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Perspectives of coagulation/flocculation for the removal of pharmaceuticals from domestic wastewater: A critical view at experimental procedures

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ABSTRACT

Literature frequently reports that colloids in aqueous matrices sorb a large fraction of pharmaceuticals. Since coagulation/flocculation removes colloids, it is expected that coagulation/flocculation in principle should be useful in concentrating pharmaceuticals in wastewater treatment, which would facilitate the treatment of these refractory compounds. In our present work, we researched the potential of coagulation/flocculation for removing pharmaceuticals from raw sewage. Results from jar tests showed that pharmaceuticals are hardly removed from sewage with coagulation/flocculation. To investigate the discrepancy between reported colloidal sorption and the lack of removal when removing colloids, we tested a commonly applied experimental setup, which makes use of ultra-filtration (UF), for determining the colloidal sorption of pharmaceuticals. The UF method under research was compared with an assessment making use of flocculation. Both methods, UF and flocculation, showed similar removal of colloids. However, during UF, the retention of pharmaceuticals reached values up to 93 ± 4 %. In contrast, when removing the colloids with flocculation, no pharmaceutical removal was observed. These results confirm that it is very likely to introduce an analysis bias in using UF membranes in the determination of colloidal sorption of pharmaceuticals. In fact, results predict an over-estimation caused by a direct retention of pharmaceuticals without any binding to colloidal matter. Overall results of the current work show that pharmaceuticals hardly sorb to colloids and herewith the absence of removal of pharmaceuticals during coagulation/flocculation is explained.

1. Introduction

In general, pharmaceuticals consumed by humans are subsequently transferred into the sewer through human excreta. Since pharmaceuticals in many cases are recalcitrant towards biological degradation, sewage treatment plants (STPs) often do not completely remove these pharmaceutical compounds [1,2]. Therefore, the main source of pharmaceuticals in surface waters is often STP effluent discharge [3]. Although the pharmaceutical concentrations in these discharges are low (ng/L to μg/L) [1,4–8], enhanced removal is necessary in order to prevent adverse effects on ecology and accumulation in the aquatic environment, especially when considering an increase in pharmaceutical consumption in Europe is observed over time [9].

1.1. Mechanisms of removal of organic micro pollutants with coagulation/flocculation

Treatment of organic micro pollutants (OMPs) in low concentrations, such as pharmaceuticals, is challenging. Hence current practice of treatment in common STPs is not sufficient yet [7,10,11]. A feasible strategy to enhance the treatment effectiveness might be to concentrate OMPs in the sludge stream prior to super critical sludge gasification. The research platform of the Dutch Water Authorities showed that supercritical gasification of sewage sludge is potentially a feasible option for future STPs [12] and this treatment would likely destroy all pharmaceutical molecules. In relatively clean water such as drinking water or ultra-pure water, the removal of pharmaceuticals by coagulation/flocculation is very poor [13–16]. However, adding organic matter before coagulation/flocculation can increase the pharmaceutical removal significantly [16]. In wastewaters rich in organic compounds, such as sewage, OMP removal up to 80 % is observed using coagulation/flocculation [4,17]. Choi et al. [18] showed that antibiotics are removed to approximately 50 % from river water applying poly-aluminium chloride. These results indicate that the presence of organic matter may enhance the removal of pharmaceuticals during coagulation/flocculation.

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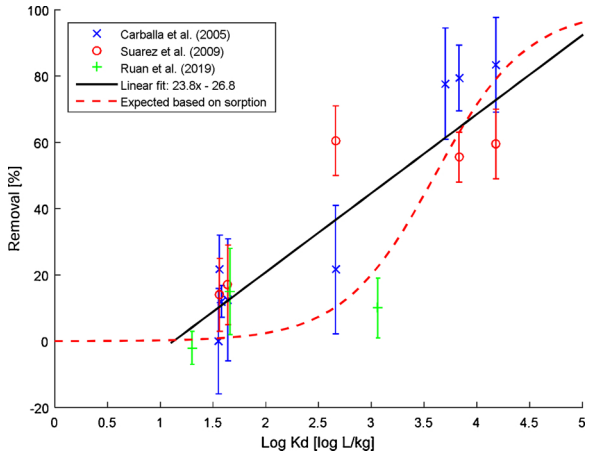

Fig. 1. Removal efficiency of pharmaceuticals and fragrances by coagulation of raw sewage measured by Carballa et al. [4], Suarez et al. [17] and Ruan et al. [1], plotted against their log K_d values (in log L/kg). A linear fit through all data points yielded the following equation: Removal % = 23.8*Log Kd – 24.8, with $r^2 = 0.63$. Although negative removals are not physically expected, all the values from the mentioned papers are included for completion. The dashed red line represents the percentage of pharmaceuticals sorbed to solids in wastewater with a typical total suspended solids concentration of 250 mg/L, which is in fact the percentage that can be expected to be removed by flocculation/coagulation. The K_d values are taken from Ternes et al. [48] except for celestolide (taken from Fernandez-Fontaina et al. [42] and naproxen taken from Barron et al. [41].

Coagulation/flocculation comprises of two different processes [19]: 1. the tendency for suspended matter to form larger aggregates promoted by altered surface properties and 2. the removal of dissolved matter by precipitation. To our knowledge, precipitation of pharmaceuticals in wastewater as a mean of removal has not been reported in literature. Therefore, if removal of pharmaceuticals due to coagulants/flocculants is observed, the responsible removal mechanism is likely linked to the removal of suspended matter that acts as a vehicle for pharmaceuticals. This would imply that there is a relation between sorption of pharmaceuticals to suspended matter (expressed by the adsorption-desorption distribution coefficient K_d [L/kg]) and their removal efficiencies by coagulation/flocculation. This hypothesis is supported by results of Carballa et al. [4], Suarez et al. [17] and Ruan et al. [1], that show that coagulation in raw sewage yields a more or less linear relationship between removal efficiencies and log K_d values of OMPs (Fig. 1); the higher the sorption, the higher the removal efficiency. In addition, the observation is made that pharmaceuticals in MilliQ water, so without solids, are hardly removed by coagulation [16].

1.2. Plain sorption mechanism

The pharmaceuticals sorbed to solids, described by the sorption coefficient K_d, may be removed from wastewater by removing the solids. In that case, pharmaceutical removal during coagulation/flocculation can be predicted based on the K_d values. In this study, this mechanism is referred to as *plain sorption*. In Fig. 1 the percentage of sorbed pharmaceuticals in wastewater with a typical total suspended solids (TSS) concentration of 250 g/L is displayed (red dashed line), plotted against the log K_d. When a suspended solids removal efficiency of 100 % due to coagulation/flocculation is assumed, the red dashed line describes the removal of pharmaceuticals by the *plain sorption mechanism*. The formula of this line is given in Eq. (1), with K_d as sorption coefficient (in L/kg) and TSS as total suspended solids (in kg/L).

$$\text{Removal percentage} = 100 \cdot \frac{k_d}{\left(\frac{1}{TSS} + k_d\right)} \quad (1)$$

In the higher log K_d range (> 3.5), the observed removal percentages correspond well with the percentages of predicted removal. However, in the lower log K_d ranges (< 3.5), lower removal is predicted by the *plain sorption* mechanism then what was measured. In order to optimize the removal efficiency of pharmaceuticals, the mechanism of removal by flocculation and coagulation should be understood, starting with the explanation of the difference in predicted and empirically observed removal in raw sewage.

1.3. The colloid mechanism

In Fig. 1 there seems to be a discrepancy between predicted removal based on the K_d value (red dashed line) and observed removal in the low K_d value range. This discrepancy could be explained by the role of colloids. Colloids are often said to play an important role in the fate of pharmaceuticals [20–23]. Table 1 shows the sorption to colloids reported in literature which indicates that even pharmaceuticals with low reported K_d values, such as carbamazepine, can have strong affinity with colloids. Since coagulation/flocculation can be applied to remove particulates of colloidal size [19] and colloids are reported to bind a disproportionally large fraction of pharmaceuticals, colloids could explain the difference between expected removal of pharmaceuticals during coagulation/flocculation and observed removal. The possibility of removal of colloidally sorbed pharmaceuticals with coagulation/flocculation, is referred to as the *colloid mechanism* in this study. With the *colloid mechanism*, a larger fraction of pharmaceuticals can be removed from water with coagulation/flocculation than what is expected based on the K_d value (*plain sorption mechanism*) because there is a disproportionally large fraction of pharmaceuticals sorbed to colloids.

1.4. Aims of this study

The hypothesis of this study is that pharmaceuticals can be removed from wastewater by coagulation/flocculation of pharmaceutical containing colloids. This was tested by studying the removal of 16 measured pharmaceuticals in raw wastewater when applying coagulation/flocculation. After it appeared that pharmaceuticals could not be removed in the mentioned test, we investigated the discrepancy between reported colloidal sorption of pharmaceuticals and the lack of removal when removing colloids. To this end we tested a commonly applied experimental setup for determining the colloidal sorption of pharmaceuticals. Colloids were removed from a solution containing pharmaceuticals in two ways: by commonly applied ultra-filtration (UF) and by flocculation. The removal efficiencies of pharmaceuticals were compared.

2. Materials and methods

2.1. Flocculation experiment

The flocculation of wastewater was conducted using municipal sewage (pH = 7.3, T = 18.0 °C, TSS) of 250.5 ± 6.3 mg/L, volatile suspended solids (VSS) of 185 ± 6.3 mg/L) of the sewage treatment plant (STP) Leiden Noord, The Netherlands (140.000 P.E.). Raw sewage was collected as a grab sample during dry weather conditions. On this batch of sewage, three types of settling conditions were applied. As a reference condition (RS) were sewage was settled without the addition of coagulants/flocculants. In a second batch, cationic acrylamide based low charged flocculant (Core Shell 71305) was dosed to a final concentration of 10 ppm (sample C). The third sample was treated with a mixture of organic coagulant (Nalco 8190; poly ampholitic; high MW) and the cationic flocculant Core Shell 71305 with final concentrations of 10 and 2 PPM respectively (sample M). The flocculant dosages were

Table 1
Overview of reported colloidal sorption of several pharmaceuticals and endocrine disruptors.

	Colloid fraction	Propranolol	Sulfonamides	Carbamazepine	Indomethacine	Diclonfenac	Estrogens	Endocrine disruptors
STP effluent, river water and ground water	1 kDa-7μm	45 %	40 %	22 %	39 %	37 %		
STP effluent	1 kDa-1.5μm						1-60 %	
STP effluent, river and sea water	1 kDa- 0.7 μm							10-29 %
STP effluent	1 kDa- 0.7 μm	10-40 %	4-12 %					
River water	5 kDa- 0.7 μm					22–33 %		
Lake water	1 kDa – 0.7 μm		7 % – 35 %					
Colloids extracted from topsoil sedimentation	< 1 μm							
STP influent	1 kDa-1.0 μm		5 %- 60 %	7 % – 10 %	12 % – 22 %		8 % – 48 %	

	Tamoxifen	Meclofenamic Acid	Ketoprofen	Naproxen	Clofibric Acid	Ibuprofen	Tetracycline	Reference
STP effluent, river water and ground water								Maskaoui and Zhou [24]
STP effluent								Holbrook et al. [25]
STP effluent, river and sea water								Zhou et al. [26]
STP effluent	31-43 %	6.5-26 %						Yang et al. [27]
River water			10-14 %	17-36 %	22–33 %	9-28 %		[20]
Lake water								[28]
Colloids extracted from topsoil sedimentation							50 %	[22]
STP influent						0 % – 11 %		[23]

Table 2
Removal efficiencies (%) of pharmaceuticals during settling without chemical additions (RS); flocculation with cationic (C) flocculant and flocculation with organic coagulant (M).

	RS	C	M
Atenolol	14 ± 4	−5 ± 6	2 ± 8
Atorvastatin	−17 ± 1	−2 ± 1	7 ± 1
Bezafibraat	−23 ± 5	21 ± 3	−5 ± 3
Carbamazepine	14 ± 6	−11 ± 5	13 ± 6
Enalapril	3 ± 3	−10 ± 3	1 ± 8
Gemfibrozil	12 ± 4	−4 ± 6	−5 ± 4
Hydrochlorthiazide	−6 ± 6	−7 ± 7	4 ± 6
Ibuprofen	−5 ± 5	−13 ± 6	−3 ± 5
Lidocaine	−9 ± 8	−9 ± 7	−4 ± 7
Losartan	−10 ± 9	−13 ± 7	−18 ± 9
Metoprolol	28 ± 4	−10 ± 4	3 ± 7
Oxazepam	−2 ± 3	16 ± 2	19 ± 2
Sotalol	16 ± 3	−7 ± 3	4 ± 7
Temazepam	−6 ± 4	15 ± 2	19 ± 4
Theophylline	16 ± 5	−7 ± 4	−32 ± 6
Trimetoprim	−17 ± 4	−7 ± 3	−2 ± 4

based on optimal turbidity removal in previous tests (data not shown). The blade used for stirring was 25 by 75 mm in total (shaft attached in the middle). The beaker sample size was 1.8 L. The flocculant and/or coagulant were added during 3 min stirring at 200 rpm (velocity gradient 400 G/s), followed by 60 s of stirring at 30 rpm (velocity gradient 11 G/s) and a 30 min settling period. Pharmaceutical concentrations as well as general wastewater parameters were analysed.

2.2. Humic substance removal experiments

A test was performed to verify the possibility of an analysis bias in ultra-filtration (UF) for the determination of colloidal sorption of pharmaceuticals. To this end, humic substances (HS) removal in combination with pharmaceutical removal by UF was compared to removal by coagulation/flocculation. A 1.0 g/L stock solution of HS was prepared by adding humic salts (Sigma 53680) into a 100 mM phosphate buffer adjusted to pH 13 and stirred for 1 h. The pH was adjusted to 7 with hydrochloric acid and the stock solution was filtered over AP40 glass fibre filters under vacuum. From the stock solution, 100 mg/L HS solutions were prepared for the UF and coagulation/flocculation experiments. The solution contained 43 commonly used pharmaceuticals (Table 3) in concentrations of 600, 100 and 20 ng/L (depending on the compound). In half of the samples, HS were removed by coagulation/flocculation using Caldic (Rotterdam, the Netherlands) P1502 cationic flocculant. Pharmaceutical and HS concentrations before and after flocculation were measured in triplicate to determine the removal efficiencies. For the other half of the samples, UF was performed with a ceramic 1 kDa tubular membrane as described in Shang et al. [29], operated at 5 bar trans membrane pressure and 1 m/s cross flow velocity. A 20 L stock solution was used. After 30 min of operating the UF setup, a sample of 1 L was taken from the permeate and feed solution and analysed for pharmaceutical and HS concentrations. The pharmaceutical removal efficiencies were determined with clean water removal (10 mM phosphate buffer) as a blank.

2.3. Analytical techniques

Test kits (Hach Lange, Germany) were used to measure the concentrations of total phosphorus (LCK 350), total nitrogen (LCK338) and COD (LCK 514). TSS and VSS were measured according to standard methods [30]. Turbidity was measured with a Hach 2100 N (Hach Lange, Germany). The pharmaceutical concentrations were measured, using an ultra-performance liquid chromatograph coupled to a mass spectrometer (UPLC-triple quad MS; Waters Micromass, United States, MA). Before analysis, 100 mL of the wastewater samples were 10x

Table 3
The log K_d, log K_{ow} and native concentrations in wastewater of the investigated pharmaceuticals. Log K_{ow} values obtained from Chemspider.com. Pharmaceuticals, which shows a native concentration in wastewater are not bound to colloids, except for oxazepam, metoprolol, temazepam and paroxetine.

Compound	Log K_{ow} []	Charge at neutral pH []	Measured Log K_d primary sludge [log L/Kg]	Log K_d of primary sludge from literature [log L/Kg]	Sewage concentration [ng/L]
Atenolol	0.43	1	1.66 ± 0.00	1.04[4] 1.98 ± 0.63[5]	2844 ± 26
Atorvastatin	5.08	−1	2.04 ± 0.05	2.00 ± 0.17[7]	54 ± 2
Bezafibraat	3.99	−1	1.913 ± 0.00	–	258 ± 5
Bisoprolol	2.20	1	2.39 ± 0.00	–	50 ± 1
Carbamazepine	2.77	0	1.66 ± 0.14	1.55[2] 1.40[4] 2.50 ± 0.65[5] 1.95 ± 0.37[9]	917 ± 11
Chloramphenicol	0.88	0 to − 1	3.09 ± 0.61	–	N.D.
Clofibrinic acid	3.84	0	1.573 ± 0.01[1]	0.7[4]	N.D.
Coffeine	−0.55	0	N.A.	1.15[4]	30923 ± 1205[1]
Cyclofosfamide	0.10	0	1.889 ± 0.01	1.74 ± 0.36[3]	N.D.
Diazepam	3.08	0	2.345 ± 0.03	1.64 ± 0.59[3] 2.14 ± 0.19[9]	N.D.
Diclofenac	4.26	−1	2.310 ± 0.02[1]	1.82 ± 0.35[2] 2.66 ± 0.07[3] 2.02[4] 2.29 ± 0.69[5] 2.13 ± 0.25[6] 2.18 ± 0.22[9]	N.D.
Enalapril	0.59	0 to -1	1.87 ± 0.03	–	277 ± 11
Fenazon	1.22	0	1.945 ± 0.02	–	N.D.
Fenofibrate	5.28	0	N.A.	–	30 ± 39
Fenofibric acid	4.36	0	2.023 ± 0.00	–	N.D.
Furosemide	1.75	−1	1.449 ± 0.05	2.10 ± 0.32[6] 220[10]	1377 ± 68
Gemfibrozil	4.39	1 to 2	2.40 ± 0.07	1.36 ± 1.00[5] 2.11 ± 0.27[9]	299 ± 26
Hydrochlorthiazide	−0.58	0	0.68 ± 0.38	1.91 ± 0.23[6]	2752 ± 233
Ibuprofen	3.84	1 to 2	2.26 ± 0.00[1]	1.58 ± 0.38[3] 0.98 ± 0.33[5] 2.32 ± 0.232	4103 ± 360
Ifosfamide	0.10	0	1.90 ± 0.03	1.34 ± 0.64[3]	N.D.
Iopromide	−0.44	0 to 1	1.86 ± 0.00	0.84[2]	40517 ± 478
Ketoprofen	3.61	0	1.76 ± 0.04	2.35 ± 0.80[5]	N.D.
Lidocaine	2.84	1	2.33 ± 0.00	–	234 ± 12
Lincomycin	−0.32	1	1.94 ± 0.03	–	N.D.
Losartan	5.08	0 to -1	1.26 ± 0.81[1]	–	3877 ± 50
Metformin	−1.36	1	2.34 ± 0.00	–	89298 ± 916[1]
Metoprolol	1.76	1	1.30 ± 0.00	1.26[4]	1127 ± 16
Naproxen	2.88	0	1.85 ± 0.00	1.00[2] 1.56[4] 2.16 ± 0.23[9]	2797 ± 56
Oxacillin	1.70	1	2.18 ± 0.03	–	4 ± 14
Oxazepam	2.92	0	1.89 ± 0.32	2.90 with (R^2 = 0.90)[8]	602 ± 3
Paracetemol	0.91	0	N.A.	1.51[4]	29305 ± 268[1]
Paroxetine	3.15	0	N.A.	4.15 with (R^2 = 0.96)[8]	112 ± 10
Pravastatin	1.65	−1	1.93 ± 0.00	–	1694 ± 98
Primidone	1.12	0	1.99 ± 0.00	–	9 ± 2
Propranolol	2.58	1	2.29 ± 0.00	2.52[4] 2.81 ± 0.75[5]	24 ± 2
Salicylic acid	1.98	−1	2.30 ± 0.54	1.36[3]	34535 ± 1165
Sotalol	−0.40	1	2.34 ± 0.00		3012 ± 14
Sulfametoxazol	0.79	0 to -1	2.30 ± 0.10	1.36[2] 1.18[4] 0.51 ± 1.41[5] 2.21 with (R^2 = 0.77)[8] 2.43 ± 0.38[9]	288 ± 7
Sulfaquinoxaline	3.08	1	2.25 ± 0.03	–	N.D.
Temazepam	2.79	0	2.27 ± 0.31	–	355 ± 4
Theophylline	−0.77	0 to 1	1.40 ± 0.40	–	3811 ± 98
Tiamulin	4.50	1	2.88 ± 0.00	–	N.D.

(*continued on next page*)

Table 3 (*continued*)

Compound	Log K_{ow} []	Charge at neutral pH []	Measured Log K_d primary sludge [log L/Kg]	Log K_d of primary sludge from literature [log L/Kg]	Sewage concentration [ng/L]
Trimetoprim	1.28	1	2.49 ± 0.00	1.83[4] 2.63 ± 0.56[5] 2.59 with (R^2 = 0.98)[8] 2.30 ± 0.16[9]	122 ± 3

[1] Values are an indication.
[2] [32] values for mesophilic digested sludge.
[3] [48].
[4] [41], values for digested sludge.
[5] [46].
[6] [45].
[7] [45], values for wastewater.
[8] [43].
[9] [44], values for secondary sludge.
[10] [47], unknown what type of sludge is used.

diluted and pre-treated with solid phase extraction (SPE) using 6CC HLB Waters Oasis cartridges and eluted with HPLC grade methanol. In the analysis, 43 pharmaceutical compounds were measured as named in Table 3. The pharmaceuticals were separated by injection of 50 µL extract on an UPLC (Waters Acquity; Waters, Etten-Leur, the Netherlands) equipped with a binary pump, a Waters Acquity UPLC BEH C18 column. The eluate was ionised using electrospray ionisation and the pharmaceuticals were analyzed on a Quattro Xevo triple quadrupole Mass selective Detector (Waters Micromass). Quantification was performed using an external calibration series of 8 concentrations of a standard mixture of the selected pharmaceuticals. Details of the analysis method can be found in [31]. The recovery of pharmaceuticals from wastewater during the SPE-extraction and analysis on UPLC-tQ-MS was investigated by spiking a parallel sample. Data with the following criteria were included in the results if the concentrations were > 10 ng/L; the recoveries between 50 % and 140 % and the variation coefficient of removal as < 10 % points. Flocculated wastewater was filtered through a Whatman Grade 1 filter (11 µm) and diluted (10x) before analysing the particles size distribution (PSD). The HS concentrations were determined spectrophotometrically by absorption at 465 nm in combination with a calibration line. PSD was determined using a Hiac (Indianapolis, United States) particle counter within the range 0.4 µm–5 µm. The volume percentages of wastewater fractions were determined using a Malvern Mastersizer 2000 and was performed by Delft Solids Solutions in Delft, the Netherlands.

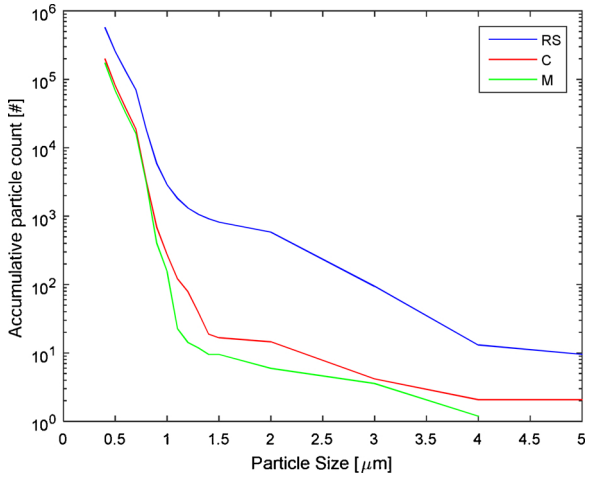

Fig. 2. Particles counts between 0.4 and 5.0 µm of raw sewage after settling (RS) and after chemically enhanced settling with flocculant (C) and coagulants (M).

2.4. K_d value determination

The K_d values of 43 pharmaceuticals were determined by using an adjusted method of Carballa et al. [32]. 1 L of primary sludge from STP Leiden Noord (TS = 17 g/L) was spiked 50–1500 ng/L with 43 pharmaceuticals and incubated overnight at 4 °C. An unspiked sample was incubated under the same conditions. From both samples, both the solid and the liquid phases were analysed for pharmaceutical concentrations. An extra internal standard spiked before injection in the UPLC showed that there was a strong suppression of the signal by the solid matrix. Therefore, K_d values were determined based on the aqueous phases of the experiments only. The assumption was made that there is no bioconversion during the over-night incubation.

3. Results and discussion

3.1. Flocculation of raw sewage

To test the possibility of removing pharmaceuticals from sewage, a jar test was performed. The addition of coagulant (sample M) and flocculant (sample C) showed to have a positive effect on the removal of suspended solids and COD compared to settling without chemical addition (RS). COD removal was enhanced with 54 % and 52 % in sample C and sample M, respectively. The TSS removal was doubled in sample C and M compared to RS. With flocculant (C) and coagulant (M) addition, the removal of small particles of 0.4–5.0 µm (Fig. 2) was increased with 65 % and 50 %, respectively.

The concentrations of 43 pharmaceuticals were determined before and after settling in the jar tests. The removal efficiencies by settling, with or without coagulant/flocculant dosing were calculated (Table 2). Because the sewage was not spiked with pharmaceuticals, only pharmaceuticals already present in the sampled sewage were detected. In the column 'Sewage concentration' of Table 3, the influent concentrations are given.

The data show that there is almost no removal of the measured pharmaceuticals in any settling method (Table 2). This is in concordance with the *sorption only mechanism*: the log K_d values of the pharmaceuticals range from 0.68 (hydrochlorthiazide) to 2.49 (trimethoprim) and thus a removal between 0%–7% was predicted following this theory. The negative removals were caused by the experimental error.

3.2. Discrepancy between colloidal sorption and removal observed in this work

Although colloids were removed with coagulation/flocculation (difference between RS and C or M in Fig. 2), no clear pharmaceutical

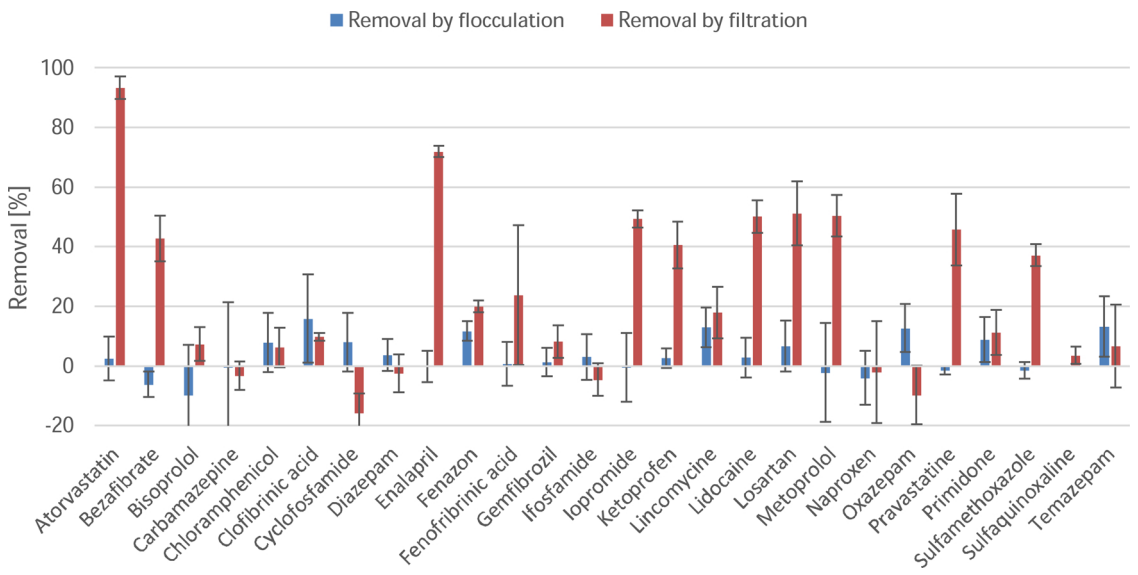

Fig. 3. Removal efficiencies of pharmaceuticals when removing humic substances by flocculation and ultra-filtration. When using ultra-filtration, significant removal can be observed of pharmaceuticals, often leading to the erroneous conclusion that pharmaceuticals are attached to colloids.

removal was observed (Table 2). A removal was expected regarding the reported sorption of pharmaceuticals to colloids in literature (Table 1). This difference may be explained by an analysis bias in the quantification of colloidally bound pharmaceuticals: in many studies colloidal sorption is determined by UF with a nominal size exclusion cut-off level for colloids as low as 1 KDa [23–27]. This is very close to the weight of pharmaceutical molecules themselves (0.2-0.3 kDa). Using these small pore sizes in the filtration of colloids raises the question if retaining pharmaceuticals is a matter of sorption to retained colloids, as is often stated, or mere retention of non-sorbed pharmaceutical molecules in the filter during filtration. In matrices with relatively little amounts of colloids such a ground and drinking water, a filtration over a filter with nominal pore sizes between 0.09 kDa – 0.3 kDa retains over 90 % of the pharmaceuticals [33–35]. In the lower range of the cut-off (0.09 kDa), the retention is dominated by steric size exclusion. In the higher range (0.270 kDa) both steric size exclusion and electrostatic repulsion causes the removal of these large molecules [33,36,37]. However, also larger pore sizes have been shown to retain pharmaceuticals; Burba et al. [38] showed that over 70 % of diclofenac in colloid free water is retained with a 1 kDa cut-off polyethersulfon (PES) membrane. But also, in matrices with colloids, the pharmaceuticals retention of the membrane may be guided by other factors than colloidal sorption: for 0.270 kDa membranes, cake built-up on the membrane surface can decrease pharmaceutical retention [39]. Therefore, using membrane filtration with membrane pore sizes of $\leq$1 kDa for colloidal sorption determination, may yield unreliable results because of direct filtration of the pharmaceuticals or by pharmaceutical interactions with the cake layer on the membrane.

3.3. Ultra-filtration of pharmaceuticals

To test the possibility of direct removal (retention) of unbound pharmaceuticals by UF, an experiment was performed in which colloids in a solution with pharmaceuticals, were removed in two ways: by UF and by flocculation. The pharmaceutical removal during the removal of colloids (in the form of HS) by UF was compared to pharmaceutical removal with colloids removal by flocculation. In Fig. 3 the pharmaceutical removal efficiencies of the UF and flocculation experiment are shown. In both cases, the removal of HS was near complete: 91 % with UF and 85 % with flocculation. However, the pharmaceuticals were not removed in case of flocculation. When UF was applied, concomitant with the removal of colloids, the pharmaceuticals avorstatine, bezafibrate, enalapril, iopromide, ketoprofen, lidocaine, losartan, metoprolol and pravastatine were removed with efficiencies exceeding 40 %. No correlation was found between removal percentage of pharmaceuticals obtained by UF and the log K_d value or the octanol partition coefficient log K_{ow} (Table 3). Because the removal of HS with UF and flocculation were comparable, the difference in pharmaceutical removal efficiency cannot be explained by sorption to HS. These results show that the use of UF for determining colloidal sorption, may lead to overestimation of pharmaceuticals sorbed to colloids. What factors play a role in the removal with UF should be investigated further.

4. Conclusion

Pharmaceuticals were not removed from sewage by settling, even when coagulation/flocculation was applied. Therewith the hypothesis of this study was rejected. Despite the reports of colloidal sorption of pharmaceuticals in literature, and the fact that colloids are removed during coagulation/flocculation, the measured 16 pharmaceuticals were apparently not attached to these colloids. For the determination of colloidal sorption of pharmaceuticals, many authors use a lower cut-off as low as 1 kDa for colloids during UF filtration. In a comparison of pharmaceutical removal in an experiment where colloids were removed by coagulation/flocculation and an experiment where colloids were removed by UF, it was observed that the 1 kDa cut-off can cause direct retention of pharmaceuticals. Direct retention may lead to an overestimation of colloidal sorption of pharmaceuticals. This possible overestimation using UF for estimating colloidal sorption of pharmaceuticals may explain why there is no observed removal of pharmaceuticals when applying coagulation/flocculation on sewage. It can be concluded that coagulation/flocculation is not a good method to concentrate pharmaceuticals during the treatment of municipal sewage.

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Declaration of Competing Interest

There are no conflicts of interest in the publication of the manuscript.

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