Solid Phase Extraction-LC-MS/MS Method for Determining Pharmaceuticals and Personal Care Products (PPCPs) and Their Removal in Drinking Water Treatment Process

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1. Introduction

The occurrence of pharmaceuticals and personal care products (PPCPs) in the environment has become an emerging issue. They are concerned to have an influence on human health and water environment as organic contaminants. PPCPs have diverse chemical characteristics ; hydrophobicity, biodegradability and so on[1)] . Therefore, the behavior of PPCPs in water purification treatment process is expected to make clear because of their possibility that PPCPs may remain in tap water[2)]. We have investigated the occurrence of PPCPs which were reported persistence in the aquatic environment in water sources with simultaneous analysis by LC-MS/MS since 2005. The purpose of this study is to modify solid-phase extraction (SPE) method with an addition of target compounds. We also report the results of the behavior of PPCPs in water treatment process using developed SPE method.

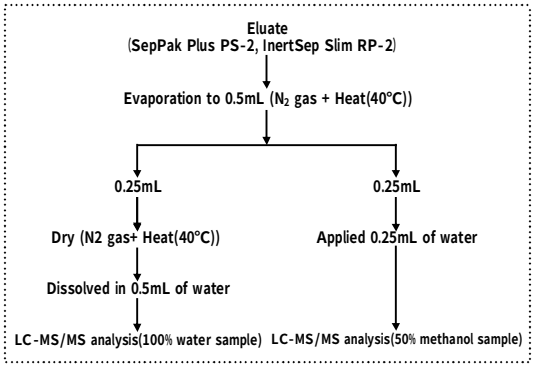

Figure 1 Eluate concentration process

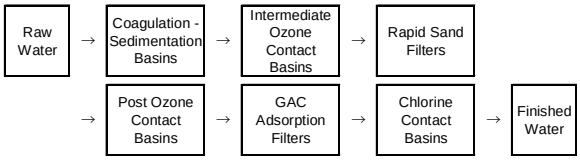

Figure 2 Advanced water treatment system of Kunijima purification plant

2. Materials and Methods

2.1 Target PPCPs

We chose 73 PPCPs for analysis which were reported to detect in the aquatic environment and were able to analyze with SPE-LC-MS/MS method.

2.2 SPE Method

Water samples were extracted with automatic SPE concentrator (GL science Co.). SepPak Plus PS-2 cartridge (Waters Co.) was coupled on the top of InertSep Slim RP-2 cartridge (GL science Co.). The cartridges were previously conditioned with 10mL of 0.1% formic acid/methanol, 15mL of methanol, and 15mL of ultrapure water. 400mL of the samples adjusted pH value to 3 with (1+10) hydrochloric acid were passed through the cartridges at 5mL/min. After washing the cartridges with 10mL of ultrapure water at 5mL/min, they were dried with a stream of nitrogen gas for 70min. Before elution, the cartridges were separated, and then eluted with 14mL of methanol, respectively. The eluates were concentrated in a water bath (40℃) under a gentle stream of nitrogen , and were divided in half, one for preparing 100% water sample, the other for water : methanol =50% : 50% sample (**Figure 1**).

2.3 Instrumental analysis

LC-MS/MS analysis was performed using an Acquity UPLC system (Waters Co.) coupled to a Quattro Premier XE triple quadrupole mass spectrometer (Waters Co.) according to the previous report[3)]. 0.05% of formic acid and 100% of acetonitrile were used for the gradient methods of LC analysis.

3. Results and Discussion

3.1 Improvement of the SPE method

Table 1 shows average recovery rates of five replicates of the samples containing 100ng/L of PPCPs in ultrapure water, coefficients of variation (CV%) , and limits of quantification (LOQ) (concentrations at S/N =10) of each substance. In the previous method[3)], we only prepared the samples of which the final solvent was 100% of water as shown in **Figure 1**. Using that method, the average recovery rates of some compounds marked with black circles in **Table 1** exceeded 150%, or the coefficients of variation were above 20%. Therefore, the eluate concentration process was modified to prepare the samples of which the final solvent was 50% of methanol so that the target compounds would be highly soluble in addition to preparing 100% water sample. The modified method provided the average recovery rate of almost all compounds between 50% and 150%. CV% and correlation coefficients of linear standard curve of all target compounds were also improved below 20% and higher than 0.99, respectively. PPCPs concentration was determined by 100% water sample or 50% methanol sample as shown in **Table 1** indicated with circles based on the extraction recovery rate and the chromatographic peak form. The recovery rates of some PPCPs spiked in raw water were more than 20% lower or higher than those spiked in ultrapure water due to matrix effects. Therefore, in determining PPCPs of the sample containing large amount of matrix, 200ng/L of PPCPs was added to the samples prior to extraction, and the recovery rates of PPCPs were calculated to correct the impact of matrix effects on the variation of the

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recovery rates[4].

3.2 Behavior of PPCPs in water treatment process at Kunijima water purification plant

Kunijima water purification plant in Osaka city is applied to the advanced water treatment system which is combined with ozone treatments and granular activated carbon (GAC) adsorption process. **Figure 2** describes the treatment scheme of the purification plant. We determined concentrations of PPCPs in water samples of each treatment process five times from April to August in 2009.

The average concentrations of 30 compounds marked with squares in **Table 1** exceeded LOQ in raw water. But only those of Iopamidol and Iohexol were above LOQ in finished water. **Figure 3** and **Figure 4** show the average concentrations of some PPCPs at each process in advanced water treatment. Most of the average concentrations of 30 PPCPs significantly declined in intermediate ozone treated water, and the number of compounds decreased to 6 of which the average concentrations were more than LOQ. The average concentrations of Iopamidol and Iohexol fell to about 50% and 30% of those of raw water in intermediate ozone treated water and finished water, respectively. These results suggest that the advanced water treatment system could efficiently remove PPCPs and that intermediate ozone treatment is very effective for PPCPs removal.

Table 1 Recovery rates of SPE and average concentrations of raw water

*		Compounds Name	LOQ (ng/L)	Water 100% Recovery (%)	Water 100% CV% (n=5)	Methanol 50% Recovery (%)	Methanol 50% CV% (n=5)	*	*		Compounds Name	LOQ (ng/L)	Water 100% Recovery (%)	Water 100% CV% (n=5)	Methanol 50% Recovery (%)	Methanol 50% CV% (n=5)	*
○	1	Iopamidol	2	45	3.9			■	●	38	Mepirizole	0.6	62	7.8	66	6.0	
○	2	Acetaminophen	2	65	3.9			▒	●	39	Carbamazepine	0.8	101	3.6	93	2.1	▒
○	3	Iopromide	20	85	5.2				●	40	Tylosin	0.7	37	16.5	56	6.6	
○	4	Caffeine	10	86	3.6			■	●	41	Isopropylantipyrine	0.5	60	6.1	56	8.5	
○	5	Amantadine	4	72	1.5			▒	●	42	Cyproheptadine	0.5	22	24.3	82	2.5	
○	6	Salicylamide	0.8	58	10.7	55	9.3	□	●	43	Azelastine	2	24	25.9	86	2.1	
○	7	Antipyrine	0.2	69	1.3	68	4.0	□	●	44	Oxatomide	2	25	23.4	78	2.8	
○	8	Primidone	0.2	99	2.0	93	3.1	□	●	45	Clarithromycin	1	31	18.7	83	3.5	□
○	9	Metoprolol	0.6	82	3.7	89	4.5	□	●	46	Clofibric acid	0.7	96	1.6	88	4.2	□
●	10	Ketotifen	0.6	34	21.7	82	3.4		●	47	Bezafibrate	2	134	3.1	89	2.9	▒
○	11	Salicylic acid	10	64	4.3	57	5.0		●	48	Clemastine	2	16	25.6	82	2.6	
○	12	Sulfadimethoxine	0.4	77	5.6	79	5.0		●	49	Terfenadine	3	45	42.4	74	5.2	
●	13	Diphenhydramine	0.9	48	15.2	85	3.3	□	●	50	Etodolac	0.5	90	1.4	60	3.6	▒
●	14	Diltiazem	0.8	37	17.7	85	2.8	□	●	51	Diclofenac	3	162	2.0	87	3.6	□
●	15	Phenytoin	10	117	5.6	103	9.7		●	52	Ibuprofen	10	100	14.6	73	9.5	
●	16	Trihexyphenidyl	4	35	14.9	91	3.9		●	53	Mefenamic acid	0.7	132	2.1	73	3.6	□
●	17	Piroxicam	0.2	45	17.6	49	3.1		●	54	Fenofibrate	4	45	23.5	39	10.8	
●	18	Sulindac	0.6	152	0.8	88	3.8		○	55	Cotinine	4	55	5.4			▒
●	19	Verapamil	1	31	26.0	88	3.6		○	56	Ioversol	16	52	4.8			▒
●	20	Tolmetin	0.5	98	2.4	83	3.5		○	57	Iohexol	50	70	7.8			■
●	21	Naproxen	2	103	4.6	85	4.9		○	58	Ioxilan	10	77	6.8			
●	22	Fenbufen	3	153	1.9	93	2.8		○	59	Pirenzepine	0.5	74	5.4			□
●	23	Ketoprofen	2	110	1.3	91	3.1		○	60	Trimethoprim	2	82	3.9			□
●	24	Crotamiton	0.5	28	20.8	36	12.9	■	○	61	Metoclopramide	2	65	7.0			
●	25	Diphenylpyraline	1	34	19.7	89	2.3		○	62	Disopyramide	1	71	5.0			▒
●	26	Diflunisal	3	174	0.7	89	4.2		●	63	Propranolol	1	43	13.3	91	2.4	
●	27	Indometacin	0.8	178	4.1	69	4.7	□	●	64	Haloperidol	3	36	17.5	91	1.8	
●	28	Acemetacin	0.9	188	7.7	77	3.3		●	65	Digoxin	1	71	3.2	70	5.7	
●	29	Flufenamate	2	184	3.3	81	3.2		●	66	Imipramine	3	21	24.1	83	2.6	
○	30	Theophylline	10	102	2.4			■	●	67	Furosemide	3	81	2.9	67	3.1	
○	31	Atenolol	0.8	90	1.2			▒	●	68	Fluvoxamine	2	4	21.1	61	5.8	
○	32	Sotalol	0.5	89	1.1				●	69	Amitriptyline	2	19	25.3	87	2.6	
○	33	Sulpiride	0.9	95	2.7			▒	●	70	Nalidixic acid	2	100	9.6	85	6.2	
○	34	Sulfamethoxazole	1	70	6.7			□	●	71	Fenoprofen	2	112	3.1	87	4.4	
○	35	Ethenzamide	0.7	66	7.7	64	9.8	□	●	72	Glibenclamide	2	114	6.0	81	3.8	
○	36	Tenoxicam	0.6	61	14.0	61	3.9		●	73	Gemfibrozil	2	122	6.2	96	7.0	
○	37	Phenacetin	0.9	84	4.3	81	7.0										

* ○ : Determined with 100% water sample
● : Determined with 50% methanol sample

* : Average concentrations of raw water

■ : More than 100ng/L
▒ : More than 10ng/L and below 100ng/L
□ : Below 10ng/L

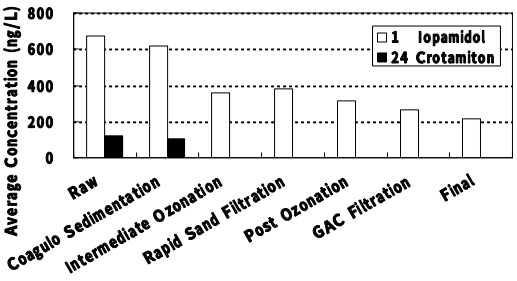

Figure 3 PPCPs in Advanced Water Treatment (No.1)

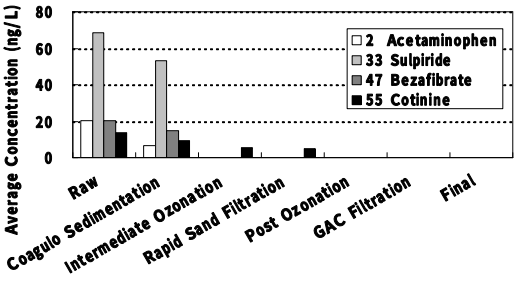

Figure 4 PPCPs in Advanced Water Treatment (No.2)

4. References

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