Status of Pharmaceuticals and Personal Care Products (PPCPs) in River Water and Wastewater and Evaluation of their Effects on Aquatic Organisms

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1. Introduction

There is growing concern over the presence of pharmaceuticals and personal care products (PPCPs) in the water environment. Many PPCPs have been reported in river water and treated wastewater. The inherent biological effect of PPCPs due to their medical properties could have an adverse effect on the aquatic ecosystem.

However, information about environmental fates and ecotoxicological data of PPCPs is still limited for assessing the risk that PPCPs pose to the large number of aquatic lives in the water environment.

In this study, we investigated the occurrence and fate of PPCPs in rivers affected by different wastewater loads, and also evaluated the biological effects of PPCPs found in those rivers using bioassays. Based on the results, the river water was evaluated from the viewpoint of the effects of PPCPs on aquatic lives.

2. Methods

2.1 PPCPs in river water and wastewater

Surveys were conducted in two rivers. One has a large basin (16,840 km^2) and receives a variety of wastewaters from households, farmland, stockbreeders and manufactures, with and without appropriate treatment. Samples were collected from surface waters in the mainstream, confluences of major tributaries and major distributaries. Wastewater effluents were also collected from wastewater treatment plants which discharge the effluent directly into the river.

The other has a small basin (37 km^2) and its watershed is densely populated. Surface waters were collected at 2 points; the upstream receiving treated wastewater from septic tanks and the tributary downstream where a nearly complete sewerage system is provided with the treatment plant outside the river basin.

Subjects of PPCPs without triclosan were analyzed by LC-MS/MS, and

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triclosan was analyzed by GC-MS.

2.2 Ecotoxicity evaluation of PPCPs

Eleven substances that were found in treated wastewater were applied for five bioassays: Bacteria test, algal growth inhibition test, protozoan test, crustacean test and frog embryo teratogenesis assay. PPCPs were dissolved in dimethyl sulfoxide (DMSO) and diluted with culture medium to the required concentration.

3. Results

In the river with a large basin, fifty-seven out of 75 PPCPs were detected. As the sampling points located on the lower reaches, the number of detection and detected concentrations were high. Concentrations were generally high in the following order: the effluents, surface water in the tributaries, and surface water in the mainstream. Calculating the total load of PPCPs into the river, the major part was estimated to come from the tributaries.

In the urban small river, concentrations of PPCPs were different according to the watershed conditions, higher concentration in the watershed with lower sewerage ratio. The concentrations at the upstream where does not yet have a developed sewerage system were quite high; on the other hand, those at the tributary downstream where the sewerage system is well developed are as low as the concentrations of the river with a large basin.

From the bioassays, it was revealed that two antibiotics inhibited algal growth and antibacterial triclosan had a strong effect on many of the species. The triclosan concentration of EC50 or LC50 ranged from 0.01 to 1 mg/L, and because triclosan is widely used in soap and dental rinse, this PPCP should be of concern.

Ecological risk was evaluated by comparing the river water concentrations at the urban small river and the ecotoxicity results. Because NOEC calculated from chronic toxicity data was obtained only for algae, the predicted no-effect concentration (PNEC) was calculated using the values of NOEC by AGI test and an assessment factor of 100. For the environmental concentration, we used the measured environmental concentration (MEC). At the upstream, MEC/PNEC values for triclosan, clarithromycin and azithromycin were higher than 1; therefore, there is a high possibility that these pharmaceuticals affect aquatic lives. At the tributary downstream, MEC/PNEC values for all PPCPs were less than 1. Thus, the watershed where does not yet have a developed sewerage system is at a higher ecological risk from PPCPs.

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1. Introduction

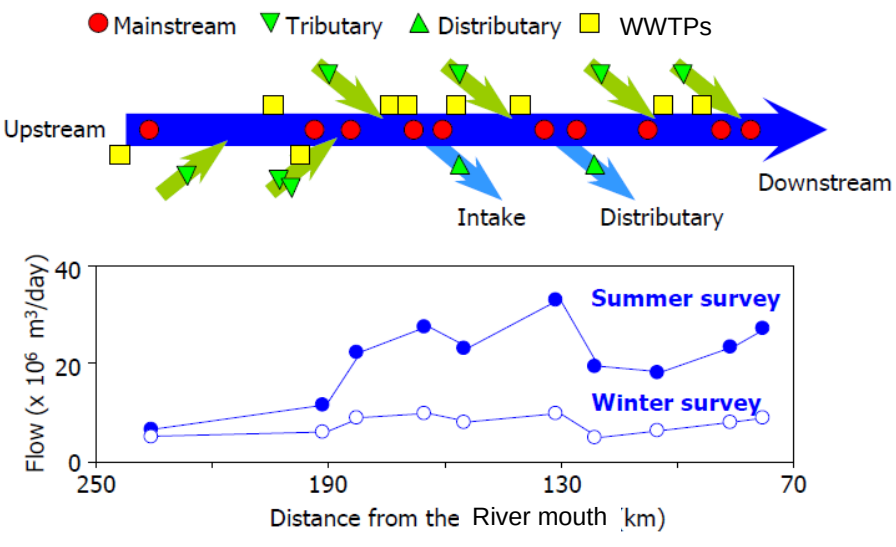
- Growing public concern about the environment pollution of pharmaceuticals and personal care products (PPCPs).
- For assessing the risk of PPCPs on aquatic lives, information about environmental fates and ecotoxicological data of PPCPs is still limited.
- In this study, we investigated
  - the occurrence and fate of PPCPs in rivers affected by different wastewater loads
  - the biological effects of PPCPs using bioassays.

-Based on the results, the river water was evaluated from the viewpoint of the effects of PPCPs on aquatic lives.

2. Methods

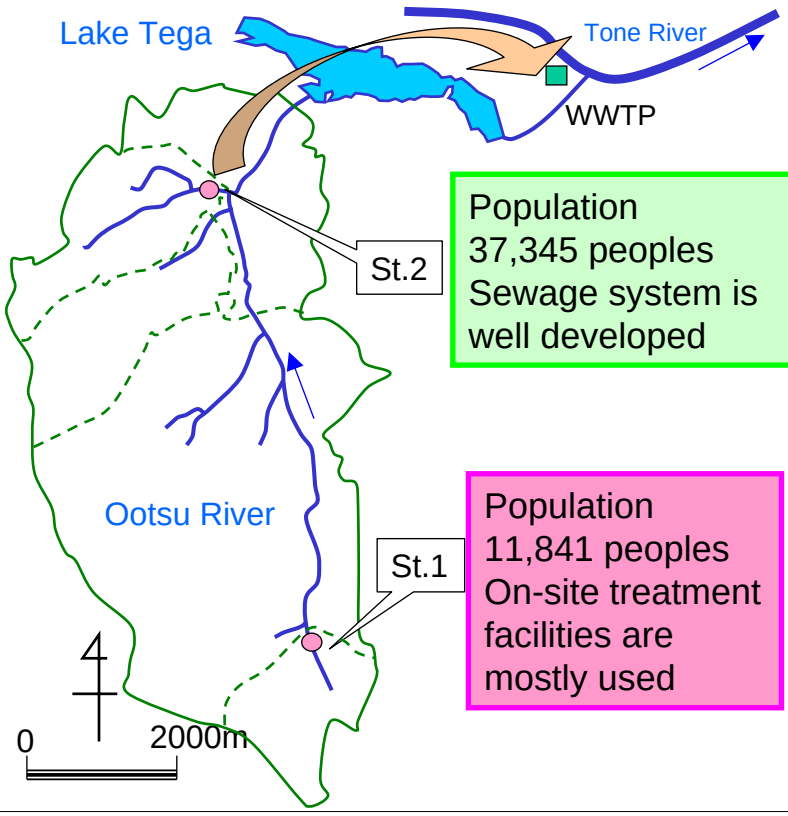
2.1 PPCPs in river water and wastewater

-River with a large basin (16,840 km2)



receiving a variety of wastewaters from households, farmland, stockbreeders and manufactures

- Urban river with a small basin (37 km2)



having some small tributaries

In downstream river basin, the sewage system is well developed

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Upstream river basin does not yet have a developed sewerage system

Target PPCPs

Use	Name
Non-steroidal anti-inflammatory drug	acetaminophen, antipyrine, ethenzamide, ibuprofen, indomethacin, mefenamic acid, naproxen, diclofenac, fenoprofen, isopropylantipyrine, mepirizole, crotamiton, ketoprofen
Antibiotic	nalidixic acid, trimethoprim, 2-quinoxainecarboxylic acid*#, azithromycin, benzylpenicillin*, chloramphenicol*, clarithromycin, danofloxacin*, levofroxacin, norfloxacin*, oxytetracycline*, tetracycline*, thiamphenicol*, tilmicosin*, sulfadimethoxine*, sulfadimizine*, sulfamethoxazole*, sulfamonomethoxine*
Antiarrhythmic	atenolol, disopyramide, metoprolol, propranolol,sotalol
Bronchodilator	clenbuterol, salbutamol, terbutaline, theophylline
Vasodilator	diltiazem, dipyridamole, Verapamil
Psychoneurotic agent	chlorpromazine, amitriptyline, imipramine, haloperidol, sulpiride
Antihyperlipidemic	bezafibrate, clofibric acid#, gemfibrozil
Anticonvulsant	carbamazepine, primidone
Anticholinergic agent	diphenidol, scopolamine, tolperisone
Other	caffeine (stimulants), cyclophosphamide (immunosuppressant), promethazine (antihistamines), carbazochrome (hemostatics), dextromethorphan (antitussive drug), ifenprodil (cerebral circulation improver), metoclopramide (dopamine receptor antagonist), tolbutamide (anti-diabetics), pentxifylline (blood viscosity-deducing agent), prednisolone (corticosteroid drug), N,N-diethyl-m-tolamide (insect-repellent), griseofulvin (antifungal drug), furosemide (diuretics), pirenzepine (peptic ulcer agent)

*: veterinary drug; #: metabolite

2.2 Ecotoxicity evaluation of PPCPs

- Bacteria (Microtox®) Bio-liminescent inhibition (EC50)

- Algae
  Algal Growth Inhibition Test (EC50, NOEC)

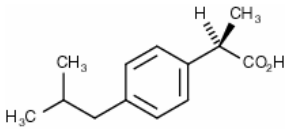
- Crustaceans
  Acute toxicity test : DaphToxkit (EC50)

- Amphibians
  Toxicity on development of embryo (LC50)

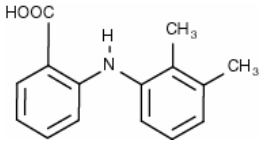
- Protozoa
  Growth inhibition test (EC50)

- 11 substances for bioassays

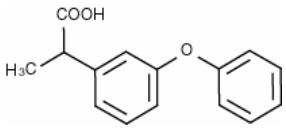
Anti-inflammatoris



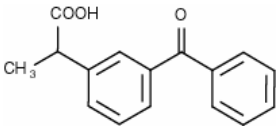
Ibuprofen



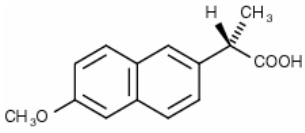
Mefenamic acid



Fenoprofen

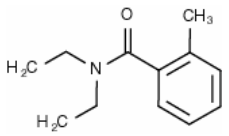


Ketoprofen



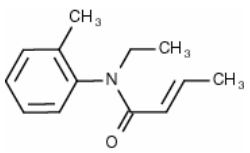
Naproxen

Insect repellent



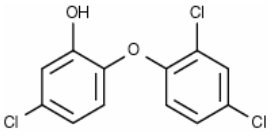
Diethyltoluamide (DEET)

Antipruritic

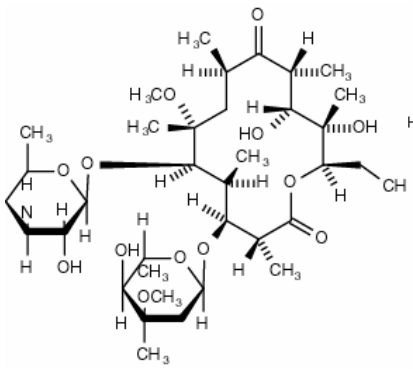


Crotamiton

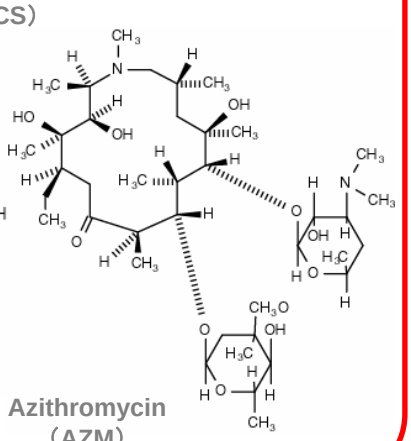
Antibacterial, Antibiotic



Triclosan
（TCS）

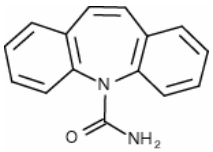


Clarithromycin
（CAM）



Azithromycin
（AZM）

Anticonvulsant



Carbamazepine
（CBZ）

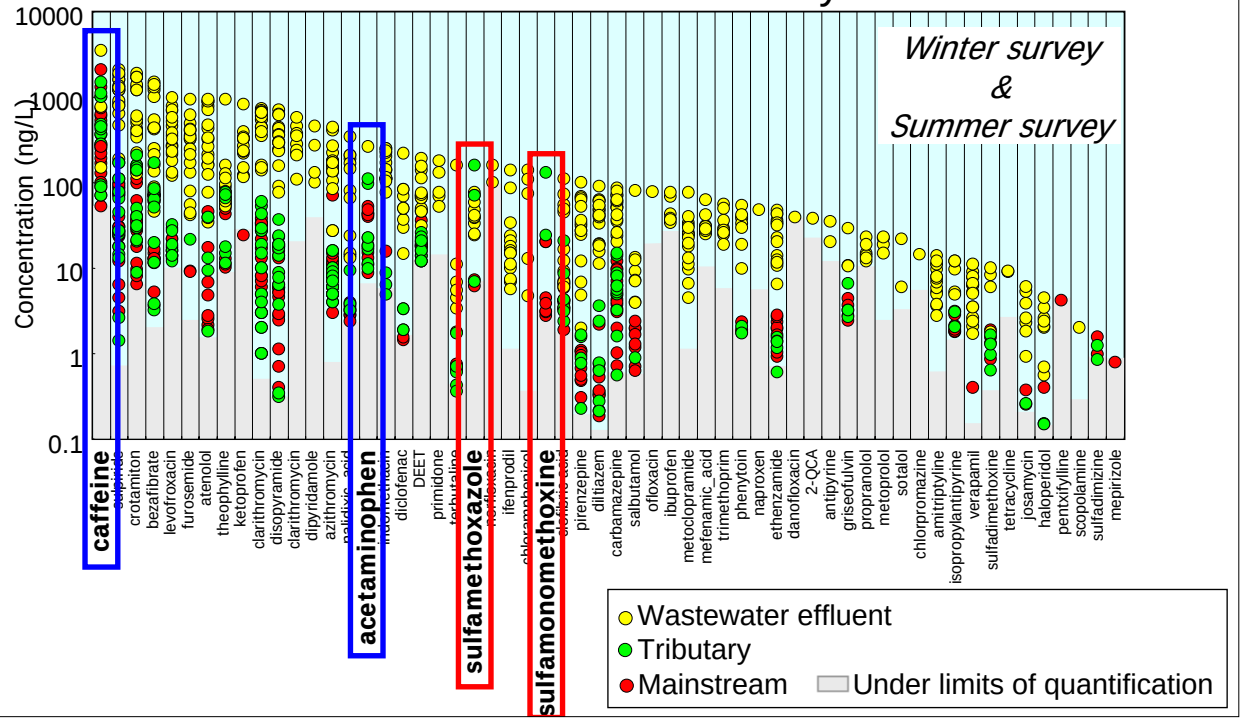
Maximum concentration on bioassay = 10mg/L

3. Results

- PPCP concentration in river with a large basin

-57 PPCPs were detected in one or more samples

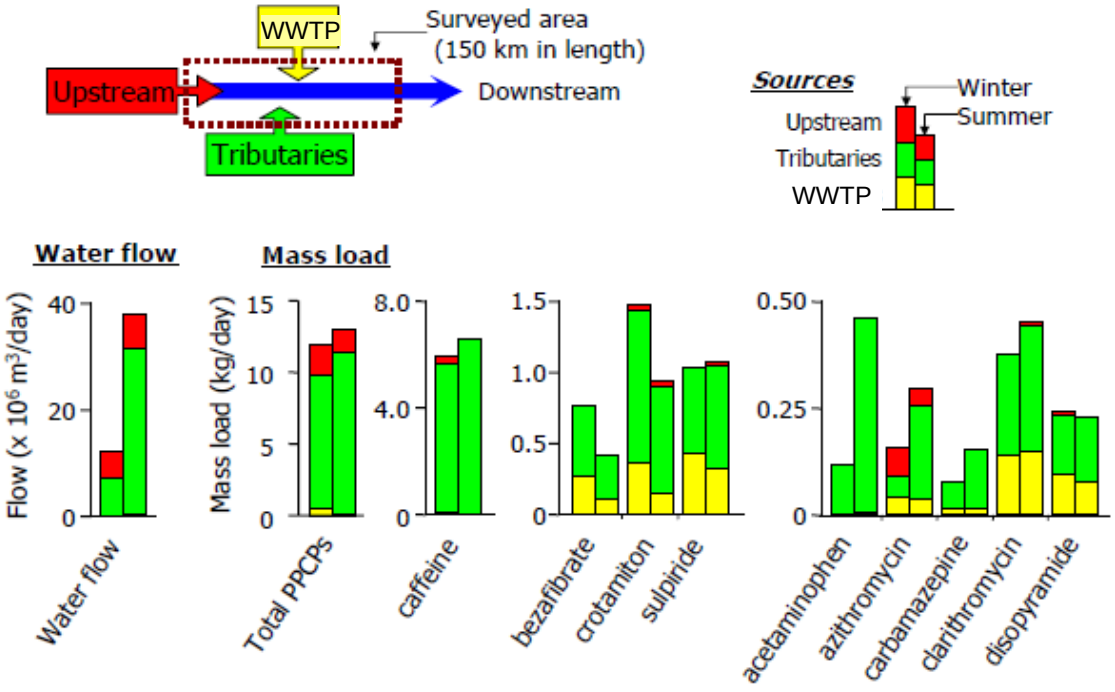
-Concentration : Effluent > Tributary > Mainstream



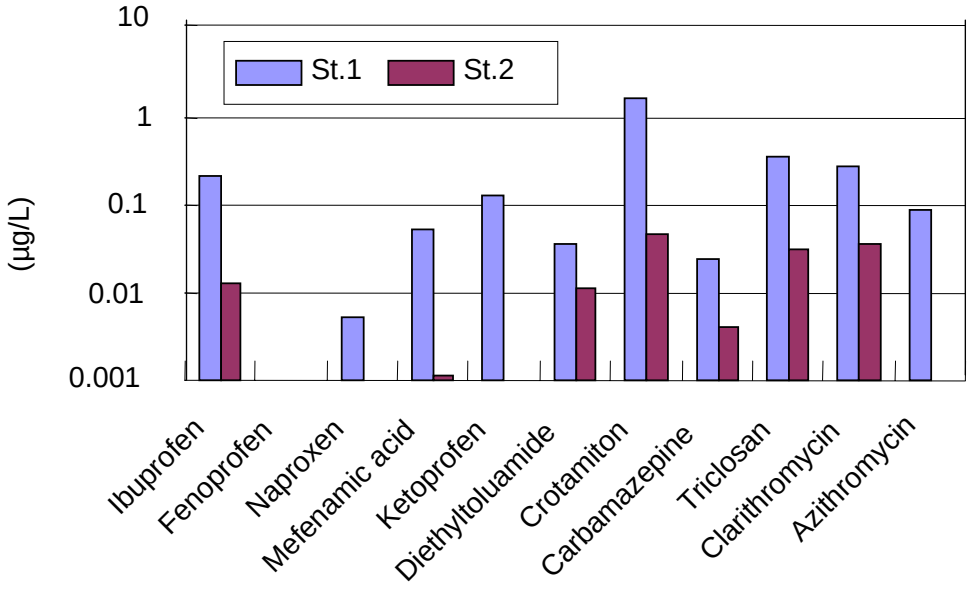
Source distribution of PPCPs

-The tributaries were dominant as PPCPs source.

-Large load of caffeine (easily biodegradable) suggests that sewerage systems in the tributaries are insufficient.



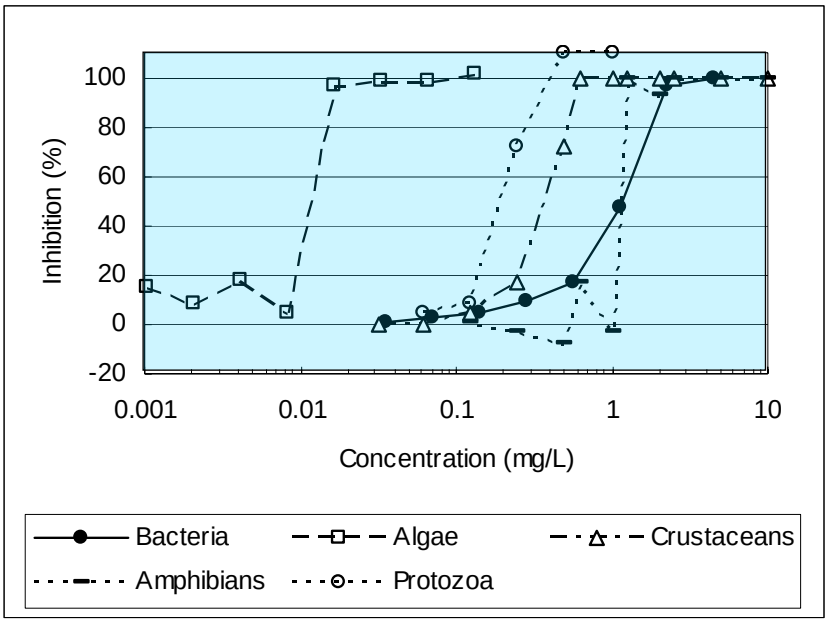
- PPCP concentration in urban small river



St.1: without a developed sewerage system
⇒20 - 1600ng/L

St.2: the sewerage system is well developed
⇒n.d. - 50ng/L

- Bioassays of PPCPs



Concentration-response curve of each bioassay on triclosan

Bioassay results

		Bacteria 15min	Algae 96H		Crustaceans 48H	Amphibian 96H	Protozoa 96H
		EC50	EC50	NOEC	EC50	LC50	EC50
Anti-inflammatory	Ibuprofen	11.3*	2.3	0.52	N.E.	N.E.	4.1
	Fenoprofen	10.4*	5.7	2.1	N.E.	N.E.	16.9*
	Naproxen	18.5*	3.7	0.52	N.E.	N.E.	-
	Mefenamic acid	10.2*	5.4	2.1	N.E.	5.2	2.4
	Ketoprofen	20.4*	2.0	1.0	2.3	N.E.	N.E.
Insect repellent	Diethyltoluamide	21.2*	4.1	0.52	N.E.	N.E.	-
Antipruritic	Crotamiton	19.6*	3.5	2.1	N.E.	N.E.	-
Anticonvulsant	Carbamazepine	28.3*	48.9*	0.52	N.E.	N.E.	-
Antibacterial Antibiotic	Triclosan	0.52	0.012	0.0083	0.26	0.82	0.21
	Clarithromycin	N.E.	0.012	0.0052	N.E.	N.E.	N.E.
	Azithromycin	N.E.	0.019	0.0052	N.E.	N.E.	N.E.

(mg/L)

[N.E.]: no effects for setting concentration, [*]: extrapolation value
[-]: no data, [yellow letter]: additional data

- First approach for risk evaluation for PPCPs

- The predicted no-effect concentration (**PNEC**) was calculated from the values of NOEC examined by AGI test using an assessment factor of **100**.
  [PNEC = NOEC÷100]

- The concentration of PPCPs actually measured at each observation station as
  Measured Environmental Concentration (**MEC**).

- **MEC/PNEC** < 0.1 ; Acceptable
  0.1<=**MEC/PNEC** <1 ; Needs further survey
  1<=**MEC/PNEC** ; Needs detailed evaluation

Results of First approach for risk evaluation for PPCPs

	PNEC [NOEC/100] (μg/L)	St.1			St.2		
		MEC (μg/L)	MEC/PNEC	Assessment	MEC (μg/L)	MEC/PNEC	Assessment
Ibuprofen	5.21	0.22	0.042	Acceptable	0.01	0.002	Acceptable
Fenoprofen	20.83	0.00	0.000	Acceptable	0.00	0.000	Acceptable
Naproxen	5.21	0.01	0.001	Acceptable	0.00	0.000	Acceptable
Mefenamic acid	20.83	0.05	0.002	Acceptable	0.00	0.000	Acceptable
Ketoprofen	10.41	0.13	0.012	Acceptable	0.00	0.000	Acceptable
Diethyltoluamide	5.21	0.03	0.007	Acceptable	0.01	0.002	Acceptable
Crotamiton	20.83	1.60	0.077	Acceptable	0.05	0.002	Acceptable
Carbamazepine	5.21	0.03	0.005	Acceptable	0.00	0.001	Acceptable
Triclosan	0.08	0.36	4.322	Needs detailed evaluation	0.03	0.372	Needs further survey
Clarithromycin	0.05	0.28	5.378	Needs detailed evaluation	0.03	0.653	Needs further survey
Azithromycin	0.05	0.09	1.671	Needs detailed evaluation	0.00	0.000	Acceptable

4. Conclusion

- In a river with a large basin, PPCP concentrations were in the order of effluents > tributaries > mainstream. Major load of PPCPs was estimated to come from the tributaries.
- In the urban small river, concentrations of PPCPs were different according to the watershed conditions, higher concentration in the watershed with lower sewerage ratio..
- The antibiotics “Clarithromycin and Azithromycin” affected the algae but did not affect the other lives.
- Triclosan had affected all lives. The sensitivity of these lives to Triclosan was in the order of algae > protozoa > crustaceans > bacteria > amphibians.
- Thus the effects of PPCPs varied according to species of lives.

- Three PPCPs (Triclosan, Clarithromycin and Azithromycin) posed an eco-toxiclogical risk in this observed rivers.
- The eco-toxicological risk in the water basin that does not yet have a developed sewerage system is higher than that well developed the sewerage system.