Environmental Science
Processes & Impacts

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c5em00505a

Seasonal variation of pharmaceutical concentrations in a river/lake system in Eastern Finland†

Axel Meierjohann,* Jenny-Maria Brozinski and Leif Kronberg

In this study, the concentrations of 15 pharmaceuticals were monitored during four seasons (February, May, July, and November 2010) along a 32 km stretch of a highly wastewater polluted watercourse (River Rakkolanjoki, Lake Haapajärvi) in Eastern Finland. The aim was to study the seasonal variation in the elimination of the pharmaceuticals and the stability of the compounds along the watercourse. The analysis was carried out using a liquid chromatography tandem mass spectrometry (LC-MS/MS) method combined with extraction and preconcentration on HLB solid phase extraction (SPE) cartridges. Pharmaceutical concentrations were determined at 9 points along the watercourse, and loads and removal of parent compounds were calculated using flow data from the discharge point and the last sampling point. The pharmaceuticals were found in concentrations ranging from low ng l^{-1} to low μg l^{-1} values at the discharge point and at concentrations of 0–556 ng l^{-1} at the last sampling point. The rate of elimination of the pharmaceutical load was significantly higher in May and July than in February and November. There were clear differences in the stability of the individual compounds along the watercourse. Carbamazepine was not eliminated during any season, while ibuprofen, ketoprofen and sertraline were fully eliminated over the studied stretch of river during the summer months. Other compounds showed continuous elimination independent of the season, indicating different elimination paths, such as sorption, biodegradation and phototransformation, for the studied compounds.

Received 7th October 2015
Accepted 23rd January 2016

DOI: 10.1039/c5em00505a

rsc.li/process-impacts

Environmental impact

The work described in this article uses a river/lake system with a single point source of wastewater effluent and a long residence time, to assess the fate of pharmaceuticals in the aquatic environment during different seasons. This makes it possible to determine the effect of temperature and light on the persistence and degradation pathways of pharmaceuticals and thus the possible environmental impact under environmental conditions.

Introduction

Pharmaceuticals used for the prevention and treatment of human illnesses are excreted either metabolized or unchanged into municipal wastewater through urine and feces. The elimination of these compounds in wastewater treatment plants (WWTPs) varies greatly, depending on the compound, the type of treatment, and the season of the year.[1–3] This leads to a constant discharge of pharmaceuticals into the recipient water bodies. Although the concentrations of these compounds in the environment are in the ng l^{-1} to low μg l^{-1} range, the constant exposure to a mixture of compounds has to be considered a potential risk for the aquatic environment.

Previous studies have shown that some psychoactive drugs can cause behavioral changes at concentrations close to those found in the environment, and are significantly lower than those needed to cause acute toxicity.[4–6] Also physiological changes in aquatic organisms have been connected to the presence of pharmaceuticals.[7–9]

While there have been many studies conducted on the occurrence of pharmaceuticals in the aquatic environment, relatively few have monitored pharmaceuticals over long distances in rivers and extended residence times downstream from a point source. This is partially due to the fact that few sites are suited for this type of study. Many rivers receive discharges not only from one but several WWTPs, or the dilution factor is too large to allow quantification over a long distance.[10]

Some studies on the seasonal variation in concentrations of pharmaceuticals downstream from WWTPs have been conducted; many of these have been performed in warm climates where seasonal changes in concentrations are due to changes in

Laboratory of Organic Chemistry, Åbo Akademi University, Biskopsgatan 8, 20500 Turku, Finland. E-mail: axel.meierjohann@abo.fi; Tel: +358 (0)2 2154138

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c5em00505a

precipitation and dilution rather than changes in elimination rates through phototransformation, biodegradation, and/or adsorption processes.[11,12]

In the current work, the concentration and the loads of 15 highly used pharmaceuticals were determined in water samples, by liquid chromatography tandem-mass spectrometry (LC-MS/MS), taken along a distance of 32 km of a highly contaminated watercourse with only one point source of WWTP effluent and a low dilution of the recipient water. The study was conducted in the winter (February), spring (May), summer (July) and autumn (November), making it possible to compare elimination rates during the different seasons.

Experimental

Chemicals and reagents

Stock solutions (1 mg ml^{-1}) of all pharmaceuticals and internal standards were prepared in HPLC grade methanol and stored at −20 °C. Working solutions were prepared by diluting the standards in LC-MS grade acetonitrile and purified water from a Millipore Simplicity 184 system (Millipore S.A.S., Molsheim, France) by demand.

The analytical standards of (purity ≥ 98%) atenolol, bezafibrate, carbamazepine, citalopram, diclofenac, fluoxetine, ibuprofen, ketoprofen, naproxen, sotalol, metoprolol and internal standards alprenolol, 10,11-dihydrocarbamazepine and D_5-fluoxetine were purchased from Sigma Aldrich Inc. (St. Louis, USA). Bisoprolol hemifumarate was obtained from Heuman Pharma GmbH (Nürnberg, Germany). Sertraline, D_3-sertraline, venlafaxine, and D_3-naproxen, were purchased from Toronto Research Chemicals (North York, ON, Canada). The chemical purities of all deuterated standards were 98% and isotopic purities were 99%. Citalopram was a gift from a pharmaceutical company.

Characteristics of the sampling area

The River Rakkolanjoki (Fig. 1) receives wastewater effluent from the WWTP of the city of Lappeenranta in Eastern Finland. The WWTP processes wastewater from approximately 60 000 population equivalents.

The river begins at the discharge point of the WWTP, with the effluent being its source. In the upper reaches the river is approximately 2 m wide, 50 cm deep and has an annual average flow rate of approximately 0.9 $m^3 s^{-1}$. The flow rate has a strong seasonality with a maximum in April during the snowmelt (5.5 $m^3 s^{-1}$) and significantly lower flow rates in winter (0.2 $m^3 s^{-1}$ in January, February and December) (Fig. S1 ESI†). This also causes a strong variation in the residence time of the water in the upper stretch of the river ranging from 1 to 48 h, with a median of 32 h. Twenty kilometers downstream from the discharge point the river enters Lake Haapajärvi, a shallow eutrophic lake with a medium depth of 1.4 m (maximum depth of 4 m) and a surface area of 220 ha. The residence time of the water in the lake varies from 6 to 220 days with a median of 159 days. On the opposite side of the lake, 3 km from the river entry point, the river continues. This part of the river is 4–10 m wide and has an average flow rate of 1.5 $m^3 s^{-1}$ with a similar seasonal variability as the upper stretch. The water flows along this stretch of the river for about 9 km before reaching the Russian border. The residence time here ranges from 1 to 8 h with a median of 5 h. The drainage basin of the studied watercourse is 215 km^2.

The quality of the river water can be considered as a worst-case scenario as it contains 5–83% wastewater effluent (average 53%) in the upper part (calculated for the entry point into Lake Haapajärvi) and 4–34% in the lower stretch (average 22%). This trait makes it a good platform for studying the fate of pharmaceuticals. Due to the geographic location (61°N; 28°E) of the river there is also a strong seasonality. In winter the temperatures are below freezing, the days are short with little sunshine and the river is covered by ice. Under these conditions phototransformation can be excluded as an elimination pathway, and the extent of biodegradation will be minimal. The opposite conditions are prevailing in summer. The close to continuous daylight and warm water temperatures create excellent conditions for both phototransformation and biodegradation of pharmaceuticals. The average temperatures measured at the weather station of Åbo Akademi University were −7.7 °C in February, 11.3 °C in May, 21.6 °C in July and −1.4 °C in November of 2010. The average sun intensity was 33 W m^{-2} in February, 182 W m^{-2} in May, 233 W m^{-2} in July and 18 W m^{-2} in November of 2010.

Sampling

Samples were taken four times in 2010: on February 22, May 25, July 07 and November 29. Grab samples (1 L) were taken at seven points along the river; at the discharge point, and at points 6.2; 12.8; 19.5; 22.9; 28.9 and 31.7 km from the WWTP. Samples were also collected at two points in the lake (20.2 and 21.6 km from the WWTP). Two additional samples along the river (13.7 and 19.4 km from the WWTP) were collected in November. The samples were stored in dark Nalgene HDPE bottles at −20 °C until work-up.

In addition to the samples taken from the River Rakkolanjoki, samples were collected from two main tributaries (small creeks with low impact on the total flow), as well as one agricultural ditch to eliminate the chance of these rivers influencing the mass flow calculations. Samples from the river's main tributaries were taken approximately 1 km upstream from the river junction while samples from the agricultural ditch were taken approximately 50 m upstream from the river junction. Samples at the tributaries were only taken during the November sampling campaign.

Sample work-up

The extraction and LC-MS/MS analysis were carried out using a modified version of the methods described and characterized in of Daneshvar *et al.*[13,14] and Vieno *et al.*[1]

The samples were divided into two 400 ml sub samples, one sub sample for analyses of acidic compounds and the other for analysis of basic and neutral compounds. Prior to filtration with Whatman GF/C glassfiber filters (1.2 μm), 200 ng of the internal standards was added to each sample. The pH of the samples

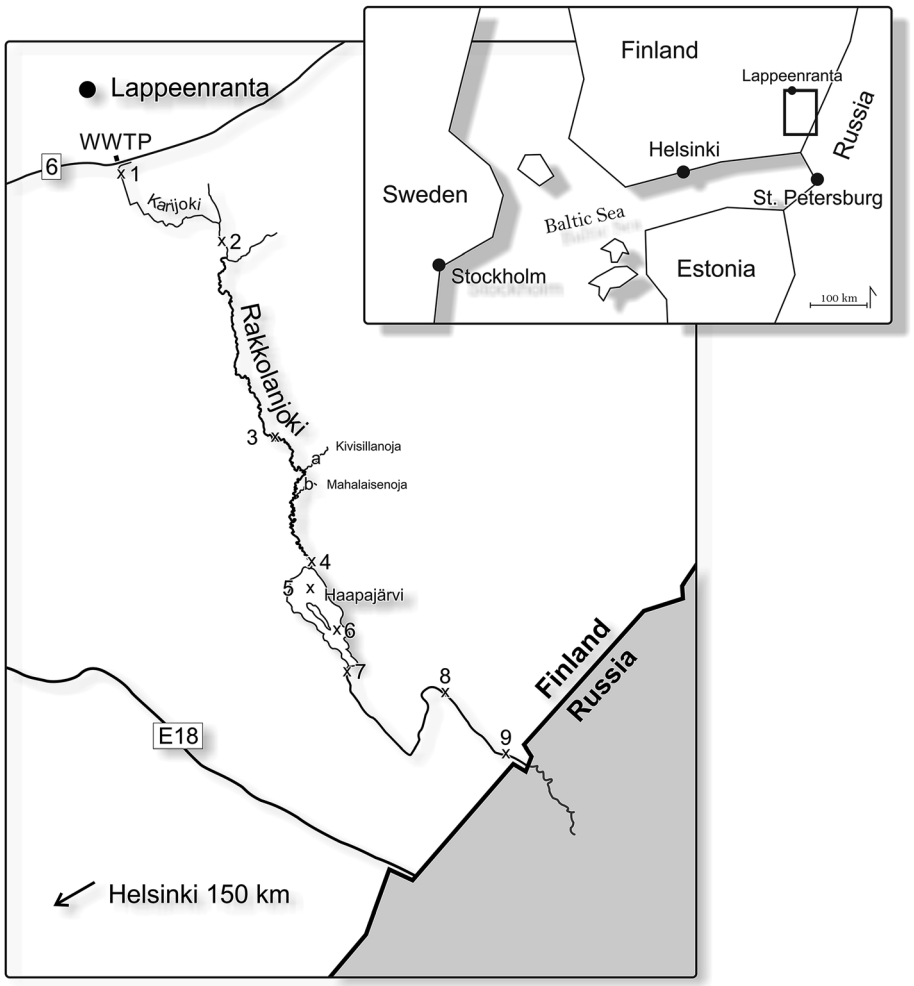

Fig. 1 The River Rakkolanjoki with sampling points 1–9 along the river, and points a and b at the tributaries Kivisillanoja and Mahalaisenoja.

used for the analysis of neutral and basic compounds was adjusted to 10 with 1 M NaOH, while the pH of the samples used for the analysis of acidic compounds was adjusted to 2 with concentrated HCl. Solid phase extraction was carried out using Waters Oasis HLB (3 cm^3, 60 mg; Waters, Milford, MA) cartridges that were preconditioned with 10 ml of methanol and 10 ml of water at the pH of the respective sample. The sample was then passed through the cartridge at approximately 6 ml min^{-1}.

Elution of the analytes from the SPE cartridge was carried out using 4 ml of acetonitrile. The extracts were dried under nitrogen and then redissolved in 500 μl 4% acetonitrile in a 0.5% aqueous solution of acetic acid for the analysis of basic compounds, and 500 μl 10% acetonitrile in 10 mM aqueous NH_4OH for the analysis of acidic compounds. The extracts were kept at −20 °C until analysis.

LC-MS/MS analysis

The extracts were analyzed using a Micromass QuattroMicro triple quadrupole mass spectrometer with electrospray ionization (Waters, Milford, MA), coupled to an Agilent 1100 series HPLC equipped with a binary pump, a vacuum degasser, an auto sampler and a thermostatted column oven. For chromatographic separation of the analytes, a Waters X-bridge analytical column (C18, 2.1 × 50 mm, 3.5 μm) with a guard column of the same material (2.1 × 5 mm) was used. The triple quadrupole mass spectrometer was run in MRM mode and the monitored transitions as well as the spectrometric conditions are presented in Table 1.

For acidic compounds, the elution was carried out with 10 mM NH_4OH in water (A) and acetonitrile (B). The column was eluted isocratically with 3% B for one minute followed by a linear gradient to 65% B over the course of 9 min. The percentage of acetonitrile was held at this value for 1 min and then returned to the initial value over the next min. The system was given eight minutes to equilibrate before the next injection. The flow rate was 300 μl min^{-1} and the injection volume was 30 μl.

For basic compounds, the elution was carried out with water (A) and acetonitrile (B), both containing 0.5% acetic acid. The eluent initially consisted of 3% acetonitrile and the percentage of acetonitrile was raised to 65% in a linear gradient over 14 min. The percentage of acetonitrile was kept at 65% for one minute before returning to the initial conditions over the next

Table 1 The analyzed pharmaceuticals, with their MRM transitions, internal standards and limits of quantification

Analyte	Ion mode	Precursor ion (m/z)	Product ion (m/z)	Cone voltage (V)	Collision energy (eV)	Limit of quantification (ng l^{-1})	Internal standard	Accuracy% (250 ng l^{-1})	CV% (250 ng l^{-1})
Bezafibrate	ESI^-	360	274	23	18	4	Fenoprop	103	2
Diclofenac	ESI^-	294	250	15	12	10	Fenoprop	104	2
Ketoprofen	ESI^-	253	209	14	8	30	Fenoprop	91	2
Naproxen	ESI^-	229	170	11	16	3	Naproxen-D3	87	9
Ibuprofen	ESI^-	205	161	15	8	10	Fenoprop	104	2
Fenoprop	ESI^-	267	195	15	13	na	IS	N/A	N/A
Naproxen-D3	ESI^-	232	188	11	16	na	IS	N/A	N/A
Sotalol	ESI^+	273	255	19	12	1	Alprenolol	126	8
Atenolol	ESI^+	267	145	33	25	2	Alprenolol	123	6
Acebutolol	ESI^+	337	116	37	29	2	Alprenolol	104	2
Metoprolol	ESI^+	268	133	32	24	3	Alprenolol	109	5
Bisoprolol	ESI^+	326	116	33	21	1	Alprenolol	106	3
Citalopram	ESI^+	325	109	20	23	1	Alprenolol	101	3
Venlafaxine	ESI^+	278	121	27	20	1	Alprenolol	107	3
Carbamazepine	ESI^+	237	194	30	19	1	Dihydrocarbamazepine	101	3
Fluoxetine	ESI^+	310	148	13	10	50	Sertraline-D3	103	12
Sertraline	ESI^+	306	275	23	13	1	Sertraline-D3	119	5
Dihydrocarbamazepine	ESI^+	239	194	36	23	na	IS	N/A	N/A
Sertraline-D3	ESI^+	309	275	23	13	na	IS	N/A	N/A

minute. The system was then given eight minutes to equilibrate before the next injection. The flow rate was 300 μl min^{-1} and the injection volume was 30 μl.

Quantification

For the quantification, a calibration curve was made by spiking 400 ml of tap water with the analytes at concentrations of 2.5, 25, 250, 1250 and 2500 ng l^{-1} as well as 200 ng of the internal standards. The calibration samples were then extracted as described above. The calibration curve was fitted using linear regression with $r^2 > 0.97$. A sample of blank tap water was worked-up together with the calibration curves. The internal standard method was used for the quantification of pharmaceuticals. The LOQs given in Table 1 were calculated from samples, to account for matrix suppression, and set to be the lowest concentration giving a s/n value of 10. The accuracy and precision of the method for the different compounds at 250 ng l^{-1} ($n = 6$) can be found in Table 1. Blank samples were run throughout the batch and showed no significant carry over effect.

Flow rates of river water

The flow rate of effluent was obtained from the WWTP and the flow rate of the river water at the last sampling point was recorded by the Centre for Economic Development, Transport and the Environment (ELY Centre), South Karelia. ELY Centre also provided the modelled data for the flow rate entering Lake Haapajärvi at sampling point four. The flow rate of the WWTP effluent and the flow rate at the last sampling point were used for the calculation of pharmaceutical loads entering and exiting the studied watercourse as well as the residence time in the lower stretch of the river. The modeled data was used to calculate the residence time in the upper stretch of the river as well as Lake Haapajärvi. Between February, July and November there was no significant difference in flowrates at the sampling time, while the flowrate in May was double that of the other months. Graphs showing the flowdata can be found in the ESI.†

Short term variability of concentrations

To assess the variability of pharmaceutical inflow and to give approximate error margins for the grab sampling, the relative standard deviation for the concentrations of the last three points was calculated. These points are a few hours apart, while the flowrate does not change in this part of the river, meaning that these samples can be treated as parallel samples, taken with a gap of a few hours. The relative standard deviation of the loads entering the watercourse between the different sampling occasions was calculated to give an estimation of the variation in the incoming loads. The results are given in Table 2.

Results and discussion

Occurrence of pharmaceuticals

The incidence of detection for all studied pharmaceuticals was calculated for the last sampling point and as a total of all samples. The highest number of the studied pharmaceuticals detected at the last sampling point was in February with 14 out of the 15 compounds detected, followed by November with 12 compounds detected and May and July, with only 8 and 9 compounds detected at the last sampling point, respectively. Fluoxetine could not be detected in any of the samples (Table S1a–d ESI†).

Considering the percentage of compounds detected over all sampling points, February had the highest value at 94%, followed by November 84%, July with 74% and May with 73%. The lowest incidence of detection over all sampling points and

Table 2 RSDs of the concentrations of pharmaceuticals at the discharge point, and at the last three sampling points

	Sotalol	Atenolol	Acebutolol	Metoprolol	Bisoprolol	Citalopram	Venlafaxine	Carbamazepine	Sertraline	Bezafibrate	Diclofenac	Ketoprofen	Naproxen	Ibuprofen
RSD effluent	39	62	29	6	18	171	151	38	43	58	20	32	103	171
RSD February points 7–9 (%)	15	30	20	15	89	27	3	46	8	19	4	34	10	26
RSD May points 7–9 (%)	13	11	8	11	17	28	21	8	N/A	20	4	N/A	31	N/A
RSD July points 7–9 (%)	10	10	8	10	11	29	16	4	N/A	13	31	N/A	26	N/A
RSD November points 7–9 (%)	16	25	12	17	32	87	28	14	N/A	12	12	N/A	20	11

seasons was observed for sertraline (49%), while bezafibrate, diclofenac, naproxen, sotalol, atenolol, metoprolol, bisoprolol and carbamazepine were detected in all the collected and analyzed samples.

No pharmaceuticals were detected in the tributaries, making it possible to consider the Lappeenranta WWTP as the only point source of pharmaceuticals in the studied stretch of the River Rakkolanjoki.

Concentrations of pharmaceuticals

Concentrations of the studied pharmaceuticals at the discharge point vary from low μg l^{-1} for metoprolol, carbamazepine, naproxen and ibuprofen, to low ng l^{-1} for the antidepressants venlafaxine, sertraline and citalopram (Table S1a–d ESI†).

Between the sampling months, the concentrations of the single compounds at the discharge point did not vary dramatically (Table 2). The exceptions are ibuprofen, naproxen, venlafaxine and citalopram which had very high relative standard deviations at the discharge point. In the case of naproxen and ibuprofen this is due to elevated concentrations in May. This high concentration may be due to the high flow of water in the treatment plant during the snowmelt causing poor efficiency in the treatment. Another concentration maximum was noted for the antidepressants venlafaxine and citalopram in November samples.

In general, the concentrations of the compounds were higher at all 9 sampling points in the February and November samples than in the May and July samples. Accordingly, most of the compounds could be traced down to sampling point 9 in February and November.

Along the studied watercourse, the concentrations of pharmaceuticals decreased after entering the river (from point 1 to 2). This first decrease can be mainly attributed to dilution. Thereafter, the concentration remained relatively stable in the upper stretch of the river. A second drastic decrease in concentration was observed between points four and five, where the river enters the lake. While this decrease can also largely be attributed to dilution with lake water, for some compounds the magnitude of this decrease was affected by the season (seasonal variation, see the discussion below on pharmaceutical loads). No further decrease in concentration was observed between sampling point 5 and 6 (Fig. 2) indicating that the lake is well mixed, with very little concentration gradient along its length. After the lake the concentration remains stable most likely due to the short residence time and lack of significant influx of water in the lower river stretch.

Loads and removal of pharmaceuticals

The load of each pharmaceutical was calculated at the first and last sampling point by multiplication of the measured concentrations with the flowrate. The loads during the different seasons can be found in Fig. 3a–d.

The total load of the studied pharmaceuticals entering the river was approximately 75 g per day in February, July and November, but it doubled to 142 g per day in May. This rise in pharmaceutical load was largely due to the loads of naproxen and

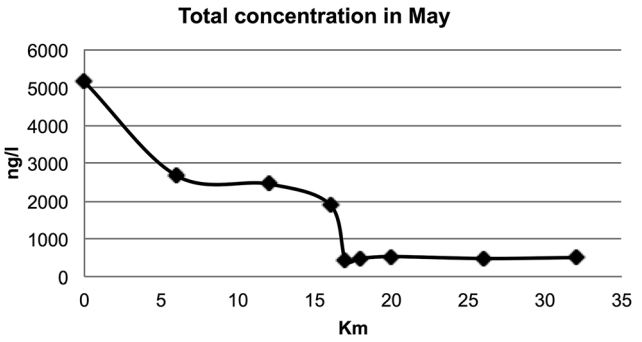

Fig. 2 Total concentration (ng l^{-1}) of pharmaceuticals along the River Rakkolanjoki in November. The points mark the concentrations at the sampling points. The line is included as a guideline for the eye.

ibuprofen being five to thirty-fold higher than during other sampling periods. The only other significant change in the incoming loads between sampling events was observed in November, when the loads of the antidepressants citalopram and venlafaxine increased 15–30-fold. In February, the pharmaceutical load at the last sampling point was 70 g per day, whereas it was 79 g per day at the discharge point, *i.e.* nearly the entire discharged load reached sampling point 9. In May, July and November, the loads at point 9 were significantly lower than at the discharge point (May: 52 of 132 g per day, July: 21 of 65 g per day and November: 28 of 67 g per day, for pharmaceutical load at point 9 *vs.* discharge point 1, respectively). This suggests a temperature and light dependent removal of the total pharmaceutical load. The comparatively higher loads at the last sampling point in May might be in part due to the higher flow rate and thus shorter residence time in that period. Factoring in the residence time to calculate the removal rate confirmed this, showing that the removal rate in May is comparable to that in July.

When comparing the relative loads (calculated as load at the last sampling point divided by load at the discharge point), the compounds can be divided into four categories according to differences in removal in the different sampling months (Fig. 4a–d).

Carbamazepine is the only compound not eliminated along the studied watercourse (Fig. 4a). The finding is in good agreement with earlier studies showing that carbamazepine is very stable in the aquatic environment.[15] The relative loads above one for carbamazepine during some seasons, can be partially explained due to possible fluctuations in incoming carbamazepine concentrations, but also deconjugation of carbamazepine phase II metabolites has been observed in earlier studies which could lead to higher loads downstream.[2] The second category of compounds includes those compounds that are eliminated to the same degree in all sampling months. This category is represented by acebutolol, bisoprolol and bezafibrate (Fig. 4b). Bezafibrate was found to be the most stable of these compounds with 51–71% of the initial load reaching the last sampling point. Previously, it has been suggested that bezafibrate does not undergo phototransformation or any other abiotic processes such as hydrolysis in river water. Also, the compound has a low affinity to solids and sediments.[16–18] Biodegradation of bezafibrate depends strongly on the

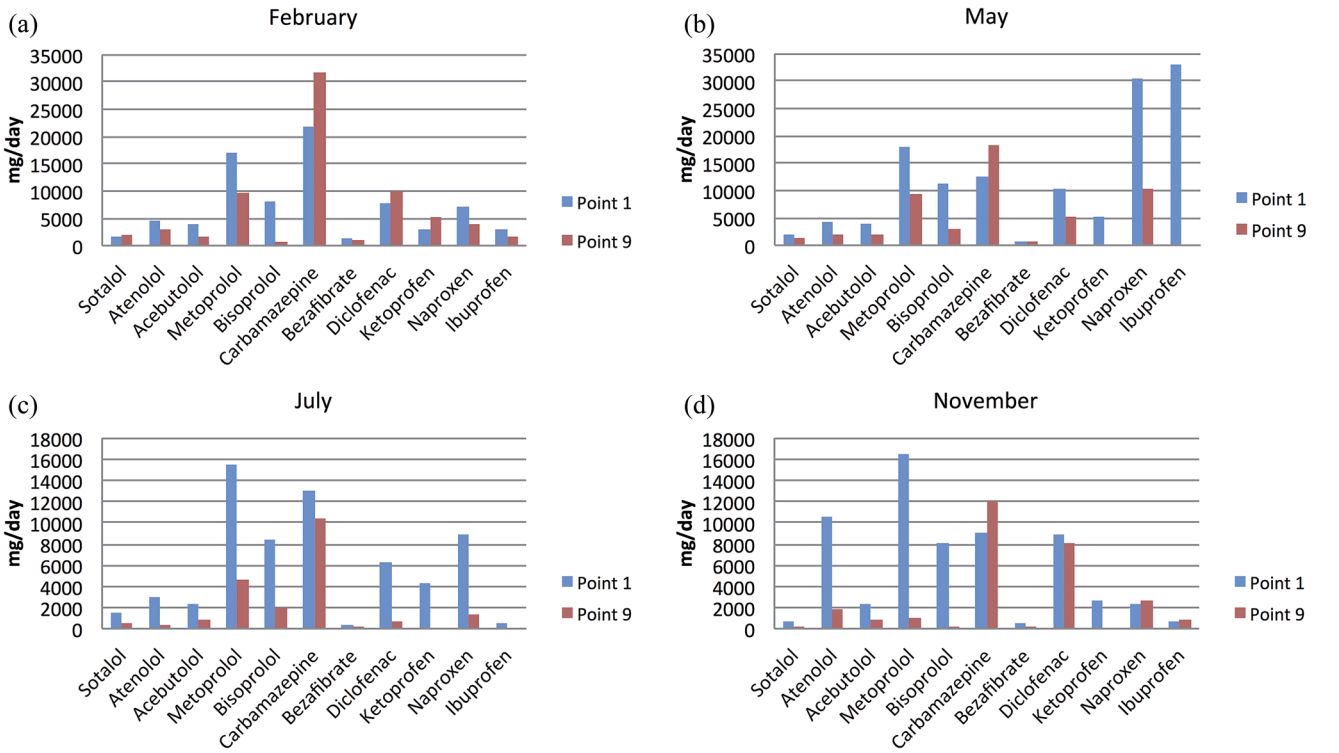

Fig. 3 (a) Loads at the first and last sampling point in February. (b) Loads at the first and last sampling point in May. (c) Loads at the first and last sampling point in July. (d) Loads at the first and last sampling point in November.

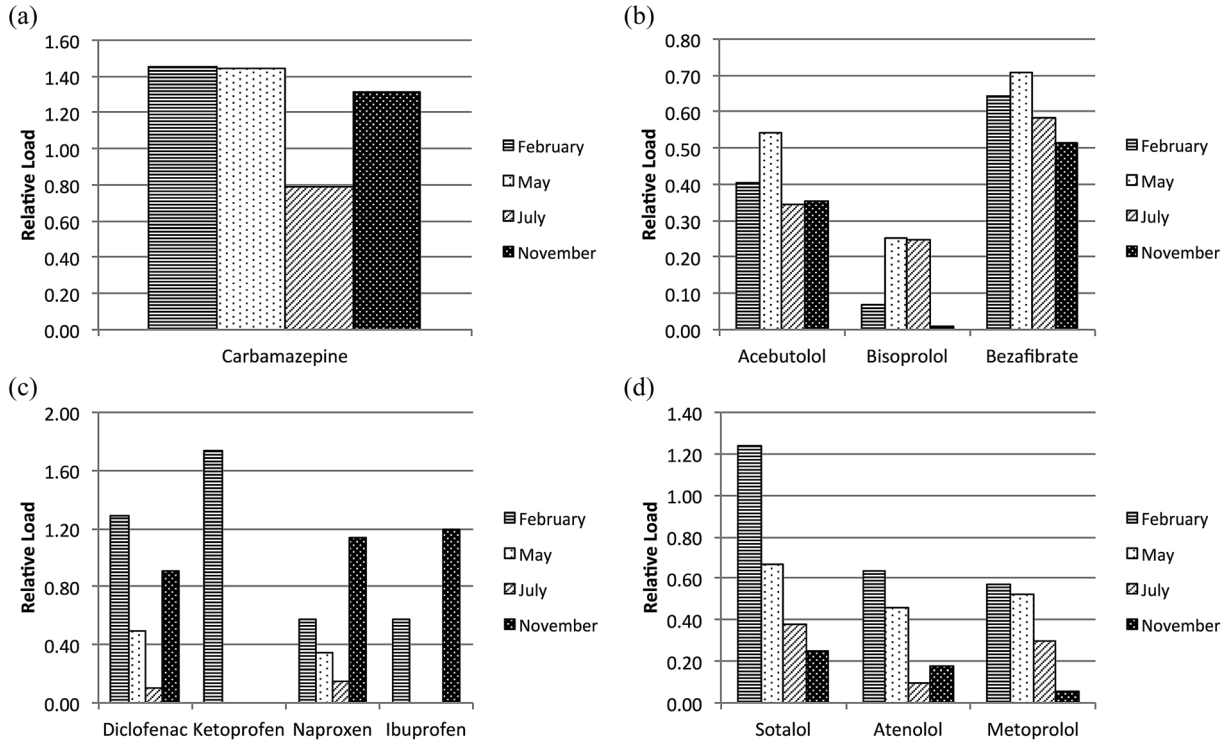

Fig. 4 (a) Relative loads of carbamazepine at the last sampling point given in percent of the load at the first sampling point. (b) Relative loads of acebutolol, bisoprolol and bezafibrate at the last sampling point given in percent of the load at the first sampling point. (c) Relative loads of diclofenac, ketoprofen, naproxen and ibuprofen at the last sampling point given in percent of the load at the first sampling point. (d) Relative loads of sotalol, atenolol and metoprolol at the last sampling point given in percent of the load at the first sampling point.

microorganisms present and has been found to be insignificant in some of the sediments studied by Radke *et al.*[18] This leads us to believe that the observed low and constant removal rate of bezafibrate may be attributed to sorption to suspended solids and sediments during the long residence time in this system. Slightly less than half of the initial load of acebutolol could be detected at sampling point 9. The compound has been found to be poorly photodegraded in light over 280 nm and does not undergo biodegradation.[19,20] It is adsorbed to particles more easily than bezafibrate and for these reasons sorption is most likely the main elimination pathway in the studied watercourse. Over 75% of bisoprolol was lost when the compound reached the last sampling point. This loss was of about the same magnitude during all seasons. Since bisoprolol has be found at high concentrations in sediments,[17] the loss of the compound can be explained by sorption to particles and sediments.

The nonsteroidal anti-inflammatory drugs (NSAIDs) belong to the third category of compounds (Fig. 4c). The loss of these compounds shows a significant seasonal pattern, with low degrees of removal in winter and autumn, and high removal rates in May and July. Earlier studies have shown that diclofenac is very prone to phototransformation[21,22] which is supported by the removal rates observed in this study in May and July (51% and 90%, respectively). Ibuprofen had the highest fluctuation in incoming concentrations at the discharge point of the studied compounds, leading to downstream concentrations higher than those at the discharge point in some cases. Despite this, the complete removal during May and July as well as low removals in February and November show a clear seasonality in ibuprofen degradation. Ibuprofen is known to be readily biodegraded in river water and the compound has been shown to have a low affinity to sediments.[22–24] Biodegradation is temperature dependent and it consequently proceeds faster in May and July. Naproxen is known to undergo both direct photolysis[25] and biodegradation.[23] Similar to ibuprofen, there is a high degree of fluctuation in effluent concentrations of naproxen, which makes it more difficult to compare the loads from the first sampling point with those at the last. However, there still seems to be a higher degree of removal during spring and summer, which is consistent with the results of naproxen biodegradation studies.[23,25] Ketoprofen could only be detected down to the last sampling point in February, where no removal of this compound was observed. Ketoprofen is very photosensitive[26] and known to readily undergo biodegradation.[27] This high sensitivity to both bio- and phototransformation can explain that ketoprofen has the lowest stability of all NSAIDs in this river. Despite being fully removed even in November, it was found further downstream than in May and July, showing a likely dependence on sunlight and temperature in the removal efficiency. Another reason for the higher-than-expected removal rate in November may be due to the long residence time in the river-lake system. Samples taken in November entered the watercourse as early as September, when temperatures are still significantly warmer.

The fourth category of the studied compounds is represented by the beta blockers sotalol, atenolol and metoprolol (Fig. 4d). The highest load of these compounds at the last sampling point

was found in February and it gradually decreases during the following months. Atenolol and metoprolol were removed to a certain extent all year round (>36% and >43%, respectively) suggesting that sorption contributes partially to the removal,[17] while biodegradation[28] by bacterial communities which are active until later in the fall, is most likely contributing to the removal. The seasonal removal pattern of sotalol, with no removal in February suggests that biodegradation is the main process responsible for the elimination of the compound. As with ketoprofen the very high removal rate measured for the compounds belonging to this group in November may be due to the long residence time.

Conclusions

Most of the 15 studied pharmaceuticals were detected in samples taken along the watercourse and could be traced over long distances down the watercourse. The concentrations at the discharge point did not vary significantly at different sampling times with the exceptions of raised concentrations of naproxen and ibuprofen in May, and higher concentrations of antidepressants in November. The degree of elimination of the parent compound in the aquatic environment varied considerably both between compounds and seasons, suggesting different mechanisms of elimination. This data indicated that the aquatic environment downstream of WWTP in northern latitudes is contaminated mainly with the parent compounds during winter months, while in the summer time most of the NSAIDs are lost, and possible contamination and exposure to aquatic fauna are due to metabolites or transformation products.

Acknowledgements

The authors would like to thank Maa- ja vesitekniikan tuki ry, The Advisory Board on Environmental and Sustainability Subjects in Research and Education at Åbo Akademi University and The Finnish Graduate School for Environmental Science and Technology for funding, the Centre for Economic Development, Transport and the Environment, South Karelia for their help with the sampling, and Jukka Höytämö from the Centre for Economic Development, Transport and the Environment, South Karelia for the flow data model. The authors would also like to thank Kurt Lundqvist from Åbo Akademi University for providing the weather data.

References

1 N. M. Vieno, T. Tuhkanen and L. Kronberg, *Environ. Sci. Technol.*, 2005, **39**, 8220–8226.
2 N. Vieno, T. Tuhkanen and L. Kronberg, *Water Res.*, 2007, **41**, 1001–1012.
3 T. A. Ternes, *Water Res.*, 1998, **32**, 3245–3260.
4 T. Brodin, J. Fick, M. Jonsson and J. Klaminder, *Science*, 2013, **339**, 814–815.
5 T. W. Valenti Jr, G. G. Gould, J. P. Berninger, K. A. Connors, N. B. Keele, K. N. Prosser and B. W. Brooks, *Environ. Sci. Technol.*, 2012, **46**, 2427–2435.
6 H. de Lange, W. Noordoven, A. Murk, M. Lürling and E. Peeters, *Aquat. Toxicol.*, 2006, **78**, 209–216.
7 J. Schwaiger, H. Ferling, U. Mallow, H. Wintermayr and R. Negele, *Aquat. Toxicol.*, 2004, **68**, 141–150.
8 R. Triebskorn, H. Casper, A. Heyd, R. Eikemper, H. Köhler and J. Schwaiger, *Aquat. Toxicol.*, 2004, **68**, 151–166.
9 B. Hoeger, B. Köllner, D. R. Dietrich and B. Hitzfeld, *Aquat. Toxicol.*, 2005, **75**, 53–64.
10 S. Wiegel, A. Aulinger, R. Brockmeyer, H. Harms, J. Löffler, H. Reincke, R. Schmidt, B. Stachel, W. von Tümpling and A. Wanke, *Chemosphere*, 2004, **57**, 107–126.
11 G. A. Loraine and M. E. Pettigrove, *Environ. Sci. Technol.*, 2006, **40**, 687–695.
12 L. Jiang, X. Hu, D. Yin, H. Zhang and Z. Yu, *Chemosphere*, 2011, **82**, 822–828.
13 A. Daneshvar, J. Svanfelt, L. Kronberg, M. Prévost and G. A. Weyhenmeyer, *Chemosphere*, 2010, **80**, 301–309.
14 A. Daneshvar, J. Svanfelt, L. Kronberg and G. A. Weyhenmeyer, *Environ. Sci. Pollut. Res.*, 2010, **17**, 908–916.
15 M. Clara, B. Strenn and N. Kreuzinger, *Water Res.*, 2004, **38**, 947–954.
16 B. F. d. Silva, A. Jelic, R. López-Serna, A. A. Mozeto, M. Petrovic and D. Barceló, *Chemosphere*, 2011, **85**, 1331–1339.
17 M. Lahti and A. Oikari, *Chemosphere*, 2011, **85**, 826–831.
18 M. Radke and M. P. Maier, *Water Res.*, 2014, **55**, 63–73.
19 A. Y. Lin, C. Lin, H. Tung and N. S. Chary, *J. Hazard. Mater.*, 2010, **183**, 242–250.
20 A. Piram, A. Salvador, C. Verne, B. Herbreteau and R. Faure, *Chemosphere*, 2008, **73**, 1265–1271.
21 J. Eriksson, J. Svanfelt and L. Kronberg, *Photochem. Photobiol.*, 2010, **86**, 528–532.
22 D. Löffler, J. Römbke, M. Meller and T. A. Ternes, *Environ. Sci. Technol.*, 2005, **39**, 5209–5218.
23 L. J. Fono, E. P. Kolodziej and D. L. Sedlak, *Environ. Sci. Technol.*, 2006, **40**, 7257–7262.
24 H. R. Buser, T. Poiger and M. D. Müller, *Environ. Sci. Technol.*, 1999, **33**, 2529–2535.
25 J. L. Packer, J. J. Werner, D. E. Latch, K. McNeill and W. A. Arnold, *Aquat. Sci.*, 2003, **65**, 342–351.
26 V. Matamoros, A. Duhec, J. Albaigés and J. M. Bayona, *Water, Air, Soil Pollut.*, 2009, **196**, 161–168.
27 J. B. Quintana, S. Weiss and T. Reemtsma, *Water Res.*, 2005, **39**, 2654–2664.
28 U. Kunkel and M. Radke, *Water Res.*, 2012, **46**, 5551–5565.

