Application Note

Environmental

# Analysis of Pharmaceuticals and Personal Care Products (PPCPs) as Contaminants in Drinking Water by LC/MS/MS Using Agilent Bond Elut PPL


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## Abstract

This work describes the development of a fast and robust workflow using offline solid phase extraction (SPE) Agilent Bond Elut PPL followed by LC/MS/MS for the analysis of multiclass pharmaceuticals and personal care product (PPCPs) contaminants in drinking water. Various SPE products were investigated, and Bond Elut PPL SPE was selected as having the best performance for this application. The PPL method was then optimized step-by-step. The quantitation result demonstrates that the average recoveries of 39 PPCPs spiked with two concentration levels were in the range of 79% to 127% with RSD below 20%. The limit of quantitation (LOQ) was in the range of 0.5 to 13 ng/L.

# Experimental

## Chemicals and reagents

All reagents and solvents used in sample preparation were HPLC or analytical grade, and the reagent and solvents used in the LC/MS analysis were LC/MS-grade. Acetonitrile (ACN) and methanol (MeOH) were from Honeywell (Muskegon, MI, USA). Formic acid (FA), ammonium formate, and ascorbic acid were obtained from Anpel (Shanghai, China). Monopotassium phosphate was obtained from J&K Scientific Ltd. (Beijing, China). Ammonium fluoride and ethylenediaminetetraacetic acid disodium salt dihydrate ($Na_2EDTA$) were obtained from Sigma-Aldrich. All target standards and internal standards at 100 µg/mL in acetonitrile, were purchased from Alta (Tianjin, China) and stored at –20 °C. Penicillin and cephalosporin solutions were freshly made with 100 µg/mL in 1:1 ACN:water before usage, for stability.

## Equipment and consumables

- Eppendorf Centrifuge 5810R (Hamburg, Germany)
- Agilent Bond Elut PPL, 6 mL cartridge, 500 mg (part number 12255001)
- Agilent Bond Elut SPE Reservoir 60 mL (part number 12131012)
- Adapter cap for 1, 3, and 6 mL Bond Elut Cartridges, 15/pk (part number 12131001)
- Agilent Vac Elut 20 Manifold (part number 12234101)

## Instrument conditions

LC/MS/MS detection was performed on an Agilent 1290 Infinity II LC system. This consisted of the Agilent 1290 Infinity II high speed pump (G7120A), the Agilent 1290 Infinity II multisampler (G7167B), and the Agilent 1290 Infinity II multicolumn thermostat (G7116B). These were coupled to an Agilent triple quadrupole LC/MS (G6470A) with an Agilent Jet Stream Electrospray ion source. Agilent MassHunter Workstation software was used for data acquisition and analysis. Table 1 lists the LC/MS/MS method conditions. The MRM transitions and settings are listed in Table 2.

**Table 1.** LC/MS/MS method conditions.

| LC/MS/MS Parameter | Setting | | |
|---|---|---|---|
| Column | Agilent ZORBAX RRHD Eclipse Plus C18, 2.1 × 100 mm, 1.8 µm (p/n 959758-902) | | |
| Column Temperature | 40 °C | | |
| Autosampler Temperature | 10 °C | | |
| Injection Volume | 10 µL | | |
| Mobile Phase | A) Water, containing 4.5 mM ammonium formate, 0.5 mM ammonium fluoride, 0.1% formic acid<br>B) Methanol, containing 4.5 mM ammonium formate, 0.5 mM ammonium fluoride, 0.1% formic acid | | |
| Gradient | Time (min)<br>0<br>1<br>3<br>8<br>10<br>15<br>16<br>19 | %B<br>2<br>2<br>20<br>30<br>40<br>70<br>98<br>98 | Flow rate (mL/min)<br>0.35 |
| Stop Time | 19 min | | |
| **Source Parameters** | | | |
| Gas Temperature | 300 °C | | |
| Gas Flow | 10 L/min | | |
| Nebulizer | 40 psi | | |
| Sheath Gas Temperature | 350 °C | | |
| Sheath Gas Flow | 11 L/min | | |
| Ionization Mode | Positive | | |
| Capillary Voltage | +3,500 | | |
| Nozzle Voltage | +500 | | |
| **Time Segments** | | | |
| Agilent 1290 Infinity II binary system | | | |
| Start Time (min) | Scan type | Div valve | Delta EMV (+) |
| 0 | DMRM | To Waste | 0 |
| 2.8 | DMRM | To MS | 400 |
| 19 | DMRM | To Waste | 0 |

**Table 2.** MRM conditions for the targeted analytes.

| Compound Name | Precursor Ion | Product Ion | RT (min) | Fragmentor | Collision Energy | Cell Accelerator Voltage |
|---|---|---|---|---|---|---|
| 1,7-Dimethylxanthine | 181.1 | 124.0 | 4.7 | 116 | 22 | 4 |
| | | 69.1 | | | 34 | |
| | | 42.2 | | | 46 | |
| 4-Acetamidophenol-$^{13}C_2$-$^{15}N$ | 155.1 | 110.9 | 3.9 | 93 | 14 | 4 |
| | | 65.0 | | | 34 | |
| Acetaminophen | 152.1 | 110.1 | 3.9 | 111 | 18 | 4 |
| | | 93.1 | | | 26 | |
| | | 65.1 | | | 38 | |
| Ampicillin | 350 | 160.0 | 6.6 | 113 | 10 | 4 |
| | | 114.0 | | | 36 | |
| | | 106.0 | | | 16 | |
| Carbamazepine | 237.1 | 194.0 | 13.8 | 136 | 22 | 4 |
| | | 179.0 | | | 42 | |
| | | 165.0 | | | 50 | |
| Ceftiofur | 524 | 241.0 | 11.8 | 146 | 6 | 5 |
| | | 126.0 | | | 40 | |
| | | 124.7 | | | 58 | |
| Cephalexin | 348.1 | 174.1 | 6.1 | 116 | 2 | 4 |
| | | 158.2 | | | 2 | |
| | | 106.0 | | | 40 | |
| Cephalexin-d5 | 353.1 | 158.1 | 6.1 | 88 | 6 | 4 |
| | | 111.0 | | | 30 | |
| Cephradine | 350.1 | 175.9 | 7.1 | 102 | 17 | 4 |
| | | 157.9 | | | 8 | |
| | | 107.8 | | | 30 | |
| Cinoxacin | 263.1 | 245.1 | 10.2 | 85 | 14 | 4 |
| | | 217.1 | | | 22 | |
| | | 189.0 | | | 30 | |
| Ciprofloxacin | 332.1 | 314.0 | 6.9 | 149 | 20 | 4 |
| | | 288.0 | | | 20 | |
| | | 245.0 | | | 40 | |
| Ciprofloxacin-d8 | 340.2 | 322.2 | 6.9 | 131 | 26 | 4 |
| | | 235.0 | | | 46 | |
| Clarithromycin | 748.5 | 590.4 | 15.3 | 100 | 18 | 5 |
| | | 158.0 | | | 30 | |
| | | 83.1 | | | 55 | |
| Cloxacillin | 436 | 277.0 | 14.6 | 70 | 12 | 4 |
| | | 160.0 | | | 12 | |
| Dehydronifedipine | 345.1 | 284.1 | 14.1 | 146 | 30 | 4 |
| | | 268.1 | | | 30 | |
| Diltiazem | 415.2 | 178.0 | 13.3 | 141 | 26 | 4 |
| | | 150.0 | | | 50 | |
| | | 109.0 | | | 55 | |
| Diphenhydramine | 256.2 | 167.0 | 12.3 | 80 | 14 | 4 |
| | | 165.0 | | | 54 | |
| | | 152.0 | | | 46 | |

| Compound Name | Precursor Ion | Product Ion | RT (min) | Fragmentor | Collision Energy | Cell Accelerator Voltage |
|---|---|---|---|---|---|---|
| Enrofloxacin | 360.2 | 342.2 | 7.3 | 156 | 20 | 4 |
| | | 316.2 | | | 16 | |
| | | 245.1 | | | 32 | |
| Erythromycin | 734.5 | 576.2 | 14.3 | 172 | 6 | 5 |
| | | 157.8 | | | 18 | |
| | | 82.8 | | | 54 | |
| Erythromycin-$^{13}$C-d3 | 738.5 | 161.8 | 14.3 | 141 | 30 | 5 |
| | | 82.7 | | | 58 | |
| Flumequine | 262.1 | 244.1 | 13.3 | 108 | 12 | 4 |
| | | 202.0 | | | 32 | |
| | | 126.0 | | | 52 | |
| Fluoxetine | 310.1 | 148.1 | 14.5 | 106 | 6 | 4 |
| | | 91.0 | | | 10 | |
| | | 44.2 | | | 14 | |
| Fluoxetine-d5 | 315.2 | 153.1 | 14.5 | 83 | 4 | 4 |
| | | 95.0 | | | 50 | |
| | | 44.1 | | | 10 | |
| Ormetoprim | 275.2 | 259.1 | 6.4 | 90 | 30 | 4 |
| | | 123.1 | | | 26 | |
| | | 81.1 | | | 54 | |
| Oxacillin | 402.1 | 243.0 | 14.2 | 106 | 10 | 4 |
| | | 160.0 | | | 14 | |
| Oxolinic acid | 262.1 | 243.9 | 11.1 | 114 | 20 | 4 |
| | | 159.9 | | | 45 | |
| Penicilline G | 335.1 | 176.1 | 13.1 | 85 | 2 | 4 |
| | | 160.1 | | | 2 | |
| Penicilline G-d7 | 342.1 | 183.1 | 13.1 | 85 | 10 | 4 |
| | | 160.1 | | | 10 | |
| Sarafloxacin | 386.1 | 368.1 | 8.3 | 150 | 20 | 4 |
| | | 342.1 | | | 20 | |
| | | 299.1 | | | 40 | |
| Sarafloxacin-d8 | 394.2 | 376.1 | 8.3 | 131 | 22 | 4 |
| | | 350.0 | | | 18 | |
| | | 303.1 | | | 30 | |
| Sulfacetamide | 215 | 155.9 | 3.5 | 80 | 4 | 4 |
| | | 108.0 | | | 16 | |
| | | 92.0 | | | 20 | |
| Sulfachloropyridazine | 285 | 156.0 | 6.7 | 108 | 12 | 4 |
| | | 108.1 | | | 24 | |
| | | 92.1 | | | 24 | |
| Sulfadiazine | 251.1 | 156.0 | 4.1 | 100 | 8 | 4 |
| | | 108.1 | | | 20 | |
| | | 92.1 | | | 28 | |
| Sulfadimethoxine | 311.1 | 156.0 | 10.5 | 141 | 16 | 4 |
| | | 108.1 | | | 28 | |
| | | 92.1 | | | 36 | |
| Sulfadoxine | 311.1 | 156.0 | 7.7 | 126 | 16 | 4 |
| | | 92.1 | | | 32 | |

| Compound Name | Precursor Ion | Product Ion | RT (min) | Fragmentor | Collision Energy | Cell Accelerator Voltage |
|---|---|---|---|---|---|---|
| Sulfamerazine | 265.1 | 156.0 | 4.9 | 114 | 12 | 4 |
| | | 108.0 | | | 20 | |
| | | 92.1 | | | 28 | |
| Sulfameter | 281.1 | 215.1 | 5.6 | 150 | 20 | 4 |
| | | 156.0 | | | 20 | |
| | | 108.0 | | | 35 | |
| Sulfamethazine | 279.1 | 186.1 | 6.0 | 116 | 12 | 4 |
| | | 124.0 | | | 21 | |
| | | 92.1 | | | 38 | |
| Sulfamethazine-d4 | 283.1 | 124.0 | 6.0 | 103 | 30 | 4 |
| | | 96.0 | | | 34 | |
| Sulfamethizole | 271 | 156.0 | 5.7 | 112 | 9 | 4 |
| | | 92.0 | | | 29 | |
| Sulfamethoxazole | 254.1 | 156.0 | 6.9 | 108 | 12 | 4 |
| | | 92.1 | | | 24 | |
| Sulfamethoxazole-d4 | 258.1 | 160.0 | 6.9 | 90 | 14 | 4 |
| | | 96.1 | | | 30 | |
| Sulfaphenazole | 315.1 | 158.1 | 9.7 | 150 | 40 | 4 |
| | | 92.0 | | | 40 | |
| Sulfapyridine | 250.1 | 156.0 | 4.7 | 150 | 17 | 4 |
| | | 92.0 | | | 29 | |
| Sulfaquinoxaline | 301.1 | 156.0 | 11.1 | 118 | 16 | 4 |
| | | 92.0 | | | 32 | |
| Thiabendazole | 202 | 175.0 | 6.8 | 130 | 24 | 4 |
| | | 131.0 | | | 36 | |
| | | 65.0 | | | 52 | |
| Thiabendazole-d4 | 206.1 | 179.0 | 6.7 | 141 | 30 | 4 |
| | | 135.1 | | | 42 | |
| Trimethoprim | 291.2 | 261.1 | 5.5 | 151 | 18 | 4 |
| | | 230.0 | | | 20 | |
| | | 123.1 | | | 24 | |
| Trimethoprim-d3 | 294.2 | 230.1 | 5.5 | 90 | 26 | 4 |
| | | 123.1 | | | 26 | |
| Tylosin | 916.5 | 772.4 | 14.3 | 280 | 30 | 5 |
| | | 174.1 | | | 40 | |
| | | 101.0 | | | 56 | |

## Sample preparation

Tap water was collected from the Shanghai municipal water supply. To 1 L of water, 30 mg of ascorbic acid, 5.848 g of monopotassium phosphate, and 0.5 g of $Na_2EDTA$ were added and mixed thoroughly until completely dissolved. A portion of the water sample was then spiked appropriately with standard solution at various levels, and internal standard solution at 1 mg/L. Water samples were then extracted following the SPE procedure, using Bond Elut PPL as shown in Figure 1.

Figure 2 shows the LC/MS/MS MRM chromatogram of the targets in the fortified water sample at 20 ng/L.

**SPE cleanup:** Agilent Bond Elut PPL, 6 cc 500 mg, 125 µm (p/n 12255001)

**Condition/equilibrate**
6 mL of methanol
6 mL of water

**Load**
Install the reservoir to the SPE cartridge, and load 200 mL of water sample from the pretreatment.

**Wash**
Wash with 10 mL of water, then dry for 5 minutes with gentle vacuum.

**Elute 1**
Elute with 6 mL of 0.5% FA in 1:1 MeOH:ACN, then apply vacuum for 10 minutes to dry the sorbent.

**Elute 2**
Elute with 6 mL of 1% $NH_3 \cdot H_2O$ in 1:1 MeOH:ACN and apply vacuum to drain the cartridge until there is no visible liquid left.

**Mix**
Mix eluents 1 and 2.

**Dry and reconstitute**
Dry the eluent under $N_2$ in a 35 °C water bath and reconstitute with 2 mL of 10/90 MeOH/$H_2O$.

**LC/MS/MS analysis**
Transfer the reconstituted sample to LC vails and inject for instrumentation analysis.

**Figure 1.** Agilent Bond Elut PPL SPE procedure for water sample extraction.

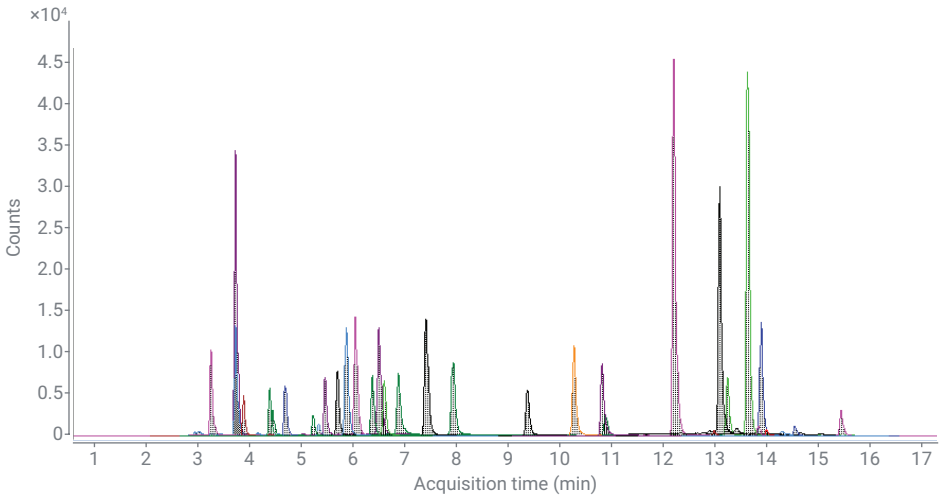


**Figure 2.** LC/MS/MS MRM chromatogram of targets in tap water sample at 20 ng/L.

## Results and discussion

### Sample preparation optimization

The optimization of the SPE method included following three parameters: SPE product selection, sample loading conditions, and target elution conditions.

### SPE sorbents selection

Four commercially available SPE products were investigated using 50 mL of neat standard solution: Agilent Bond Elut Plexa, Agilent Bond Elut ENV, Agilent Bond Elut PPL, and HLB, with the same loading process. The sample loading process refers to EPA method 1694[1] where the sample was adjusted to a pH of 2 with 1 M HCl. The elution was conducted with 100% MeOH, except Bond Elut PPL, which recommends acidic and basic sequential elution for multiclass target analysis in the user guide.[2] The recovery results of the representative targets in Figure 3 show that Bond Elut PPL delivered best recoveries overall. For some of the targets, such as erythromycin and penicillin G, the recoveries show extremely low values, no matter which SPE products are used for extraction, which might be relevant to degradation during sample preparation.

### Loading conditions

Chlorine residuals in drinking water can react with some antibiotics and cause a stability issue on the targets. It was reported that ascorbic acid can be an effective chlorine-quenching agent without affecting the analysis and stability of antibiotics in water.[3] As a result, ascorbic acid was added to the drinking water to remove chlorine, thus preserving the sensitive targets. Other than the EPA method, some literature has suggested acidic loading for antibiotic drugs or PPCPs, to enhance lipophilicity to achieve strong retention on the sorbent.[4] However, the acidic

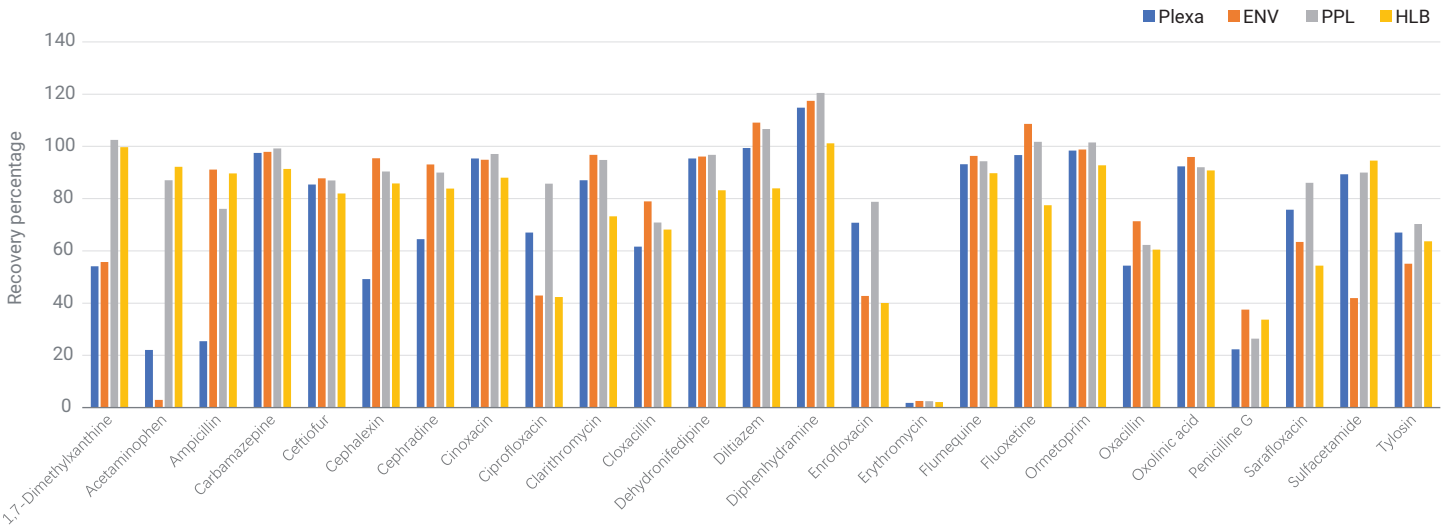


**Figure 3.** Comparison of different SPE products for the extraction of representative targets.

condition caused low recoveries and higher variability of erythromycin and penicillin G, which could result in the method failure. To verify the applicability of the sample loading condition, both acidic and neutral loading were tested for comparison. The results in Figure 4 show that, for erythromycin and penicillin G, the neutral loading condition delivered higher recoveries than acidic loading condition, while for the rest of the targets, similar results were obtained with both loading conditions. Additionally, the stability of the PPCPs in neutral water and acidified water (pH 2) was tested under room temperature for 12 hours, by monitoring the analyte responses using LC/MS/MS with sampling every 90 minutes. As shown in Figure 5, the acidic sample condition caused degradation of the penicillins and macrolides significantly and rapidly. Conversely, these targets showed much better stability in the neutral sample over time. As a result, the neutral sample loading condition was applied to the final SPE method.

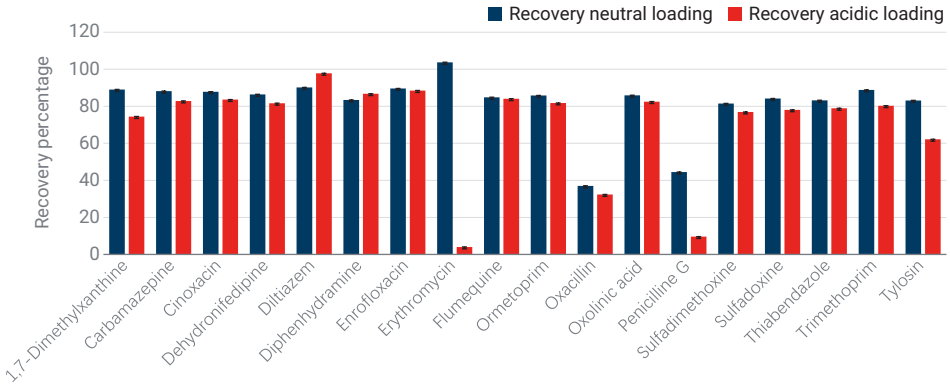


**Figure 4.** Recovery and reproducibility comparison with neutral sample loading and acidic sample loading for representative PPCPs (n = 5).

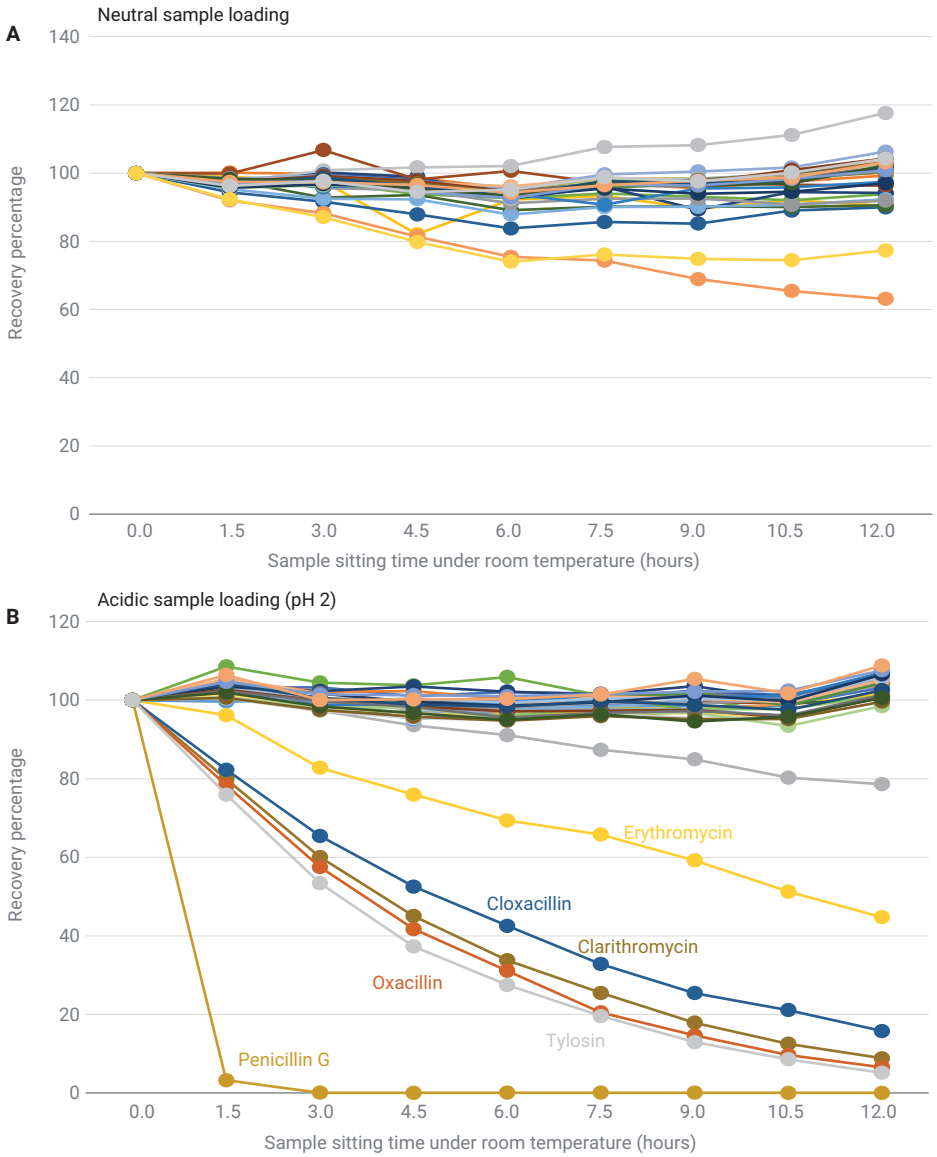


**Figure 5.** Stability study of the PPCPs in neutral and pH of 2 acidic buffered solution at room temperature.

## Elution condition

As recommended in the Bond Elut PPL guidelines[2], neutral elution with MeOH provides good recoveries for most of the targets, while acidic or basic elution using acidified or alkaline solvent or solvent mixture improves certain analyte recoveries significantly. For multiclass target analysis, acidic and basic sequential elution delivers the best comprehensive results.[2] Thus, the different conditions for elution were investigated in consideration of both targets' recoveries and acid labile compound stability. The results shown in Figure 6 confirm the necessity of acidic-basic sequential elution to achieve the acceptable recoveries for all of targets in this application.

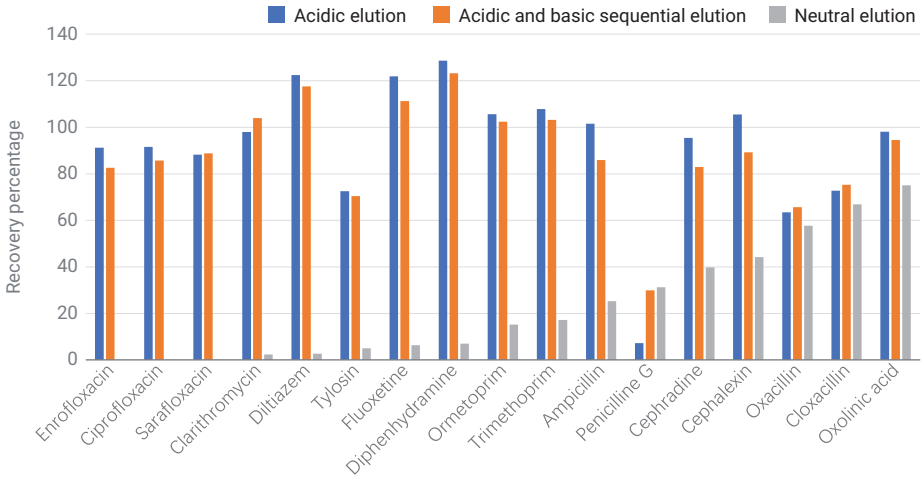


**Figure 6.** Comparison of the different sample elution conditions for representative PPCPs.

## Method validation

The quantitative method validation includes calibration curve linearity, limit of quantification (LOQ), analyte recovery, and precision at both low and high spiking levels. The detailed quantitation results are shown in Table 3. Ten or more calibration standards were used to generate calibration curves over the dynamic range from 0.05 ng/mL to 25, 50, or 100 ng/mL, depending on various targets which correspond to 0.5 to 1,000 ng/L spiking level in the water sample. Linear regression fit and $1/x^2$ weighting were used. Excellent calibration curve linearity was demonstrated with correlation coefficients ($R^2$) >0.992 for all of targets. The low QC spiking level at 5 ng/L was analyzed with seven replicates, and the method detection limit (MDL) was defined as 3.14 times the standard deviation (SD), while the lower LOQ is calculated to be four times the MDL.[5,6] The LOQs of the PPCPs ranged from 0.5 to 13 ng/L in drinking water. Acceptable recoveries (79% to 127%) were achieved, except the high recovery of 1,7-dimethylxanthine at the low spiking level (5 ng/L), caused by positive contribution from the matrix background. Method reproducibility was demonstrated with less than 20% RSDs for all analytes at both spiking levels.

**Table 3.** Method quantitation results for 39 PPCPs in drinking water with LC/MS/MS.

| Analytes | IS | Calibration Range (ng/L) | $R^2$ | LOQ (ng/L) | 5 ng/L Spiking Level (n = 5) | | 20 ng/L Spiking Level (n = 5) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | LQC-Rec% | LQC-RSD | HQC-Rec% | HQC-RSD |
| 1,7-Dimethylxanthine | Trimethoprim-d3 | 0.5 to 1,000 | 0.9992 | 3.1 | 150 | 3.3% | 109 | 1.9% |
| Acetaminophen | 4-Acetamidophenol-$^{13}C_2$-$^{15}N$ | 0.5 to 1,000 | 0.9999 | 1.4 | 102 | 2.1% | 107 | 0.7% |
| Ampicillin | Penicilline G-d7 | 0.5 to 1,000 | 0.9995 | 4.6 | 95 | 9.1% | 79 | 4.1% |
| Carbamazepine | Trimethoprim-d3 | 0.5 to 250 | 0.9923 | 0.5 | 112 | 0.6% | 109 | 1.3% |
| Ceftiofur | 4-Acetamidophenol-$^{13}C_2$-$^{15}N$ | 0.5 to 1,000 | 0.9996 | 2.8 | 90 | 2.0% | 88 | 4.1% |
| Cephalexin | Cephalexin-d5 | 0.5 to 1,000 | 0.9997 | 12.9 | 103 | 18.0% | 107 | 7.4% |
| Cephradine | Trimethoprim-d3 | 0.5 to 1,000 | 0.9995 | 7.2 | 104 | 13.5% | 94 | 9.1% |
| Cinoxacin | Ciprofloxacin-d8 | 0.5 to 1,000 | 0.9955 | 1.8 | 100 | 2.6% | 123 | 2.2% |
| Ciprofloxacin | Ciprofloxacin-d8 | 0.5 to 1,000 | 0.9979 | 2.0 | 90 | 3.8% | 103 | 0.7% |
| Clarithromycin | Trimethoprim-d3 | 0.5 to 1,000 | 0.9980 | 0.9 | 108 | 1.1% | 109 | 3.1% |
| Cloxacillin | 4-Acetamidophenol-$^{13}C_2$-$^{15}N$ | 0.5 to 1,000 | 0.9999 | 5.2 | 93 | 9.7% | 98 | 2.2% |
| Dehydronifedipine | Trimethoprim-d3 | 0.5 to 1,000 | 0.9991 | 0.7 | 105 | 1.2% | 107 | 1.8% |
| Diltiazem | Ciprofloxacin-d8 | 0.5 to 1,000 | 0.9988 | 1.1 | 104 | 1.7% | 127 | 4.3% |
| Diphenhydramine | Ciprofloxacin-d8 | 0.5 to 1,000 | 0.9931 | 0.9 | 110 | 1.3% | 118 | 3.7% |
| Enrofloxacin | Ciprofloxacin-d8 | 0.5 to 1,000 | 0.9990 | 2.6 | 114 | 4.0% | 122 | 2.8% |
| Erythromycin | Erythromycin-$^{13}$C-d3 | 0.5 to 1,000 | 0.9994 | 8.6 | 105 | 11.4% | 119 | 2.9% |
| Flumequine | Erythromycin-$^{13}$C-d3 | 0.5 to 250 | 0.9978 | 5.2 | 100 | 8.5% | 115 | 1.1% |
| Fluoxetine | Fluoxetine-d5 | 0.5 to 1,000 | 0.9989 | 0.9 | 109 | 1.5% | 111 | 0.8% |
| Ormetoprim | Sulfamethazine-d4 | 0.5 to 250 | 0.9982 | 1.6 | 115 | 2.4% | 116 | 2.4% |
| Oxacillin | Penicilline G-d7 | 0.5 to 1,000 | 0.9997 | 3.6 | 98 | 5.4% | 89 | 2.0% |
| Oxolinic acid | Trimethoprim-d3 | 0.5 to 500 | 0.9981 | 1.2 | 113 | 1.7% | 106 | 3.2% |
| Penicilline G | Penicilline G-d7 | 0.5 to 1,000 | 0.9991 | 4.1 | 91 | 6.9% | 107 | 1.7% |
| Sarafloxacin | Sarafloxacin-d8 | 0.5 to 1,000 | 0.9993 | 1.7 | 98 | 2.9% | 105 | 0.7% |
| Sulfacetamide | Sulfamethoxazole-d4 | 0.5 to 500 | 0.9922 | 1.0 | 88 | 1.5% | 87 | 1.1% |
| Sulfachloropyridazine | Cephalexin-d5 | 0.5 to 1,000 | 0.9983 | 4.0 | 96 | 4.9% | 88 | 3.4% |
| Sulfadiazine | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9935 | 0.7 | 86 | 1.2% | 83 | 1.5% |
| Sulfadimethoxine | Trimethoprim-d3 | 0.5 to 1,000 | 0.9958 | 1.6 | 98 | 3.0% | 101 | 1.8% |
| Sulfadoxine | Trimethoprim-d3 | 0.5 to 500 | 0.9962 | 2.0 | 104 | 2.9% | 104 | 1.3% |
| Sulfamerazine | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9951 | 0.7 | 99 | 1.3% | 99 | 1.6% |
| Sulfameter | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9967 | 2.6 | 101 | 4.8% | 104 | 2.7% |
| Sulfamethazine | Sulfamethazine-d4 | 0.5 to 1,000 | 0.9941 | 1.5 | 100 | 2.1% | 108 | 1.2% |
| Sulfamethizole | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9996 | 1.7 | 86 | 3.9% | 83 | 1.7% |
| Sulfamethoxazole | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9997 | 1.7 | 101 | 3.1% | 101 | 1.3% |
| Sulfaphenazole | Sulfamethoxazole-d4 | 0.5 to 1,000 | 0.9971 | 0.8 | 102 | 1.3% | 97 | 1.6% |
| Sulfapyridine | Sulfamethoxazole-d4 | 0.5 to 500 | 0.9948 | 1.5 | 100 | 1.7% | 96 | 2.6% |
| Sulfaquinoxaline | Cephalexin-d5 | 0.5 to 1,000 | 0.9995 | 4.7 | 94 | 5.5% | 80 | 4.2% |
| Thiabendazole | Thiabendazole-d4 | 0.5 to 1,000 | 0.9952 | 1.4 | 106 | 1.5% | 105 | 1.8% |
| Trimethoprim | Trimethoprim-d3 | 0.5 to 1,000 | 0.9943 | 2.2 | 105 | 3.1% | 109 | 1.6% |
| Tylosin | Thiabendazole-d4 | 0.5 to 1,000 | 0.9988 | 3.4 | 92 | 6.3% | 104 | 5.5% |

## Conclusion

A reliable analytical method was developed for multiclass multiresidue analysis of PPCPs in drinking water using the Agilent Bond Elut PPL SPE extraction, followed by LC/MS/MS detection. The method was validated for quantitative analysis based on LOQs, recoveries and precisions, and calibration ranges. This was demonstrated to be a robust and reliable method for routine monitoring of the PPCPs in drinking water, and has potential extension to environmental water analysis.

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