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# Comparison of four extraction methods for the analysis of pharmaceuticals in wastewater

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ABSTRACT

As one category of the most urgent emerging pollutants, pharmaceuticals have provoked much public and scientific attention due to widespread contamination in aquatic environment. In this study, two active methods by Oasis HLB and MCX and two passive methods by XAD-16 and XAD-16/7 were evaluated for determining the concentrations of 10 pharmaceuticals (carbamazepine, clofibric acid, diclofenac, gemfibrozil, ibuprofen, ketoprofen, naproxen, paracetomol, terbutaline and triclosan) in reclaimed wastewater. Recoveries of the target pharmaceuticals extracted by MCX were higher than HLB except for diclofenac and ketoprofen. For the passive methods, the addition of polar resin XAD-7 improved the recovery compared with the addition of XAD-16 only. The mean recoveries of the target analytes by XAD-16/7 ranged from 22 to 75.8%. The limit of quantification (LOQ) ranged between 25 and 280 ng/L. In addition, by comparing the accuracy and precision of XAD-16/7 method and MCX method, we further demonstrated that the XAD-16/7 method can be satisfactorily used for the analysis of pharmaceuticals in wastewater samples. We applied the method to some wastewater samples from sewage treatment plant (STP) nearby Riverside, CA to track the concentration change of pharmaceuticals in the treatment processes. The result shown that pharmaceuticals were effective reduced in STP mostly by activated sludge.



## 1. Introduction

The occurrence and fate of pharmaceutical residues in the aquatic environment have attracted considerable attentions in recent years [1–3]. These trace organic compounds have been detected in surface waters and even in drinking water. They and their metabolites entered the aquatic environment mainly via municipal or hospital wastewater discharges, and sewage treatment plant (STP) effluents [4–7].

Although the concentrations of these compounds are relative low in water (ng/L–μg/L), continuous release and chronic exposure to these substances can result in adverse effects on aquatic life and potential risk to human health [8]. Schwaiger et al. [9] and Mimeault et al. [10] reported that prolonged exposure to diclofenac and gemfibrozil causes toxic effects and bioaccumulation in fish. A review by Daughton and Ternes [11] suggested possible health effects of long-term exposure to pharmaceuticals via drinking water.

Therefore, it is important to develop analytical methods for the detection of pharmaceuticals at trace level to study their occurrence, behaviour, and fate in aquatic environments. Solid phase extraction (SPE) is the most commonly used method [12–17] for concentrating pharmaceuticals from water samples. Oasis HLB, with its hydrophilic–lipophilic balance, is widely used for the extraction of pharmaceuticals with a wide range of polarities and pH values [18–20]. Oasis MCX is a mixed-mode strong cation-exchanger, therefore provides both ion-exchange and reversed-phase retention and can adsorb polar, non-polar, neutral and cationic compounds simultaneously from aqueous media. MCX has been successfully employed to extract a wide range of pharmaceuticals and synthetic hormones from water matrices [21–23].

Passive samplers, due to relatively inexpensive and simple to use, are increasingly employed to assess the spatial and temporal trends of a wide variety of organic contaminants in environmental media [24–27]. The nonpolar XAD resins are generally used for adsorption of organic substances from aqueous systems. Magnér et al. [28,29] used XAD-2 to make bag-SPE for the analytes in wastewater. However, the extraction efficiencies were lower with the bag-SPE sampler compared to the HLB, especially for the polar compounds. XAD-7 is the only “moderately polar” XAD resin now available, and XAD-16 is more efficient than XAD-2 due to higher surface area [30], thus XAD-16 was used in this study. Furthermore, XAD-7 was added to test if it could improve the extraction efficiency in this study.

Most methods for the determination of trace pharmaceuticals utilize high/ultra performance liquid chromatography coupled with detection by tandem mass spectrometry (HPLC/UPLC–MS/MS) [16–23]. Tandem mass spectrometry (MS/MS), such as

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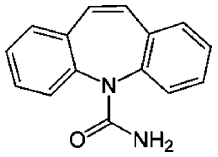
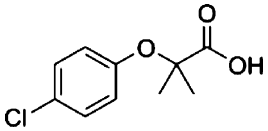
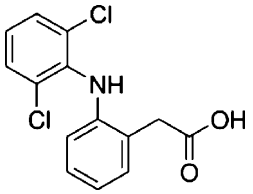
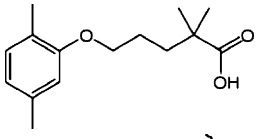
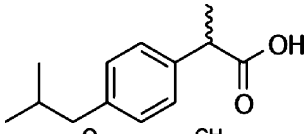
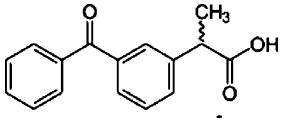
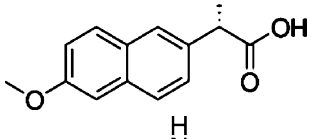
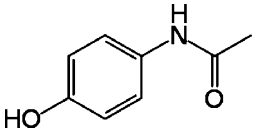
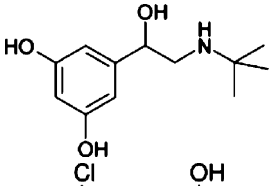
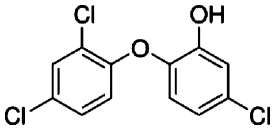
**Table 1**
CAS numbers, therapeutic class, log Kow, p*Ka* and structures for the selected pharmaceuticals.

| Compound | CAS | Type | log Kow[a] | p*Ka*[a] | Structure |
|---|---|---|---|---|---|
| Carbamazepine | 298-46-4 | Anti-epileptic | 2.67 | 13.94 |  |
| Clofibric acid | 882-09-7 | Lipid regulator | 2.6 | 3.46 |  |
| Diclofenac | 15307-79-6 | NSAID | 4.06 | 4.18 |  |
| Gemfibrozil | 25812-30-0 | Lipid regulator | 4.39 | 4.75 |  |
| Ibuprofen | 15687-27-1 | NSAID | 3.72 | 4.41 |  |
| Ketoprofen | 22071-15-4 | NSAID | 2.81 | 4.23 |  |
| Naproxen | 22204-53-1 | NSAID | 3.2 | 4.2 |  |
| Paracetamol | 103-90-2 | Analgesic | 0.7 | 1.7 |  |
| Terbutaline | 23031-32-5 | Broncho-dilator | 0.48 | 9.11 |  |
| Triclosan | 3380-34-5 | Antibiotic | 4.8 | 7.8 |  |

NSAID: non-steroidal anti-inflammatory drug.
[a] Values are from SciFinder Scholar™ 2006.

triple-quadrupoles (QqQ) and quadrupole time-of-flight (QTof), are often used for analysis of pharmaceuticals in environmental samples [16,28,29]. However, the matrix effect caused by co-eluting substances present in the extract is one of the major drawbacks of electrospray ionization (ESI) source, which could lead to signal suppression or enhancement, and then relatively high detection limits and decreased reproducibility [20,31,32]. Moreover, not all the environmental researchers can afford high cost of LC–MS/MS. In contrast, gas chromatography–mass spectrometry (GC–MS) is much more common in environmental laboratories. Using a GC–MS allows less costly and easier operation than LC–MS/MS. The main challenge in the analysis of pharmaceuticals using GC–MS is the high polarities due to functional groups with active hydrogens, such as –OH, amines, amides, et al. Therefore, derivatization was conducted prior to GC–MS to reduce the polarity and enhance their mobility on the GC column [15,33,34].

The objectives of this study were to (1) compare the extraction efficiency of two active methods, HLB and MCX; (2) develop a passive method by testing if addition of the XAD-7 would improve the extraction efficiency of XAD-16 only, and (3) assess the passive

**Table 2**
Retention times and mass spectrometric data for *tert*-BDMS derivatives of selected compounds.

| Compound | Retention time | Molecular weight | Primary ions | Secondary ions |
|---|---|---|---|---|
| Carbamazepine | 18.98 | 236.3 | 193 | 194, 293 |
| Clofibric acid | 12.42 | 214.6 | 143 | 273, 271 |
| Diclofenac-Na | 19.44 | 318.1 | 352 | 214, 409 |
| Gemfibrozil | 15.98 | 250.3 | 243 | 179, 307 |
| Ibuprofen | 12.82 | 206.3 | 263 | 264, 161 |
| Ketoprofen | 18.29 | 254.3 | 311 | 295, 312 |
| Naproxen | 17.13 | 230.3 | 287 | 185, 288 |
| Paracetamol | 15.20 | 151.2 | 322 | 379, 248 |
| Terbutaline hemisulfate salt | 19.03 | 274.3 | 482 | 483, 484 |
| Triclosan | 17.66 | 289.5 | 347 | 200, 345 |
| D3-Ibuprofen | 12.84 | 209.3 | 266 | 267, 268 |
| D3-Paracetamol | 15.22 | 154.2 | 325 | 251, 326 |

method by comparing with the better active method in objective (1).

## 2. Experimental

### 2.1. Chemicals and materials

Carbamazepine, clofibric acid, diclofenac (sodium salt), ketoprofen, naproxen, and terbutaline (hemisulfate salt) were purchased from MP Biomedicals (Solon, OH). Gemfibrozil, ibuprofen, and paracetomol were obtained from Sigma (St. Louis, MO) and triclosan from Fluka (St. Louis, MO). The surrogate standard, [$^2H_3$]-ibuprofen (D3-ibuprofen) and [$^2H_3$]-paracetomol (D3-paracetomol) were purchased from C/D/N Isotopes Inc. (Quebec, Canada). Chemical structures, CAS registry numbers of the compounds are shown in Table 1. Stock solutions of the reference compounds were prepared in methanol and stored at −20 °C. *N*-*tert*-butyldimethylsilyl-*N*-methyltrifluoroacetamide (MTBSTFA) (Sigma–Aldrich, St. Louis, MO) was used as the derivatizing reagent.

Methanol, ethyl acetate (pesticide grade), ammonium hydroxide solution (25%) and hydrochloric acid were purchased from Fisher Scientific (Pittsburgh, PA) and sodium azide from RICCA Chemical Company (Arlington, TX). Deionized water was prepared with a Milli-Q water purification system. Amberlite XAD-16 (particle size 20–60 μm) was obtained from Alfa Aesar (Ward Hill, MA) and XAD-7 (particle size 20–60 μm) from Acros Organics (Morris Plains, NJ). The woven polyester fabric was purchased from Jo-Ann Fabrics & Crafts (Moreno Valley, CA). Glass fiber pre-filter was obtained from Whatman (Maidstone, UK). Oasis HLB and MCX columns (60 mg, 3 mL) were purchased from Waters (Milford, MA).

### 2.2. Sampling procedure

In May 2010, wastewater samples were collected from STP near Riverside, California. The influent water was treated by a conventional activated sludge process, followed by primary sedimentation, aeration, and secondary clarification. After the secondary treatment, the effluent was continuous backwash sand filtrated, and ultraviolet light (UV) disinfected. Samples were collected at different stages of treatment: the influent, wastewater treated by activated sludge, secondary clarified effluent, and UV disinfected effluent. The samples, collected in glass bottles, were immediately transported to the lab, passed through glass fiber prefilters, and stored at 4 °C after adding 0.5% (w/v) sodium azide until further analysis.

### 2.3. Extraction and clean-up procedure

#### 2.3.1. SPE method

For SPE, 100 mL of water samples or standard solutions were spiked with internal standard at a final concentration of 1 ng/mL. The sample was adjusted to pH 2 with HCl (37%) prior to extraction. The columns were conditioned with 2 mL methanol and 2 mL deionized water, followed by loading of the sample at a flow rate of 5 mL/min. The cartridges were dried under nitrogen, and HLB was eluted with 2 mL methanol [12,14,16,18,33], while MCX was eluted with 2 mL 2% ammonium hydroxide in methanol [21–23].

The eluates were evaporated to dryness with a gentle stream of nitrogen at 35 °C, and redissolved in 900 μL of ethyl acetate, then transferred into the GC vial, and 100 μL of MTBSTFA was added. The GC vials were put into GC oven at 70 °C for 60 min for derivatization prior to GC–MS analysis [15,35,36].

#### 2.3.2. XAD method

The XAD-bag samplers were made from woven polyester fabrics, which were welded with an impulse hand sealer (American International Electric, Whittier, CA, USA). The bag was filled with 60 mg XAD-16 resin, or 30 mg XAD-16 + 30 mg XAD-7 resins.

The samplers were wetted in methanol and placed in glass-bottles filled with 100 mL water samples or standard solutions spiked with internal standard at final concentration of 1 ng/mL. The samplers were equilibrated with the solutions for 4 h under gentle mixing at 40 rpm on a shaker. Then they were left to dry on a paper-towel for 10 min, and ultrasonicated for 10 min in 2 mL MeOH. Our preliminary test showed that sorption equilibrium was reached in less than 4 h, and more than 96% were desorpted from XAD-bag after ultrasonicating in 2 mL MeOH for 10 min. The final extracts were evaporated, redissolved and derivatized following the procedure as described above. Possible losses of XAD sorbent during sampling were checked by weighting XAD-bag before and after sampling.

### 2.4. Detection with GC–MS

Concentrations of pharmaceuticals were determined with an Agilent 6890N GC with 5975C MSD equipped with an Agilent 7683B automatic liquid sampler. A HP-5MS GC column (30 m, 0.25 mm i.d., 0.25 μm film thickness) was used in chromatographic separation with helium as the carrier gas at a constant flow rate of 1.2 mL/min. Injector temperature was 250 °C. The GC oven temperature was programmed from 70 °C (held for 1 min) to 120 °C at 20 °C/min, then to 250 °C at 10 °C/min, thereafter to 270 °C at 5 °C/min and held for 3 min. The total analysis time for each GC run was 23 min. A 2 μL sample was injected in pulsed splitless mode. Mass spectra were obtained in electron impact ionization (EI) mode (70 eV) with selected ion monitoring (SIM) and a filament delay time of 11 min. The GC–MS interface, ion source and quadrupole temperatures were set at 280, 230 and 150 °C, respectively. The retention time and fragment were obtained by injecting single standard of compounds under full scan. Primary and secondary ions used for quantification and monitoring are shown in Table 2.

### 2.5. Quantification

A nine point calibration curve, spanning from 10 to 4000 ng/L, were prepared in 100 mL aqueous solution. A constant amount of surrogate standards (100 ng) was added. Samples were then subjected to SPE or XAD as described above. The use of labeled surrogates compensates for differences in extraction yields between different analytes, and for variations between water samples with regard to physico-chemical properties. D3-ibuprofen and D3-paracetomol were used as internal standards. D3-ibuprofen was selected for the quantification of clofibric acid, diclofenac, gemfibrozil, ibuprofen, ketoprofen and naproxen, while for carbamazepine, paracetomol, terbutaline and triclosan, D3-paracetomol was used. Quantification was performed using the calibration curves with an inverse weighing factor ($1/x$) of the internal standard.

### 2.6. Method validation

The recovery of the method was determined by spiking 1 mL known concentrations (20, 100 and 500 ng/mL) of analytes into 100 mL influent and effluent samples (triplicates each). The absolute recovery of analytes was calculated by dividing the peak area difference of spiked and nonspiked sample with the peak area of spiked quantities. The instrumental detection limit (IDL) and instrumental quantification limit (IQL) were set as signal to noise (S/N) ratio of 3 and 10, respectively, obtained from serial dilution of standards. The limit of detection (LOD) was determined by calculating S/N ratios of each compound from wastewater samples. By extrapolation to a S/N ratio of 3, LOD concentrations were obtained. The limit of quantification (LOQ) of the method was determined in the same way as the LOD, but with a S/N ratio of 10 instead. The accuracy of both SPE and XAD methods was evaluated by intra-day and inter-day reproducibility. The precision of the method was determined by calculating the relative standard deviation (RSD). Statistical treatment of data (significance level) was carried out using the statistical software SPSS 16.

## 3. Result and discussion

### 3.1. Instrumental performance

Fig. 1 shows a typical chromatogram for a standard solution (100 ng/mL). Carbamazepine and terbutaline cannot be separated (19.03 min), and extraction ion chromatograms (EIC) were used to quantification based on the ions in Table 2. Briefly, the total peak area of carbamazepine and terbutaline was integrated together at first. EIC was used to obtain the peak area of terbutaline by extracting ion 482, 483 and 484 (Table 2), then the peak area of carbamazepine was calculated by subtracting the peak area of terbutaline from the total peak area. EIC is also applied to the quantification of ibuprofen/D3-ibuprofen (12.82 min), and paracetamol/D3-paracetamol (15.20 min).

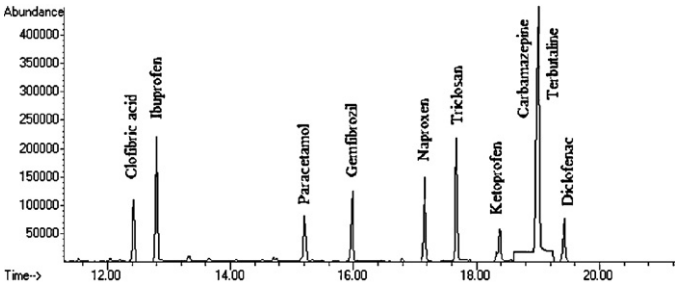



**Fig. 1.** GC–MS chromatograms of target analytes (100 ng/mL).

The peak area repeatability obtained from five repeated injections of a spiked effluent sample was lower than 7% (Table 3) from the RSD, reflecting the stability of the equipment. Values of IDL for the test analytes range from 1 to 10 pg, while the IQL range from 2 to 20 pg (Table 3).

The linearity of the calibration curve for each analyte was tested in the range shown in Table 3. Linearity was evaluated by statistical methods measuring the coefficient of determination ($R^2$) which quantify the goodness of fit of the linear regression. The developed GC–MS procedure exhibits satisfactory linearity ($R^2 > 0.98$) for all the analytes [29,34].

### 3.2. Evaluation of recovery

The recovery and precision of the method, when applied to the analysis of spiked influent and effluent wastewaters, are shown in Fig. 2. The recoveries of the pharmaceuticals from influent samples varied from 5.8 (terbutaline) to 85.4% (ketoprofen) and from 29.6 (paracetamol) to 84.4% (naproxen), with an average of 55.0 for HLB and 67.9% for MCX, respectively. For effluent samples, on the other hand, the recoveries ranged from 7.1 (terbutaline) to 87.3% (diclofenac) and from 37.6 (paracetamol) to 87.6% (naproxen), with an average of 57.1 for HLB and 72.3% for MCX, respectively. The precision of the recovery was satisfactory with relative standard deviations (RSD) below 8%. The recovery of MCX was higher than HLB ($p < 0.01$), suggesting that better extraction efficiency were obtained by MCX.

The recoveries from influent samples varied from 13.1 (paracetamol) to 59.1% (naproxen) and from 20.3 (paracetamol) to 69.3% (triclosan), with an average of 41.1 for XAD-16, and 49.1% for XAD16/7, respectively. For effluent samples, the recoveries ranged from 12.9 (paracetamol) to 65.8% (naproxen) and from 22 (terbutaline) to 75.8% (triclosan), with an average of 45.5 for XAD-16 and

**Table 3**
Instrumental performance and validation data.

| Compound | Repeatability of peak area (RSD, %) ($n = 5$) | IDL[a] | IQL[a] | Instrumental linear range[a] | $R^2$ |
|---|---|---|---|---|---|
| Carbamazepine | 1.5 | 1.0 | 2.0 | 2.0–2000 | 0.9951 |
| Clofibric acid | 4.8 | 4.0 | 10.0 | 10.0–2000 | 0.9832 |
| Diclofenac | 6.9 | 4.0 | 10.0 | 10.0–2000 | 0.9819 |
| Gemfibrozil | 1.9 | 2.0 | 10.0 | 10.0–2000 | 0.9871 |
| Ibuprofen | 3.8 | 2.0 | 4.0 | 4.0–2000 | 0.9941 |
| Ketoprofen | 5.5 | 4.0 | 10.0 | 10.0–2000 | 0.9863 |
| Naproxen | 5.6 | 2.0 | 4.0 | 4.0–2000 | 0.9892 |
| Paracetamol | 6.7 | 10.0 | 20.0 | 20.0–2000 | 0.9918 |
| Terbutaline | 5.0 | 1.0 | 2.0 | 2.0–2000 | 0.9936 |
| Triclosan | 2.4 | 2.0 | 4.0 | 4.0–2000 | 0.9912 |

[a] pg injected.

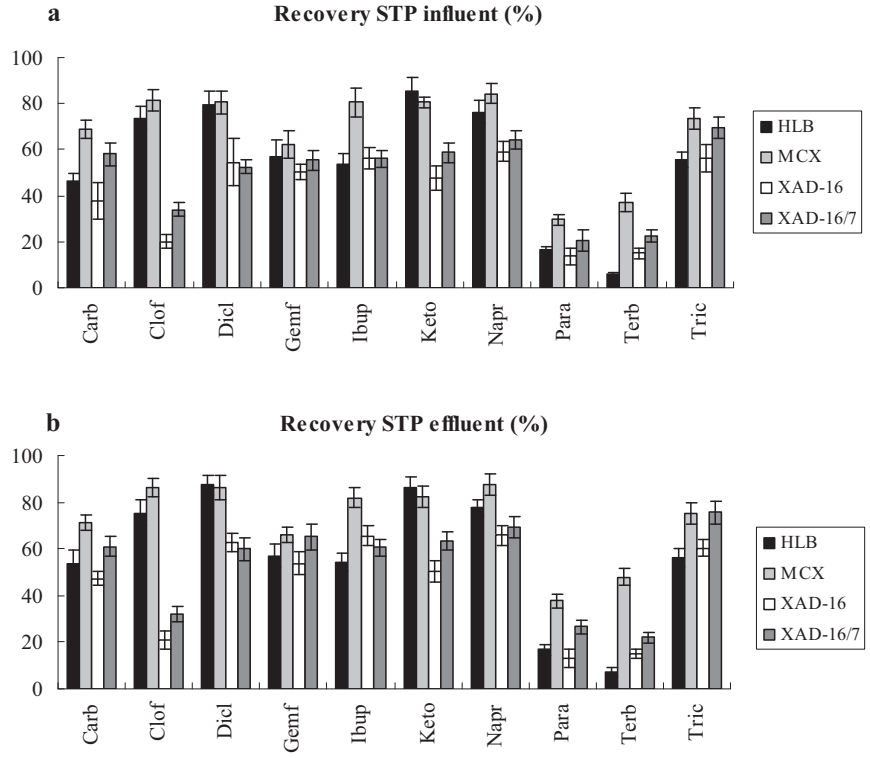



**Fig. 2.** Recovery and precision of the four methods used from spiked wastewater: (a) influent and (b) effluent.

53.6% for XAD16/7, respectively. The precision of the recovery was satisfactory for effluent, with RSD below 6%. However, the RSD of recoveries for influent samples were higher, such as carbamazepine (8.2%) and diclofenac (10.3%).

For all the 4 extraction methods, the mean recovery of effluent was not significant higher than that of influent ($p > 0.05$), which is different from the research using ESI source [18–21], indicating that no obvious matrix effect were observed via GC–MS. The low recoveries of paracetamol and terbutaline by the four methods are most likely due to the water-soluble properties of these compounds. They have the lowest logarithms octanol–water partition coefficient (log Kow) (0.48 and 0.7, respectively) of all of the analytes in this study (Table 1). This was similar with the result from Lavén et al. [21], where they reported recoveries of paracetamol and terbutaline were 11.4 and 43.4%, respectively. Addition of XAD-7 improves the extraction efficiency for most compounds ($p < 0.01$) with the exception of ibuprofen and dicolfenac, which is partially because of their higher log Kow.

### 3.3. Validation of the method

Method accuracy was calculated as the RSD of concentrations obtained from intra-day and inter-day determination. The results summarized in Table 3 reflect the good accuracy of the method. The RSD of intra-day reproducibility were lower than 9%. Values of inter-day RSD, however, were somewhat higher, such as clofibric acid and diclofenac. The reason for these deviations was partially because the spiked method we used. In this work, the concentrations of pharmaceuticals were calculated based on analysis of samples spiked with all the 10 analytes at three concentration levels (0.2, 1 and 5 ng/mL). Thus, it raised a high requirement to equipment that the linearity and linear range of analytes should be good enough, because even small variations in the different concentration levels of target analytes can have negative effects on the accuracy of the method. However, it was a disadvantage of GC–MS compared with a HPLC–QqQ-MS.

Finally, LOQ of the 10 analytes in the XAD 16/7 extracts were below 180 ng/L with the exception of paracetamol (Table 3), demonstrating that the method is suitable for detection of trace levels (ng/L) of pharmaceuticals in natural waters. Although the LOQ were higher than other studies [3,14,18,21], they can be compensated by increasing the concentrated factor. In this work we used concentrated factor of 100 for influent and effluent wastewaters. If needed, the concentrated factor can be easily increased to 500 by choosing a start-volume of 500 mL or a final-volume of 0.2 mL instead.

### 3.4. Comparison of the two sample pre-treatment methods

Analytical procedures using different extraction methods and GC–MS for the simultaneous determination of the 10 pharmaceuticals from effluent wastewater have been proposed. The GC–MS method allows the separation and identification of the analytes with low detection limits.

Recoveries obtained from the XAD 16/7 ranged from 20.3 to 69.3% and 22 to 75.8%, respectively, for the influent and effluent waters. As shown in Fig. 2, compared with MCX method, the recoveries of XAD were lower for most compounds ($p < 0.01$), which is the advantage of MCX column. For gemfibrozil and triclosan with higher log Kow, however, the recoveries of XAD were similar to those of MCX method ($p > 0.05$).

Table 4 presents the results of the intra-day and inter-day standard deviations for the extraction procedures. In general, the intra-day precision of MCX was higher than XAD ($p < 0.05$), but the different procedures show similar RSD at inter-day reproducibility ($p > 0.05$).

Overall, XAD method offers a fast extraction procedure for extracting the pharmaceuticals in wastewater, but lower extraction

**Table 4**
Analytical method performance and validation data.

| Compound | Reproducibility of determination (RSD, %) | | | | XAD-16/7 | | | |
|---|---|---|---|---|---|---|---|---|
| | Intra-day precision ($n=3$) | | Inter-day precision ($n=6$) | | LOD (ng/L) | | LOQ (ng/L) | |
| | MCX | XAD-16/7 | MCX | XAD-16/7 | Influent | Effluent | Influent | Effluent |
| Carbamazepine | 4.7 | 4.7 | 7.5 | 8.2 | 12 | 7 | 40 | 25 |
| Clofibric acid | 5.2 | 7 | 11.4 | 13.1 | 55 | 25 | 180 | 83 |
| Diclofenac | 4.6 | 6.3 | 10.3 | 12.5 | 50 | 22 | 165 | 75 |
| Gemfibrozil | 2.3 | 5.1 | 7.9 | 10.8 | 24 | 14 | 80 | 48 |
| Ibuprofen | 2.6 | 3.9 | 5.4 | 6.1 | 16 | 12 | 55 | 40 |
| Ketoprofen | 4.8 | 7.5 | 9.8 | 8.9 | 40 | 25 | 130 | 84 |
| Naproxen | 5.1 | 8.3 | 10.7 | 10.3 | 20 | 12 | 68 | 40 |
| Paracetamol | 5.4 | 7.1 | 8.3 | 9.9 | 86 | 50 | 290 | 170 |
| Terbutalin | 3 | 5.6 | 8.5 | 9.2 | 35 | 15 | 120 | 50 |
| Triclosan | 2 | 5.8 | 8.4 | 8.8 | 20 | 13 | 70 | 45 |

**Table 5**
Comprehensive comparison of results with other studies.

| Instrument | GC–MS (present study) | | | | UPLC-TQD [19] | | | UPLC-QqQ [23] | | | UPLC-QTof [28,29] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MCX (%) | XAD 16/7 (%) | IDL (pg) | LOQ (ng/L) | HLB (%) | IDL (pg) | LOQ (ng/L) | MCX (%) | IDL (pg) | LOQ (ng/L) | XAD 2 (%) | IDL (pg) | LOQ (ng/L) |
| Carbamazepine | 71.4 | 61 | 1 | 25 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | 53.8 | 0.47 | 30 |
| Clofibric acid | 86.3 | 31.9 | 4 | 83 | n.a. | n.a. | n.a. | 59.3 | 1 | 0.5 | n.a. | n.a. | n.a. |
| Diclofenac | 86.1 | 59.9 | 4 | 75 | 84 | 8.2 | 53 | 71.5 | 2 | 0.5 | 55.5 | n.a. | 45 |
| Gemfibrozil | 66.2 | 65.2 | 2 | 48 | 102 | 12.8 | 18 | n.a. | n.a. | n.a. | 24.6 | 1.8 | 300 |
| Ibuprofen | 81.9 | 60.7 | 2 | 40 | 120 | 52.4 | 247 | 66.7 | 2 | 0.5 | 35.9 | 1.5 | 45 |
| Ketoprofen | 82.4 | 63.4 | 4 | 84 | 84 | 6.4 | 72 | 38 | 2 | 2.5 | 57.9 | 1.1 | 120 |
| Naproxen | 87.6 | 69.3 | 2 | 40 | 84 | 7.6 | 30 | 64.1 | 2 | 1.5 | 37.9 | 1.8 | 40 |
| Paracetamol | 37.6 | 26.6 | 10 | 170 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| Terbutaline | 47.9 | 22 | 1 | 50 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | 20.7 | 1.5 | 120 |
| Triclosan | 75.2 | 75.8 | 2 | 45 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |

n.a.: not available.

recovery in comparison with MCX extraction procedures. However, this method avoids the use of organic solvents and clean-up steps, thus reducing the operation and the sample preparation time with similar reproducibility. Furthermore, the cost is substantially lower and can be used for analyzing large number of samples and in situ investigation.

Moreover, we compare our results with other studies [19,23,28,29]. As shown in Table 5, the IDL of GC–MS were similar to those of UPLC-QqQ [23] and UPLC-QTof [28,29], and lower than UPLC-TQD (quadrupole–hexapole–quadrupole) [19]. The recoveries of MCX in this study were higher with exception of gemfibrozil and ibuprofen concentrated by HLB [19]. The recoveries of XAD 16/7 were higher than XAD-2 [28,29]. The LOQ in this study were significantly higher than that by Kasprzyk-Hordern et al. [23], where they use a concentrated factor of 2000 by concentrating water samples from 1000 mL to 0.5 mL.

### 3.5. Application to real samples

The XAD method developed in this work was applied in the analysis of wastewater from a STP near Riverside, CA (Table 6).

**Table 6**
Concentrations (μg/L) of pharmaceuticals in wastewaters from a sewage treatment plant near Riverside, CA.

| Compound | Influent | Activated sludge | Secondary clarify | Effluent |
|---|---|---|---|---|
| Carbamazepine | 2.1 | 0.76 | 0.65 | 0.39 |
| Clofibric acid | <LOQ | <LOQ | <LOQ | <LOQ |
| Diclofenac | 3.2 | 0.15 | 0.12 | <LOQ |
| Gemfibrozil | 8.4 | 1.4 | 0.89 | 0.65 |
| Ibuprofen | 21 | 2.2 | 0.12 | 0.06 |
| Ketoprofen | 1.5 | 0.02 | <LOQ | <LOQ |
| Naproxen | 14 | 1.8 | 0.15 | 0.08 |
| Paracetamol | 77 | 0.33 | 0.40 | 0.18 |
| Terbutaline | 0.31 | <LOQ | <LOQ | <LOQ |
| Triclosan | 1.8 | 0.09 | 0.09 | 0.05 |

Clofibric acid was not found, and terbutaline was only found in influent water at 0.31 μg/L. Other substances were detected at >1 μg/L in influent water. Although high concentrations of paracetamol, ibuprofen and naproxen were found in influent water, they were effectively reduced in the STP. Diclofenac and ketoprofen were totally removed from wastewater after treatment. Moreover, carbamazepine, gemfibrozil and triclosan were also effectively reduced, with an average removal efficiency of 90.3%. Most compounds were removed by activated sludge, suggesting a potential capability to control the contaminant of pharmaceutical.

## 4. Conclusion

In this paper, we present a passive sampling method using XAD-16 and XAD-7 resins and analysis of the chemicals by GC–MS. The addition of XAD-7 improves the recovery compared with XAD-16 only. The new method was validated and compared with MCX method, which have a higher mean recovery than HLB. Different procedures show similar reproducibility for most compounds. With low solvent consumption, easy operation, short extraction and running time, the new procedure was successfully applied to determine the concentrations of 10 pharmaceuticals in wastewater. Further research will test applicability of this method to field measurement, other compounds and media.

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