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## Effect of sewage sludge type on the partitioning behaviour of pharmaceuticals: a meta-analysis†

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Assessment of the fate of pharmaceutical residues in the environment involves the measurement or prediction of their sewage sludge partition coefficient ( $K_d$ ). Sewage sludge can be classified into four types: primary, activated, secondary and digested, each one with different physical and chemical properties. Published studies have measured  $K_d$  for pharmaceuticals in a variety of sludge types. This paper discusses the variability of reported  $K_d$  values of pharmaceuticals in different types of sewage sludge, using a dataset generated from the literature. Using a meta-analysis approach, it was shown that the measured  $K_d$  values depend on the type of sludge used in the test. Recommendations are given for the type of sludge to be used when studying the partitioning behaviour of pharmaceuticals in waste water treatment plants. Activated sludge is preferred due to its more homogenous nature and the ease of collection of consistent samples at a plant. Weak statistical relationships were found between  $K_d$  values for activated and secondary sludge, and for activated and digested sludge. Pooling of  $K_d$  values for these sludge types is not recommended for preliminary fate and risk assessments. In contrast, statistical analyses found stronger similarities between  $K_d$  values reported for the same pharmaceutical in primary and activated sludges. This allows the pooling of experimental values for these two sludge types to obtain a larger dataset for modelling purposes.

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### Water impact

Active pharmaceutical ingredients (API) in waste water treatment plants partition between aqueous and sludge phases. Understanding this behaviour is important for regulatory purposes. A partition coefficient ( $K_d$ ) describes how chemicals distribute between these phases and can be measured experimentally using specific tests. A number of  $K_d$  values have been published for APIs in a range of sludge types. This paper undertakes a meta-analysis of these  $K_d$  values to investigate how the partitioning is affected by the different sludge types and if there are correlations between the datasets. This information is useful to make initial predictions of the fate of an API during treatment processes and may reduce the need to undertake time-consuming OECD tests in preliminary environmental risk assessments.

## Introduction

Over the past decade the environmental fate of active pharmaceutical ingredients (APIs) and personal care products and their potential effects on organisms have been investigated.<sup>1</sup> Municipal and hospital waste effluents are the most

important sources of APIs entering the aquatic environment.<sup>2,3</sup> Although some APIs are removed by waste water treatment plants (WWTPs), many substances are not fully biodegraded during treatment processes.<sup>4</sup> In this case, the partitioning behaviour of the API between sludge and aqueous phases at WWTPs is the key indicator of their subsequent environmental fate. The distribution of APIs between these two phases is described by the partition coefficient  $K_d$ . It is defined as the dimensionless ratio of the equilibrium concentrations (expressed as  $\text{L kg}^{-1}$ ) of the substance in the sludge and aqueous phases:

$$K_d = [\text{API}]_{\text{sludge}} / [\text{API}]_{\text{aqueous}} \quad (1)$$

The  $K_d$  values of APIs in different sewage sludges have been reported in many studies.<sup>5–18</sup>

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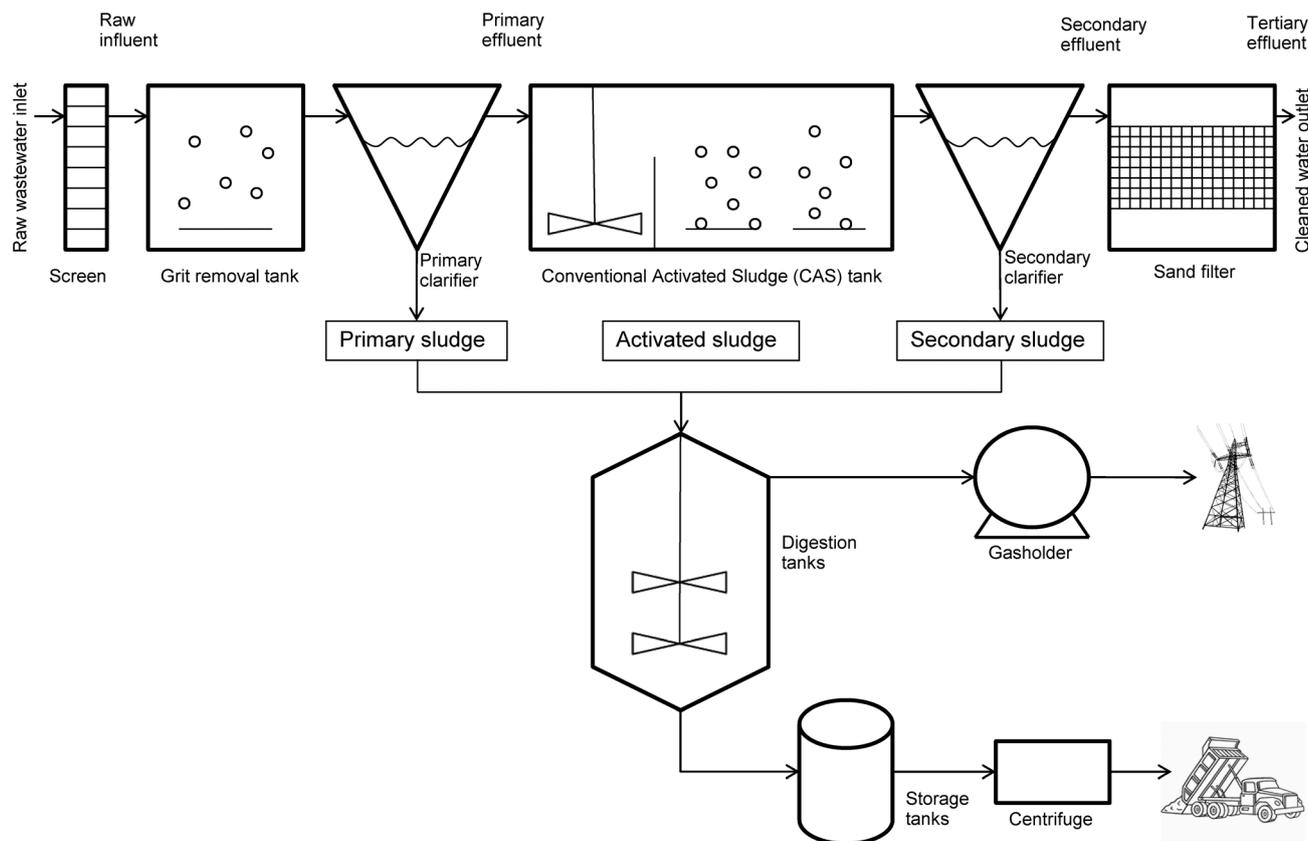


Fig. 1 Typical waste water treatment plant processes.

nervous system drugs and hormones). The authors reported  $K_d$  values in four types of sewage sludge (primary, activated, secondary or digested) and their classifications were used directly in the meta-analysis. This type of analysis does not take account of any small variations in experimental conditions used in the studies to ascertain the  $K_d$  values.

### Type of sludge

Primary sludge was collected just after the grit removal stage and before the first clarifier in some papers, or just after the primary clarifier in others (Fig. 1). In some papers the primary clarifier had no secondary sludge recirculation; while in others it did.<sup>6,9,16,17</sup> Activated sludge was always sampled in the activation tank in the nitrification zone.<sup>11,13,17</sup> Secondary sludge was collected in the secondary clarifier. However, there were differences in sludge age and secondary clarifier volume.<sup>6,16</sup> Anaerobically digested sludge was sampled from the digester. Only one paper reported the type of digester (mesophilic or thermophilic) and sludge age.<sup>10</sup>

The key physico-chemical properties (pH, total suspended solids (TSS), total organic carbon (TOC), volatile suspended solids (VSS) and chemical oxygen demand (COD)) of the four sludge types, where available, are detailed in Table 1.

### Sorption data

All the experimentally derived  $K_d$  values were calculated using a linear isotherm. Due to the relatively small number of

studies the data were grouped by sludge type regardless of any sampling differences. When an API had more than one  $K_d$  value for the same type of sludge, the values were averaged and the mean was used. APIs were only included if  $K_d$  values were available for more than one type of sludge. This resulted in a set of 79 APIs associated with a set of 196  $K_d$  values (Table 2). Few of these APIs had  $K_d$  values available in the literature for all sludge types.

### Statistical analysis

To assess any similarities in sorption behaviour between sludge types several statistical tests were performed. Some of these tests require the data to have a normal distribution, and a Box-Cox plot revealed that a log transformation was required to normalise the data and stabilise the variation. The effectiveness of the transformation was confirmed for the transformed data using normal probability plots. First, the correlations between the measured  $\ln K_d$  values of the APIs on different pairs of the four sludge types available in the literature were calculated (Table 3). Pearson correlation coefficients were considered significant if their associated  $p$ -value was below 0.05. Initially, a multiple comparison between the  $\ln K_d$  values for the different sludge types was performed using a Tukey test. However, the results of this test were adversely affected by the sparseness of the data set. For example, there are several large values of  $K_d > 10^3$  for primary sludge that have no corresponding measurement for



**Table 2** Partition coefficients ( $K_d$ ) reported in the literature for active pharmaceutical ingredients with different types of sewage sludge. Where multiple values are available the mean value is stated, with the relative standard deviation in parentheses

Compound	$K_d$ activated	$K_d$ primary	$K_d$ secondary	$K_d$ digested
Acetaminophen	595.0 (134.3) <sup>a,b</sup>	18.0 (89.8) <sup>a,b</sup>	—	—
Alfuzosin	—	1800.0 <sup>c</sup>	1200.0 <sup>c</sup>	—
Amitriptyline	4555.0 <sup>a</sup>	4897.0 (23.0) <sup>a,c</sup>	5020.0 (120.6) <sup>c,d</sup>	1049.0 <sup>e</sup>
Androstenedione	156.0 <sup>a</sup>	174.0 <sup>a</sup>	—	—
Androsterone	579.0 <sup>a</sup>	534.0 <sup>a</sup>	—	—
Atenolol	44.0 (40.4) <sup>a,b,f</sup>	200.3 (112.9) <sup>a,b,c</sup>	2800.0 <sup>c</sup>	11.0 <sup>e</sup>
Atorvastatin	198.0 <sup>a</sup>	216.0 <sup>a</sup>	—	—
Atracurium	—	350.0 <sup>c</sup>	1600.0 <sup>c</sup>	—
Azelastine	—	6400.0 <sup>c</sup>	470.0 <sup>c</sup>	—
Biperiden	—	820.0 <sup>c</sup>	750.0 <sup>c</sup>	—
Bisoprolol	40.0 <sup>f</sup>	—	110.0 <sup>c</sup>	—
Bupropion	—	85.0 <sup>c</sup>	140.0 <sup>c</sup>	—
Caffeine	30.0 <sup>a</sup>	30.0 <sup>a</sup>	—	14.0 <sup>e</sup>
Carbamazepine	53.8 (97.0) <sup>a,b,f,g,h</sup>	102.3 (154.9) <sup>a,b,h,i</sup>	120.6 (140.0) <sup>d,i,j</sup>	39.5 (9.7) <sup>e,h,j</sup>
Chlorprothixene	—	38 000.0 <sup>c</sup>	20 000.0 <sup>c</sup>	—
Citalopram	—	540.0 <sup>c</sup>	2105.0 (127.3) <sup>c,d</sup>	282.0 <sup>e</sup>
Clofibrilic Acid	25.5 <sup>g</sup>	—	4.8 <sup>j</sup>	5.0 <sup>e</sup>
Clomipramine	—	17 000.0 <sup>c</sup>	6700.0 <sup>c</sup>	—
Clotrimazol	—	32 000.0 <sup>c</sup>	34 000.0 <sup>c</sup>	8128.0 <sup>e</sup>
Clozapine	1642.0 <sup>a</sup>	1730.0 <sup>a</sup>	—	—
Cyclophosphamide	—	55.0 <sup>j</sup>	2.4 <sup>j</sup>	—
Cyproheptadine	—	11 000.0 <sup>c</sup>	3600.0 <sup>c</sup>	—
Desloratadine	—	3700.0 <sup>c</sup>	2900.0 <sup>c</sup>	—
Diazepam	91.8 (109.7) <sup>a,f,h</sup>	125.0 (115.0) <sup>a,h,j</sup>	21.0 <sup>i</sup>	—
Diclofenac	55.3 (104.2) <sup>b,g,h</sup>	384.7 (43.3) <sup>b,h,i,j</sup>	16.0 <sup>i,j</sup>	77.5 (50.2) <sup>e,h</sup>
Dicycloverine	—	1400.0 <sup>c</sup>	1700.0 <sup>c</sup>	—
Dilantin	81.0 <sup>a</sup>	45.0 <sup>a</sup>	—	—
Donepezil	—	3600.0 <sup>c</sup>	970.0 <sup>c</sup>	—
Duloxetine	—	13 000.0 <sup>c</sup>	2900.0 <sup>c</sup>	—
Erythromycin	116.0 (51.2) <sup>b,h</sup>	309.0 <sup>b</sup>	—	190.0 <sup>e</sup>
Estradiol (E2)	787.8 (64.1) <sup>a,g,h,k</sup>	560.0 <sup>a</sup>	—	375.5 (69.7) <sup>l,h</sup>
Estrilol	63.0 <sup>a</sup>	58.0 <sup>a</sup>	—	—
Estrone (E1)	424.2 (42.8) <sup>a,g,h,k</sup>	636.0 <sup>a</sup>	—	352.1 (62.7) <sup>l,h</sup>
Ethinylestradiol (EE2)	763.0 (69.2) <sup>a,g,h,k</sup>	515.3 (84.3) <sup>a,h,j</sup>	349.0 <sup>j</sup>	414.1 (100.4) <sup>l</sup>
Ezetimibe	—	2300.0 <sup>c</sup>	3000.0 <sup>c</sup>	—
Fexofenadine	—	2700.0 <sup>c</sup>	360.0 <sup>c</sup>	—
Fluoxetine	—	10 000.0 <sup>c</sup>	7400 (26.8) <sup>c,d</sup>	—
Flutamide	—	1500.0 <sup>c</sup>	750.0 <sup>c</sup>	—
Gemfibrozil	54.8 (75.3) <sup>a,b,g</sup>	34.0 (45.8) <sup>a,b</sup>	—	—
Glibenclamide	239.0 <sup>b</sup>	1941.0 (120.9) <sup>b,c</sup>	1300.0 <sup>c</sup>	—
Glimepiride	—	2100.0 <sup>c</sup>	960.0 <sup>c</sup>	—
Haloperidol	—	10 000.0 <sup>c</sup>	2900.0 <sup>c</sup>	—
Hydrochlorothiazide	20.2 <sup>b</sup>	25.8 <sup>b</sup>	—	—
Hydroxyzine	819.0 <sup>a</sup>	989.0 (30.2) <sup>a,c</sup>	720.0 <sup>c</sup>	—
Ibuprofen	32.4 (127.3) <sup>g,h,m</sup>	14.8 (50.3) <sup>b,h,i</sup>	183.6 (136.0) <sup>c,i,j</sup>	31.4 (28.8) <sup>h,j</sup>
Ifosfamide	—	22.0 <sup>j</sup>	1.4 <sup>j</sup>	—
Indomethacin	39.0 <sup>g</sup>	—	—	214.0 <sup>e</sup>
Iopromide	10.0 <sup>h</sup>	10.0 <sup>i</sup>	11.0 <sup>j</sup>	10.0 (43.4) <sup>h,j</sup>
Irbesartan	—	700.0 <sup>c</sup>	940.0 <sup>c</sup>	—
Ketoconazole	—	9700.0 <sup>c</sup>	8500.0 <sup>c</sup>	—
Ketoprofen	22.5 (40.9) <sup>b,g</sup>	226.0 <sup>b</sup>	—	—
Loperamide	—	14 000.0 <sup>c</sup>	5500.0 <sup>c</sup>	—
Loratidine	3321.0 <sup>b</sup>	2336.0 <sup>b</sup>	—	—
Maprotiline	—	6700.0 <sup>c</sup>	4500.0 <sup>c</sup>	—
Mefenamic acid	434.0 <sup>b</sup>	294.0 <sup>b</sup>	—	—
Meprobamate	30.0 <sup>a</sup>	42.0 <sup>a</sup>	—	—
Metoprolol	65.0 <sup>f</sup>	—	—	18.0 <sup>e</sup>
Mianserin	—	3000.0 <sup>c</sup>	910.0 <sup>c</sup>	—
Naproxen	24.0 <sup>g</sup>	217.0 <sup>i</sup>	217.0 <sup>i</sup>	29.0 <sup>e,h</sup>
Nefazodone	—	14 000.0 <sup>c</sup>	8300.0 <sup>c</sup>	—
Nortriptyline	—	—	6200.0 <sup>k</sup>	600.0 <sup>e</sup>
Omeprazole	107.0 <sup>a</sup>	130.0 <sup>a</sup>	—	—
Oxazepam	13.0 <sup>f</sup>	790.0 <sup>c</sup>	1100.0 <sup>c</sup>	—
Paroxetine	—	14 000.0 <sup>c</sup>	11 650.0 (40.7) <sup>c,d</sup>	—
Phenylphenol	347.0 <sup>a</sup>	652.0 <sup>a</sup>	—	—
Pizotifen	—	4700.0 <sup>c</sup>	3100.0 <sup>c</sup>	—



Table 2 (continued)

Compound	$K_d$ activated	$K_d$ primary	$K_d$ secondary	$K_d$ digested
Primidone	18.5 (87.9) <sup>a,f</sup>	45.0 <sup>a</sup>	—	—
Progesterone	—	750.0 <sup>c</sup>	1100.0 <sup>c</sup>	—
Propranolol	354.5 (10.2) <sup>b,f</sup>	641.0 <sup>b</sup>	—	331.0 <sup>e</sup>
Repaglinide	—	170.0 <sup>c</sup>	210.0 <sup>c</sup>	—
Risperidone	861.0 <sup>a</sup>	1432.0 <sup>c</sup>	650.0 <sup>c</sup>	—
Roxithromycin	282.0 <sup>h</sup>	400.0 <sup>i</sup>	170.0 <sup>i</sup>	49.0 (70.8) <sup>h,l</sup>
Sertraline	—	35 000.0 <sup>c</sup>	24 000.0 (41.2) <sup>c,d</sup>	1883.0 <sup>e</sup>
Sotalol	18.0 <sup>f</sup>	—	360.0 <sup>c</sup>	—
Sulfamethoxazole	205.0 (54.4) <sup>b,h,n</sup>	161.6 (129.9) <sup>b,c</sup>	370.0 <sup>c</sup>	24.7 (103) <sup>e,h,l</sup>
Testosterone	157.0 <sup>a</sup>	178.0 <sup>a</sup>	—	—
Tramadol	447.0 <sup>f</sup>	110.0 <sup>c</sup>	190.0 <sup>c</sup>	—
Trimethoprim	195.0 (28.6) <sup>a,b,h,n</sup>	356.0 (26.1) <sup>a,b,c</sup>	420.0 <sup>c</sup>	68.0 <sup>e</sup>
Verapamil	1501.0 <sup>a</sup>	1722.0 (6.4) <sup>a,c</sup>	400.0 <sup>c</sup>	—

<sup>a</sup> Stevens-Garmon *et al.* 2011 (ref. 17). <sup>b</sup> Radjenović *et al.* 2009 (ref. 13). <sup>c</sup> Hörsing *et al.* 2011 (ref. 16). <sup>d</sup> Lajeunesse *et al.* 2012 (ref. 18). <sup>e</sup> Barron *et al.* 2009 (ref. 12). <sup>f</sup> Wick *et al.* 2009 (ref. 14). <sup>g</sup> Urase and Kikuta 2005 (ref. 9). <sup>h</sup> Suárez *et al.* 2008 (ref. 11). <sup>i</sup> Joss *et al.* 2005 (ref. 8). <sup>j</sup> Terres *et al.* 2004 (ref. 6). <sup>k</sup> Andersen *et al.* 2005 (ref. 29). <sup>l</sup> Carballa *et al.* 2008 (ref. 10). <sup>m</sup> Stuer-Lauridsen *et al.* 2000 (ref. 5). <sup>n</sup> Göbel *et al.* 2005 (ref. 7).

some of the other sludge types. Differences in the mean  $K_d$  values thus reflect the coverage of reported values rather than intrinsic differences between the sludge types. Therefore, for each pair of sludge types a paired sample *t*-test was performed to assess their similarity, using only cases where  $K_d$  values were available for both sludge types. A 95% confidence level was applied, together with a Bonferroni correction to reduce the risk of a Type I error due to multiple comparisons (Table 4). Finally, linear regression was used to quantify the relationships between the  $\ln K_d$  values obtained on the four different sludge types. As regression of the  $\ln K_d$  values of one sludge type onto another involves errors in both variables, orthogonal, or total least squares, regression was used, rather than the usual ordinary least squares regression. The results of these three statistical tests were used in combination to assess the feasibility of inferring the  $\ln K_d$  value of an API on one sludge type from its measured value on another sludge type.

Table 3 Correlations between reported  $\ln K_d$  values for active pharmaceutical ingredients with different types of sewage sludge

		$K_d$ activated	$K_d$ primary	$K_d$ secondary	$K_d$ digested
$K_d$ activated	Correlation coefficient	1			
	<i>p</i> -value				
$K_d$ primary	<i>n</i>	45			
	Correlation coefficient	0.72	1		
	<i>p</i> -value	<0.001			
$K_d$ secondary	<i>n</i>	40	73		
	Correlation coefficient	0.48	0.85	1	
	<i>p</i> -value	0.027	<0.001		
$K_d$ digested	<i>n</i>	21	51	55	
	Correlation coefficient	0.82	0.88	0.80	1
	<i>p</i> -value	<0.001	<0.001	<0.001	
	<i>n</i>	19	19	16	23

## Results and discussion

The literature search identified 14 papers satisfying the criteria for the meta-analysis. This relatively small number of publications reflects the fact that the study of the fate of APIs in the environment is relatively new, especially compared with many other classes of regulated pollutants (*e.g.* certain pesticides) that have been extensively investigated for many decades. As further work on the sorption behaviour of APIs within a WWTP is undertaken, the resultant data can be used to augment and strengthen the comparisons presented here.

### Activated and primary sludge

The correlation coefficient between the  $\ln K_d$  values of activated and primary sludge was 0.72 with a *p*-value <0.001 (Table 3). This indicated that the sorption behaviour of the APIs in the dataset for these sludge types was similar. The paired sample *t*-test for the  $\ln K_d$  activated– $\ln K_d$  primary sludge pair gave a *p*-value of 0.08 (Table 4). This was above the Bonferroni-corrected threshold value of  $p = 0.05/6 = 0.0083$ , indicating that these two sludge types behave similarly. The confidence interval associated with the *t*-test included zero, also showing that there was no significant difference between the sorption behaviour of these two sludges.

The orthogonal regression of  $\ln K_d$  activated against  $\ln K_d$  primary gave a regression coefficient of 0.96, an intercept of 0.54 and a RMSE (the root mean square of the orthogonal distance from the data points to the regression line) of 0.81 (Fig. 2). These results showed that activated and primary sludge have similar sorption properties for a diverse set of APIs ( $n = 40$ ). These findings are consistent with the observation that primary and activated sludge have similar physico-chemical properties; both have a relatively neutral pH, high TOC and comparable COD (Table 1).

Within a WWTP there are several distinct stages where partitioning takes place. The first of these occurs in the primary clarifier.<sup>22</sup> Hence primary sludge is the result of all the partitioning processes occurring prior to and including the



**Table 4** Paired sample *t*-tests for reported  $\ln K_d$  values for active pharmaceutical ingredients with different types of sewage sludge

	Paired differences			95% confidence interval of the difference		<i>t</i>	<i>p</i>
	<i>n</i>	Mean	Standard deviation	Lower	Upper		
$\ln K_d$ activated– $\ln K_d$ primary	40	–0.33	1.16	–0.70	0.04	–1.79	0.082
$\ln K_d$ activated– $\ln K_d$ secondary	21	–0.57	1.78	–1.38	0.24	–1.47	0.157
$\ln K_d$ activated– $\ln K_d$ digested	19	0.58	0.93	0.13	1.03	2.73	0.014
$\ln K_d$ primary– $\ln K_d$ secondary	51	0.42	1.16	0.09	0.75	2.58	0.013
$\ln K_d$ primary– $\ln K_d$ digested	19	1.18	0.99	0.70	1.65	5.19	<0.001
$\ln K_d$ secondary– $\ln K_d$ digested	16	1.52	1.57	0.69	2.36	3.88	0.001

*t* = Student's *t*-statistic. *p* = *p*-value associated with the *t*-test.

primary clarifier (Fig. 1). As shown above, partitioning in activated sludge was similar to that in primary sludge. This means that partitioning in the WWTP would be similar in all compartments of the WWTP up to and including the activation tank.

It should be noted that, although the average reported  $K_d$  values for activated and primary sludge were found to be similar, a higher variability in  $K_d$  values was observed for some APIs with primary sludge than for activated sludge. For example, in primary sludge,  $K_d$  values ranging from 194 to 501 were reported for the anti-inflammatory diclofenac, from 20 to 314 for the anti-convulsant carbamazepine, from 46 to 460 for the cardiovascular drug atenolol, from 32 to 320 for the antibiotic sulfamethoxazole and from 251 to 427 for the antibiotic trimethoprim. This may have been due to differences in the location of the sampling point. In most cases primary sludge was collected after the first clarifier, while in a few instances material was collected by sedimentation/filtration of influent wastewater. By comparison, in activated sludge the variability in  $K_d$  values was lower, ranging from 16 to 128 for diclofenac, 17 to 135 for carbamazepine, 30 to 64 for

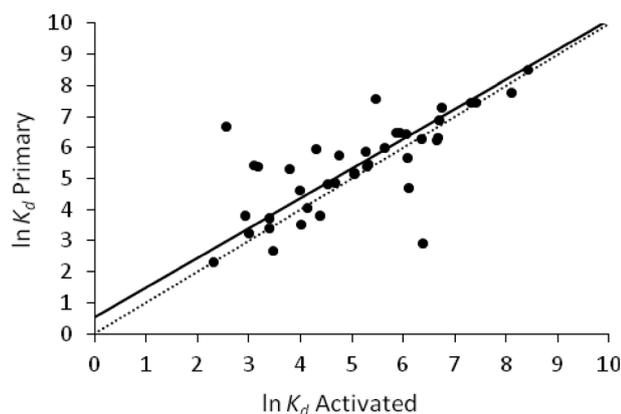
atenolol, 77 to 282 for sulfamethoxazole and 119 to 253 for trimethoprim (Table 2). This was attributed to the activated sludge being a more homogeneous material due to the aeration process used in the activation tank. These differences aside, analysis of the available data suggests that using either activated or primary sludge would lead to similar measured values of  $K_d$ .

#### Activated and secondary sludge

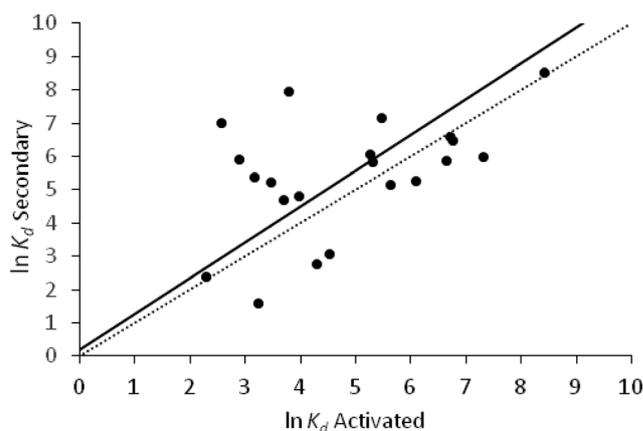
The correlation coefficient between the  $\ln K_d$  values of activated and secondary sludge was 0.48 with a *p*-value = 0.027 (Table 3). This was lower than the correlation coefficient between activated and primary sludge. The paired sample *t*-test indicated that there was no significant difference between the  $\ln K_d$  values for activated and secondary sludge.

The regression analysis of these two sludge types for the available dataset (*n* = 21) gave a RMSE of 1.22 (Fig. 3).

In a WWTP, secondary sludge is formed mainly from activated sludge which has been allowed to settle, and their physico-chemical properties, with the exception of TSS, are



**Fig. 2** Plot of  $\ln K_d$  values reported for active pharmaceutical ingredients in primary sludge ( $\ln K_d$  primary) against activated sludge ( $\ln K_d$  activated). The orthogonal regression equation was  $\ln K_d$  primary =  $0.96 \ln K_d$  activated + 0.54 (solid line), RMSE = 0.81, *n* = 40 compounds. The dotted line indicates the diagonal ( $y = x$ ).



**Fig. 3** Plot of  $\ln K_d$  values reported for active pharmaceutical ingredients in secondary sludge ( $\ln K_d$  secondary) against activated sludge ( $\ln K_d$  activated). The orthogonal regression line was  $\ln K_d$  secondary =  $1.08 \ln K_d$  activated + 0.20 (solid line), RMSE = 1.22, *n* = 21. The dotted line indicates the diagonal ( $y = x$ ).



broadly similar (Table 1). This would suggest that the sorption properties of these two sludges would be similar, but this was not supported by our analysis of the data reported in the literature. It is difficult to explain these statistical results. Sorption of pharmaceuticals to sewage sludge is a complex process. Unlike some other environmental media, such as soils, the partitioning mechanisms involved are not well understood. The bulk properties commonly used to characterise sewage sludge may not be adequate to describe fully these interactions and the inclusion of other properties of the matrix such as cation-exchange capacity may be required.

### Activated and digested sludge

A higher correlation coefficient (0.82,  $p < 0.001$ ) was found between the  $\ln K_d$  values of activated and digested sludge (Table 3). The paired sample  $t$ -test gave  $p = 0.014$ , showing no difference between activated and digested sludge; however, the confidence interval did not contain 0 (Table 4). The orthogonal regression of these  $\ln K_d$  values ( $n = 19$ ) gave a RMSE of 0.84 with a regression coefficient of 0.99 and intercept 0.20 (Fig. 4).

These observed differences between the sorptive properties of activated and digested sludge may be influenced by their physico-chemical properties and the availability of oxygen. Generally, digested sludge is more basic than activated sludge (Table 1). The pH of the sludge affects the sorption of ionic compounds and will be more influential for APIs with  $pK_a$  values in the range 6–9. There were differences in other physico-chemical properties, such as TOC, TSS and VSS, between these sludge types but their effect on sorption is more difficult to predict. Sorption may also have been affected by local variations of the bacterial population in the digester.

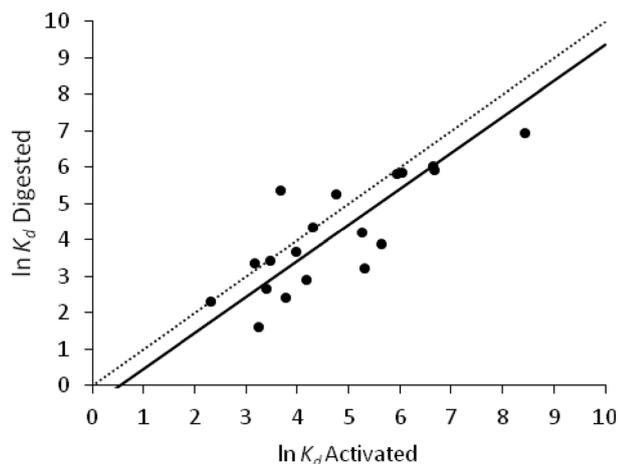


Fig. 4 Plot of  $\ln K_d$  values reported for active pharmaceutical ingredients in digested sludge ( $\ln K_d$  digested) against activated sludge ( $\ln K_d$  activated). The orthogonal regression line was  $\ln K_d$  digested =  $0.99 \ln K_d$  activated  $-0.54$  (solid line), RMSE = 0.64,  $n = 19$ . The dotted line indicates the diagonal ( $y = x$ ).

### Primary and secondary sludge

In a WWTP a portion of primary and secondary sludge is mixed to form the sludge which is fed in to the anaerobic digester (Fig. 1). Secondary sludge is formed after the activation treatment in which microorganisms biodegrade some compounds and generate new biomass material. Therefore, the primary and secondary sludge may be expected to have different sorption characteristics for APIs. The correlation coefficient between the  $\ln K_d$  values of primary and secondary sludge was 0.85 with a  $p$ -value  $< 0.001$  (Table 3). The paired sample  $t$ -test gave a  $p$ -value of 0.013, above the critical value, but the confidence interval was slightly to the right of 0, providing some evidence that primary and secondary sludge were similar in terms of their partitioning properties.

The orthogonal regression of the  $\ln K_d$  values for primary and secondary sludge ( $n = 51$ ) gave a RMSE of 0.81, a regression coefficient of 1.06 and intercept  $-0.81$  (Fig. 5). This indicated that the sorption properties of APIs between primary and secondary sludge were correlated, with APIs sorbed more strongly to primary sludge than to secondary sludge (Fig. 5).

Some differences in the physico-chemical properties of primary and secondary sludge are apparent (Table 1). Most notably, TSS is markedly lower for secondary sludge compared with primary sludge. A smaller difference between TOC values suggests that the higher TSS value in primary sludge is mainly due to inorganic material.

### Primary/secondary and digested sludge

Anaerobic digestion of sludge leads to changes in the physico-chemical properties of the sludge (Table 1). Therefore the partitioning behaviour for both primary and secondary sludge was expected to differ from the behaviour for anaerobically digested sludge. However, both primary and secondary

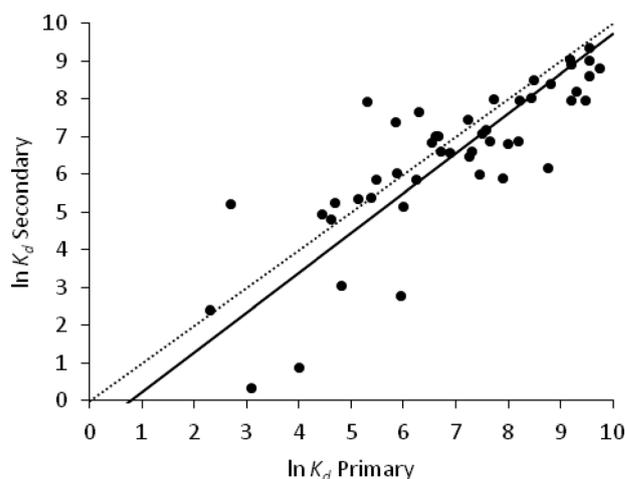


Fig. 5 Plot of  $\ln K_d$  values reported for active pharmaceutical ingredients in secondary sludge ( $\ln K_d$  secondary) against primary sludge ( $\ln K_d$  primary). The orthogonal regression line was  $\ln K_d$  secondary =  $1.06 \ln K_d$  primary  $-0.81$  (solid line), RMSE = 0.81,  $n = 51$ . The dotted line indicates the diagonal ( $y = x$ ).







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