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Multi-component quantitative analysis of pharmaceuticals and personal care products in the environment by LC-MS/MS with fast polarity switching

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Introduction

Pharmaceuticals and personal care products (PPCPs) constitute a group of emerging contaminants which have received considerable attention in recent years. Monitoring of PPCPs in the environment is vital as many of these compounds are ubiquitous, persistent and biologically active with recognised endocrine-disruption functions. Given the hazardous nature of these compounds, there is a need to provide fast and sensitive multi-residue methods that are able to analyze multiple classes of compound within one analytical procedure. Here we report a new multi-residue UHPLC-ESI-QqQ method that utilizes fast polarity switching with an optimized chromatographic gradient that removes matrix effects and results in excellent ng/L detection levels. Furthermore, we have evaluated the performance of polarity switching in comparison to dedicated single polarity experiments.

Materials and Methods

Natural river and lake water was collected from the Shiga region (Japan) and spiked, without any sample pre-treatment, at a range of concentration levels (1 – 10000 ng/L) with 15 PPCPs.

Table 1. Analytical conditions.

UHPLC	
LC system:	Nexera (Shimadzu, Japan)
Analysis Column:	Shim-pack XR-ODSIII (2.0 mmI.D. x 50 mmL., 1.6 µm)
Mobile Phase A:	0.1% Formic acid - Water
Mobile Phase B:	Acetonitrile
Gradient Program:	0%B (0-6 min) – 80%B (16 min) – 100%B (16.01-18 min) – 0%B (18.01-21 min)
Flow rate:	0.4 mL/min
Column Temperature:	40°C
Injection Volume:	40 µL

MS	
MS system:	LCMS-8080 (Shimadzu, Japan)
Ionization:	ESI (positive/negative)
Nebulizing Gas Flow:	3.00
Curtain Gas Flow:	3.50
Heating Gas Flow:	12.00
Probe Temperature :	450°C
HSID Temperature :	300°C

A higher sensitivity triple quadruple mass spectrometer (LCMS-8080, Shimadzu, Japan) operating in SRM mode with fast polarity switching (20 msec) was used for the detection of positively and negatively charged analytes.

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Results

Analysis of PPCPs spiked in environmental water

As a result of the complex matrix in which PPCPs are present, the occurrence of ion suppression/enhancement can reduce MS/MS detection limits. For this reason, an optimized gradient was developed that focused target analytes at the head of the chromatographic column while allowing the interfering environmental matrix to be eluted (Fig. 1).

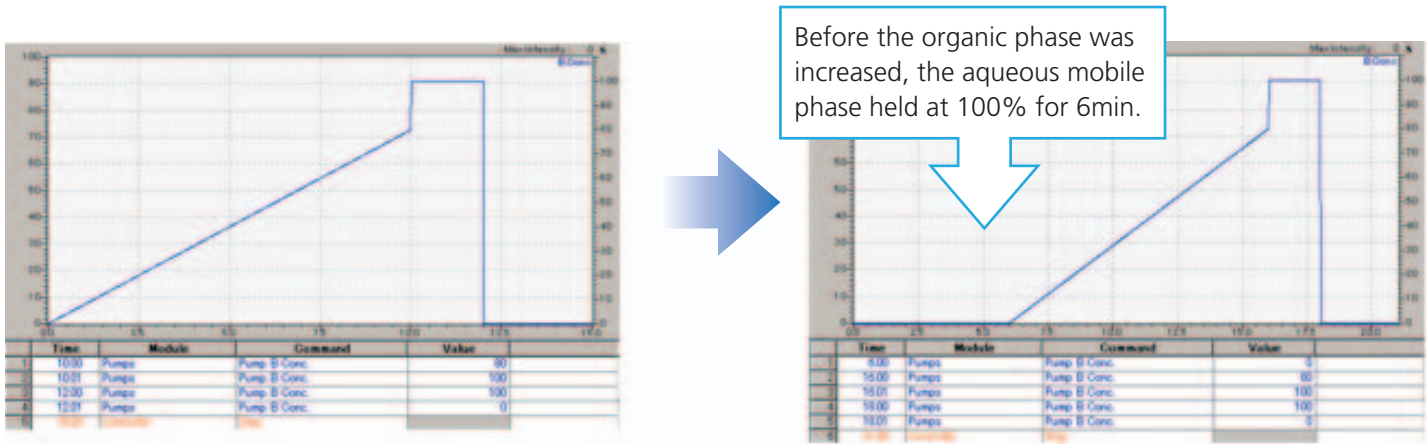

Fig. 1 Gradient program of LC.

All compounds were measured by SRM with fast polarity switching (20 msec) for multi-component analysis. Excellent limits of quantification were achieved in the range 1 – 50 ng/L for nearly all studied compounds, with outstanding linearity ($R^2 > 0.999$). The analysis results of 15 PPCPs are shown in Table 2, Fig. 2 shows calibration curves for three selected PPCPs: Carbamazepine, Albeterol and Ibprofen.

Table 2 MRM mode parameters and analysis results for each PPCPs.

Compound	Polarity	Transition	LOQ (ng/L)		%Recoery (100 ng/L)	
			River	Lake	River	Lake
Albuterol	pos	240.20>148.20	5	5	148	112
Acetaminophen	pos	152.10>110.30	50	50	80	87
Trimethoprim	pos	291.20>230.20	5	25	143	118
Sulfamethoxazole	pos	254.00>92.30	25	50	104	76
Carbamazepine	pos	237.10>194.20	1	2.5	94	68
Dehydronifedipine	pos	345.20>284.10	5	25	97	75
Naproxen	pos	231.10>185.20	10	25	99	76
Antipyrine	pos	189.00>56.20	10	25	106	82
Doxycycline	pos	445.00>428.00	100	50	79	56
Isopropylantipyrine	pos	231.00>189.00	2.5	5	103	82
Warfarin	pos	309.00>163.00	5	10	86	60
	neg	307.00>161.20	25	50	91	103
Ibuprofen	neg	205.30>161.40	50	50	106	87
Gemfibrozil	neg	249.30>121.30	25	50	114	77
Triclocarban	neg	313.10>160.20	25	25	120	98
Triclosan	neg	287.00>34.90	50	100	105	74

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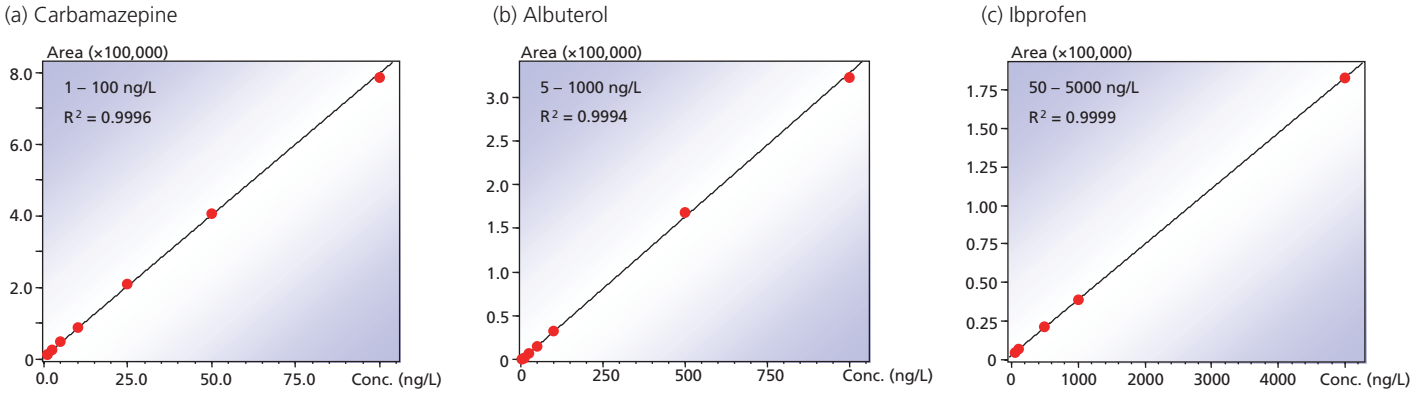

Fig. 2 Calibration curves for Carbamazepine (a), Albeterol (b) and Ibprofen (c); (a) was spiked in river water, (b) and (c) were spiked in lake water.

Polarity Switching

To evaluate the capability of polarity switching the data quality obtained was compared to dedicated positive or negative analysis.
Data quality obtained during polarity switching experiments was directly comparable to that achieved during dedicated positive or negative analysis (Fig. 3).
Long term stability was investigated by making 100 injections over 10 hours. Polarity switching data indicates excellent stability over the analysis time (Fig. 4, Table 3).

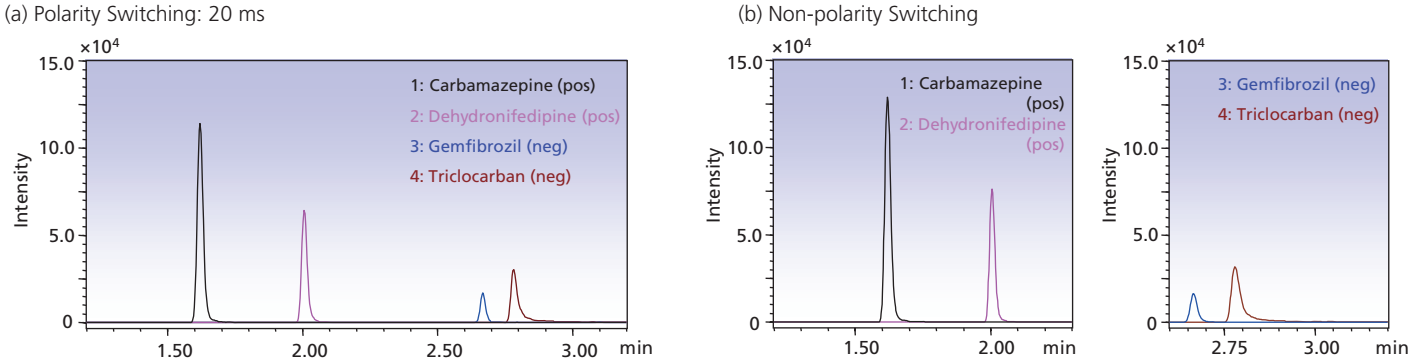

Fig. 3 Comparison of polarity switched analysis (a) and non-polarity switched analysis (positive only or negative only analysis) (b).

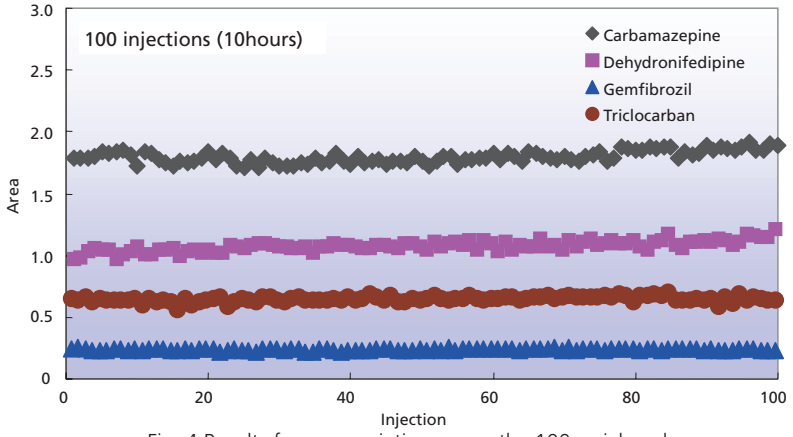

Fig. 4 Results for area variation across the 100 serial analyses.

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Table 3 Analysis results for respective compounds.

Compound	Polarity	Transition	%RSD
Carbamazepine	pos	237.10 > 194.20	2.70
Dehydronifedipine	pos	345.20 > 284.10	3.94
Gemfibrozil	neg	249.30 > 121.30	3.10
Triclocarban	neg	313.10 > 160.20	3.52

Conclusion

- Optimization of the LC gradient program resulted in the reduction of matrix effect and the recoveries of 70 – 120 % for almost all studied compounds.
- Using LCMS-8080, excellent sensitivity and linearity were obtained for PPCPs spiked in environmental water samples.
- Fast polarity switching results were shown to be comparable to dedicated single polarity experiments for the analysis of PPCPs in environmental samples.

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