Environmental Pollution 258 (2020) 113792

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Ny-Ålesund-oriented organic pollutants in sewage effluent and receiving seawater in the Arctic region of Kongsfjorden☆

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ARTICLE INFO

Article history:
Received 4 July 2019
Received in revised form
9 December 2019
Accepted 10 December 2019
Available online 13 December 2019

Keywords:
Arctic
Ny-Ålesund
LC-HRMS
Nontarget screening
Effluent

ABSTRACT

Ny-Ålesund, one of four permanent settlements on Spitsbergen in Svalbard, is a research town that includes scientific institutes from many countries. Because of daily-used chemicals (e.g., pharmaceutical and personal care products (PPCPs)) used by residents in the area, generated sewage is considered as a point source in the Kongsfjorden. The aim of the present study was to identify and quantify organic pollutants in the effluent and along the shoreline and offshore via target, suspect, and non-target screening using liquid chromatography–high-resolution mass spectrometry. We tentatively identified 30 compounds using the suspect and non-target screening methods in effluent samples from our first visit to the settlement in 2016. Among these, 3 were false positive, 24 were confirmed, and the 3 remaining compounds were not confirmed because of a lack of reference standards. Of the confirmed, 21 were quantifiable and considered target compounds for the 2nd year study. The quantified compounds in the effluent samples in 2017 totaled 17, including PPCPs, pesticides, perfluorinated compounds, and their metabolites. Some of the compounds, such as caffeine, paraxanthine/theophylline, acetaminophen, cetirizine, diethyl toluamide (DEET), and icaridin, were also detected in the receiving seawater. The concentration range was from 4 to 280,000 ng/L in the effluent and 2–98 ng/L in the seawater. Other 24 compounds were tentatively identified in the second-year effluent samples. Five were further confirmed using reference standards. Prioritization was performed on the 47 substances screened in Ny-Ålesund using the exposure and toxicity index. As the result, the top seven substances of concern present were perfluorooctanesulfonic acid (PFOS), triphenyl phosphate (TPHP), irbesartan, DEET, acetaminophen, caffeine, and paraxanthine/theophylline. As the effluent was identified as a source of the concerned organic pollutants, an emission reduction strategy should take place for protection of Arctic Fjorden environment.

1. Introduction

The Arctic is the northernmost polar region on the planet and thus considered a pollution-free area. Unfortunately, a number of studies have reported the occurrence of anthropogenic pollutants such as polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), perfluorinated compounds (PFCs), and pharmaceuticals in this far-remote environment (Butt et al., 2010a, b; R. Wang et al., 2015; Zhu et al., 2015). The presence of these organic pollutants in Arctic media is mainly attributed to transportation via either sea currents or the atmosphere. Previous studies found that the North Sea flowing into the Arctic region was contaminated with benzotriazoles and clofibric acid as well as caffeine (Weigel et al., 2002; Wolschke et al., 2011). It is well known that mercury and methyl mercury in the Arctic mainly occur via atmospheric transportation (Steffen et al., 2015). Thus, the contamination of the Arctic has been largely considered the consequence of remote transportation of pollutants.

Kongsfjorden is an inlet on the west coast of Spitsbergen, an island that is part of the Svalbard archipelago in the Arctic Ocean. The inlet is 6.4 km long and ranges in width from 6.4 to 14.5 km.

☆ This paper has been recommended for acceptance by Eddy Y. Zeng.

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https://doi.org/10.1016/j.envpol.2019.113792
0269-7491/

Ny-Ålesund, on the southern shore of Kongsfjorden, is one of only four permanent settlements on Spitsbergen and has a number of scientific bases established by 10 countries, including Germany, Japan, England, Norway, the Netherlands, Italy, France, China, Sweden, and Korea. The northernmost functional civilian settlement in the world has a year-round permanent population of 30–35 with a summer population reaching 120. There is a sewage treatment plant, which runs without chemical/microbial treatment, but retains sewage in 4-linked tanks (5 tons each, 20 tons in total) for approximately 40–50 h before discharge to the Fjorden. As the influent carries particulate matters (mainly soil) into the tanks, sorption onto particles and/or biodegradation by microbes originating in the soil are the expected elimination mechanisms. The effluent is discharged four times per day with approximately 2–2.5 ㎥ at each event. Thus, the effluent discharged along the shore of Ny-Ålesund is a point source for the Kongsfjorden. However, information regarding pollution of the Arctic region from a point source is limited. A previous study of contamination in Longyearbyen and Tromsø, in Svalbard, southeast of Ny-Ålesund, reported occurrences of pharmaceuticals in effluent and seawater (Kallenborn, 2009; Weigel et al., 2004). However, a source-oriented study had not been conducted, to our knowledge, in the region. Therefore, it was necessary to study pollutant generation, concentration, and concentration change around the area caused by the discharged effluent from Ny-Ålesund as a point source in the Arctic region.

During recent years, the development of analytical screening techniques such as suspect and non-target screening (SNTS) has facilitated contaminant prioritization. SNTS is an analytical technique to identify substances without a reference standard. Suspect screening is performed based on a database of known substances, while non-target screening is able to identify peaks corresponding to unknown chemicals (Aalizadeh et al., 2016). To perform this analysis technique, high-resolution mass spectrometry (HRMS) such as Orbitrap™ and time-of-flight (TOF), which offer high mass accuracy and resolution, is required. HRMS is capable of detecting numerous compounds in an aquatic environment because of its high sensitivity and selectivity in full scan analysis (Aalizadeh et al., 2016; Avagyan et al., 2016; Gago-Ferrero et al., 2015; Richardson and Ternes, 2018; Schymanski et al., 2014).

The aim of present study was to identify prior organic pollutants by SNTS using liquid chromatography-high resolution mass spectrometry (LC-HRMS) and monitor the occurrences and concentrations in the effluent and receiving seawaters in the Kongsfjorden.

For identification of prior pollutants, a sampling campaign, followed by SNTS, was conducted on Ny-Ålesund during the summer of 2016. After selection of quantifiable priority pollutants and preparation of quantitative analyses, the occurrences and concentrations were investigated via target/suspect/non-target screening during the following year.

2. Materials and methods

2.1. Chemical and standards

Detail about 32 reference standards and 15 isotopically labeled internal standards (ILIS) used confirmation/quantitative analysis for the tentatively identified substances and other chemicals are given in SI.1.

2.2. Sample collection

The first sampling was undertaken from July 5th to 10th, 2016, for the identification of major pollutants using SNTS. The samples included effluent ($n = 6$), receiving shoreline ($n = 8$)/offshore seawater ($n = 4$), glacier ($n = 1$), and surface water ($n = 1$) (used as a drinking water source). The effluent samples and receiving seawaters were considered sources of major pollutants whereas the glacial and surface water were used to recognize background contaminations. During the following summer (August 21st to 26th, 2017), target screening for prior pollutants and SNTS for extra pollutants were performed for 10 effluent and shoreline ($n = 15$)/offshore ($n = 6$) seawater samples. The sampling points were selected with consideration for the direction of discharge and the current flow at the Kongsfjorden as shown in Fig. 1. Detailed information regarding sampling method, sampling sites, and dates are provided in the SI.2 and Table S1.

2.3. Sample storage and pretreatment

To avoid cross contamination between the effluent and seawater samples, sample pretreatments were separately performed with independent apparatus sets. The pretreatment was performed in two steps. During the first step, sample loading onto a solid-phase extraction (SPE) cartridge and drying of the cartridge were performed at a laboratory of the Arctic Science Base in Ny-Ålesund. All dried cartridges were packed with aluminum foil and a plastic bag to prevent sample contamination. After transportation to Korea, the second step was to extract analytes from the cartridges. The detailed pretreatment procedure is described in SI.3.

2.4. Instrumental parameters

The chromatographic analyses were conducted using a liquid chromatographic (LC) system (Dionex UltiMate 3000 XRS, Thermo Fisher Scientific) coupled to an HRMS (Q-Exactive plus, Thermo Fisher Scientific). The detailed about instrumental parameters is showed in SI.3.

2.5. Identification of major pollutants (via SNTS)

For suspect screening, we used the data processing software Trace Finder 4.1 (Thermo Fisher Scientific) to isolate the suspected peaks and Xcalibur (Thermo Fisher Scientific, USA) to confirm the TraceFinder 4.1 results. To develop the suspected compound list, the EFS high-resolution, accurate-mass (HRAM) compound database (EFS DB, Thermo Fisher Scientific), which includes 1,729 substances related to environmental and food safety, was used as a main source of candidates. Furthermore, another 133 emerging pollutants not in the EFS DB, such as pharmaceuticals, organophosphate flame retardants (OPFRs), and PFCs recognized via comprehensive monitoring/screening studies (Green et al., 2008; Woudneh et al., 2015), were also added to the list. In total, 1,862 compounds were included in a suspected candidate list which was used for data-dependent tandem mass spectrometry (MS/MS fragment) data acquisition. Non-target screening was performed using Compound Discoverer 2.0 (Thermo Fisher Scientific) based on the mzCloud database, which provides searchable, accurate MS/MS fragment data for a number of compounds such as pharmaceuticals, personal care products, pesticides, industrial chemicals, metabolites, etc. Detailed about the workflow for suspect and non-target screening is depicted in SI (SI.4, Fig. S1A and B).

2.6. Quantitative analysis for major pollutants (via target screening)

TraceFinder 4.1 was used for quantitative analysis based on the internal standard method. A method of quantitative analysis was established for 21 substances out of the 24 confirmed. A reliable quantitative analysis was not feasible for amoxicillin, lidocaine and

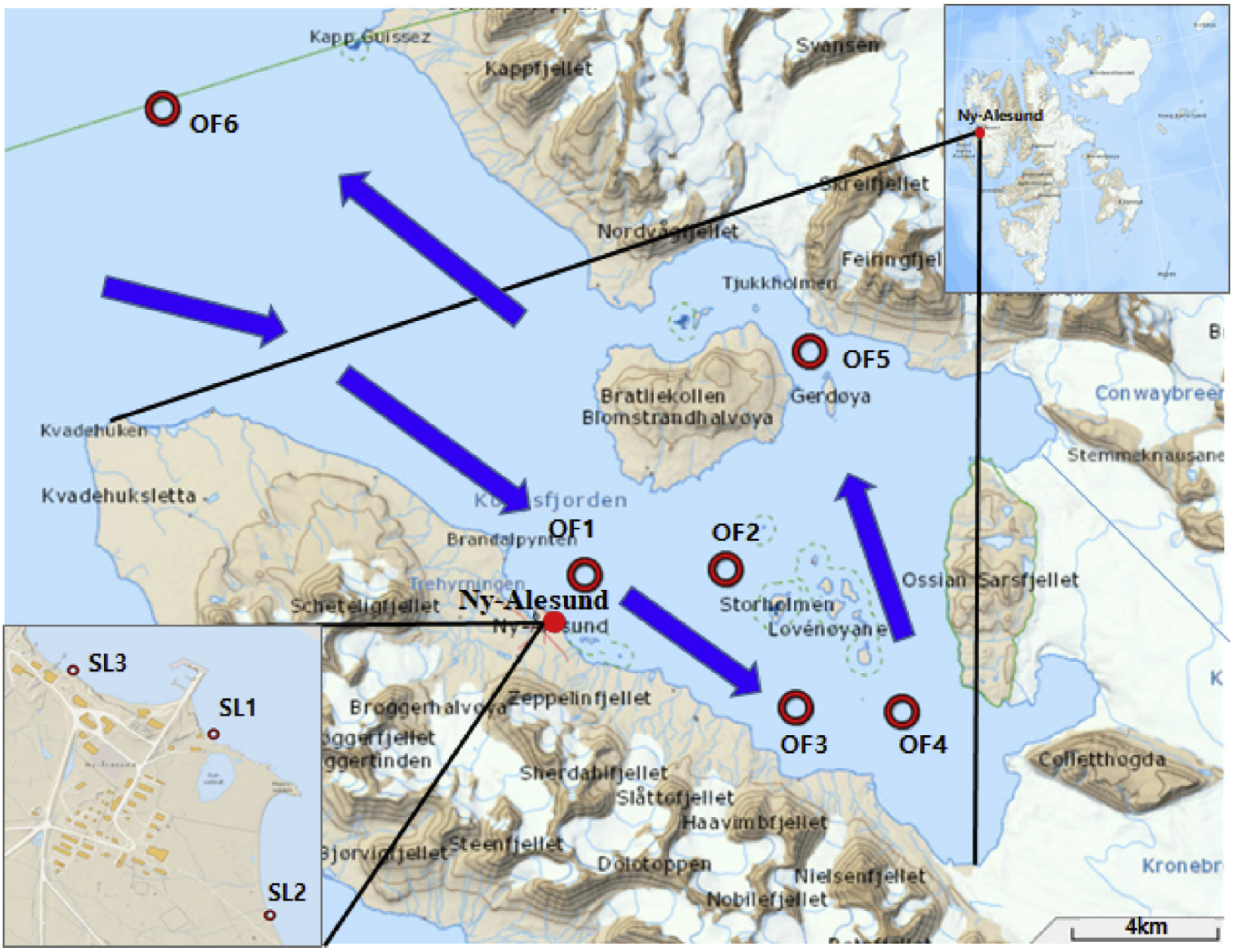


Fig. 1. Sampling sites around Ny-Ålesund. SL1-3 indicate the shoreline sampling points whereas OF1-6 indicate offshore sampling points. The blue arrows describe the seawater current direction in the Kongfjorden. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

sulfonate because the linearity of the R^2 value was poor at low and medium concentration ranges. For a peak suspected to be paraxanthine and/or theophylline, the two substances were quantified as one substance because they could not be perfectly separated. Method performance was evaluated through verification of linearity, precision, and recovery. Procedure for recovery test is described in SI (SI.5, Figs. S2A and B). The 12-point calibration curves were constructed using the extracts from the identical SPE procedure for the water samples ranging from 1 to 200 ng/L or 200 to 2000 ng/L. Precision values were calculated as the standard deviation of five-times measurement at a concentration of 100 ng/L during the day. The limits of detection (LODs) and quantification (LOQs) were calculated using S/N ratio of 3 and 10, respectively.

3. Results and discussion

3.1. Method performance

3.1.1. Quantitative analysis

Table 1 shows the linearity of the calibration curve, analytical precision, LOD, LOQ, and recovery for the target compounds selected from results of the 1st year. Across all of the calibration range, the R^2 for target compounds exceeded 0.9940 with good linearity. The index of precision as measured by relative standard deviation was less than 25%, the LOD ranged from 0.1 to 1 ng/L, and the LOQ ranged from 0.5 to 5 ng/L. However, the precision and accuracy for 2-acetaminophenol, acetaminophen, caffeine, cetirizine, paraxanthine/theophylline and triphenylphosphine oxide were not guaranteed as their concentrations were above 2000 ng/L, the maximum quantification range.

Absolute recovery for the targets with artificial seawater was in the range of 72–110%, whereas the results with DI water were in the range of 74–114%. Results of relative recovery in the effluent matrix for 16 out of 21 targets ranged from 80 to 120%, showing the reliability of the quantification method. The relative recovery for the Fjorden seawater was not estimated, as we were unable to bring extra seawater samples for the recovery test due to limited sample transportation from Ny-Ålesund.

3.1.2. Suspect and non-target screening

Notably, some peaks excluded from the tentative identification via SNTS were potential candidates for a false negative error. Even though exclusion filters such as peak area threshold are appropriate for the purpose of identifying major pollutants, some apparent candidate peaks were filtered out given the lack of information. For example, 32 peaks were filtered out during step 7 of suspect screening because of the absence of fragment data. To identify false or true negatives for the 32 deleted peaks, MS/MS fragment acquisition of the corresponding ions was conducted by renewing the inclusion list with 32 candidates. As a result of the

Table 1
Information on the 21 target compounds.

Compounds	Formula	Log K_{ow}[a]	RT	R^2	LOD (ng/L)	LOQ (ng/L)	Precision (RSD, %)	Abs. recovery		Rel. recovery
								Artificial seawater	DI water	effluent
2-Acetaminophenol	C8H9NO2	0.6	2.8	0.9988	1.0	5.0	17	84	98	88
5,6-dimethyl benzimidazole	C9H10N2	2.3	3.4	0.9996	0.1	0.5	6	76	94	102
8-methoxypsoralen	C12H8O4	2.1	5.4	0.9997	0.1	0.5	6	87	98	93
Acetaminophen	C8H9NO2	0.3	1.9	0.9997	0.1	0.5	19	94	90	115
Antipyrine	C11H12N2O	0.6	3.6	0.9999	0.1	0.5	7	72	94	101
Caffeine	C8H10N4O2	0.2	3.0	0.9996	0.1	2.0	22	96	95	81
Carbendazim	C9H9N3O2	1.6	2.6	0.9999	0.1	0.5	6	98	88	108
Cetirizine	C21H25ClN2O3	−0.6	7.2	0.9948	0.1	1.0	19	92	99	85
Diethyl toluamide	C14H11Cl2NO2	2.3	10.4	0.9999	0.1	5.0	2	110	81	130
Diclofenac	C12H17NO	4.0	6.8	0.9992	0.5	1.0	2	74	95	105
Icaridin	C12H23NO3	2.6	7.6	0.9962	1.0	2.0	6	94	74	104
Metoprolol	C15H25NO3	1.7	3.9	1.0000	0.1	0.5	2	90	96	126
N,N-dimethyl-N′-phenylsulfamide	C8H12N2O2S	1.2	5.0	0.9996	0.1	1.	5	72	99	97
Naproxen	C14H14O3	3.1	7.9	0.9999	0.1	0.5	1	75	99	101
Paraxanthine/theophylline	C7H8N4O2	−0.4	2.3	0.9998	0.5	2.0	4	88	93	110
PFHxS	C6HF13O3S	4.3	9.0	0.9997	0.1	1.0	1	95	101	79
PFOA	C8HF15O2	4.8	10.4	0.9999	0.1	0.5	0	97	114	65
PFOS	C8HF17O3S	4.5	11.2	0.9999	0.1	0.5	13	91	97	116
Pyrimethanil	C12H13N3	3.2	6.1	0.997	0.1	0.5	2	104	94	100
Tributyl phosphate	C12H27O4P	3.8	12.1	0.997	0.5	2.0	4	90	79	36
Triphenylphosphine oxide	C18H15OP	3.1	7.8	0.9972	0.1	1.0	10	96	98	103

[a] A log octanol-water partition coefficient (log K_{ow}) of approximately 21 compounds was estimated using KOWWIN v1.67 or 1.68.

measurement, MS/MS fragments were still not acquired for 14 masses which should have been excluded for a type of error. Among others, fragment patterns for 16 peaks were inconsistent with any of the MS/MS database, indicating true negative results. Only two peaks for amoxicillin and lidocaine were finally confirmed using reference standards. Thus, two meaningful compounds were falsely excluded along with other 30 uncertain or false peaks, indicating 6.7% false negative errors in the suspect screening step.

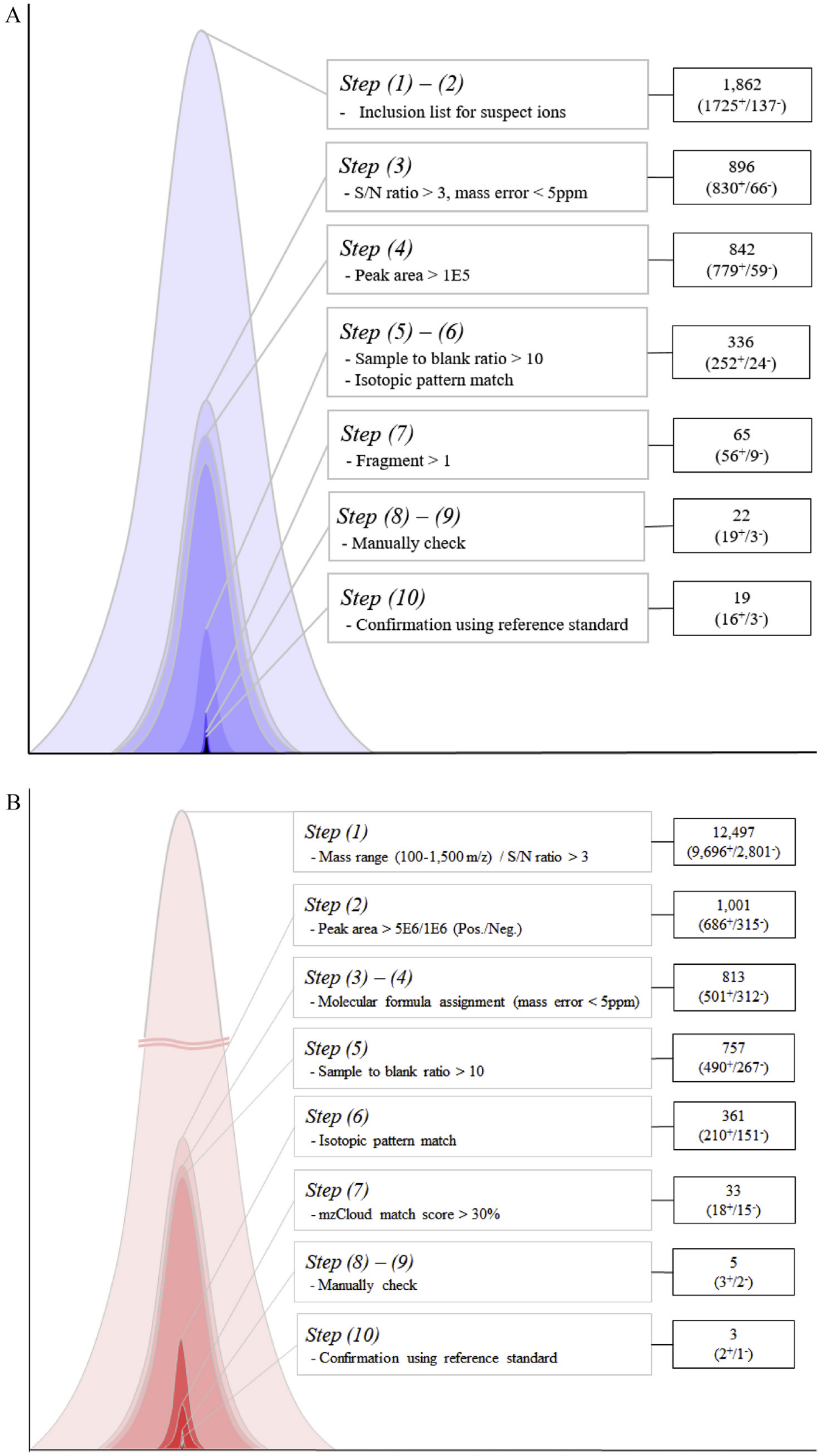
During non-target screening, 328 peaks were excluded from the tentatively identified candidates, regardless of MS/MS fragment acquisition, because of the absence of MS/MS information in mzCloud. These false/true negative candidates were re-investigated with help of MS/MS fragment data prediction system (Metfrag) as supplementary tool to mzCloud. After excluding 275 peaks deviating from parameters such as the intensity threshold (<10,000,000) and peak shape check, 53 candidate peaks remained as candidates for false negatives. Of these, 41 candidate peaks were excluded via a mass error check of MS/MS fragments, and a total of seven candidate peaks were tentatively identified via a manual check with MS/MS fragment data prediction using Metfrag. However, six of these candidates were not considered environmental pollutants. Finally, just one identification (5-Ethyl-2-methyl-2-oxido-1,3,2-dioxaphosphinan-5-YL methyl methyl-phosphonate) (Fig. S5) was suspected of being a false negative.

Consequently, the validation test for SNTS resulted in 22 true positives (19 with suspect and 3 with non-target screening, described in below section), 3 false positives (12-hydroxy dodecanoic acid, allethrin, 3,4-dimethoxycinnamic acid), and 2 false negatives (amoxicillin, lidocaine). The identified false positive/negative errors are a part of total errors. In particular, there should be more unidentifiable false negatives because we considered a limited number of peaks as false candidates ruled out by step 7 in suspect and non-target screening. Nevertheless only 2 false negatives out of 32 candidates could be acceptable for a reasonable sacrifice for a fast workflow in the suspect screening. Most substances tentatively identified via SNTS were unambiguously confirmed by authentic reference standards and only three candidate peaks (11%) were false positives. The false positives rate is comparable or even lower than those of a previous study (Singer et al., 2016). This can be attributed to the manual checking step, which is time consuming but essential to minimize false positive errors.

3.2. Identification of major pollutants via SNTS (with 1st year samples)

The SNTS results for the effluent samples collected during 2016 are shown in Fig. 2A and B, respectively. In the suspect screening, approximately 900 peaks, on average, measured in positive and negative ESI modes, were consistent with compounds in the suspect list. Of these, peaks with an area of <100,000 were excluded. Approximately 40% of these satisfied isotopic pattern simulations for the corresponding molecular formula. Of these, only 65 peaks with MS/MS fragment information passed the criteria set in TraceFinder 4.1 and were considered the software-aid results for candidates. The candidates were then manually checked for their peak shape, isotopic pattern, appearance in the blank, MS/MS fragment, etc. The fragments were compared to and cross-checked with available databases, e.g., mzCloud and MassBank. During the manual check, 43 peaks could not be identified mainly because of the bad peak shape and/or lack of consistent fragments. The promising 22 peaks were suggested as final candidates for potential major pollutants in the effluent. Thanks to the commercial availability of reference standards, except for two OPFRs (i.e., tris(1-chloro-2-propanyl) phosphate (TCIPP) and tris(2-butoxyethyl) phosphate (TBEP)), orthogonal chemical confirmations were successfully conducted for 19 compounds out of the 20 standards. The only one false positive was allethrin whose peak was approximately 7 min behind that of the suspect. This error could be avoided if RT plausibility was checked in advance, indicating the importance of RT estimation.

During the confirmation of the substances, 181.072 m/z was proposed for two isomer compounds, i.e., paraxanthine and theophylline (mass error: Δ −0.77 ppm). Paraxanthine and theophylline are major metabolites of caffeine accounting for 80% and 4% of the total metabolism, respectively (Miners and Birkett, 1996). Unfortunately, these compounds were not separately



+/- : identified /confirmed candidates/substances in the positive mode (+)/in the negative mode (-).

Fig. 2. Identified or confirmed candidates/substances in the effluent in 2016 using suspect (A) and non-target screening (B).

identified with our separating LC method and, thus considered as one for the corresponding peak.

In addition to 19 confirmations, two other substances in suspect list were confirmed through false negative checking as described above. Consequently, the suspect screening recognized 21 substances in effluent, which are classified into six groups: ten pharmaceutical and personal care products (PPCPs) (8-methoxypsoralen, acetaminophen, antipyrine, caffeine, cetirizine, diclofenac, metoprolol, naproxen, amoxicillin, and lidocaine), two fungicides (pyrimethanil and carbendazim), two insect repellents (DEET and icaridin), one metabolite (of caffeine, paraxanthine/theophylline), two OPFRs (tributyl phosphate (TBP) and triphenyl phosphine oxide (TPPO)), three PFCs (perfluorooctane sulfonic acid, perfluorooctanoic acid, and perfluorohexane sulfonate), and one other (byproduct of acetaminophen (2-acetaminophenol)) (Table S2, Table S3).

In the non-target data processing using Compound Discoverer 2.0, the number of candidates with high uncertainty was effectively reduced by setting a lower limit for the peak area (<5 × e6 for (+) and <1 × e6 for (−) mode) and the mzCloud matching score (<30%) for fast and efficient isolation of prior pollutants (Fig. 2B). Some peaks failed to obtain a feasible molecular formula and were filtered out. Finally, five unexpected substances were tentatively identified. With corresponding reference standards, three were then confirmed as xylene sulfonate (surfactant), N,N-dimethyl-N′-phenylsulfamide (metabolite of dichlofluanid), and 5,6-dimethylbenzimidazole (Table S2). In total, SNTS yielded successful confirmations for 24 substances in effluent (Table S2, Table S3). Any of peaks detected in glacier and surface water samples were not evident for anthropogenic substances, indicating the free of background contaminations.

3.3. Quantitative analysis for 2nd year samples

Since it was revealed in 1st year results that 21 of the 24 confirmed substances were quantifiable, target analysis for samples collected in 2017 was conducted with these compounds.

As a result, 17 of the 21 targets were detected in all effluent samples (n = 10) (Table S4.). Fig. 3 shows the target compounds and their average concentrations in the effluent samples. Antipyrine, 8-methoxypsoralen, carbendazim, and TBP were not evident. Nine substances (2-acetaminophenol, acetaminophen, caffeine, cetirizine, DEET, icaridin, metoprolol, paraxanthine/theophylline, TPPO) had a greater concentration than 1 μg/L in at least one of the effluent samples. Paraxanthine/theophylline showed the greatest average concentration of 280 μg/L, followed by caffeine (230 μg/L) and acetaminophen (60 μg/L), making these the top 3 major substances present.

All detected pharmaceuticals (acetaminophen, cetirizine, diclofenac, naproxen) belonged to the top-200 drugs in 2017 based on prescriptions (ClinCalc DrugStats Database). DEET and icaridin are repellents recommended by World Health Organization (Sorge, 2009). TPPO has been extensively used as a synthetic intermediate in pharmaceutical products and as a ligand for many transitional metals (Hu et al., 2010). Also, it is a typical flame retardant (Alygizakis et al., 2016). The occurrence of TPPO in environmental media has already been reported (R. Z. Wang et al., 2015; Rodil et al., 2012; Bollmann et al., 2012), and is present at a relatively

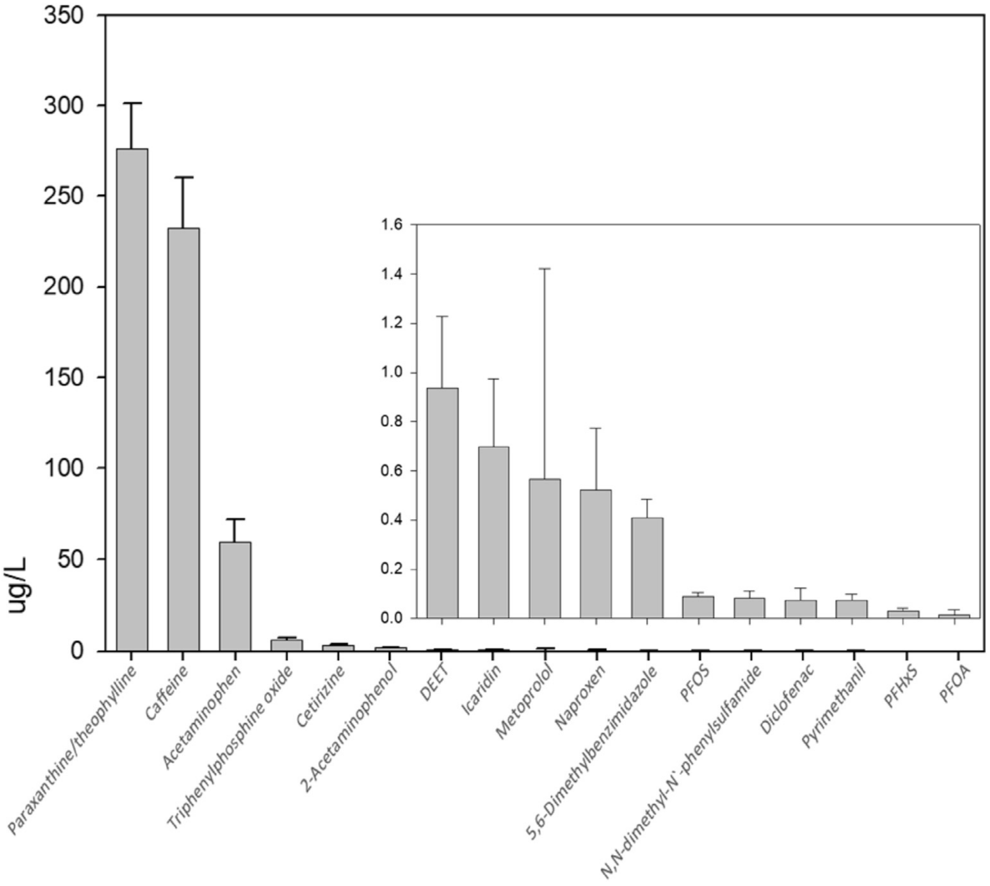


Fig. 3. Average concentrations of target compounds in the effluent samples collected in 2017.

higher concentration in Ny-Ålesund. In previous studies, PFCs have been recognized as persistent contaminants in the Arctic environment (Müller et al., 2011; Zhao et al., 2012) and atmospheric and oceanic currents have generally been proposed as their transport mechanisms (Butt et al., 2010b). However, we identified the sewage treatment plant in Ny-Ålesund as the point source for PFCs in the Fjorden.

The cumulative average concentration of the 17 substances detected in the effluent over 5 days was calculated as 580,000 ng/L (510,000 ng/L for caffeine and the metabolite, 64,000 ng/L for pharmaceuticals, 6600 ng/L for flame retardant, 1600 ng/L for insect repellents, 100 ng/L for PFCs, 87 ng/L for fungicide and the metabolite, and 2000 ng/L for other (impure acetaminophen)). Considering the amount of effluent discharged (approximately 10 tons/day) from the sewage treatment plant, approximately 5.9 g/day of the measured pollutants are discharged into the Fjorden. Weigel et al. (2004) reported that caffeine (30,200–126,000 ng/L), diclofenac (30 ng/L), DEET (10–60 ng/L) and metoprolol (70 ng/L) were detected in the effluent of sewage treatment plant in Tromsø, which does not use microbial treatment processes. In the effluent of the sewage treatment plant in Longyearbyen, caffeine (501-50,704 ng/L) and diclofenac (30-1074 ng/L) were detected (Kallenborn, 2009). In the present study, the substances such as caffeine, DEET and metoprolol showed higher concentration than those measured in any other studies on Arctic regions, while the diclofenac was detected lower concentration. Thus, it is uncertain whether the Ny-Ålesund effluent discharged into Kongsfjorden is safe for the receiving Fjorden environment.

As the result of seawater analysis, six substances including insect repellents (DEET, icaridin) and pharmaceuticals and metabolites (acetaminophen, caffeine, cetirizine, paraxanthine/theophylline) were detected along the shoreline, which was expected to be contaminated by the effluent (Table S5.). The average concentrations at shoreline 1 (n = 5) and concentration ratios of shoreline/effluent are shown in Fig. 4. The ratio is an indicator to show the degree of decrease in the concentrations as the substances released from the effluent are dispersed out to the shoreline. Thus, a high ratio of shoreline/effluent concentration indicates a less decrease in shoreline concentration from the effluent probably because the substance is more persistent in saltwater environment. In the effluent, paraxanthine/theophylline and caffeine showed higher concentrations than the other substances, but relatively lower concentration ratios of shoreline over effluent (Fig. 4). Inversely, the ratios for insect repellents are significantly higher than those for the other substances, indicating these biocides are more persistent in the shoreline. DEET, along with other major substances (i.e., caffeine, paraxanthine/theophylline), was also detected below LOQ level at offshore sites (OF1 and OF2) (Table S6.). Outdoor activities and inhabitants in Ny-Ålesund increase during the summer, and thus the amount of insect repellent used accordingly could increase. In addition, the hydrolytically stable property of DEET (Keith et al., 2017), proved in the present study with the higher ratios, can result in the less decrease in the shoreline concentration compared to the origin and the occurrence even in offshore environments.

All substances detected at shoreline 1 except acetaminophen were also detected at shorelines 2 and 3, and only caffeine and paraxanthine/theophylline appeared in the quantitative analysis for offshore samples (Fig. S3A, Fig. S3B, Fig. S4).

3.4. Additional identification in 2nd year samples

As a result of SNTS to identify additional substances in the effluent collected in 2017, nine substances including five PPCPs (acetylsalicylic acid/salicylic acid, ethyl paraben, ketoprofen, metformin, and sumatriptan), one fungicide (pyroquilon), and three OPFRs chemicals (triphenyl phosphate (TPHP), TCIPP, and TBEP) from suspect screening and 11 substances including three PPCPs (adenosine, diethanolamine, and nicotinyl alcohol), four metabolites (1,3,7-trimethyluric acid, 1,7-dimethyluric acid, desthiobiotin, and theobromine), four other (cyclamic acid, N,N-dimethylaniline, saccharin, and triethyl citrate) from non-target screening were tentatively identified. Since acetylsalicylic and salicylic acids could not be separated via the pretreatment and analytical methods used in this study, these were expressed as a single substance. Through the step to check false negative errors in SNTS as previously described, four more substances, i.e., amoxicillin, irbesartan, lidocaine and caprylamidopropyl betaine, were additionally identified.

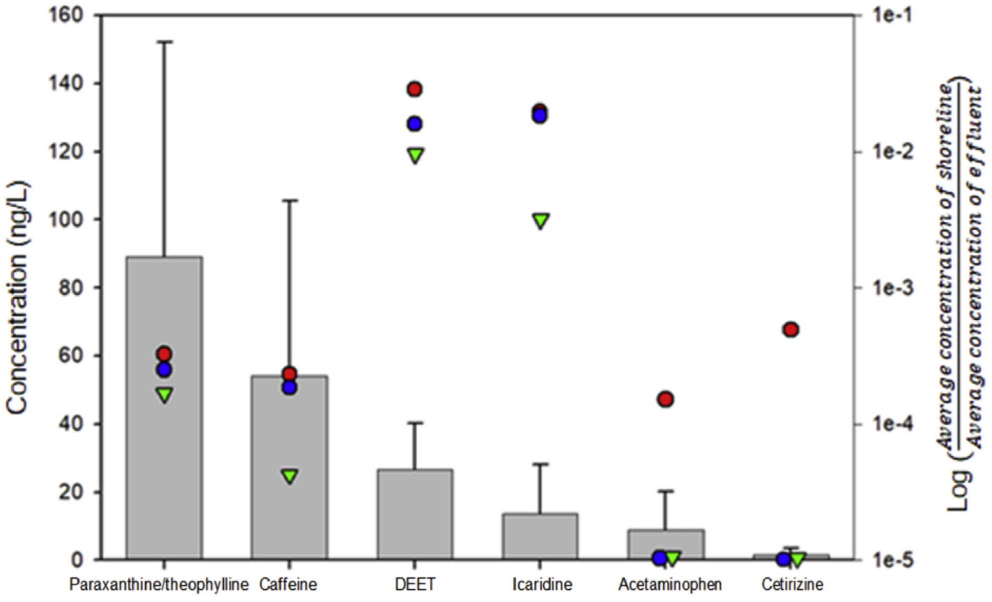


Fig. 4. Average concentrations detected from the shoreline (1) in 2017 and concentration ratio of shoreline/effluent (ratio = $\frac{\textit{Average concentration of shore line}}{\textit{Average concentration of effluent}}$). ●: Shoreline (1)/effluent, ●: Shoreline (2)/effluent, ▼: Shoreline (3)/effluent.

Among those 24 tentatively identified cases, 5 peaks were successfully confirmed using the reference standards of metformin, acetylsalicylic acid/salicylic acid, amoxicillin, irbesartan, and lidocaine (Tables S7 and S8). Peak, isotopic pattern, and MS/MS spectrum information on the remained 19 substances are depicted in SI (Fig. S6~S24).

Among the tentatively identified metabolites, 1,3,7-trimethyluric acid and theobromine are direct metabolites of caffeine and 1,7-dimethylfuric acid is a metabolite of paraxanthine which is a major metabolite of caffeine (Chandrasekaran and Karunasagar, 2014). Desthiobiotin is a synthetic metabolite and an analog of biotin, which is vitamin B7. Of the other groups, N,N-dimethylaniline is used as intermediate in the manufacture of dyes and specialized industrial chemicals, and triethyl citrate is used as a plasticizer for polyvinyl chloride. Cyclamic acid and saccharin are artificial sweeteners used as food additives.

Of the tentatively identified substances, all pharmaceuticals except adenosine, nicotinyl alcohol, salicylic acid and ketoprofen, belong to the top 200 pharmaceuticals based on 2017 prescriptions (ClinCalc DrugStats Database). Additionally, diethanolamine, used as a surfactant in consumer products such as soaps, shampoos, cleaners, and cosmetics, was classified as Group 2B- possibly carcinogenic to humans by the International Agency for Research on Cancer (IARC) 2012 (IARC, 2013). Ethyl paraben, used as a preservative in drugs and cosmetics and in food packaging, has been evaluated as ‘harmful to aquatic organisms’ in a previous paraben toxicity study (J. Lee et al., 2018). In a U.S. Environmental Protection Agency (EPA) survey, TBEP and TBP, both identified in the present study, were listed as high production volume chemicals (U.S. EPA, 1996). Consequently, recent studies have reported the presence of OPFRs in aquatic terrestrial, biotic, and atmospheric environments (Hallanger et al., 2015; He et al., 2017; S. Lee et al., 2018; Shi et al., 2016; Wolschke et al., 2015) and even in remote areas such as polar regions. Two studies speculated that the contamination of the Arctic area with OPFRs is likely a result of long-distance transport, as has been the case with POPs (Möller et al., 2012; Pantelaki and Voutsa, 2019). However, as the present study identified and/or quantified OPFRs in the effluent, the point source in the Arctic also cannot be ignored.

3.5. *Substances of concern*

For the 47 substances that were quantitatively detected or tentatively identified from the 2016 and 2017 effluent samples using target and SNTS, prioritization was made by considering risk-relevant parameters such as maximum concentration or peak intensity, detection frequency, log octanol-water partition coefficient (log K_{ow}), and toxicity value (EC50) if available (Tables S9 and S10). Each parameter was classified into 4 levels which indicate risk potential. Circle marking as an index of significance was assigned according to the estimated classification level (up to 4 circles given for each parameter). Thus, substances with more circles were considered riskier, or pollutants of concern, in the environment.

Detailed information on classification and circle marking is provided in Table S9.

PFOS and TPHP obtained the highest number of circles for exposure index and toxicity index, followed by irbesartan, DEET, acetaminophen, caffeine and paraxanthine/theophylline. These were thus our top seven substances of concern. PFCs displayed relatively low overall concentrations, but were classified as high risk because of relatively high log K_{ow} and detection frequency. It is noteworthy that PFOS was designated a POP in the Stockholm Convention of 2009. PFOA and PFHxS are also under review for POPs listing due to persistence, bioaccumulation, and toxicity (Stockholm Convention, 2016). Despite the relatively low exposure index, TPHP was ranked 2nd due to its high toxicity index. TPPO, TBEP, and TCIPP showed lower toxicity indexes than other OPFRs (TPHP, TBP). However, it is noteworthy that the degradation products or water sonolysis by-products of TPPO are more toxic than the parent substance to *Aliivibrio fischeri*, which is present in the marine environment (Emery et al., 2005). Irbesartan, found to be persistent or bioaccumulative in a previous study (Howard and Muir, 2013) was scored 3rd place for intensity, log $K_{ow,}$ and detection frequency, even without toxicity data available. Irbesartan was obtained five circles for exposure index as detected in effluent and seawater samples, despite relatively low peak intensity. In addition, toxicity data (EC50) could not be obtained via ECOTOX, but showed a relative high toxicity index due to high low K_{ow}. DEET and icaridin, which are classified as toxicity category III with some acute toxicity by the U.S. EPA, occupied relatively high spots with eight and seven circles, respectively (US EPA. New Pesticide Fact Sheet, 2005; Profile, 1998). While DEET is considered a low risk to aquatic biota, icaridin is reported to be toxic to salamander larvae (Costanzo et al., 2007; Almeida et al., 2018). Acetaminophen, caffeine, and paraxanthine/theophylline showed high exposure index scores, but scored only eight circles because of their relatively low toxicity index. Diclofenac, which has a higher log K_{ow} than other indexes, has been suggested as an indicator for wastewater treatment in Switzerland (Indicator-substances, 2010) and shown to be biotoxic (Der Beek et al., 2016). Cetirizine, which is known to degrade only slightly during wastewater treatment (Bahlmann et al., 2012), and metformin, one of the most abundant medicines discharged into the environment in recent years (Niemuth and Klaper, 2015), acquired 7 circles due to high exposure indexes. Carbendazim, classified by the U.S. EPA as Group C (possible human carcinogen) (Cohen, 1984), had the highest toxicity value, but was ranked relatively low because of its low concentration, detection frequency, and log K_{ow}.

3.6. *Limitation and implications*

In the present study, 17 substances were quantitatively analyzed while additional 10 were orthogonally confirmed, remaining extra 20 as tentatively identified substances in the Ny-Ålesund effluents, respectively. The quantitative and qualitative results were achieved with a single instrumental setup (LC-ESI-HRMS), which is a valuable approach for non-volatile, polar, and/or stable compounds. Thus, there are likely more substances present that were barely measurable with our analytical method, but would be detectable with different chromatogram and ionization approaches, e.g. GC-EI and LC-APCI. In addition, the peak area thresholds (<1E5 for suspect screening and <5E6/1E6 for non-target screening) for the detected candidate peaks might have excluded some substances of concern. These limitations of the instrument used and the peak screening process likely resulted in unidentified false negatives. Nevertheless, the 47 substances identified are firstly recognized as major organic pollutants from Ny-Ålesund effluent in the Arctic environment. Most of these are already known elsewhere, but their exposure risk (Table 2) had never been estimated in the Arctic area. It was also confirmed that some substances such as caffeine and its metabolites occur at measurable levels in the Kongsfjorden and even in a remote offshore area. This is attributable to the insufficient treatment of wastewater in Ny-Ålesund, which also leads to relatively higher concentrations of identified substances in the effluent than has been measured in other Arctic regions (Weigel et al., 2004; Kallenborn, 2009). Even though the overall load is low due to the low volume of effluent, the sewage treatment plant should be recognized as a point source producing organic pollutants in the Fjord. Furthermore, it is expected that the number of

Table 2
Prioritization for substances detected/identified in the effluent based on exposure (i.e. maximum concentration/peak intensity and detection frequency) and toxicity indices (i.e. Log K_{ow}, and toxicity value (EC50)). In total, 16 circles can be assigned according to classifications for each index. The substances are ranked by the number of circles for prioritization.

Compound	Priority index		Total	Rank
	exposure index	toxicity index	○	
PFOS	🔴🔴🟠🟠🟠	🔵🔵🔵🔵🟣	10	1
TPHP	🔴🔴🟠	🔵🔵🔵🔵🟣🟣🟣	10	1
Irbesartan	🔴🔴🟠🟠🟠	🔵🔵🔵🔵	9	3
DEET	🔴🔴🔴🟠🟠🟠	🔵🟣	8	4
Acetaminophen	🔴🔴🔴🟠🟠🟠🟠	🟣	8	4
Caffeine	🔴🔴🔴🔴🟠🟠🟠🟠		8	4
Paraxanthine/theophylline	🔴🔴🔴🔴🟠🟠🟠🟠		8	4
PFOA	🔴🟠🟠	🔵🔵🔵🔵	7	8
Diclofenac	🔴🔴🟠	🔵🔵🔵🟣	7	8
Icaridin	🔴🔴🔴🟠🟠🟠	🔵	7	8
PFHxS	🔴🟠🟠🟠	🔵🔵🔵	7	8
Cetirizine	🔴🔴🔴🟠🟠🟠🟠		7	8
Metformin	🔴🔴🔴🟠🟠🟠	🟣	7	8
Theobromine	🔴🔴🔴🔴🟠🟠		6	14
Pyrimethanil	🔴🟠🟠	🔵🟣🟣	6	14
TPPO	🔴🔴🔴🟠🟠	🔵	6	14
N,N-dimethylaniline	🔴🔴🔴🟠	🔵🟣	6	14
2-Acetaminophenol	🔴🔴🔴🟠🟠🟠		6	14
Metoprolol	🔴🔴🔴🟠🟠🟠		6	14
TBEP	🔴🔴🔴🟠🟠	🔵	6	14
8-methoxypsoralen	🔴🔴🟠🟠🟠	🔵	6	14
1,7-dimethyluric acid	🔴🔴🔴🟠🟠🟠		6	14
1,3,7-trimethyluric acid	🔴🔴🔴🟠🟠🟠		6	14
Ethyl paraben	🔴🔴🔴🟠	🔵🟣	6	14
TBP	🔴🟠	🔵🔵🟣	5	25
Naproxen	🔴🔴🟠🟠	🔵	5	25
Ketoprofen	🔴🔴🔴🟠	🔵	5	25
Caprylamidopropyl betaine	🔴🔴🔴🔴🟠		5	25
TCIPP	🔴🔴🟠🟠	🔵	5	25
Adenosine	🔴🔴🟠🟠🟠		5	25
N,N-dimethyl-N'-phenylsulfamide	🔴🔴🟠🟠🟠		5	25
xylenesulfonate	🔴🔴🟠🟠🟠		5	25
5,6-dimethylbenzimidazole	🔴🔴🟠🟠	🔵	5	25
Carbendazim	🟠	🟣🟣🟣	4	34
Acetylsalicylic acid / salicylic acid	🔴🔴🟠	🟣	4	34
Saccharin	🔴🔴🔴🟠		4	34
Antipyrine	🔴🟠🟠🟠		4	34
Nicotinyl alcohol	🔴🔴🟠		3	38
Triethyl citrate	🔴🔴🟠		3	38
Cyclamic acid	🔴🔴🟠		3	38
Desthiobiotin	🔴🔴🟠		3	38
Pyroquilon	🔴🔴🟠		3	38
(5-Ethyl-2-methyl-2-oxido-1,3,2-dioxaphosphinan-5-yl)methyl methyl methylphosphonate	🔴🔴🟠		3	38
Diethanolamine	🔴🔴🟠		3	38
Sumatriptan	🔴🟠		2	45
Lidocaine	🟠🟠		2	45
Amoxicillin	🟠🟠		2	45

Circles in Red – Maximum concentration or peak intensity/ Orange – Detection Frequency/ Blue – Log octanol-water partition coefficient (log K_{ow})/ Purple – toxicity value (EC50).
Log octanol-water partition coefficient (log K_{ow}) were estimated with KOWWIN v1.67 or 1.68.
Toxicity values (e.g., EC50) were referred to ECOTOX DATABASE if available.
Detailed information on circle assignment is present in S.I. Table S9.

unexpected pollutants in the environment increase. This is supported by the fact that different substances were identified in the first and second years of the present study. According to a report, tourist visiting by cruise ship to the Arctic region is increasing over the recent years, which is possibly correlated to increase in concentration and diversity of pollutants (Cruising.org, 2014). In fact, a cruise ship visited in Ny-Ålesund during each the sampling periods. As population or tourist is increasing, there may be controversy to install advanced treatment processes such as microbial or oxidation treatment in the region. If state-of-the-art technology for water treatment (e.g., advanced oxidations) is not feasible in the region, as may be the case if it results in the formation of undesirable products (Lin et al., 2014), input control would be the most effective measure for reducing the output. Before adopting a control measure, it is essential to keep conducting suspect and non-target screening to identify and monitor unexpected substances. Information from the screening could be used for the prioritization of pollutants and for the selection of the most effective treatment methods. In addition, the analytical methods suggested here can also be used to trace the fate of identified organic pollutants not only in the environmental media, but also in the Arctic food web by monitoring transformation products or metabolites formed in biota. Confirmation of a major source of pollutants and correlation with the resulted bioaccumulation in Arctic biota should be further studied to expand our understanding of the fate of the identified pollutants, and to implement effective control measures for protection of the pristine nature of this region.

4. Conclusions

Overall, SNTS based on HRMS as presented in this study was successfully implemented with few false positives, which is comparable to or even lower than a previous approach (Singer et al., 2016). The present study proves that the effluent discharged from the sewage treatment plant at Ny-Ålesund in the Arctic can be a point source in the Kongsfjorden. Pharmaceuticals (particularly caffeine and its metabolites) and insect repellents were a dominant component of the detected compounds in the effluent. It is not surprising that considerable amount of the identified substances is used in the area because Ny-Ålesund accommodates many researchers as well as tourists in the summer period when we took samples. Additionally, we recognized the effluent for the first time as a point source in the Arctic region for substances such as PFCs and OPFRs, which until now have been thought to be transported to the Arctic environment either by atmospheric or sea current transport. PFOS, TPHP, irbesartan, DEET, acetaminophen, caffeine and paraxanthine/theophylline were selected as the top seven substances of concern in this study based on the parameters of concentration or intensity, detection frequency, log K_{ow}, and toxicity. Caffeine, paraxanthine/theophylline, and caprylamidopropyl betaine showed the highest concentration/intensity indexes, while acetaminophen, caffeine, paraxanthine/theophylline and cetirizine were the most detectable substances. PFOS, PFOA, TPHP, and irbesartan were evaluated as having the highest log K_{ow} value. With regards to toxicity value, TPHP and carbendazim obtained the most circles. Accordingly, caffeine and paraxanthine/theophylline were ranked the top two in the exposure index, and TPHP was ranked first for toxicity value. Suspect and non-target screening for two consecutive years resulted in the discovery of different pollutant profiles each year. It implicates that unexpected and more micropollutants will occur continuously in the area. As a novel analytical approach, SNTS along with target screening using LC-HRMS was successfully applied in the present study. Its use is suggested to identify more novel pollutants threatening Arctic environments.

CRediT authorship contribution statement

Younghun Choi: Writing - original draft, Methodology, Visualization. **Kitae Kim:** Funding acquisition, Investigation. **Deokwon Kim:** Methodology, Investigation. **Hyo-bang Moon:** Conceptualization, Validation. **Junho Jeon:** Supervision, Writing - review & editing.

Acknowledgements

This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science ICT and Future Planning (No. 2017R1C1B2010098) and by the Korea Polar Research Institute (KOPRI) project (PE19200).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2019.113792.

References

Aalizadeh, R., Thomaidis, N.S., Bletsou, A.A., Gago-Ferrero, P., 2016. Quantitative structure-retention relationship models to support nontarget high-resolution mass spectrometric screening of emerging contaminants in environmental samples. J. Chem. Inf. Model. 56, 1384–1398. https://doi.org/10.1021/acs.jcim.5b00752.

Almeida, R.M., Han, B.A., Reisinger, A.J., Kagemann, C., Rosi, E.J., 2018. High mortality in aquatic predators of mosquito larvae caused by exposure to insect repellent. Biol. Lett. 14 https://doi.org/10.1098/rsbl.2018.0526.

Alygizakis, N.A., Gago-Ferrero, P., Borova, V.L., Pavlidou, A., Hatzianestis, I., Thomaidis, N.S., 2016. Occurrence and spatial distribution of 158 pharmaceuticals, drugs of abuse and related metabolites in offshore seawater. Sci. Total Environ. 541, 1097–1105. https://doi.org/10.1016/j.scitotenv.2015.09.145.

Avagyan, R., Åberg, M., Westerholm, R., 2016. Suspect screening of OH-PAHs and non-target screening of other organic compounds in wood smoke particles using HR-Orbitrap-MS. Chemosphere 163, 313–321. https://doi.org/10.1016/j.chemosphere.2016.08.039.

Bahlmann, A., Carvalho, J.J., Weller, M.G., Panne, U., Schneider, R.J., 2012. Immunoassays as high-throughput tools: monitoring spatial and temporal variations of carbamazepine, caffeine and cetirizine in surface and wastewaters. Chemosphere 89, 1278–1286. https://doi.org/10.1016/j.chemosphere.2012.05.020.

Bollmann, U.E., Möller, A., Xie, Z., Ebinghaus, R., Einax, J.W., 2012. Occurrence and fate of organophosphorus flame retardants and plasticizers in coastal and marine surface waters. Water Res. 46, 531–538. https://doi.org/10.1016/j.watres.2011.11.028.

Butt, C.M., Berger, U., Bossi, R., Tomy, G.T., 2010a. Science of the Total Environment Levels and trends of poly- and per fl uorinated compounds in the arctic environment ☆. Sci. Total Environ. 408, 2936–2965. https://doi.org/10.1016/j.scitotenv.2010.03.015.

Butt, C.M., Berger, U., Bossi, R., Tomy, G.T., 2010b. Levels and trends of poly- and perfluorinated compounds in the arctic environment. Sci. Total Environ. 408, 2936–2965. https://doi.org/10.1016/j.scitotenv.2010.03.015.

Chandrasekaran, K., Karunasagar, D., 2014. Determination of trace elements in the Pb-Bi-eutectic system by inductively coupled plasma-quadrupole mass spectrometry after sequential removal of the matrix by precipitation. J. Anal. At. Spectrom. 29, 1720–1725. https://doi.org/10.1039/c4ja00138a.

Cohen, S., 1984. US environmental protection agency, office of pesticide programs. In: I. Pomerantz (Environmental Prot. Agency, off, pp. 5–13.

Costanzo, S.D., Watkinson, A.J., Murby, E.J., Kolpin, D.W., Sandstrom, M.W., 2007. Is there a risk associated with the insect repellent DEET (N,N-diethyl-m-toluamide) commonly found in aquatic environments? Sci. Total Environ. 384, 214–220. https://doi.org/10.1016/j.scitotenv.2007.05.036.

Cruising.org, 2014. State of the Cruise Industry 2014 ([WWW Document]).

Der Beek, T. aus, Weber, F.-A., Bergmann, A., Grüttner, G., Carius, A., 2016. Pharmaceuticals in the environment: global occurrence and potential cooperative action under the strategic approach to international chemicals management (SAICM). Ger. Fed. Environ. Agency 94.

Emery, R.J., Papadaki, M., Freitas Dos Santos, L.M., Mantzavinos, D., 2005. Extent of sonochemical degradation and change of toxicity of a pharmaceutical precursor (triphenylphosphine oxide) in water as a function of treatment conditions. In: Environment International, pp. 207–211. https://doi.org/10.1016/j.envint.2004.09.017.

Gago-Ferrero, P., Schymanski, E.L., Bletsou, A.A., Aalizadeh, R., Hollender, J., Thomaidis, N.S., 2015. Extended suspect and non-target strategies to characterize emerging polar organic contaminants in raw wastewater with LC-HRMS/MS. Environ. Sci. Technol. 49, 12333–12341. https://doi.org/10.1021/

acs.est.5b03454.

Green, N., Schlabach, M., Bakke, T., Brevik, E.M., Dye, C., Herzke, D., Huber, S., Plosz, B., Remberger, M., Schøyen, M., 2008. Screening of selected metals and new organic contaminants 2007. Phosphorous flame Retard. polyfluorinated Org. Compd. nitro-PAHs, silver, Platin. sucralose air, wastewater. Treat. Facil. Freshw. Mar. Recip. Rep. TA 2367, 2008.

Hallanger, I.G., Sagerup, K., Evenset, A., Kovacs, K.M., Leonards, P., Fuglei, E., Routti, H., Aars, J., Strøm, H., Lydersen, C., Gabrielsen, G.W., 2015. Organophosphorous flame retardants in biota from Svalbard, Norway. Mar. Pollut. Bull. 101, 442–447. https://doi.org/10.1016/j.marpolbul.2015.09.049.

He, H., Gao, Z., Zhu, D., Guo, J., Yang, S., Li, S., Zhang, L., Sun, C., 2017. Assessing bioaccessibility and bioavailability of chlorinated organophosphorus flame retardants in sediments. Chemosphere 189, 239–246. https://doi.org/10.1016/j.chemosphere.2017.09.017.

Howard, P.H., Muir, D.C.G., 2013. Identifying new persistent and bioaccumulative organics among chemicals in commerce. III: byproducts, impurities, and transformation products. Environ. Sci. Technol. 47, 5259–5266. https://doi.org/10.1021/es4004075.

Hu, F.H., Wang, L.S., Cai, S.F., 2010. Solubilities of methyldiphenylphosphine oxide in selected solvents. J. Chem. Eng. Data 55, 492–495. https://doi.org/10.1021/je900277m.

IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2013. Some chemicals present in industrial and consumer products, food and drinking-water. IARC Monogr. Eval. Carcinog. Risks Hum.

Indicator-substances, S.U., 2010. Mikroverunreinigungen, pp. 1–9.

Kallenborn, R., 2009. Pharmaceutical Residues in Arctic Marine Environments: Levels in Sewage Effluents and Receiving Sea Water Pharmaceutical Residues in Arctic Marine Environments.

Keith, S., Harper, C., Williams, R., Llados, F., Coley, C., Carlson-Lynch, H., 2017. Toxicological Profile for DEET (N,N-Diethyl-Meta-Tolumide). Agency for Toxic Substances and Disease Registry (ATSDR).

Lee, J., Bang, S.H., Kim, Y.-H., Min, J., 2018. Toxicities of four parabens and their mixtures to Daphnia magna and Aliivibrio fischeri. Environ. Health Toxicol. 33, e2018018 https://doi.org/10.5620/eht.e2018018.

Lee, S., Cho, H.J., Choi, W., Moon, H.B., 2018. Organophosphate flame retardants (OPFRs) in water and sediment: occurrence, distribution, and hotspots of contamination of Lake Shihwa, Korea. Mar. Pollut. Bull. 130, 105–112. https://doi.org/10.1016/j.marpolbul.2018.03.009.

Lin, A.Y.C., Lee, W.N., Wang, X.H., 2014. Ketamine and the metabolite norketamine: persistence and phototransformation toxicity in hospital wastewater and surface water. Water Res. 53, 351–360. https://doi.org/10.1016/j.watres.2014.01.022.

Miners, J.O., Birkett, D.J., 1996. The Use of Caffeine as a Metabolic Probe for Human Drug Metabolizing Enzymes, 27, pp. 245–249.

Möller, A., Sturm, R., Xie, Z., Cai, M., He, J., Ebinghaus, R., 2012. Organophosphorus flame retardants and plasticizers in airborne particles over the Northern Pacific and Indian Ocean toward the polar regions: evidence for global occurrence. Environ. Sci. Technol. 46, 3127–3134. https://doi.org/10.1021/es204272v.

Müller, C.E., De Silva, A.O., Small, J., Williamson, M., Wang, X., Morris, A., Katz, S., Gamberg, M., Muir, D.C.G., 2011. Biomagnification of perfluorinated compounds in a remote terrestrial food chain: Lichen-Caribou-Wolf. Environ. Sci. Technol. 45, 8665–8673. https://doi.org/10.1021/es201353v.

Niemuth, N.J., Klaper, R.D., 2015. Emerging wastewater contaminant metformin causes intersex and reduced fecundity in fish. Chemosphere 135, 38–45. https://doi.org/10.1016/j.chemosphere.2015.03.060.

Pantelaki, I., Voutsa, D., 2019. Organophosphate flame retardants (OPFRs): a review on analytical methods and occurrence in wastewater and aquatic environment. Sci. Total Environ. https://doi.org/10.1016/j.scitotenv.2018.08.286.

Profile, U., 1998. R.e.d. Facts.

Richardson, S.D., Ternes, T.A., 2018. Water analysis: emerging contaminants and current issues. Anal. Chem. https://doi.org/10.1021/acs.analchem.7b04577.

Rodil, R., Quintana, J.B., Concha-Graña, E., López-Mahía, P., Muniategui-Lorenzo, S., Prada-Rodríguez, D., 2012. Emerging pollutants in sewage, surface and drinking water in Galicia (NW Spain). Chemosphere 86, 1040–1049. https://doi.org/10.1016/j.chemosphere.2011.11.053.

Schymanski, E.L., Singer, H.P., Longrée, P., Loos, M., Ruff, M., Stravs, M.A., Ripollés Vidal, C., Hollender, J., 2014. Strategies to characterize polar organic contamination in wastewater: exploring the capability of high resolution mass spectrometry. Environ. Sci. Technol. 48, 1811–1818. https://doi.org/10.1021/es4044374.

Shi, Y., Gao, L., Li, W., Wang, Y., Liu, J., Cai, Y., 2016. Occurrence, distribution and seasonal variation of organophosphate flame retardants and plasticizers in urban surface water in Beijing, China. Environ. Pollut. 209, 1–10. https://doi.org/10.1016/j.envpol.2015.11.008.

Singer, H.P., Wössner, A.E., McArdell, C.S., Fenner, K., 2016. Rapid screening for exposure to “non-target” pharmaceuticals from wastewater effluents by combining HRMS-based suspect screening and exposure modeling. Environ. Sci. Technol. 50, 6698–6707. https://doi.org/10.1021/acs.est.5b03332.

Sorge, F., 2009. Prevention with repellent in children. Arch. Pediatr. https://doi.org/10.1016/S0929-693X(09)75313-8.

Steffen, A., Lehnherr, I., Cole, A., Ariya, P., Dastoor, A., Durnford, D., Kirk, J., Pilote, M., 2015. Atmospheric mercury in the Canadian Arctic. Part I: a review of recent field measurements. Sci. Total Environ. https://doi.org/10.1016/j.scitotenv.2014.10.109, 509–510, 3–15.

US EPA. New Pesticide Fact Sheet, 2005. United States Environmental Protection Agency.

US EPA. Office of Pesticide Programs, 1996. New Pesticide Fact Sheet. United States Environmental Protection Agency.

Wang, R., Tang, J., Xie, Z., Mi, W., Chen, Y., Wolschke, H., Tian, C., Pan, X., Luo, Y., Ebinghaus, R., 2015. Occurrence and spatial distribution of organophosphate ester flame retardants and plasticizers in 40 rivers draining into the Bohai Sea, north China. Environ. Pollut. 198, 172–178. https://doi.org/10.1016/j.envpol.2014.12.037.

Wang, Z., Na, G., Ma, X., Ge, L., Lin, Z., Yao, Z., 2015. Chemosphere Characterizing the distribution of selected PBDEs in soil , moss and reindeer dung at Ny-Ålesund of the Arctic. Chemosphere 137, 9–13. https://doi.org/10.1016/j.chemosphere.2015.04.030.

Weigel, S., Berger, U., Jensen, E., Kallenborn, R., Thoresen, H., Heinrich, H., 2004. Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsø/Norway with emphasis on ibuprofen and its metabolites, 56, 583–592. https://doi.org/10.1016/j.chemosphere.2004.04.015.

Weigel, S., Kuhlmann, J., Hühnerfuss, H., 2002. Drugs and personal care products as ubiquitous pollutants: occurrence and distribution of clofibric acid, caffeine and DEET in the North Sea. Sci. Total Environ. 295, 131–141. https://doi.org/10.1016/S0048-9697(02)00064-5.

Wolschke, H., Sühring, R., Xie, Z., Ebinghaus, R., 2015. Organophosphorus flame retardants and plasticizers in the aquatic environment: a case study of the Elbe River, Germany. Environ. Pollut. 206, 488–493. https://doi.org/10.1016/j.envpol.2015.08.002.

Wolschke, H., Xie, Z., Möller, A., Sturm, R., Ebinghaus, R., 2011. Occurrence, distribution and fluxes of benzotriazoles along the German large river basins into the North Sea. Water Res. 45, 6259–6266. https://doi.org/10.1016/j.watres.2011.09.028.

Woudneh, M.B., Benskin, J.P., Wang, G., Grace, R., Hamilton, M.C., Cosgrove, J.R., 2015. Quantitative determination of 13 organophosphorous flame retardants and plasticizers in a wastewater treatment system by high performance liquid chromatography tandem mass spectrometry. J. Chromatogr. A 1400, 149–155. https://doi.org/10.1016/j.chroma.2015.04.026.

Zhao, Z., Xie, Z., Möller, A., Sturm, R., Tang, J., Zhang, G., Ebinghaus, R., 2012. Distribution and long-range transport of polyfluoroalkyl substances in the Arctic, Atlantic Ocean and Antarctic coast. Environ. Pollut. 170, 71–77. https://doi.org/10.1016/j.envpol.2012.06.004.

Zhu, C., Li, Y., Wang, P., Chen, Z., Ren, D., Ssebugere, P., Zhang, Q., Jiang, G., 2015. Chemosphere polychlorinated biphenyls (PCBs) and polybrominated biphenyl ethers (PBDEs) in environmental samples from Ny-Ålesund and London island , svalbard , the arctic. Chemosphere 126, 40–46. https://doi.org/10.1016/j.chemosphere.2015.01.043.