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Modelling pharmaceutical concentration in the soil profile using HYDRUS 1D

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Abstract. Pharmaceuticals are an emerging class of environmental contaminants that are receiving increased attention, although their environmental fate is for the most part unknown, especially in the vadose zone. HYDRUS-1D, a model of water and solute transport in the vadose zone, was used to describe the leaching of diazepam and iopromide. Data from a soil column study was extracted from the literature that reported concentration of these two compounds at increments of 5 cm depth, along with artificial rainfall rate and total leachate collected. Values for the organic carbon-water distribution coefficient were obtained from external sources. The inverse solution was used to obtain optimized parameter estimates for α, D_L, and D_W. Predicted diazepam concentration was most sensitive to D_L, a non-measurable parameter, while the least sensitive parameter was D_W. There was good agreement between observed and predicted diazepam concentration and a low mass balance error (104% recovery). The pattern of iopromide distribution was not described well by HYDRUS-1D, and there was a large error in the final mass of solute (157% recovery). It was assumed that the poor fit was from the difference between the pKa of iopromide (9.9) and the pH of the soil (5.8), since iopromide contains many ionisable groups. This may have led to reduced sorption and higher water solubility. Decreasing the K_D led to a pattern of iopromide transport that more closely resembled the observed values, but increased the solute mass balance error. The reason for the mass error for iopromide is not known.

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Keywords. Pharmaceuticals, modeling, HYDRUS-1D, chemical transport in soil, leaching

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Introduction

Pharmaceuticals are an emerging class of environmental contaminants that have been frequently detected in both soil and water within the last decade (Kolpin et al. 2002, Kinney et al. 2006). The early 1990's saw the first attempts by scientists and government agencies to evaluate the environmental impacts of certain high volume pharmaceuticals (Jørgensen and Halling-Sørensen 2000). A review by Daughton and Ternes (1999) drew increased attention to a then under-appreciated group of contaminants, and popularized the term "Pharmaceuticals and Personal Care Products" or PPCPs. Since then, considerable attention has been given to the PPCPs, and extensive work has gone into development of methods for their analysis (e.g. USEPA 2007, Zaugg et al. 2007). There are tens of thousands of different pharmaceutical compounds produced worldwide (Kümmerer 2008), and relatively speaking, only a handful have had their environmental fate examined. Since they have only recently been recognized as pollutants, pharmaceuticals have generally not undergone the same extensive toxicity testing as the pesticides have (Daughton and Ternes 1999). In the unsaturated zone, the fate and transport of pharmaceuticals is largely unknown and is expected to be compound specific (Xu et al. 2009).

Pharmaceutical compounds are introduced into the environment following irrigation with or release into water bodies of "treated" sewage wastewater, land-application of sewage sludge, or from the utilization of animal wastes contaminated with veterinary pharmaceuticals (Oppel et al. 2004). Pharmaceuticals generally enter the wastewater stream through domestic use, excreted either unchanged or as metabolites, although the importance of point sources like hospitals or dental clinics has also been recognized (Ruhoy and Daughton 2008). Disposal of untreated municipal wastewater in water bodies was common practice in Canada until quite recently (Bonner and Wristen 1999, 2004), although treatment is sometimes limited to primary settling of solids. Even with secondary biological treatment, some pharmaceuticals like sulfonamide and lincosamide antibiotics have low removal rates (Watkinson et al. 2007). This has negative implications for wastewater treatment plant receiving waters and for land irrigated with reclaimed wastewater (Watkinson et al. 2007). It has been hypothesized that, even if pharmaceuticals are not persistent pollutants, they may act as such due to their nearly constant release into the aquatic environment (Daughton and Ternes 1999).

The analysis of environmental samples for pharmaceuticals is expensive and requires sophisticated equipment and highly trained personnel, but it is necessary in order to develop an understanding of their environmental fate. Modelling is an inexpensive tool that can also be used to predict environmental fate based on certain properties of the chemical, like water solubility, Henry's Law constant, or the octanol-water (KOW) or organic carbon-water (KOC) partition coefficients. However, without actual data for comparison it is not possible to assess how reliable the predictions are. The goal of this project was to apply a model of chemical transport in the unsaturated zone, HYDRUS-1D (Šimůnek et al. 2009), to data extracted from the literature on pharmaceutical leaching in soil. It is hoped that, if successful, HYDRUS-1D could be used in the future to take advantage of the accumulating published data regarding pharmaceutical transport in soil.

Methods

Soil column study

Data was obtained from a soil column study conducted by Oppel et al. (2004; Figure 1) according to the OECD Guidelines for the Testing of Chemicals: Leaching in Soil Columns (OECD 2004). A 30 cm glass sectionable column was re-packed with air-dried and sieved soil, in small amounts under gentle vibration to give a more consistent density. Columns were saturated with artificial rain containing 0.01 M $CaCl_2$, prior to spiking with compounds and applying artificial rain for the leaching study. In total, 20 cm of artificial rain was applied over 48 hours. ^{14}C-labelled diazepam and iopromide were applied to the soil column, which was measured using liquid scintillation counting. Soil samples were combusted and the radioactivity trapped for measurement (Oppel et al. 2004).

HYDRUS-1D

Water flow

Initially, the Van Genutchen-Mualem single porosity model was used to obtain Artificial Neural Network estimates for the soil hydraulic model parameters based on the percent sand, silt, and clay (Table 1). Simulations were run using both the single and dual porosity models. The solute transport results were identical, so the single porosity model was used for the final simulations. The upper boundary condition was atmospheric with runoff, and the lower boundary condition was a seepage face with h = 0. Time was measured in hours, with a minimum and maximum time step of 0.01 and 1 hour respectively. The simulation was run for 48 hours, with 48 time-variable boundary conditions. Water was applied at a rate of 0.416667 cm/hr to match the conditions of the column study. Initial pressure head throughout the whole column was set at 0 cm since it was saturated prior to commencing artificial rainfall (Oppel et al. 2004). A total of 301 nodes were used, resulting in a 0.1 cm node length.

Solute transport

The compounds diazepam and iopromide (Figure 2) were applied to the top of the column as an aqueous solution or dissolved in an organic solvent, to a final concentration of 100 µg/kg. Results in Oppel et al. (2004) were reported in increments of 5 cm as percent recovery of the initial amount added. This was problematic since it was not in the same format as HYDRUS-1D inputs (soil concentrations entered as µg/cm^3), and the column diameter was not reported in the paper to calculate the total volume of soil used. To resolve this, a concentration of 150 ng/cm^3 (100 ng/g with bulk density of 1.5 g/cm^3) was assumed throughout the 30 cm column. Then, it was assumed that the total concentration was initially distributed within only the top 1 cm at a concentration of 4500 ng/cm^3. Finally, to convert simulated results into the same format as the paper, the concentration from the output file NOD_INF.OUT was brought into Excel, where the concentration was summed within 5 cm increments, and expressed as a fraction of the total area.

The one-site chemical non-equilibrium sorption model was used for both pharmaceuticals. A bulk density of 1.5 g/cm^3 was assumed since it was not reported in the paper. A log(K_{OC}) value of 2.91 (K_{OC} = 813) for diazepam in soil was obtained from Barron et al. (2009). A log(K_{OC}) of 1.81 (K_{OC} = 64.6) was obtained for iopromide from Carballa et al. (2008), although it was determined in sewage sludge and not soil. The organic carbon content of the soil in this study was reported as 2.3% (Oppel et al., 2004), from which a K_D of 18.7 for diazepam and 1.49 for

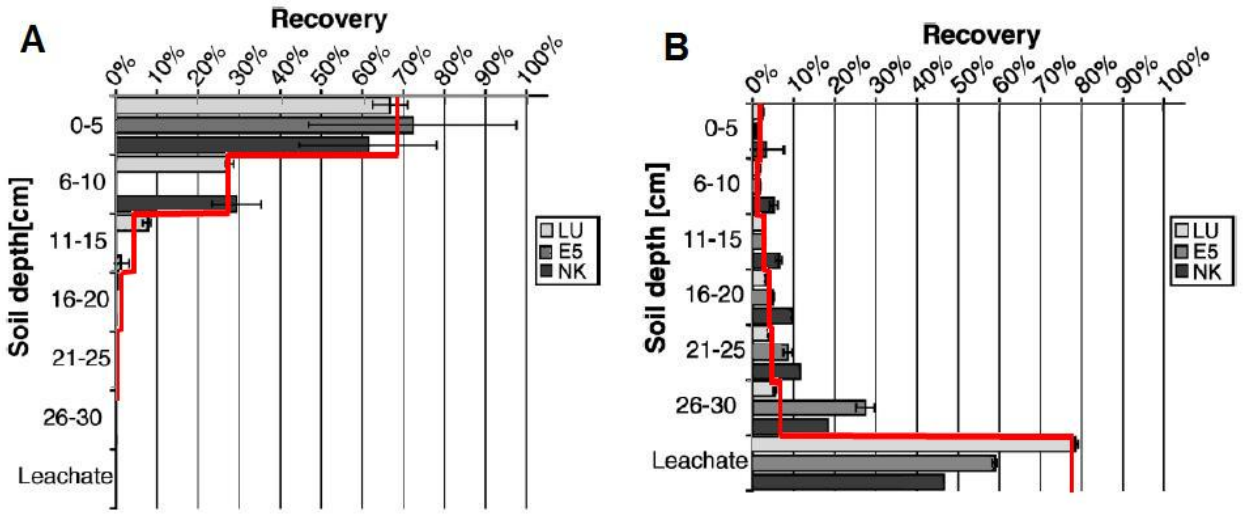

Figure 1. Data reproduced from Oppel et al. (2004) describing the concentration of diazepam (A) and iopromide (B) in the soil profile and leachate from a soil column study. The line represents the extracted values used in modelling.

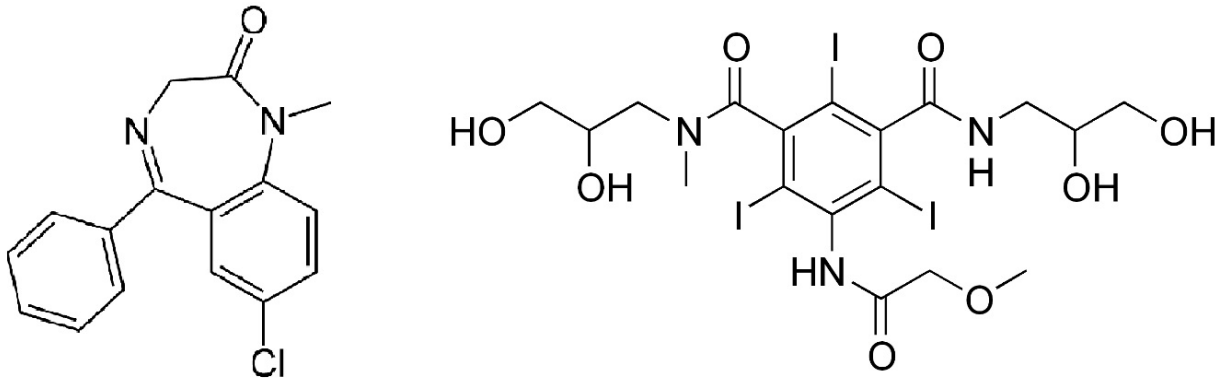

Figure 2. Chemical structures of diazepam and iopromide

Table 1. Soil particle size distribution and Van Genuchten parameters estimated using the Artificial Neural Network option in HYDRUS 1D for LUFA 2.2 loamy sand (Oppel et al. 2004).

Sand (%)	Silt (%)	Clay (%)	θ_R	θ_S	Alpha	n	K_S (cm/hr)	i
74.8	17.0	8.2	0.0413	0.3845	0.0384	1.5014	2.53542	0.5

iopromide was calculated for use in HYDRUS-1D.

Values were not given in the paper for alpha (α), the first order rate constant for solute transfer between the mobile and immobile liquid phases, for the molecular diffusion coefficient in water (D_W), or for the longitudinal dispersivity (D_L), a non-measurable parameter that is related to the pore size distribution. An initial value for α of 0.32 was obtained from an example project included with HYDRUS-1D titled "TEST 5: Solute transport with non-equilibrium cation adsorption." Simulations were run with values of α varying around this value to see the effect of α (not shown). Values for D_L are typically between 0.5 to 2 cm for lab studies and 5 to 20 cm for field or intact column studies (Prasher 2011). Values were varied within this range to test the effect of D_L since it is not measurable (not shown). The D_W is typically around 1 cm^2/day or 0.0416 cm^2/hour (Prasher 2011), so D_W was also varied around this value to examine the effect of D_W (not shown). The simulations of diazepam transport were most sensitive to D_L, and least sensitive to D_W.

For final estimates of α, D_W, and D_L, the inverse solution was used to obtain optimized parameter estimates based on the data for diazepam. The parameter estimate for D_L was validated using the data for iopromide. For α, the initial estimate was 0.3, with minimum and maximum of 0.001 and 1. The initial estimate for D_W was 0.0416, with minimum and maximum of 0.0001 and 1. For D_L, the initial estimate was 2, with minimum and maximum of 0.5 and 20. Observation nodes were set at the surface and every 2 cm for the top 8 cm, then at the center of each 5 cm increment after that, at 0, 2, 4, 6, 8, 12.5, 17.5, 22.5, and 27.5 cm. The average concentration over each 5 cm increment was entered in the corresponding observation nodes. Concentration in the observation nodes for inverse solution prediction are presented in Table 2. For iopromide, most of the compound was recovered in the leachate rather than from the soil column (Figure 1). To calculate the recovery in the leachate from simulated data, the cumulative bottom flux of iopromide at 48 hours was divided by the total amount initially present.

Results and discussion

Hydrology

There was very little hydrology information given in the paper, other than the range of the amount of leachate collected. This varied between 18.4 and 21.2 cm, and the simulated bottom water totaled between 20 to 21 cm. This indicated that the model provided an adequate simulation the hydrology, considering the minimal information available. Since the saturated hydraulic conductivity was much greater than the amount of artificial rainfall (2.5 vs. 0.4 cm/hour), by the end of 48 hours the simulated volumetric water content was lower near the surface (not shown).

Diazepam transport

Almost all of the diazepam was detected within the top 15 cm of the soil column, with none being detected in the leachate (Figure 1). Fitting the data with HYDRUS-1D reached convergence, and there was good agreement between the observed and predicted concentrations (Figure 5). The R^2 provided by HYDRUS-1D was 0.9630. Parameter estimates for α, D_L, and D_W from the inverse solution lacked precision since the confidence intervals contained zero (Table 3). The fitted value of α was close to the initial estimate of 3, so the fitted value was entered as a fixed parameter and the model was ran again. Since only two parameters were being estimated, it was hoped that it would give them more precision and confidence intervals different from zero. The confidence intervals were smaller with only two parameters (Table 4), but still contained zero. The agreement between observed and predicted

Table 2. Data obtained from Oppel et al. (2004) for diazepam and iopromide in percent recovery and as concentrations entered in HYDRUS 1D for inverse solution.

Depth	0	2	4	6	8	12.5	17.5	22.5	27.5	Leachate
Diazepam										
Recovery (%)	68	68	68	27	27	4	1	0	0	0
Concentration (ng/cm)	612	612	612	252	252	18	4.5	0	0	0
Iopromide										
Recovery (%)	2	2	2	1	1	3	4	5	7	78
Concentration (ng/cm)	18	18	18	9	9	27	36	45	63	702

Table 3. Optimized parameter estimates and 95% Confidence Intervals from inverse solution for diazepam with three and two parameters fitted.

	Three parameters fitted			Two parameters fitted	
Parameter	α	D_W	D_L	D_W	D_L
Fitted Value	0.354	1	18.2	1	14.4
95% CI	-1.86 to 2.57	-1674 to 1676	-922 to 959	-473 to 501	-873 to 875

values was still good (Figure 4), with an R^2 of 0.9631. Although the parameter estimates lack precision, the model does provide a good simulation of diazepam transport. There was a small error in the mass balance of solute, with a total recovery of 104% when all compartments were added together.

The lack of precision in parameter estimates may be due to the lower resolution of the reported data compared to that of HYDRUS-1D. Converting the data from the paper into values for the inverse solution in HYDRUS-1D is a rough approximation since it had to be assumed that concentration was constant over the 5 cm intervals. There is some error introduced, since the HYDRUS-1D model produces a curved line (Figure 3). Also, there is a limit on the number of observation points that can be included in HYDRUS-1D, which the inverse solution uses to fit the parameters. However, as this project demonstrates, it is still possible to convert high-resolution HYDRUS-1D output into lower resolution depth measurements typical of leaching experiments, and low-resolution data into a form that can be fit using the inverse solution option. It would be difficult to obtain representative samples at even 1 cm resolution from a column study, since mixing would likely occur during sampling. In the field, it would likely require excavation of an area and sampling horizontally in the profile, or very careful sampling with a proper soil probe.

Iopromide transport

The inverse solution was used to fit the parameter D_W since it was not known and is compound-specific. The estimates for α and D_L obtained from diazepam were also used for iopromide. The estimate for D_W (0.0416) was more precise than for diazepam, since the confidence interval (0.0065 to 0.077) did not contain 0. This is likely because only one parameter was fitted. A K_D of 1.49 was used initially, but poor results were obtained for simulated iopromide concentration (Figure 5). In addition, there was a large error in the mass balance of the solute (157%

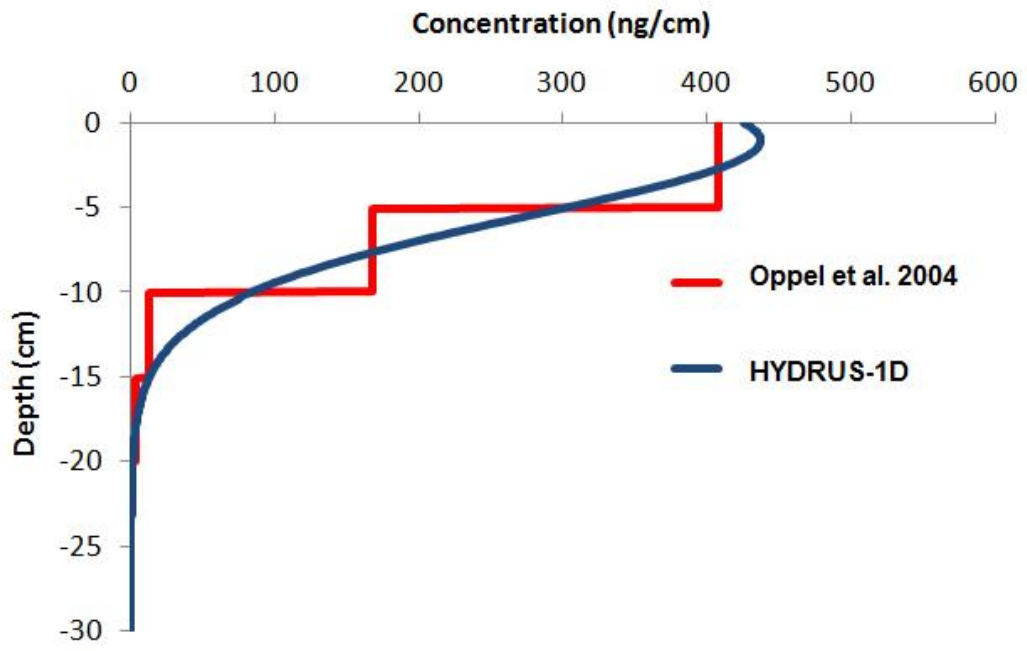

Figure 3. HYDRUS-1D output compared to the data structure used for the inverse solution

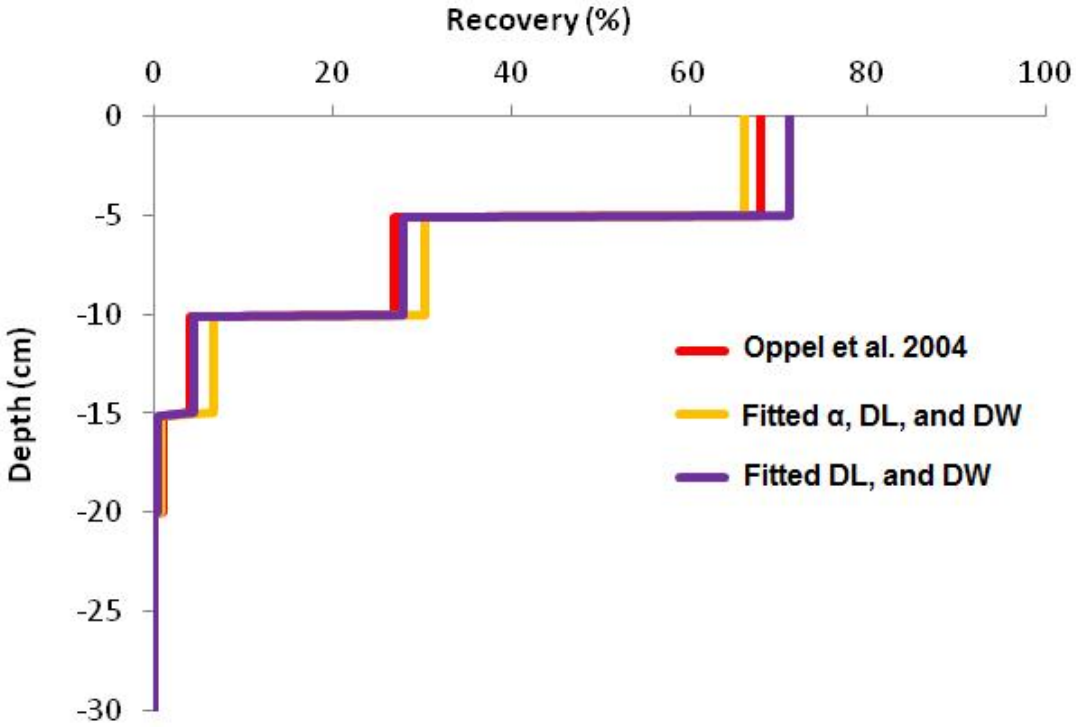

Figure 4. Final fitted data for diazepam using inverse solution to fit α, D_L and D_W, and using a fixed α and fitted estimates for D_W and D_L, in comparison to data from Oppel et al. (2004).

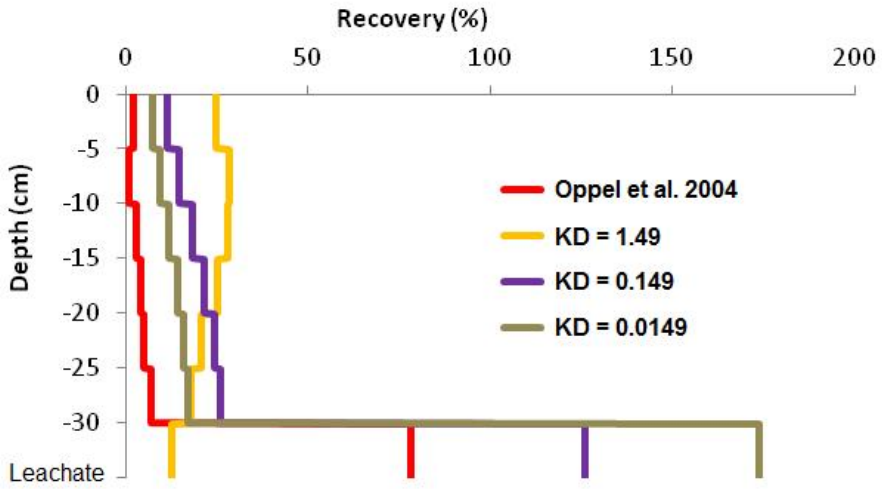

Figure 5. Observed (Oppel et al., 2004) and predicted iopromide transport with varying K_D.

recovery). The reason for this is not known. No calculation errors could be found. In addition to the mass balance error, the pattern of iopromide distribution was not simulated well (Figure 5). Based on the data from Oppel et al. (2004), much of the iopromide was transported through the column, indicating that the K_D used in this simulation may have been too high. The pKa of iopromide is reported to be 9.9 (Carballa et al. 2008), while the pH of the soil in this study was 5.8. Iopromide contains a number of functional groups capable of being protonated (Figure 2). It is possible that the low pH relative to the pKa, and therefore protonation of basic groups, led to a higher water solubility and decreased sorption with organic matter. Models based on distribution coefficients assume that sorption to organic matter is the main process affecting the solutes, but this assumption may not be true in the case of ionisable compounds (Cunningham 2008). This is especially true for compounds that have more than one ionisable functional group (Cunningham 2008), as is the case with iopromide. Decreasing the K_D caused the pattern of iopromide transport to more closely resemble the data from Oppel et al. (2004), but the mass balance error increased to a recovery of 242% and 248% at K_D of 10 and 100 times less than the literature value (Figure 5). Overall, iopromide transport was poorly described by HYDRUS-1D.

Limitations of this approach

As mentioned earlier, the main limitation of the approach taken here is the different data structure between HYDRUS-1D (solute concentration at 1 mm scale) and that reported in Oppel et al. (2004), which was given in percent recovery at 5 cm increments. A compounding factor is that the bulk density was not reported, nor was the column diameter or the amount of liquid applied in which the compounds were dissolved. It would not have been hard to determine the bulk density of the packed columns which may have improved the modelling predictions if it was reported. An initial distribution of the compounds within the soil profile had to be assumed (concentrated within top 1 cm), and it was assumed to be the same for both compounds which may not have been the case, especially for iopromide which was much more prone to leaching.

The two chemicals also have different chemical properties, and diazepam is more favorable to modelling based on the distribution coefficient K_D since it is relatively hydrophobic and with a pKa of 2.92 (Stevens-Garmon et al. 2011), most of the diazepam would not be protonated at the soil pH of 5.8. It is therefore safe to assume that sorption to organic matter is the primary

influence on diazepam transport in soil water. Iopromide on the other hand has multiple groups that can become protonated, so sorption processes would be highly pH dependent (Cunningham 2008). With a pKa of 9.9, the majority of these groups would be protonated at a soil pH of 5.8. This project highlights a known weakness in modelling pharmaceuticals based on distribution coefficients (Cunningham 2008). Like iopromide, they often contain multiple ionisable groups and environmental fate can be strongly influenced by pH.

Conclusion

HYDRUS-1D, a model of water and solute transport in the unsaturated zone, was used to describe the leaching of two pharmaceutical compounds, diazepam and iopromide. Data was obtained from the literature describing a soil column study, and values for the organic carbon-water distribution coefficient were obtained from external sources. The inverse solution was used to obtain optimized parameter estimates for α, D_L, and D_W, based on data for diazepam. These parameters were also varied to evaluate the effect of each on predicted solute concentrations. The estimates for α and D_L were tested using iopromide. Of the three parameters, predicted diazepam concentration was most sensitive to D_L, a non-measurable parameter. The least sensitive parameter was D_W. The model performed well at describing diazepam concentrations with depth, with good agreement between observed and predicted concentration and a low mass balance error. The pattern of iopromide distribution was not described well by HYDRUS-1D, and there was a large error in the final mass of solute (157% recovery). This poor representation of iopromide transport was assumed to be from a large difference between the pKa of iopromide (9.9) and the pH of the soil (5.8), since iopromide contains many ionisable groups. Diazepam is more hydrophobic and has a pKa of 2.92, so the majority would not be protonated. This may have led to reduced sorption and higher water solubility for iopromide than was predicted by the K_D. Decreasing the K_D led to a pattern of iopromide transport that more closely resembled the observed values, but increased the solute mass balance error significantly. The reason for the mass error for iopromide is not known.

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