Electronic Supplementary Information (ESI)

Predicting sorption of pharmaceuticals and personal care products onto soil and freeze-dried digested sludge using artificial neural networks

Leon Barron[a*], Josef Havel[b], Martha Purcell[a], Michal Szpak[a], Brian Kelleher[a] and Brett Paull[a]

[a] *National Centre for Sensor Research, Dublin City University, Glasnevin, Dublin 9, Republic of Ireland. (*Email: leon.barron@dcu.ie)*

[b] *Department of Chemistry, Faculty of Science, Masaryk University, Kotlářská 2, 611 37 Brno, Czech Republic.*

Table of Contents

Sections: 9 Figures: 5 Tables: 5

List of Figures

List of Tables

S 1.0 Glassware pretreatment procedures

All glassware was silanised prior to use using a single rinse of 10 % dichlorodimethylsilane solution in dichloromethane followed by twice rinsing with dichloromethane and H_2O. Any losses due to further adsorption to glassware were noted and final results corrected.

S 2.0 Particle size analysis

Particle size distribution was performed with use of a Malvern Mastersizer S instrument laser diffraction based granulometer. Air dried samples were sieved through a standard test sieve of 100 μm to remove coarse grains and organic debris and gently pulverised with mortar and pestle. Disagglomeration of grains was achieved by applying ultrasonic energy prior to analysis within the instrument presentation unit. Analysis was performed with moderate stirring and pump speeds. Obscuration of the beam was maintained between 15-30 %. Particle size distributions and physical descriptors were calculated according to the method of moments and the Folk and Ward nomenclature *(1)*. Please refer to Figure S1 for size distribution of soil particles used in this study.

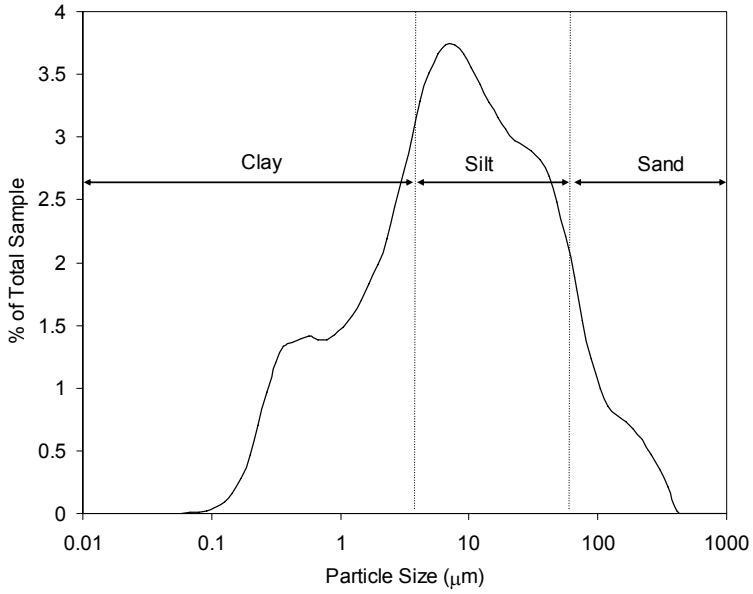

Figure S1. Particle size distribution of soil sampled from Corrstown, Co. Dublin after drying and sieving. Overall breakdown: 20 % clay, 69 % silt and 11 % sand.

1. Folk, R.L. and Ward, W.C. Brazos River bar: a study in the significance of grain size parameters. *J. Sediment. Petrol.*, 27 (1957), 3-26.

S 3.0 LC-MS/MS conditions and limits of quantification (LOQ) in soil/sludge mixtures.

All separations were carried out on a Waters Sunfire 3.5 µm, 150 x 2.1 mm analytical column at a flow rate of 0.2 mL/min. Mobile phases were 10:90 (A) and 80:20 (B) MeCN:10 mM ammonium acetate with a gradient profile as follows: 0-5 min was 100 % A; 5-28 min MeCN raised to 45 %; 28-35 MeCN raised to 80 % and kept constant for a further 10 mins. Re-equilibration time was 15 mins. Injection volumes were 10 µL. Tandem mass spectrometry was carried out on a Bruker-Daltonics Esquire~LC electrospray ion trap mass spectrometer in positive and negative ionisation modes (Table S2). All parent and fragment ions are given in Table S1 along with limits of quantification of the method. Mass spectral LOQ data was generated injecting low concentration matrix matched standards and by calculating a corresponding concentration for a signal to noise ratio of 10:1.

Table S1 MS detection masses/transitions for all test analytes, retention times and limits of quantification in all matrices studied

Compound	t_r (min)	MRM Transition or EIC m/z	LOQ water[a] – soil mixture (µg/L)	LOQ water[a] - sludge mixture (µg/L)	LOQ water[a] only (µg/L)
Amitriptyline	38.6	278>233	18	204	5
Amphetamine	14.6	136>119	160	-	128
Atenolol	6.0	267>190	1	4	3
Benzoylecgonine	17.1	290>168	1	-	1
Bezafibrate	24.8	362>316	1	-	25
Budesonide	36.2	431>413	9	68	4
Caffeine	10.7	195>138	3	30	2
Carbamazepine	29.9	237>194	0.4	4	0.5
Chloramphenicol	21.4	345>275	31	-	86
Cimetidine	14.2	253>211	5	-	12
Citalopram	33.8	325>263	9	12	2
Clofibric Acid*	19.4	213>127	35	37	51
Clotrimazole	40.6	277>165	2	205	4
Cocaethylene	30.2	318>196	1	-	42
Cocaine	26.9	304>182	1	-	1
Diazepam	36.9	285>257	1	156	1
Diclofenac*	28.0	294>250	28	-	57
Doxazosin	34.0	452>344	37	201	3
EDDP	40.6	278>249	4	-	12
Erythromycin	41.6	734>576	1	5	0.4
Flurbiprofen*	26.3	199	19	37	10
Heroin	27.6	370>268	350	-	1

Compound *(contin.)*	t_r (min)	MRM Transition or EIC m/z	LOQ[a, b] soil-water (µg/L)	LOQ[a, b] sludge-water (µg/L)	LOQ[a, b] water only (µg/L)
Indomethacin	29.8	358>174	2	90	4
Ketoprofen	23.4	255>209	6	-	13
MDMA	23.0	194>163	10	-	5
Metoprolol	38.2	268>116	0.4	2	1
Methadone	22.9	310>268	57	-	3
Naproxen*	21.8	185>170	14	31	31
Nifedipine	35.7	346	8	31	17
Nimesulide*	36.6	307>229	2	15	2
Nortriptyline	37.2	264>233	8	82	8
Papaverine	32.8	340>202	144	-	2
Paracetamol*	17.9	150	45	39	3
Phenazone	30.6	189	1	2	4
Propranolol	13.5	260>116	1	30	29
Ranitidine	5.1	315>270	5	-	20
Salbutamol	5.5	240>166	3	17	17
Salicylic Acid*	39.5	137>93	250	400	8
Sertraline	43.2	275	11	221	3
Simvastatin	17.3	441>419	18	144	3
Sulfamethazine	10.5	279>156	1	6	10
Sulfamethoxazole	13.3	254>156	2	11	6
Sulfapyridine	41.6	250.4	4	-	5
Tamoxifen	43.6	373>327	39	-	4
Temazepam	23.3	301>283	2	170	8
Tramadol	42.0	264	3	-	4
Triclocarban*	41.8	315	64	n.c.	17
Triclosan*	41.8	287/289	12	n.c.	32
Trimethoprim	17.1	291>123	1	8	8
Warfarin*	24.2	307>161	3	11	4

* Compounds detected in negative ionisation mode, all others in positive ionization mode.

[a] Data generated from the average of triplicate runs of post-equilibration spiked water-solid mixtures after centrifugation giving an approximate signal to noise ratio of 10:1 with instrument repeatability of ≤ 20 % of peak height.

[b] Water phase contained 10 mM $CaCl_2$.

Table S2 Electrospray-ion trap-mass spectrometry conditions

Parameter	Negative Mode	Positive Mode
Capillary Voltage	4500	4500
End Plate Offset (V)	-764	-561
Skimmer 1 (V)	-15	28.1
Skimmer 2 (V)	-4.4	6.7
Cap. Exit Offset (V)	-50	63.7
Octopole (V)	-1	2.51
Octopole RF (Vpp)	103.3	155.3
Octopole Delta (V)	-1.36	1.98
Lens 1	3.4; 30	-2.4; -37.8
Trap Drive	22.8	34.7
Dry Gas Flow (N_2; L/min)	8	8
Nebulizer Pressure (psi)	50	50
Dry Gas Temp. (^oC)	300	300

S 4.0 Sorption kinetics and PLE conditions for solid phase analysis

Freshly silanised flasks were filled with 0.5 g soil and shaken in 20 mL of pre-spiked 1 mg/L solutions of PPCPs in three separate sets and in triplicate. For investigation of sorption kinetics, these were allowed to shake for t = 8, 24, 30 and 48 hours. An additional flask was shaken and sampled immediately to constitute t = 0. Aliquots of 0.5 mL of the liquid phase were taken and centrifuged at 7,500 rpm for 10 min and analysed by LC-MS/MS. Soil-water mixtures were filtered through Whatman GF/C glass fibre filters to remove suspended matter and the solid portion dried under vacuum for approximately 30 mins. Soil was then transferred to 33 mL PLE cells and extraction was carried out using 50:50 MeOH:H_2O as the extraction solvent. Temperature and pressure were 60 ^oC and 1,500 psi respectively for n=2 cycles. Heat and static times were 5 mins each, flush volumes of 100 % and 60 s purge times. Extracts of ~53 mL were then dried under N_2 and reconstituted in 1 mL of 10 mM $CaCl_2$ solution and analysed directly by LC-MS/MS. Percent recoveries for those compounds studied in solid soils are given in Table S3 for n=2 replicates. Three sets of blanks were also shaken for 24 hours with liquid and solid portions treated in exactly the same way as previously described. Exactly 1 mL of two of the blank aqueous phases were dried under N_2 and reconstituted in standard for matrix matching (n=2). The third was run neat. Spiking of neat soils was carried out directly inside PLE cells for calculation of sorbed quantities and for calculation of the approximate extraction recovery. Figure S2 shows the ratio of liquid phase concentration at t hrs to concentration at 0 hrs (in spiked soil suspension) versus time (hrs). It can be seen

from these sorption kinetics profiles that, in the majority of cases, equilibriums were reached within 24 hrs. Some psychoactive compounds such as morphine and heroin with equilibration times > 24 hrs showed elevated sorption behavior from analysis liquid phases over the 48 hr timescale studied and data led to exaggeratedly large K_d values for soil-water suspensions (~1300 L/kg). When examining the quantity of heroin and morphine in the solid phase (by taking into account PLE recoveries and comparing to a matrix matched standard), it was observed that actual amounts present were far lower than expected (Figure S3 (b)) and that degradation in liquid phases was most probable and according to first order kinetics (Figure S3 (b)). Heroin showed some sorption behaviour in soils up to ~30% of expected concentration, but again decreased as equilibration time increased. PLE recoveries along with MS/MS quantification limits were insufficient to detect doxazosin to reliably determine stability in solids and data are not included in Figure S3.

Table S3 Available PPCP recovery data for PLE of solid soils

Compound [a]	**PLE % Recovery ± σ** [b]	**Compound** [a]	**PLE % Recovery ± σ** [b]
Temazepam	116±32	Bezafibrate	54±1
Amitripyline/Morphine	104±5	Sertraline	53±5
Clotrimazole	101±25	Budesonide	53±2
Indomethacin	101±5	Atenolol	50±3
Flurbiprofen	86±13	Methadone	50±4
Ketoprofen	79±5	Nifedipine	46±2
Salicylic Acid	78±20	Tramadol	45±3
Warfarin	75±14	Carbamazepine	41±4
Erythromycin	72±6	Cocaine	40±1
Meclofenamic Acid	71±15	Heroin	36±1
Nortriptyline	70±6	Sulfamethoxazole	29±2
Propranolol	69±7	Cocaethylene	29±1
Amphetamine	68±8	Clofibric Acid	28±3
Salbutamol	66±18	Caffeine	26±1
Nimesulide	65±9	Phenazone	25±2
Benzoylecgonine	63±1	Sulfapyridine	25±1
Trimethoprim	62±1	Citalopram	14±4
Diazepam	56±2	Sulfamethazine	14±1
Simvastatin	55±2	Papaverine	8±1
Metoprolol	55±1	Ranitidine	5±1
Naproxen	55±3		

[a] Recovery <5 % or data not available (inadequate LODs in solids at the working concentration range) for chloramphenicol, tramadol, cimetidine, triclosan, triclocarban, EDDP and MDMA.
[b] For n=2 replicates compared to a matrix matched standard spiked post extraction at theoretical 100 % extraction concentration.

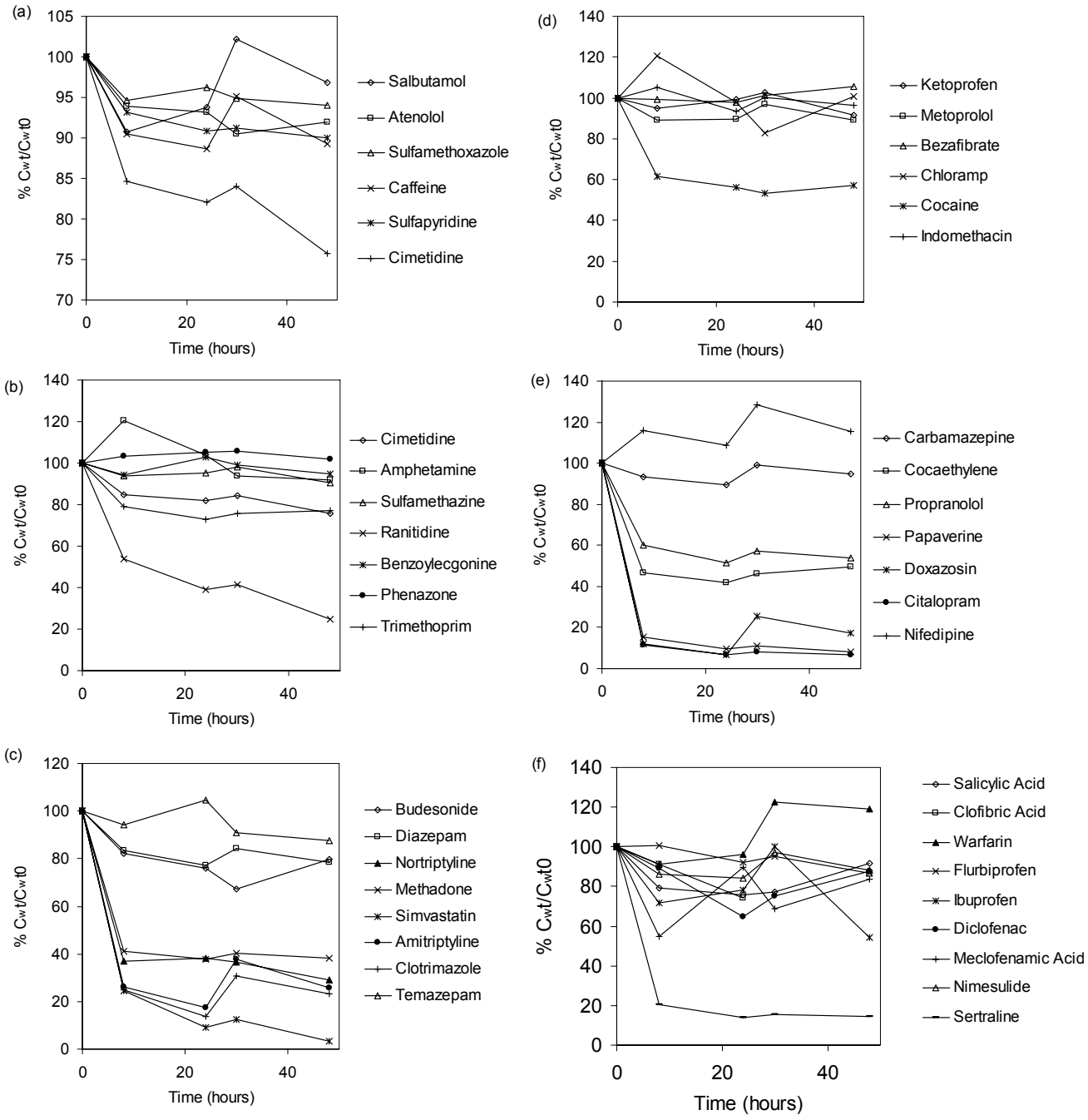

Figure S2 (a)-(f) Ratio of PPCP concentration in the liquid phase (C_wt) to concentration in liquid phase immediately after spiking (C_wt0) versus time. Data not available for triclosan, triclocarban, erythromycin or simvastatin.

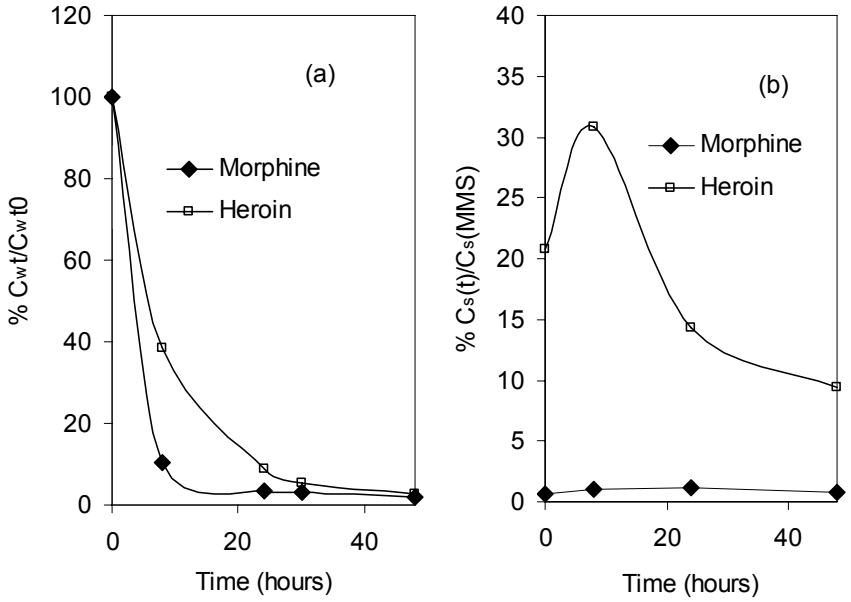

Figure S3 (a) Percentage of the liquid phase reduction in morphine and heroin levels at time, *t*, versus t=0 (b) Solid phase content of morphine and heroin over 0-48 hrs taking into account PLE recovery values for each compared to a theoretical 100 % spiked matrix matched standard C_s(MMS).

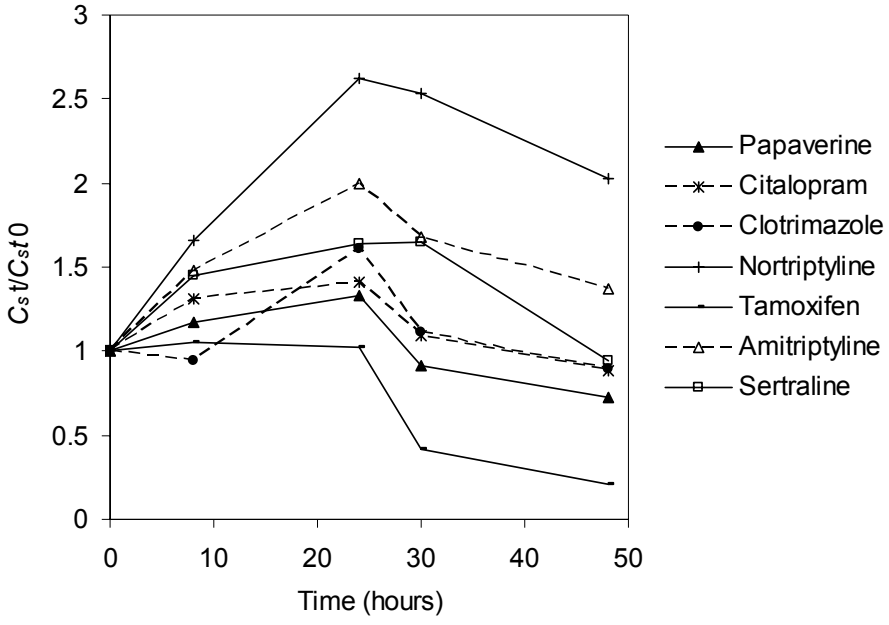

Figure S4 Possible transformation of selected PPCPs after 24 hrs. Graph represents the ratio of the total concentration of PPCP in the solid phase at t = 8, 24, 30 and 48 hrs (C_st) relative to the concentration for t=0 hrs (C_st0).

S 5.0 Calculation of K_d by the Freundlich model

Aqueous phases were analysed by LC-MS/MS to elucidate C_w (μmol/L) and this value subtracted from the total spiked concentration to determine C_s (μmol/kg). Using these data for each compound, plots of logC_s versus logC_w were constructed with the slope of the resulting fitting curves taken as n and intercept taken as logK_f. Subsequently, K_d (L/kg) was calculated from (1) below:

$$K_d = K_f . C_w^{n-1} \quad (1)$$

where K_f has units of μmol^{1-n}L^n/kg. Calculations for K_d were calculated for 3 x C_w concentrations.

S 6.0 Calculation of D_{ow}, the octanol-water distribution ratio and correlations with K_d

The D_{ow} of all compounds was calculated from (2) below:

$$D_{ow} = \frac{K_{ow}}{1+10^{|pH-pK_a|}} \quad (2)$$

where pH was 6.3 in both soil-water and sludge-water mixtures. All data was then correlated with experimentally determined K_d and shown in Figure S2

S 7.0 Determination of the organic carbon normalized sorption coefficient, K_{oc}

Measured percentage total organic carbon for the sampled soil and freeze-dried sludge were 3.77 % and 30.78 % respectively. K_{oc} was then calculated using experimentally determined K_d values using (3)

$$K_{oc} = \frac{K_d}{f_{oc}} \quad (3)$$

where f_{oc} was the fraction of organic carbon in the sample (kg_{oc}/kg_{solid})

Table S4 Data for the organic carbon normalized sorption coefficient, K_{oc}, for all compounds studied.

Compound	K_{oc} soil (L/kg_{oc})	K_{oc} sludge (L/kg_{oc})	Compound	K_{oc} soil (L/kg_{oc})	K_{oc} sludge (L/kg_{oc})
Amitriptyline	3667	3407	Methadone	2262	60
Amphetamine	801	-	Metoprolol	563	-
Atenolol	402	34	Naproxen	303	116
Benzoylecgonine	774	-	Nifedipine	292	88
Bezafibrate	396	-	Nimesulide	400	213
Budesonide	319	1459	Nortriptyline	3231	1950
Caffeine	687	46	Papaverine	149929	62
Carbamazepine	367	139	Paracetamol	880	-
Chloramphenicol	1155	-	Phenazone	228	26
Cimetidine	301	-	Propranolol	1608	1074
Citalopram	6897	916	Ranitidine	1364	-
Clofibric Acid	254	17	Salbutamol	725	35
Clotrimazole	28343	26406	Salicylic Acid	2249	75
Cocaethylene	716	-	Sertraline	3841	6116
Cocaine	609	-	Simvastatin	2350	4375
Diazepam	817	-	Sulfamethazine	248	49
Diclofenac	243	340	Sulfamethoxazole	218	35
Doxazosin	68018	26521	Sulfapyridine	218	-
EDDP	5454	-	Tamoxifen	44790	8229
Erythromycin	1877	616	Temazepam	684	-
Flurbiprofen	292	210	Tramadol	610	-
Indomethacin	895	694	Triclocarban	12053	-
Ketoprofen	241	-	Triclosan	3488	-
MDMA	480	-	Trimethoprim	719	222
			Warfarin	230	89

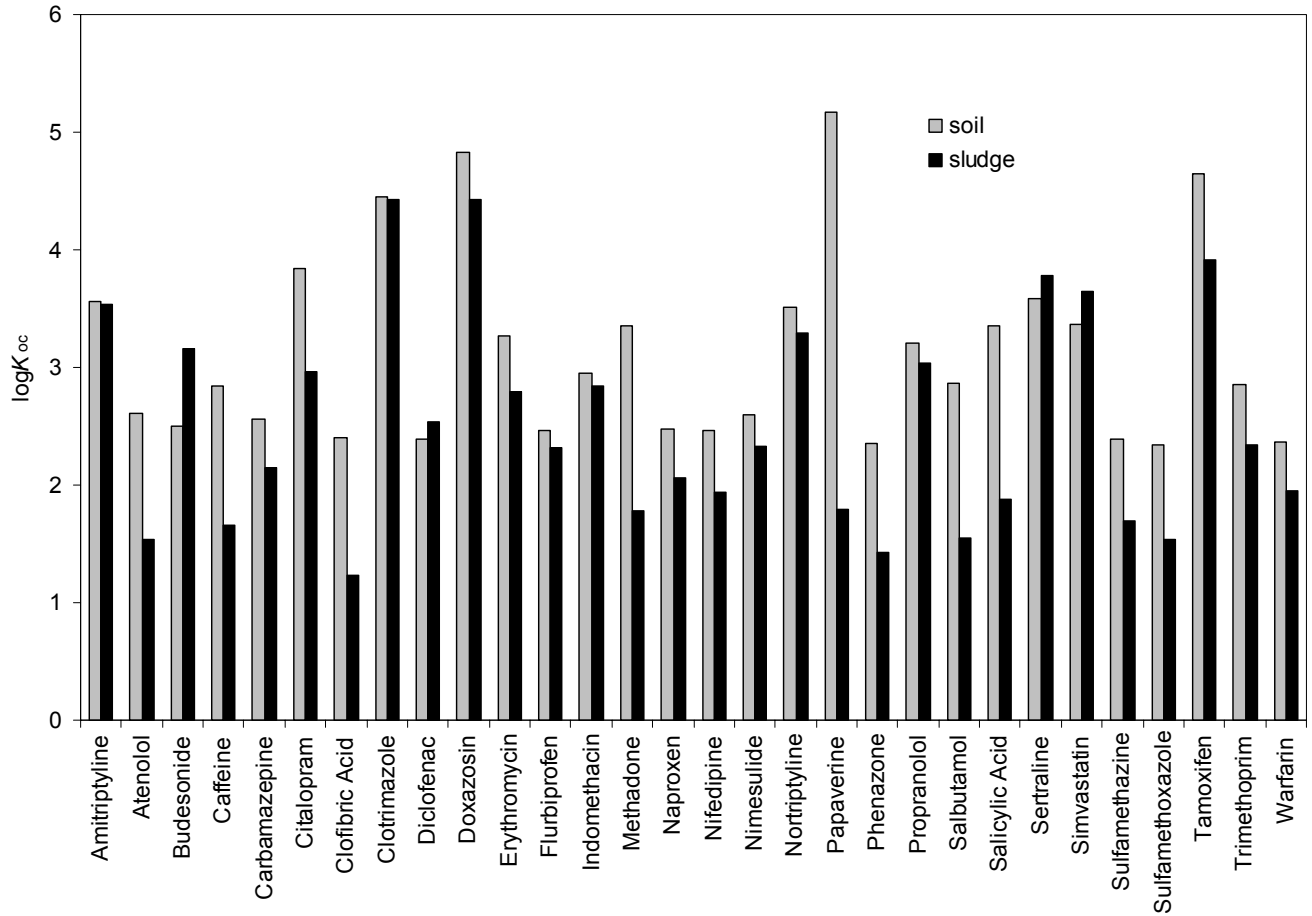

Figure S5 Comparison of logK_{oc} for PPCPs in soil and sludge sorption experiments.

S 8.0 Generation of molecular descriptors

The molecular descriptors outlined in Table S5 were generated using canonical simplified molecular input line entry specifications (SMILES). For example, amitriptyline has a SMILE of CN(C)CCC=C1C2=CC=CC=C2CCC3=CC=CC=C31. Using SMILES, QSAR data was generated using Parameter Client. Experimental pK_a and log$P$ values were sourced externally from literature cited data.

Table S5. Selection of molecular descriptors for neural network prediction of K_d

Compound Name	Empirical Formula	log$P$ Ref.	Mlog$P$	Alog$P$	pK_a Ref.	AMR	TPSA	UI	HF	AR	Σ VWV	Σ SAEN	Σ AP	Σ KHES
Amitriptyline	$C_{20}H_{23}N$	4.62 [1]	4.76	4.77	9.42 [2]	92.3	3.2	3.8	-0.9	0.52	27.6	42.8	29.4	38.3
Amphetamine	$C_9H_{13}N$	1.83 [3]	2.24	1.64	9.80 [4]	43.7	26.0	2.8	0.6	0.60	13.6	22.4	14.6	20.5
Atenolol	$C_{14}H_{22}N_2O_3$	0.16 [5]	0.93	0.67	9.20 [5]	73.5	84.6	3.0	2.0	0.32	23.5	41.0	25.0	47.2
Benzoylecgonine	$C_{16}H_{19}NO_4$	1.29 [6]	2.17	1.87	11.20 [7]	75.8	66.8	3.2	-0.3	0.26	24.4	40.4	25.7	52.3
Bezafibrate	$C_{19}H_{20}ClNO_4$	4.25 [8]	3.39	3.84	3.60 [9]	95.5	75.6	3.9	0.3	0.46	28.7	45.6	30.3	64.4
Budesonide	$C_{25}H_{34}O_6$	3.60 [10]	2.01	2.13	-	116.4	93.1	2.3	0.2	0.00	38.2	65.0	40.7	72.3
Caffeine	$C_8H_{10}N_4O_2$	-0.07 [9]	0.74	-0.10	14.00 [9]	49.3	61.8	3.0	-0.6	0.33	14.8	24.7	15.2	37.7
Carbamazepine	$C_{15}H_{12}N_2O$	2.45 [9]	2.59	2.68	13.90 [9]	71.9	48.0	3.9	0.3	0.60	20.5	30.0	21.2	41.3
Chloramphenicol	$C_{11}H_{12}Cl_2N_2O_5$	1.14 [11]	1.23	1.02	5.50 [12]	73.2	115.4	3.3	1.3	0.30	20.5	33.8	21.6	64.2
Cimetidine	$C_{10}H_{16}N_6S$	0.40 [5]	0.82	0.61	6.80 [5]	69.7	114.2	3.0	1.4	0.29	20.0	33.1	21.5	39.3
Citalopram	$C_{20}H_{21}FN_2O$	3.77 [13]	3.30	3.72	9.50 [14]	93.8	36.3	3.8	-0.8	0.46	28.6	44.9	30.0	55.6

Compound Name	Empirical Formula	log*P* (*Ref.*)	Mlog*P*	Alog*P*	pK_a (*Ref.*)	AMR	TPSA	UI	HF	AR	Σ VWV	Σ SAEN	Σ AP	Σ KHES
Clofibric Acid	$C_{10}H_{11}ClO_3$	2.58 [9]	2.38	2.73	3.46 [15]	52.6	46.5	3.0	-0.2	0.43	15.8	25.6	16.8	38.9
Clotrimazole	$C_{22}H_{17}ClN_2$	6.12 [9]	4.93	5.22	6.12 [9]	102.1	17.8	4.6	-0.9	0.82	29.5	41.6	31.0	51.0
Cocaethylene	$C_{18}H_{23}NO_4$	-	2.65	2.47	-	85.4	55.8	3.2	-0.8	0.24	27.6	46.1	29.2	53.3
Cocaine	$C_{17}H_{21}NO_4$	2.39 [16]	2.41	2.12	8.60 [17]	80.7	55.8	3.2	-0.8	0.25	26.0	43.3	27.4	51.8
Diazepam	$C_{16}H_{13}ClN_2O$	2.86 [18]	3.36	3.39	3.46 [19]	80.0	32.6	3.9	-0.8	0.55	22.8	33.2	23.9	45.6
Diclofenac	$C_{14}H_{11}Cl_2NO_2$	4.15 [9]	3.99	4.35	4.40 [20]	75.5	49.3	3.8	0.4	0.60	21.0	30.7	22.2	49.2
Doxazosin	$C_{23}H_{25}N_5O_5$	2.09 [21]	1.32	2.59	6.93 [22]	121.7	112.3	4.3	0.3	0.46	36.5	59.0	37.9	74.8
EDDP	$C_9H_{11}N$	-	4.37	4.47	-	91.4	3.2	3.8	-0.9	0.52	27.6	42.8	29.4	39.1
Erythromycin	$C_{37}H_{67}NO_{13}$	3.06 [5]	-0.14	1.65	8.90 [5]	186.0	193.9	1.6	2.0	0.00	64.4	118.5	69.0	126.
Flurbiprofen	$C_{15}H_{13}FO_2$	4.16 [9]	3.90	3.66	4.33 [9]	67.3	37.3	3.8	-0.3	0.63	20.3	31.4	21.2	48.7
Indomethacin	$C_{19}H_{16}ClNO_4$	4.27 [9]	3.32	4.21	4.50 [23]	94.3	68.5	4.3	-0.3	0.59	27.5	41.8	28.8	64.1
Ketoprofen	$C_{16}H_{14}O_3$	3.12 [9]	3.37	3.34	4.45 [9]	72.5	54.4	3.9	-0.4	0.60	21.7	33.2	22.7	49.7
MDMA	$C_{11}H_{15}NO_2$	-0.32 [24]	1.67	1.84	9.90 [25]	54.3	30.5	2.8	-0.2	0.40	17.2	28.9	18.2	28.8
Methadone	$C_{21}H_{27}NO$	3.90 [26]	4.10	4.32	9.10 [19]	97.4	20.3	3.8	-0.9	0.50	30.3	48.9	32.4	47.6
Metoprolol	$C_{15}H_{25}NO_3$	1.88 [27]	1.65	1.76	9.31 [27]	76.7	50.7	2.8	0.3	0.32	24.7	43.7	26.5	41.5
Naproxen	$C_{14}H_{14}O_3$	3.24 [1]	2.76	2.82	4.20 [9]	64.9	46.5	3.7	-0.3	0.61	19.7	31.2	20.7	42.2
Nifedipine	$C_{17}H_{18}N_2O_6$	3.17 [28]	2.07	1.77	1.00 [29]	92.2	110.5	3.7	-0.2	0.23	26.8	44.2	27.8	70.1

Compound Name	Empirical Formula	log*P* (*Ref.*)	Mlog*P*	Alog*P*	pK_a (*Ref.*)	AMR	TPSA	UI	HF	AR	Σ VWV	Σ SAEN	Σ AP	Σ KHES
Nimesulide	$C_{13}H_{12}N_2O_5S$	2.60 [30]	2.11	2.67	6.50 [30]	78.5	109.6	4.1	-0.2	0.55	21.6	34.3	22.7	61.6
Nortryptiline	$C_{19}H_{21}N$	4.39 [1]	4.53	4.24	9.70 [31]	87.0	12.0	3.8	-0.5	0.55	26.0	39.9	27.6	36.8
Papaverine	$C_{20}H_{21}NO_4$	3.00 [32]	2.44	3.50	8.07 [33]	95.5	49.8	4.2	-0.8	0.63	29.0	46.3	30.4	53.8
Paracetamol	$C_8H_9NO_2$	0.46 [9]	1.06	0.68	9.38 [2]	40.8	49.3	3.0	0.7	0.55	12.4	20.3	13.0	30.5
Phenazone	$C_{11}H_{12}N_2O$	0.17 [34]	2.31	1.62	1.45 [2]	56.9	26.9	3.2	-0.8	0.40	16.5	26.0	17.3	32.0
Propranolol	$C_{16}H_{21}NO_2$	3.48 [9]	2.53	2.54	9.49 [9]	76.8	41.5	3.6	0.3	0.55	24.0	39.6	25.5	40.7
Ranitidine	$C_{13}H_{22}N_4O_3S$	0.15 [35]	0.66	1.47	8.20 [36]	85.1	111.6	3.2	0.5	0.24	25.0	43.4	26.9	51.3
Salbutamol	$C_{13}H_{21}NO_3$	0.11 [37]	1.13	0.92	5.90 [9]	67.5	72.7	2.8	2.1	0.35	21.5	37.9	23.0	43.1
Salicylic Acid	$C_7H_6O_3$	2.36 [9]	1.64	1.17	3.50 [9]	34.5	57.5	3.0	0.7	0.60	10.3	16.6	10.7	32.0
Sertraline	$C_{17}H_{17}NCl_2$	4.30 [38]	5.15	5.00	9.16 [38]	85.7	12.0	3.7	-0.4	0.55	24.8	36.7	26.6	40.7
Simvastatin	$C_{25}H_{38}O_5$	4.68 [39]	4.00	4.64	5.50 [40]	117.7	72.8	2.3	-0.4	0.00	38.9	67.4	41.7	67.6
Sulfamethazine	$C_{12}H_{14}N_4O_2S$	0.89 [9]	1.06	1.35	7.40 [41, a]	75.2	106.4	3.9	1.3	0.60	21.1	33.6	22.4	49.8
Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	0.89 [9]	0.97	1.18	5.60 [12]	65.9	106.6	3.8	1.4	0.61	18.0	28.9	19.1	46.6
Sulfapyridine	$C_{11}H_{11}N_3O_2S$	0.02 [34]	1.15	1.43	8.40 [41, a]	67.5	93.5	3.9	1.3	0.67	18.5	28.6	19.6	45.4
Tamoxifen	$C_{26}H_{29}NO$	6.58 [42]	5.20	6.32	8.85 [43]	119.2	12.5	4.3	-0.9	0.60	35.9	55.8	38.1	54.0
Temazepam	$C_{16}H_{13}ClN_2O_2$	2.19 [44]	3.36	3.05	1.60 [44]	80.9	52.9	3.9	-0.3	0.52	23.3	34.5	24.4	51.4
Tramadol	$C_{16}H_{25}NO_2$	2.51 [45]	2.32	2.70	9.19 [45]	78.3	32.7	2.8	-0.4	0.30	25.2	43.4	27.1	38.9

Compound Name	**Empirical Formula**	**log*P* (*Ref.*)**	**Mlog*P***	**Alog*P***	**pK_a (*Ref.*)**	**AMR**	**TPSA**	**UI**	**HF**	**AR**	**Σ VWV**	**Σ SAEN**	**Σ AP**	**Σ KHES**
Triclocarban	$C_{13}H_9Cl_3N_2O$	4.90 [46]	3.99	4.52	12.77 [47]	76.9	41.1	3.8	0.5	0.60	20.6	28.9	21.9	48.3
Triclosan	$C_{12}H_7Cl_3O_2$	4.53 [48]	3.84	5.12	8.10 [49]	68.4	29.5	3.7	-0.2	0.67	18.1	25.0	19.3	43.8
Trimethoprim	$C_{14}H_{18}N_4O_3$	0.91 [9]	1.26	1.54	6.60 [9]	81.5	105.5	3.7	2.0	0.55	23.7	39.6	24.7	49.7
Warfarin	$C_{19}H_{16}O_4$	2.60 [9]	2.80	3.13	5.05 [9]	85.8	67.5	4.0	-0.4	0.48	25.8	39.4	26.9	58.0

[a] Molecule with two or more reported pK_a values. Values chosen as inputs were those closest to pH of soil/sludge-water mixture.

1 Ghasemi, J., Saaidpour, S., *Anal. Chim. Acta* 2007, **604**, 99.
2 Escuder-Gilabert, L., Molero-Monfort, M., Villanueva-Camañas, R.M., Sagrado, S., Medina-Hernández, M.J., *J. Chromatogr. B* 2004, **807**, 193.
3 Nishida, M., Yashiki, M., Namera, A., Kimura, K., *J. Chromatogr. B* 2006, **842**, 106.
4 FDA Adderall XR Capsules Product Information, 2006, www.fda.gov/cder/foi/label2005/0213035009lbl.pdf
5 Jones, O.A.H., Voulvoulis, N., Lester, J.N., *Wat. Res.* 2002, **36**, 5013.
6 HIV/OI Chemical Biological Database, 2006, Bezoylecgonine Information, http://chembd2.niaid.nih.gov/struct_search/all/url_search.asp?aids_no-001987
7 Skopp, G., Potsch, L., *Int. J. Leg. Med.* 1999, **112**, 213.
8 Paschke, A., Bruemmer, J., *Anal. Bioanal. Chem.* 2007, **387**, 1417.
9 Bones, J., Thomas, K., Nesterenko, P.N., Paull, B., *Talanta* 2006, **70**, 1117.
10 Nolen, H., Fedorak, R.N., Friend, D.R., *J. Pharm. Sci.* 1995, **84**, 677.
11 Hansch, C., Leo, A., 1987.
12 Martindale, W., *The Extra Pharmacopoeia*, The Pharmaceutical Press, London, 1993.
13 Rampono, J., Kristensen, J.H., Hackett, L.P., Paech, M., Rolland, K., Ilett, K.F., *Brit. J. Clin. Pharmaco.* 2000, **50**, 263.
14 Kwon, J.-W., Armbrust, K.L., *B. Environ. Contam. Tox.* 2008, **DOI 10.1007/s00128-008-9401-1**.
15 Witiak, D.T., Feller, D.R., Stratford, E.S., Hackney, R.E., Nazareth, R., Wagner, G., *Med. Chem.* 1971, **14**, 754.
16 Cone, E.J., Huestis, M.A., *Oral-Based Diagnostics* 2007, **1098**, 51.
17 Barkley Barnett, L., Toxicity, cocaine, http://www.medscape.com/px/trk.svr/emedsearch?exturl=http://www.emedicine.com/emerg/TOPIC102.HTM
18 Kontoyannis, S., Antimisiaris, D., Douroumis, D., *Talanta* 1999, **48**, 979.
19 Roerig, D.L., Dahl, R.R., Dawson, C.A., Warp, R.I., *Drug Metab. Dispos.* 1984, **12**, 536.
20 LaRotonda, M.I., Amato, G., Barbato, F., Silipo, C., Vittoria, A., *Chem. Biol.* 1983, **2**, 168.
21 Negwer, M., *Organic Chemical Drugs and their Synonyms*, Academie, Berlin, 1987.
22 Astra Zeneca, 2006, Product Monograph, http://www.astrazeneca.ca/documents/ProductPortfolio/CARDURA_PM_en.pdf
23 Kavvada, K.M., Murray, J.G., Moore, V.A., Coombes, A.G.A., Hanson, P.J., *Eur. J. Pharmacol.* 2006, **549**, 41.
24 Seidel, S., Singer, E.S., Just, H., Farhan, H., Scholze, P., Kudlacek, O., Holy, M., Koppatz, K., Kirvanek, M., Freissmuth, M., Sitte, H.H., *Mol. Pharmacol.* 2005, **67**, 140.
25 Pirichini, S., Distribution of 3, 4-Methylenedioxy Methamphetamine in non-conventional matricesand its application in clinical toxicology, Universitat Autonoma de Barcelona, Doctoral Thesis, 2005

26 Nekhayeva, I.A., Nanovskaya, T.N., Deshmukh, S.V., Zharikova, O.L., Hankins, G.D.V., Ahmed, M.S., *Biochem. Pharmacol.* 2005, **69**, 187.
27 Carda-Broch, S., Berthod, A., *J. Chromatogr. A* 2003, **995**, 55.
28 Lombardo, F., Shalaeva, M.Y., Tupper, K.A., Gao, F., *J. Med. Chem.* 2001, **44**, 2490.
29 Knock, G.A., Aaronson, P.I., *Brit. J. Pharmacol.* 1999, **127**, 1470.
30 Alves, M.P., Scarrone, A.L., Santos, M., Pohlmann, A.R., Guterres, S.S., *Int. J. Pharm.* 2007, **341**, 215.
31 Croes, K., McCarthy, P.T., Flanagan, R.J., *J. Chromatogr. A* 1995, **693**, 289.
32 Virtual Computational Chemistry Laboratory logP Calculator, http://146.107.217.178/lab/alogps/start.html
33 Choe, H., Lee, Y.-K., Lee, Y.-T., Choe, H., Ko, S.-H., Joo, C.-U., Kim, M.-H., Kim, G.-S., Eun, J.-S., Kim, J.-H., Chae, S.-W., Kwak, Y.-G., *J. Pharmacol. Exp. Ther.* 2003, **304**, 706.
34 Liu, X., Tanaka, H., Yamauchi, A., Testa, B., Chuman, H., *J. Chromatogr. A* 2005, **1091**, 51.
35 Zakeri-Milani, P., Tajerzadeh, H., Islambolchilar, Z., Barzegar, S., Valizadeh, H., *DARU* 2006, **14**, 164.
36 Campanero, M.A., Lopez-Orcariz, A., Garcia-Quetglas, E., Sadaba, B., de la Maza, A., *Chromatographia* 1998, **78**, 391.
37 Forbes, B., Shah, A., Martin, G.P., Lansley, A.B., *International Journal of Pharmaceutics* 2003, **257**, 161.
38 Deak, K., Takacs-Novak, K., Tihanyi, K., Noszal, B., *Med. Chem.* 2006, **2**, 385.
39 Serajuddin, A.T.M., Ranadive, S.A., Mahoney, E.M., *J. Pharm. Sci.* 1991, **80**, 830.
40 Vanderbist, F., Sereno, A., Baudier, A., ORAL PHARMACEUTICAL COMPOSITION CONTAINING A STATIN DERIVATIVE, European Patent EP1395254, 2007, http://www.freepatentsonline.com/EP1395254B1.html
41 Chienthavorn, O., Smith, R.M., *Chromatographia* 1999, **50**, 485.
42 Nadanaciva, S., Bernal, A., Aggeler, R., Capaldi, R., Will, Y., *Toxicol. in Vitro* 2007, **21**, 902.
43 Astra Zeneca, 2002, Nolvadex (Tamoxifen Citrate), http://www.fda.gov/cder/pediatric/labels/Tamoxifen.pdf
44 Graf, E., El-Menshawy, M., *Pharm. Unserer Zeit* 1977, **6**, 171.
45 Tsai, R.S., Carrupt, P.A., Testa, B., El Tayar, N., Grunewald, G.L., Casy, A.F., *J. Chem. Res.* 1993, **8**, 1901.
46 Duan, M.S., Zhao, N., Össurardóttir, Í.B., Thorsteinsson, T., Loftsson, T., *Int. J. Pharm.* 2005, **297**, 213.
47 Chu, S., Metcalfe, C.D., *J. Chromatogr. A* 2007, **1164**, 212.
48 Hagedorn-Leweke, U., Lippold, B.C., *Pharmaceut. Res.* 1995, **12**, 1354.
49 Tixier, C., Singer, H.P., Canonica, S., Mueller, S.R., *Environ. Sci. Technol.* 2002, **36**, 3482.

S 9.0 Network Architecture

Figure S6. Optimized tri-layer neural network for the prediction of K_d in soils and sludges.