-22367.65	<30-46	77.6-91.2	sludge	[42]
					15	398.1	soil	[37]
					8.1±0.6	1000	sediment	[13]
					1.3±0.3-8.1±0.6	310±60-1700±400	sediment	[20]
					7.93	0.56-12.68	sediment	[29]
					0.85-4.08	-	sediment	[24]
					460-1900	-	sludge	[70]
Cimetidine	8.73 (2.28-15.88)	199.07 (102.33-426.78)	45.63 6.78-92.67	1123.62 210.05-2229.1	199.5-616.6	724.4	sludge	[43]
					11	301.1	soil	[37]
					22	-	sediment	[61]
					142-188	-	sediment	[62]
					17	-	soil	
Diltiazem	258.19 (22.03-1022.6)	4265.79 (799.24-13182.57)	16.64 3.98-30.86	370.41 236.61-412.13	53	-	sediment	[61]
					190-869	-	sediment	[62]
					140	-	soil	
					440	-	sludge	[63]
					125.9-501.2		sludge	[44]
Mefenamic acid	6.64 (1.83-19.04)	149.04 (75.86-331.13)	3.0 0.63-6.33	64.06 64.0-64.11	294±379-434 ± 304	-	sludge	[60]
					12±2-20±5	580±60-27000±7000	sediment	[20]
					21	-	soil	[37]
					17	-	soil	[37][p]
					630.9-5011.9	-	sludge	[44]

[a] Franco and Trapp (2008), p = predicted

Table 4. Multiple-linear regression equations for predicting Kd values from sediment properties and sediment-specific physico-chemical properties of a pharmaceutical

Compound	Predictor	R^2	Regression equation [a]
Amitriptyline	Log Dow	0.793**	Kd= -349.2+ 190.06 (log Dow)
Atenolol	CEC	0.731**	Kd= -0.445+ 0.49 (CEC)
Cimetidine	Clay, OC	0.922***	Kd= 2.4+ 0.198(%clay) +0.744(%OC)
Diltiazem	Log Dow, Ex.Ca2+	0.956***	Kd= -902.75+ 543.4 (log Dow)+8.018 ($Ex.Ca^{2+}$)
Mefenamic acid	OC%	0.621**	Kd= -0.044+ 1.425 (%OC)

[a]Regression equation only for significantly correlated properties. *p<0.05, **p<0.01, ***p<0.001.

Table 5. Potential Mechanisms for the adsorption of pharmaceuticals and how they are influenced by properties of the compound and the sediment.

Compound	Potential Mechanisms	Type of interaction	Pharmaceutical properties	Sediment properties	Ranking according to sorption affinity
Amitriptyline	Hydrophobic interaction	Partitioning	Hydrophobicity	High OC%	2
Atenolol	Cation exchange	Nonspecific electrostatic interaction	Basicity	Concentration of exchangeable cations	3
Cimetidine	Hydrophobic interaction	Partitioning	Hydrophobicity	High OC%	4
	Cation exchange	Nonspecific electrostatic interaction	Basicity	Concentration of exchangeable cations	
Diltiazem	Hydrophobic interaction	Partitioning	Hydrophobicity	High OC%	1
	Cation exchange	Nonspecific electrostatic interaction	Basicity	Concentration of exchangeable cations	
Mefenamic acid	Cation bridging	Inner-sphere complex	Anionic, low valence functional group	High-valence exchangeable cations	5

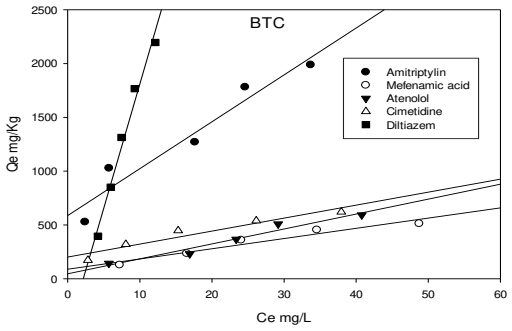
Figure captions

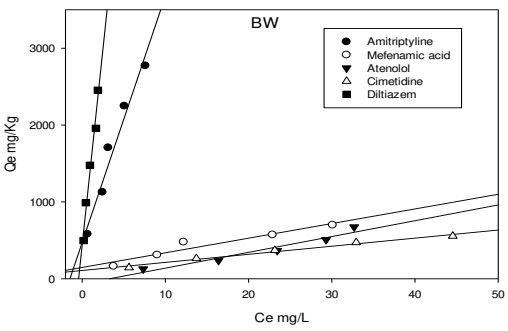
Figure 1 Adsorption isotherms of selected pharmaceuticals in sediments (20 ±2^{o}C). Initial concentrations ranged from 20 to 100 mg L^{-1}. Points represent means of three replicates.

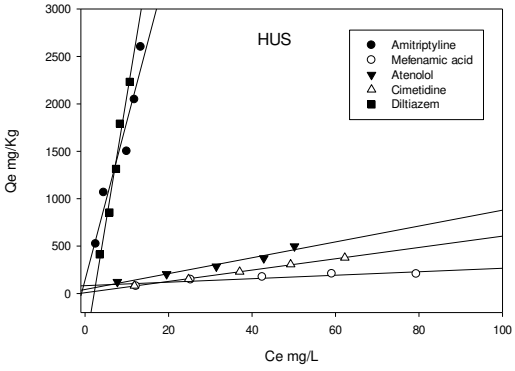
Figure 2 Kd values (±S.D.) for the study pharmaceuticals in the ten different study sediments.

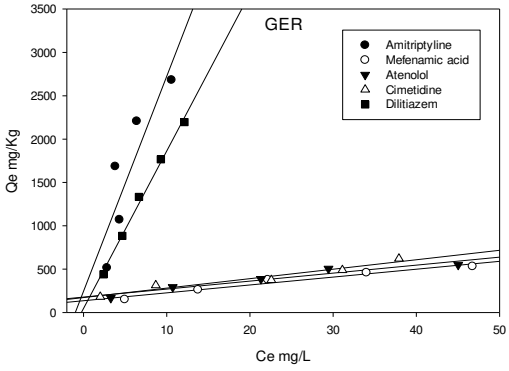
Figure 3 Correlation between experimentally obtained log Koc values and log Koc values predicted using the Franco and Trapp (2008) model for the study pharmaceuticals in the ten study sediments.

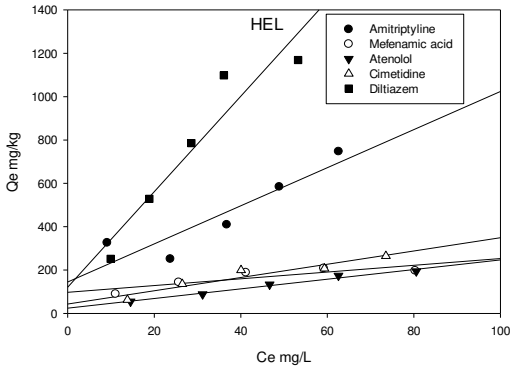
Figure 4 Correlation between Kd predicted by developed method and measured values from this study and literature.

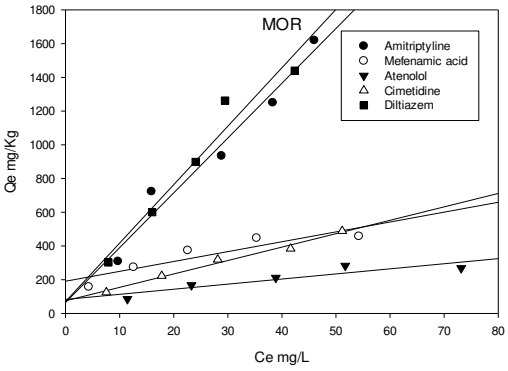

BTC
Amitriptylin
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L

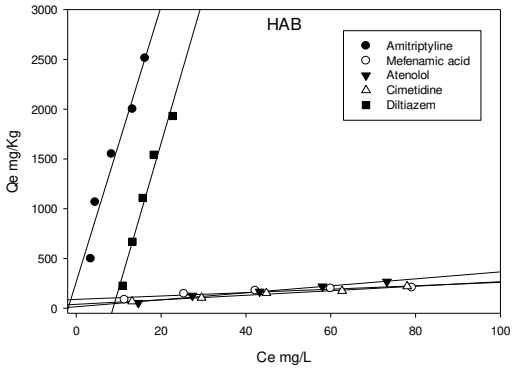

BW
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L

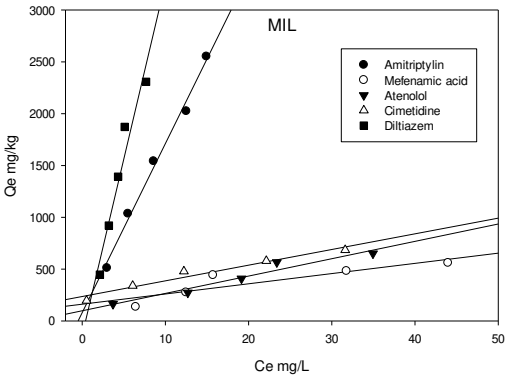

HUS
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L


GER
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Dilitiazem
Qe mg/Kg
Ce mg/L


HEL
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L


MOR
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L


HAB
Amitriptyline
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/Kg
Ce mg/L


MIL
Amitriptylin
Mefenamic acid
Atenolol
Cimetidine
Diltiazem
Qe mg/kg
Ce mg/L

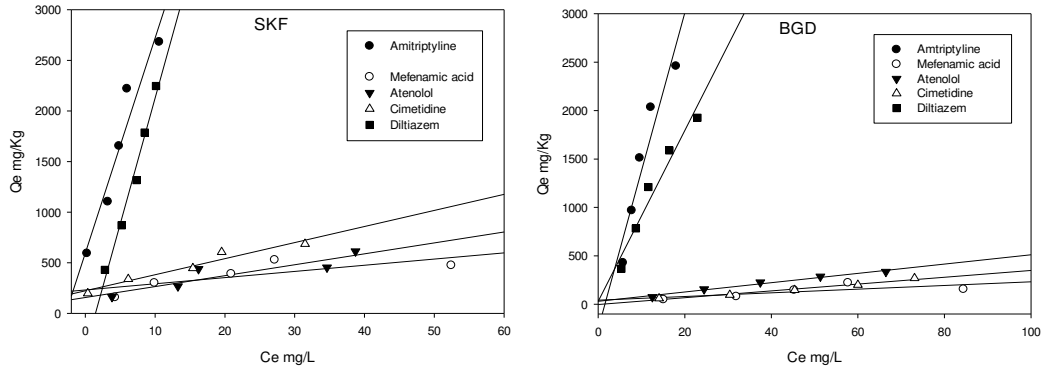


Figure 1

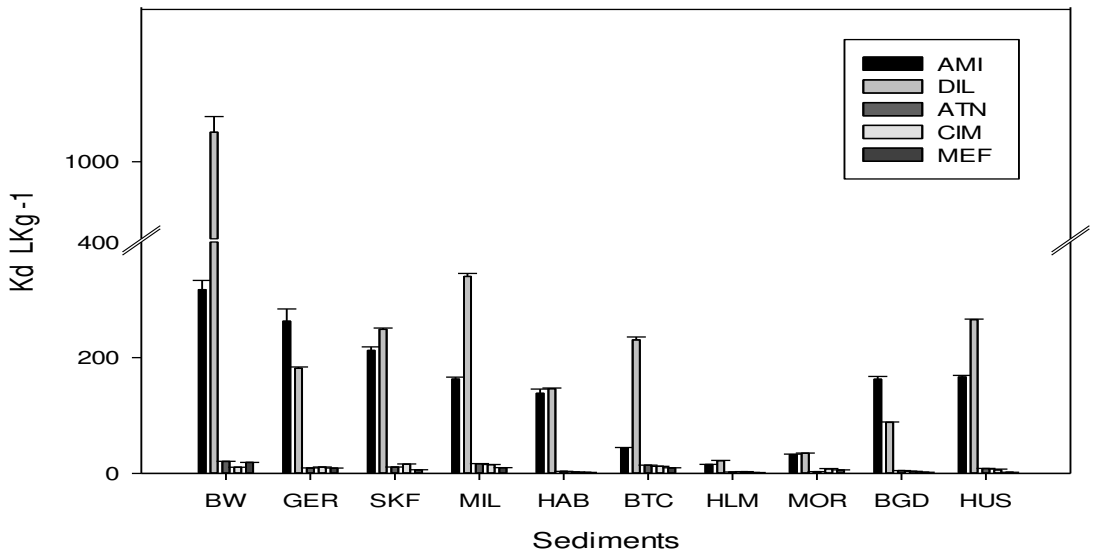


Figure 2

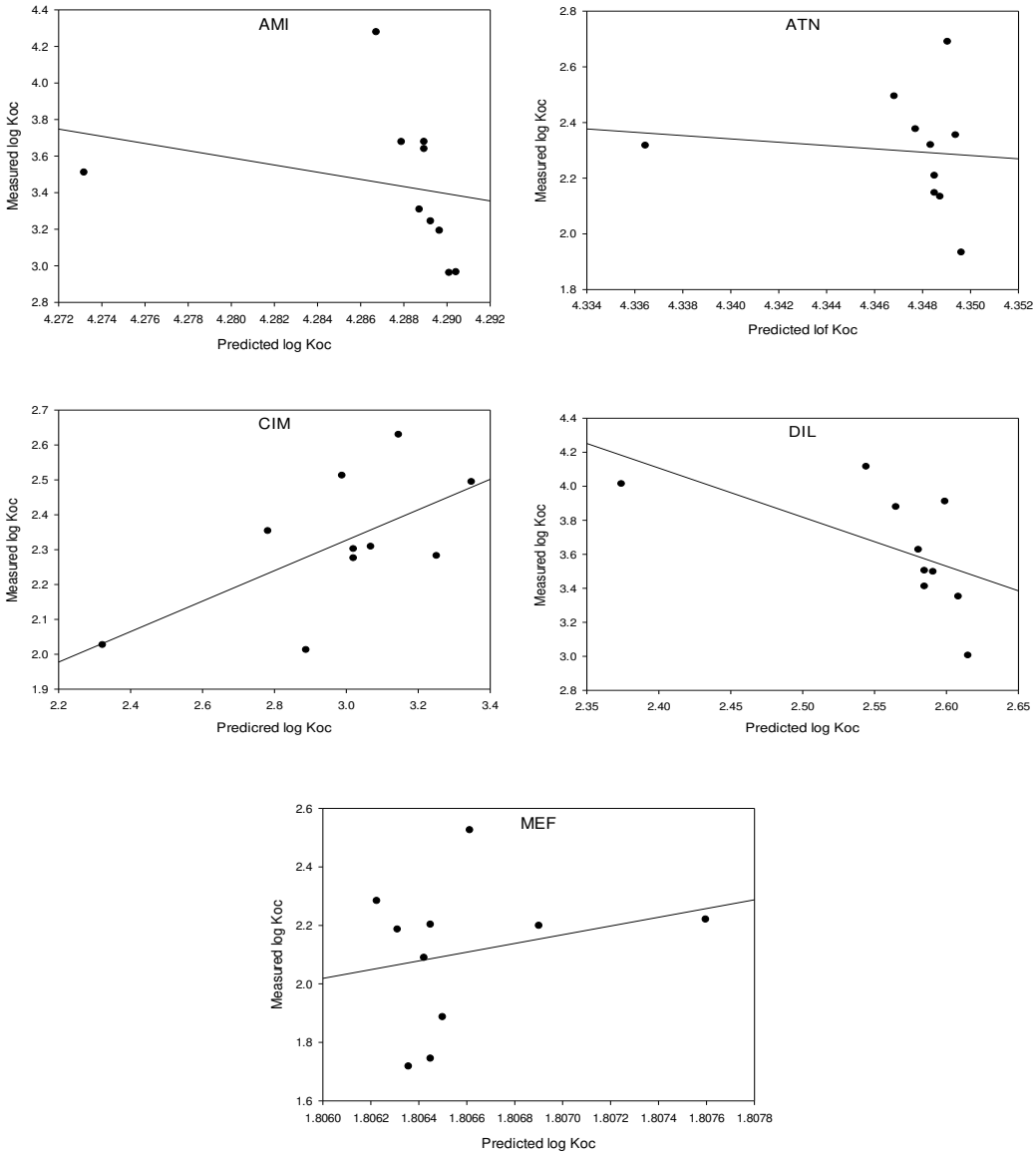

AMI
Measured log Koc
Predicted log Koc
ATN
Measured log Koc
Predicted lof Koc
CIM
Measured log Koc
Predicred log Koc
DIL
Measured log Koc
Predicted log Koc
MEF
Measured log Koc
Predicted log Koc

Figure 3

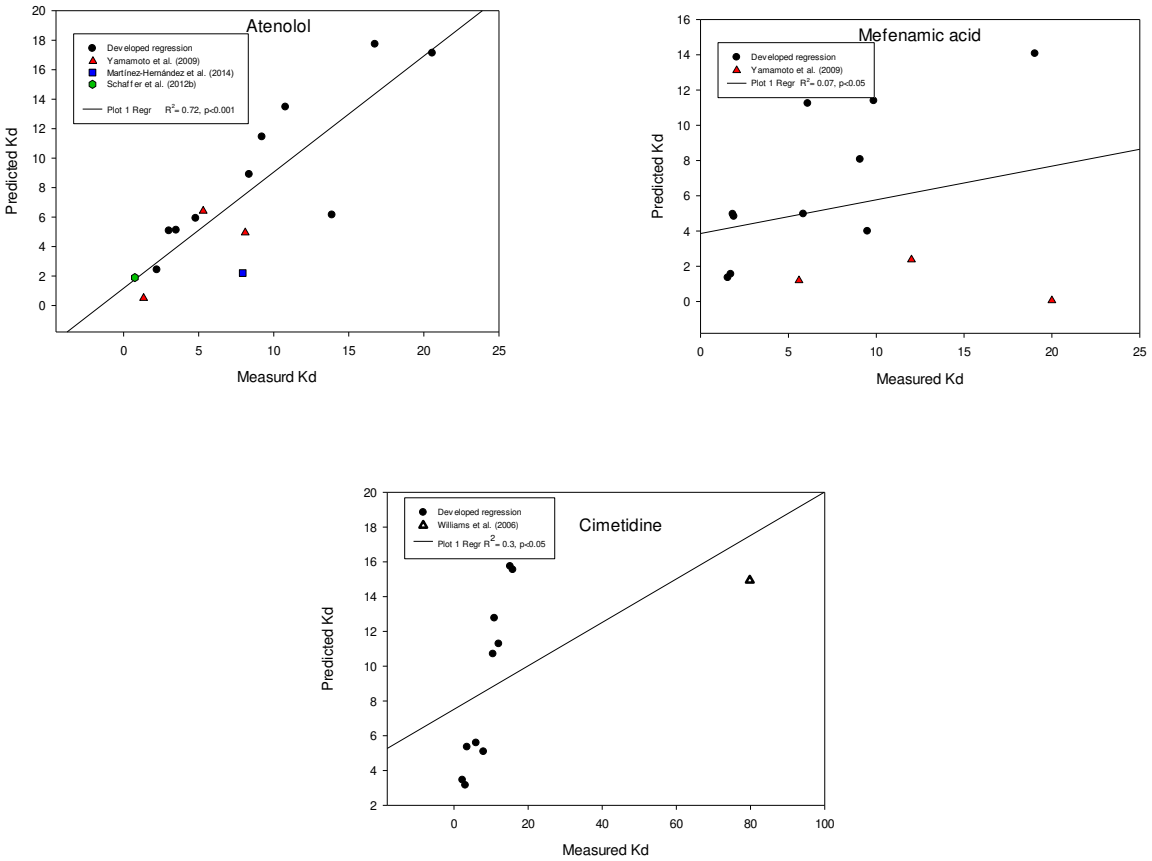

Atenolol
Developed regression
Yamamoto et al. (2009)
Martínez-Hernández et al. (2014)
Schaffer et al. (2012b)
Plot 1 Regr R²= 0.72, p<0.001
Predicted Kd
Measurd Kd
Mefenamic acid
Developed regression
Yamamoto et al. (2009)
Plot 1 Regr R²= 0.07, p<0.05
Predicted Kd
Measured Kd
Cimetidine
Developed regression
Williams et al. (2006)
Plot 1 Regr R²= 0.3, p<0.05
Predicted Kd
Measured Kd

Figure 4