PHARMACEUTICAL AND PERSONAL CARE PRODUCTS IN THE SOMEŞ RIVER BASIN, ROMANIA

Zaharie MOLDOVAN[(1)(#)], Gabriella SCHMUTZER[(1)], Florina TUSA[(1)], Roxana CĂLIN[(2)], Alfredo C. ALDER[(3)]

[(1)]*National Institute of Research and Development for Isotopic and Molecular Technology, Cluj-Napoca, 71-103, Donath Street, Romania*

[(2)]*University of Medicine and Farmacy „Iuliu Haţeganu" Cluj-Napoca, Romania*

[(3)]*Swiss Federal Institute for Aquatic Science and Technology (Eawag), CH-8600 Duebendorf, Switzerland*

[(#)]*Corresponding author: zaha@oc1.itim-cj.ro*

Abstract. The mass flows of selected pharmaceuticals and personal care products (PPCPs) were studied in the aqueous compartment of the river Someș in Romania. PPCPs distribution was correlated with wastewater treatment plant effluents in the receiving river water.

Carbamazepine, pentoxyfylline, ibuprofen, diazepam, galaxolide, tonalide and triclosan were determined in wastewater effluents with individual concentrations up to 800 ng/L. Caffeine was measured at concentrations up to 43 000 ng/L. Due to the high contamination of WWTP effluents, the receiving river was also polluted. The most abundant PPCPs measured in the Someş were caffeine, galaxolide, carbamazepine and triclosan, with concentrations ranging from 10 to 400 ng/L. The loads increased significantly after the confluence of the river Somesul Mic with the river Someşul Mare after Dej. The highest loads were observed for caffeine (800–2400 g/d), galaxolide (410–860 g/d), triclosan (200–310 g/d) and carbamazepine (170–240 g/d) suggesting the discharge of wastewater without proper treatment into the Someş. These results show that the upgrading of the WWTPs in the River Basin is of high importance to reduce the effluent load of contaminants into the Someş.

This study is a first overview of PPCPs along the Romanian stretch of the Someş River.

Key words: Pharmaceuticals, PPCPs, wastewater, surface water, GC/MS

INTRODUCTION

The widespread presence of pharmaceuticals in the aquatic environment[1-5] is due to their extensive use in medical practices[6] and incomplete removal in wastewater treatment plants (WWTP). Pharmaceuticals are designed to target specific metabolic pathways in humans and animals but there is also concern that they may pose a potential risk to aquatic organisms[7-9] at the low ng/L level. It is also assumed that PPCPs could act as pseudo-persistent compounds, because of their continual discharge into aquatic media via WWTP effluents[8-10].

Inputs of PPCPs into aquatic systems have led to their occurrence in WWTP effluent, river and marine water and ground water[1-8, 11-16]. Much of this work has been conducted in West Europe and in North America[15,17-20] but very little or no data from Eastern Europe or developing countries are available.

PPCPs concentrations in the river water are dependent on the share of wastewater discharged into the river and therefore of the dilution of the wastewater that occurs. Dilution factors are site specific and may vary depending on location and season.

Due to dilution and transformation processes, lower concentration levels are expected for drugs after they enter the aquatic environment[21]. To obtain detection limits of the order to ng/l range, the enrichment methods and very sensitive detection methods are necessary[22-25]

The absence of data for Eastern Europe is a matter of concern since use patterns and volumes differ from country to country. In this part of Europe the majority of wastewater, from highly-populated cities and industrial complex zones, is still discharged into surface waters without proper treatment or after inefficient treatment. In respect to this, it is important to determine the environmental occurrence and fate of PPCPs in wastewaters and surface waters.

The objective of the present study was to survey the occurrence and behaviour of selected PPCPs along the Someş River Basin by mass flow analysis. For this purpose, five pharmaceuticals belonging to different pharmaceutical groups, two fragrances and one antimicrobial agent were analyzed in wastewater effluents and in river waters.

The results should provide support for the improvement of the existing WWTPs and therefore minimise their loads into the aquatic environment.

EXPERIMENTAL

Sampling site area and sample preparation

The Someş watershed has 1 800 000 inhabitants in the north-west of Romania. The Someş flows from the Central to the Northwest of Transylvania. It originates south of Cluj-Napoca and flows after 370 km into the Tiza in Hungary and later into the Danube. The map of the Someş River Basin and the sampling locations are shown in Fig. 1. The average flow of the river is: 20-25 m^3/s at the sampling sites 1-3, 65-70 m^3/s at the sites 3-5 (after confluence of the river Someşul Mic with the river Someşul Mare) and 80-90 m^3/s at the sites 6-7 (after confluence with Lăpuş River).

Grab samples were collected from several locations along the Romanian river stretch of 250 km, at least 1 km up- and downstream of tributaries and effluents of WWTPs entering into the Someş. In order to have complete mixing between WWTP effluent or tributaries and the sampling point, samples were taken along the whole width (usually, situated on a bridge connecting the shores) and combined to one sample. The samples were collected at 10 sites along the 250 km river stretch between Cluj-Napoca and Satu Mare in September 2006.

Analytical methods

The following analytes were selected: acidic pharmaceuticals (ibuprofen), neutral pharmaceuticals (caffeine, carbamazepine, diazepam, pentoxyfylline), musk fragrances (galaxolide, tonalide) and an anti-microbial compound (triclosan).

The samples were acidified with 2N HCL to pH 2 and filtered on a glass fibre filter of 0.45 µm (Whatman, Maidstone, England). The detailed SPE procedure is described in an earlier paper[26]. Briefly, analytes were concentrated by solid-phase extraction performed on Oasis HLB cartridges (60 mg, Waters) and subsequently analysed on a GC/ITMS system, involving a Thermo Electron Polaris Q mass spectrometer (operated in EI mode to 70 eV) and a Trace GC ultra gas chromatograph.

The TMS derivatives were obtained by reaction with N-Methyl-N-(trimethylsilyl)-trifluoracetamide (MSTFA, Sigma) at 70^0 C for 15 min.

The gas chromatograph was equipped with a capillary column HP-5MS (30x0.25mm) with 0.25 µm film thickness. The chromatographic conditions are described elsewere[26].

Accuracy was determined by recovery studies. Two replicates were performed using river water spiked with 500 ng/L for all compounds. The calculated amount was compared with the spiked concentration. The absolute recoveries vary between 55 % and 110 %. All standards show a linear range from 10 ng/l up to 1000 ng/l. The concentrations of analytes in relation to an external calibration were measured and results were compared to a non-enriched standard solution.

The reproducibility (precision) of the entire method was determined using two replicates of wastewater and surface water, spiked with different quantities of analytes (in the range 100-500 ng/l) prior to extraction. The overall precision of the method was indicated by the range of results of duplicates and was lower than 15%.

Quantification was performed using the corresponding labelled internal standards ($^{13}C_3$-Ibuprofen, $^{13}C_3$-Caffeine, D_3-Tonalide, $^{13}C_{12}$-Triclosan, D_{10}-Carbamazepine, D_5-Diazepam) added prior to enrichment (except galaxolide which was measured relative to the tonalide-D_{10} and pentoxyfylline measured relative to D_5-Diazepam).

RESULTS AND DISCUSSIONS

The studied compounds as well as of the internal standards are shown in Table 1. The identification of compounds and quantification were performed based on diagnostic ions. In Fig. 2 ion chromatograms of caffeine, tonalide and galaxolide as well as the labelled compounds used as internal standards are shown. Detection was performed in the full-scan mode. The loads calculated for every site, upstream and downstream for caffeine, carbamazepine, galaxolide and ibuprofen, triclosan are shown in the Fig. 3 and 4 respectively. The concentrations of compounds measured in different municipal WWTP effluents are shown in Table 2.

Neutral pharmaceuticals

Carbamazepine is widely used as antiepileptic and antidepressant drug. It has been widely detected in WWTP effluents, surface waters and groundwaters in Europe and North America.

Carbamazepine is fairly persistent and its removal in WWTPs is insignificant (< 10%) [3,8,10,13,14, 27-30]. Therefore, this compound is a good tracer for evaluating whether surface water is impacted by contamination from municipal WWTP effluents[31,32.].

The concentrations in grab samples of the effluents from the WWTPs in Cluj-Napoca, Gherla, Dej, Baia Mare and Satu Mare varied between 250 and 800 ng/L. The highest concentration was measured in the effluents of the WWTP in Cluj-Napoca reflecting the higher number of inhabitants in the catchments area of this WWTP.

In the Someş, the concentrations were relatively constant, varying between 20 and 50 ng/L over the whole river stretch. Therefore, the concentrations were comparable to other European rivers. However, the dilution of the wastewater should to be considered in order to compare different studies. The loads in the Someş varied between 80 g/day in Cluj-Napoca

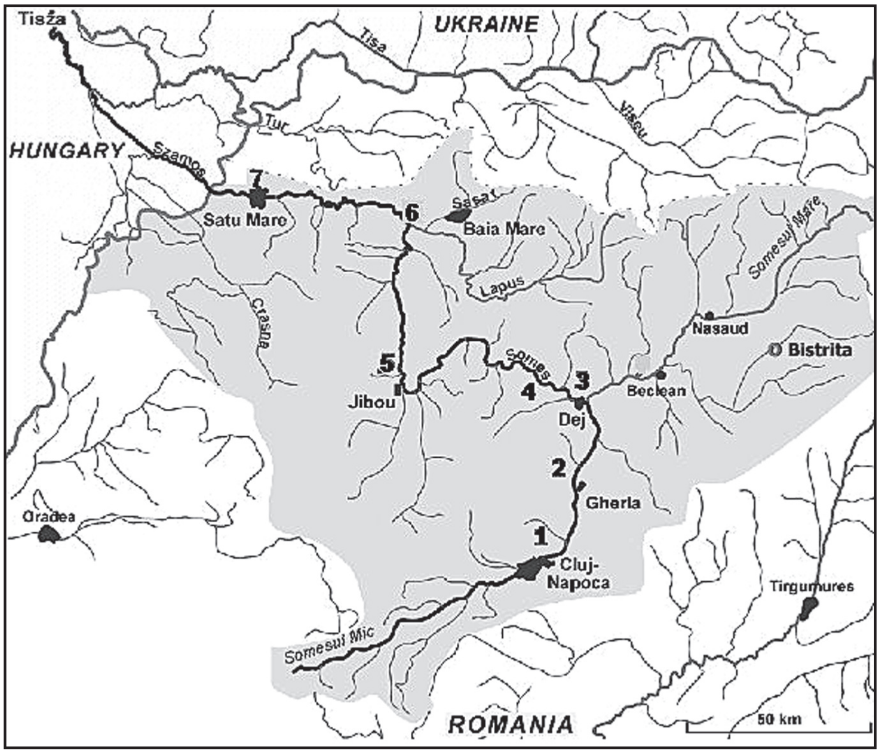

Fig. 1 Sample location on Someş River: 1) Cluj-Napoca, 2) Gherla, 3) Dej, 4) Rus, 5) Jibou, 6) Baia Mare and 7) Satu Mare

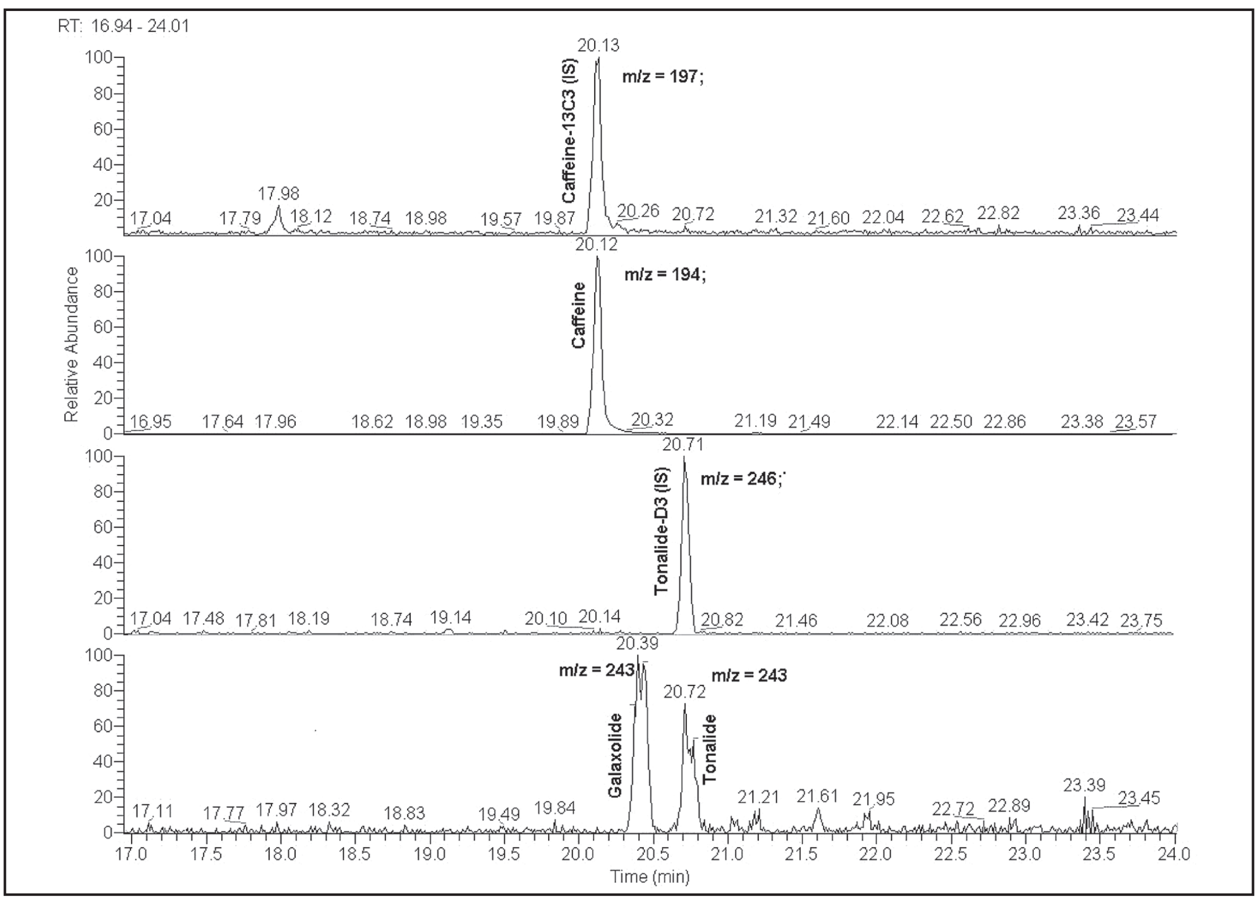

Fig. 2 Ion Chromatogram at m/z 197 (Caffeine 13C3, SI), 194 (Caffeine), 243 (Galaxolide, Tonalide) and 246 (Tonalide D3, SI) in the time range 17-24

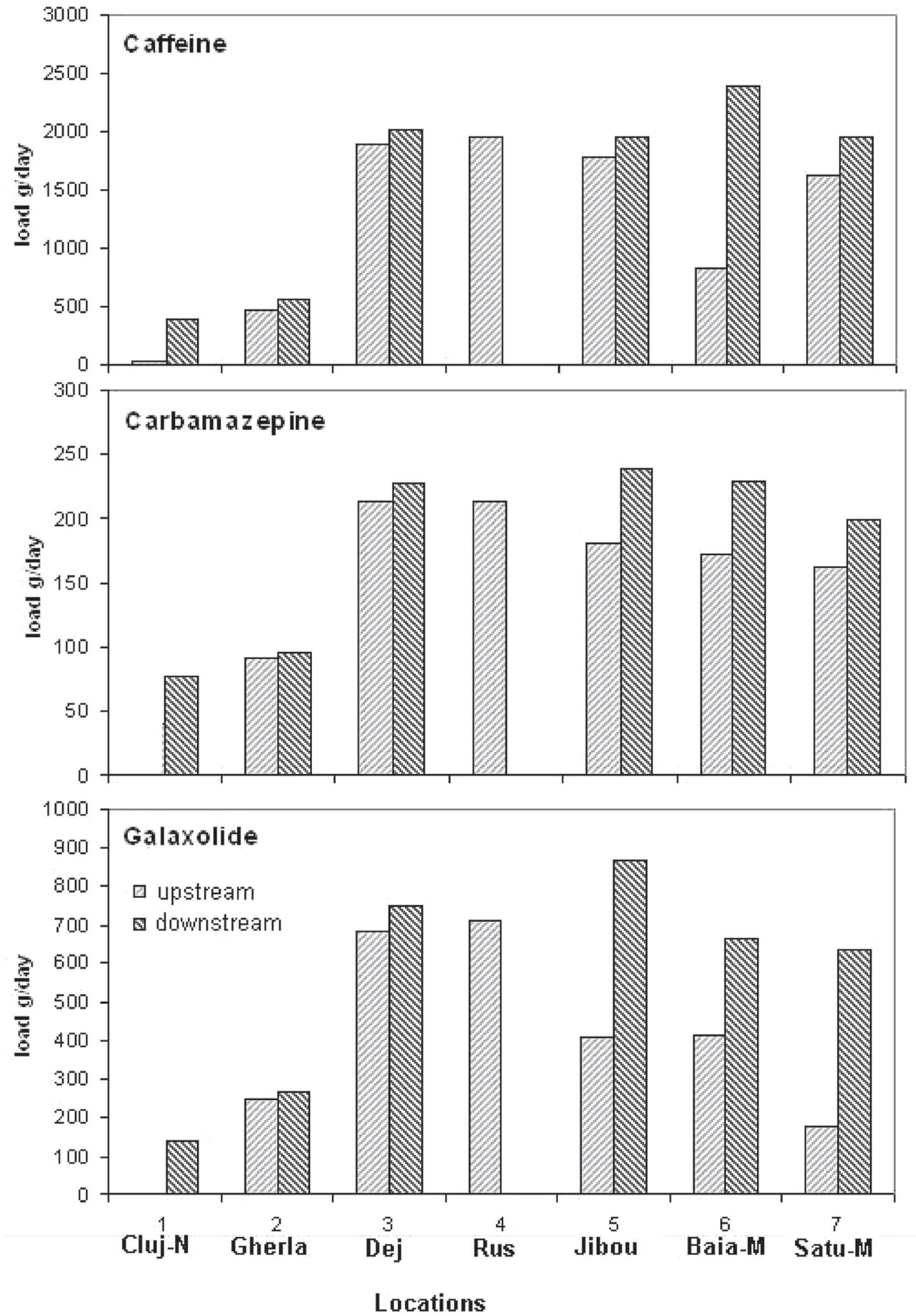

Fig. 3 Distribution of Caffeine, Carbamazepine and Galaxolide load (g/day) along of Someş River. The number 1-7 correspond to the sites from Fig. 1

Table 1 Name, CAS number, elemental, structure, molecular mass, and ion used for quantification of the studied compounds

Substance	CAS	Structure	quantification ion
Ibuprofen	15687-27-1	$C_{13}H_{18}O_2$, M=206	163
Caffeine	58-08-2	$C_8H_{10}N_4O_2$, M=194	194
Galaxolide (HHCB)	1222-05-5	$C_{18}H_{26}O$, M=258	243
Tonalide (AHTN)	1506-02-1	$C_{18}H_{26}O$, M=258	243
Triclosan	3380-34-5	$C_{12}H_7Cl_3O_2$, M=288	288
Carbamazepine	298-46-4	$C_{15}H_{12}N_2O$, M=236	193
Pentoxyfylline	6493-05-6	$C_{13}H_{18}N_4O_3$, M=278	221
Diazepam	439-14-5	$C_{16}H_{13}ClN_2O$, M=284	256

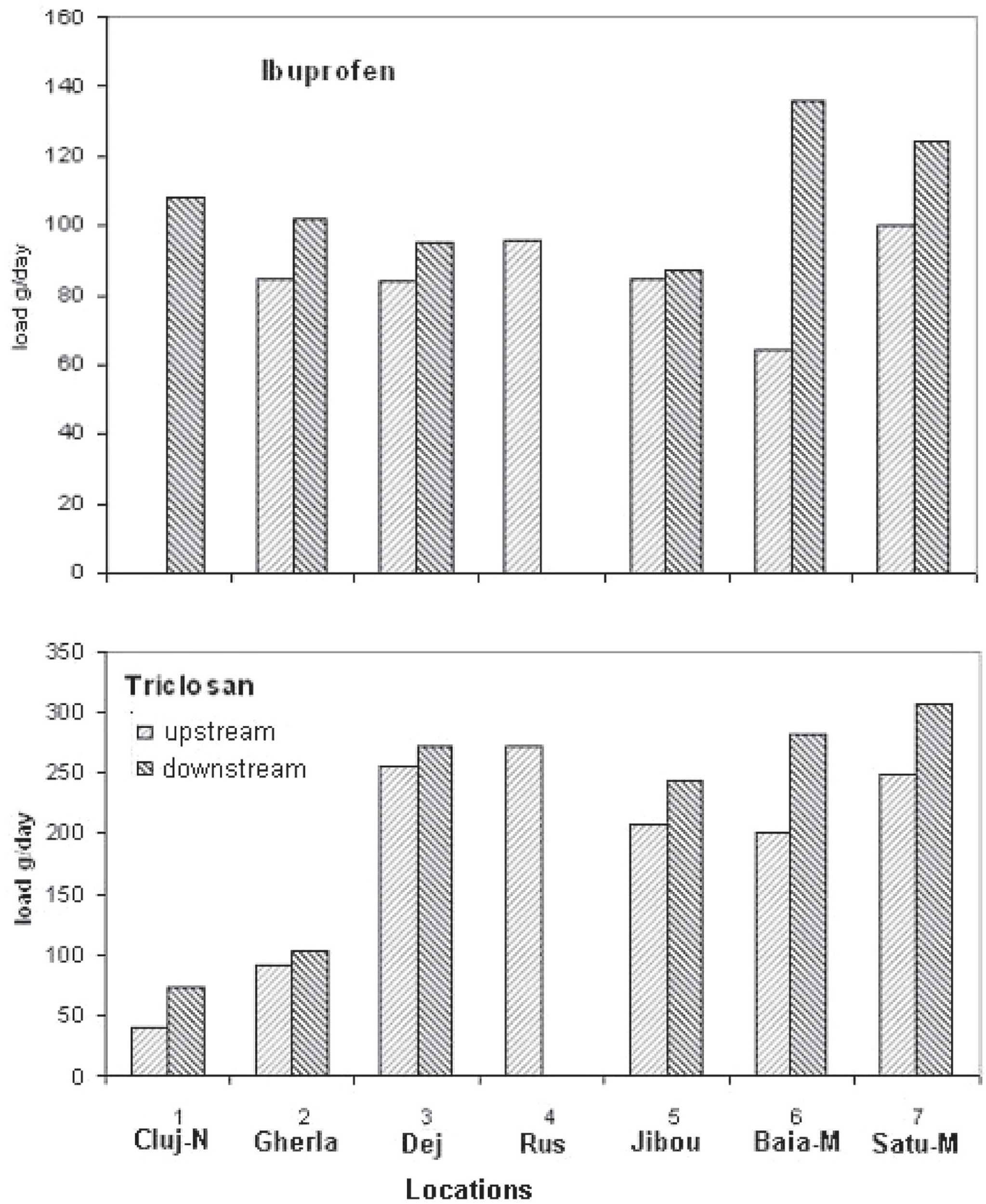

Fig. 4 Distribution of Ibuprofen and Triclosan load (g/day) along of Someş River

Table 2 Average concentration of compounds in effluent of WWTP from Cluj-Napoca (1). Gherla (2), Dej (3), Baia Mare (4) and Satu Mare (5).

Substance	Concentration (ng/l)				
	WWTP 1	WWTP 2	WWTP 3	WWTP 4	WWTP 5
Ibuprofen	14.1	302.8	340.4	209.98	416.0
Caffeine	27.1	23918.1	42560.1	23337.1	25506.8
Galaxolide	680.4	609.9	774.1	530.4	1597.2
Tonalide	71.3	135.6	38.4	60.4	281.5
Triclosan	209.5	284.2	352.9	299.5	758.1
Carbamazepine	728.7	367.8	774.1	192.8	641.3
Pentoxifylline	30.2	212.1	360.13	153.2	242.3
Diazepam	10.6	29.2	23.9	22.4	17.8

and increased to around 230 g/day after Someşul Mic and Someşul Mare merged.

The increase of the load at Dej is due to the input of the Someşul Mare river where wastewater effluents from important cities are being discharged (Bistriţa 75 000 inhabitants, Năsăud 25 000, Beclean 15 000).

Downstream of Dej, the load remained constant until Rus, decreased to about 180 g/day because of the dilution through the Almaş River and increased again to 230 g/day after the tributary Lăpuş with the wastewater effluents of Baia Mare flew into the Someşul. Assuming a total of 1 000 000 inhabitants in the Someş catchment area at Satu Mare, a discharge of 0.20 mg/person can be estimated.

Caffeine has been suggested as a potential chemical marker for domestic wastewater contamination because of its widespread usage in beverages, food and pharmaceuticals[33]. Despite the efficient removal in most WWTPs, caffeine is ubiquitously present in aquatic environment at concentrations up to 300 ng/L [1,2,26]. Poiger *et al*.[34] reported that the main source of caffeine in natural waters is untreated wastewater.

The concentrations of caffeine in the effluents from most WWTPs along the Someş River (Table 2) ranged between 24 000 and 42 000 ng/l, except in the effluent of the WWTP in Cluj-Napoca where it was around 30 ng/l. The low concentrations in the effluent refer to the efficient removal in this WWTP in contrast to the other WWTPs located at the Someş. Therefore, the concentrations in untreated or hardly treated wastewater were up to three orders of magnitude higher than in the treated effluent of the WWTP in Cluj-Napoca. The caffeine concentration along the Someş after Cluj-Napoca was relatively constant, varying between 230 and 330 ng/L and were thus comparable to other European Rivers.

The calculated loads of caffeine along Someş (Table 2) were below 600 g/day in the river stretch 1-3 (Someşul Mic) and increased up to 2 400 g/day after the confluence with Someşul Mare (location 3 at Dej).

The loads at Dej of the persistent carbamazepine increased 2–3 times. The loads of caffeine, that is well degraded in upgraded WWTPs, increased by a factor of 4 downstream the WWTP in Cluj-Napoca and this refers to discharges of untreated wastewater into the Someş River.

The distribution of load along of Someş River shows that: a) the loads of caffeine are proportional to the number of inhabitants living in the respective catchments; b) the caffeine is biodegraded *in situ* in the segment of slow flow conditions, between sites 5 and 6 along 50 km, and c) only the WWTP at site 1, in Cluj-Napoca, is working efficiently, the load of caffeine being small close to Cluj considering the high population (above of 350 000).

After site 3 (Dej), the caffeine load is high due to the discharge of only mechanically treated wastewater or due to poor biological treatment from localities situated at Someşul Mare as: Bistriţa (75 000 inhabitants), Năsăud (50 000), and Beclean (15 000). A high caffeine load was observed at site 6 (Baia Mare) due to the relatively high number of inhabitants (200 000) and this implies that the WWTP at Baia Mare is probable working inefficiently. The contribution of wastewater from Baia Mare to the caffeine load was 1 000 g/day. Considering that after consumption only 10% is excreted unmetabolised and knowing the concentration of caffeine in commercial products, an average consumption of 90 000 cups of coffee per day was estimated. This number corresponds to approximately half of the number of inhabitants and this consumption is consistent with the real situation in this region.

The concentration of *pentoxyphylline* in the effluent of the WWTP Cluj Napoca was low (< 30 ng/l) but in other effluents (see Table 2) in the concentration ranged between 150 and 360 ng/l. This behaviour leads to the conclusion that this compound is efficiently removed in upgraded WWTPs and therefore may be a marker for untreated wastewater. The low concentrations measured for pentoxyphylline along the Someş River surface water (<LOQ) is impacted. The main source of pentoxyphylline in the Someş Valley is probably the Hospital Units in Cluj-Napoca.

The concentrations of *diazepam* (psychiatric drug used as tranquilliser) was also always below the LOQ. Other authors reported also only trace concentrations of diazepam in rivers[13, 21, 26].

Acidic pharmaceuticals

Ibuprofen is a widely used antiphlogistic drug which is frequently found in wastewater effluents and surface waters[2,4,25] probably because of the high rates of usage of this compound to treat the symptoms of colds, aches and pains, or for the treatment of arthritic conditions. In the UK, ibuprofen was detected in receiving waters at concentrations of up to 5.0 µg·L^{-1}[11].

The concentrations of ibuprofen in the effluent of the WWTP in Cluj-Napoca was 14 ng/l but in the effluents of the other WWTPs the concentrations ranged between 150 and 350 ng/L. Ibuprofen is significantly (> 90%) transformed in upgraded WWTPs and the relatively high concentrations in the effluents downstream of Cluj-Napoca reflect the poor efficiency of those WWTPs.

The ibuprofen concentrations along the Someş varied between 10 and 60 ng/L. These concentrations are low compared to values of 200ng/L reported for USA in surface waters[35]. The loads along the Someş were relatively constant, ranging from 65 to 124 g/d as it can be seen in Fig. 4. The loads of ibuprofen decreased slightly (12-25%) in river stretches downstream of a WWTP and upstream of the next WWTP, *e.g.* in the river stretches (45-90 km) downstream Cluj-Napoca-upstream Gherla, downstream Rus- upstream Jibou, downstream Jibou-upstream Baia Mare, suggesting a relatively slow elimination in the Someş River.

Musk fragrances

Synthetic musks are often used in cosmetics, perfumes, shampoos, detergents, fabric softeners, household cleaning products and are therefore discharged quantitatively after their use into wastewater. There are indications that the polycyclic musks which are slowly biodegradable [36,37] are not only found in various environmental compartments, but also in the aquatic food chain as well as in fatty tissue and mothers' milk[38].

Polycyclic musks show a high affinity for particles and have been described to occur as ubiquitous contaminants[39,40]. The most widely used polycyclic musks are galaxolide (HHCB) and tonalide (AHTN). An elimination of at least 50% for galaxolide and tonalide in WWTPs is seen, mainly due to sorption onto sludge.[30,37,41,42]

Buerge *et al.* have shown that galaxolide and tonalide are two potential anthropogenic markers for domestic wastewater in surface waters[42].

The concentrations of galaxolide and tonalide in the effluents of the different WWTPs in the Someş catchment ranged between 500-700 and 40-130 ng/L, respectively (Table 2). Taking into account the number of inhabitants living in the catchment area of the WWTP in Cluj-Napoca (around 350 000) and comparing it to the other WWTP (with much smaller population living in the respective catchment area), it can be seen that similar concentrations of galaxolide were measured in the effluents. Because of the bad working conditions of these WWTPs (WWTP 2-7) the wastewater is only mechanically treated and the wastewater is discharged without or with only poor biological treatment to the receiving water.

The load of galaxolide measured in the river stretch between location 1 and 3 (Someşul Mic) was around 250g/day and went up to 700g/day at site 3 (Dej) after Someşul Mic and Someşul Mare merge into the Someşul. At locations 3 and 7, the difference of the loads between down- and up-stream of the cities is significant, leading to the conclusion that this compound is strongly removed, probably mainly due to sorption [47,53] (favoured by slow flowing conditions of the Someş). Tonalide was detected above the LOQ only shortly after the discharge of wastewater downstream of the WWTP at concentrations ranging between 20-34 ng/l. The low concentrations of tonalide are in agreement to its strong sorption[36].

Antimicrobial agents

Triclosan is a widely used biocide, used as a disinfectant in personal care products such as skin creams and hand soaps[43,44]. It is ubiquitously present in the aquatic environment[18]. It has been shown that triclosan is efficiently eliminated in WWTPs, with removal rates up to 99%[44] and significantly adsorption to sewage sludge[43]. During the summer season, direct phototransformation appears to be a major elimination pathway of triclosan in surface waters[45].

The concentrations in WWTP effluents varied between 200 and 350 ng/L and the loads in the Someş increased along the river. The lower concentrations detected at site 1 (Cluj-Napoca) again support the conclusion that the WWTP in Cluj-Napoca (site 1) was working more efficiently than the other WWTPs. At site 3, the load increased to 250 g/day by contribution of Someşul Mare River, which receives mainly poorly, treated wastewaters.

The transport in the Someş caused a decrease of triclosan in river stretches downstream of a WWTP and upstream of the next WWTP (*e.g.* stretches downstream Rus- upstream Jibou, downstream Jibou-upstream Baia Mare) probably mainly due to direct photo-transformation, although sorption to the sediment may also play a significant role.

CONCLUSIONS

1) This study has established an overview of the mass flows of five pharmaceuticals, two polycyclic musks and one disinfectant (triclosan) in the river Someş. The usage patterns, as well as the concentrations and loads, are comparable to those in other European countries and in North America.

2) The calculated loads showed at every site downstream site 3 (Dej), a significant increase of triclosan, carbamazepine, galaxolide and caffeine. This suggests that the WWTPs, at locations 3–7, are inefficient and the wastewater is discharged into the river without proper treatment.

3) The efficiency of wastewater treatment varied strongly, from very efficient WWTPs to very poor WWTPs. Therefore, it is crucial that several WWTPs in the Someş Valley watershed need to be improved in order to reduce the discharge of contaminants into the Someş River.

4) In this study, the loads along the Someş River can be classified in three groups:

- The loads of caffeine and galaxolide ranged between 200-2400 g/day and significantly different loads were calculated up- and down-stream of WWTPs
- The loads group of carbamazepine and triclosan were relatively constant along the river and the loads varied between 100-250 g/day.
- The loads of ibuprofen were below 100 g/day and very constant along the river.

5) Pharmaceuticals may be used as anthropogenic markers for domestic wastewater contamination of surface waters.

ACKNOWLEDGEMENTS

This work was financed by the Swiss National Science Foundation (SNSF), the Swiss Agency for Development and Cooperation (SDC) and the Romanian Ministry for Education and Research (MEC) within the framework of the Swiss-Romanian cooperation program on "Environmental Science and Technology in Romania - ESTROM". The reported study was performed in the project PHARMSOMES focusing on environmental exposure of pharmaceuticals in the Someş Valley Watershed in Romania.

REFERENCES

[1] S. D. Richardson and T. A. Ternes, *Anal Chem.,* 2005, **77**, 3807-3838.

[2] S. S. Verenitch, C. J. Lowe and A. Maznuder, *J. Chromatogr., A,* 2006, **1116**, 193-203.

[3] M. J. Gómez, Mira Petrović, A. R. Fernández-Alba and D. Barcelo, *J. Chromatogr., A,* 2006, **114**, 224-233.

[4] S. Castiglioni, R. Bagnati, D. Calamari, R. Fanelli and E. Zuccato, *J. Chromatogr., A,* 2005, **1092**, 206-215.

[5] K. Bester, *Chemosphere*, 2004, **57**, 863-870.

[6] P. K. Jjemba, *Ecotixicol. Environ. Saf.,* 2006, **63**, 113-130.

[7] R. Hirsh, T. A. Ternes, K. Haberer and K. L. Kratz, *Sci. Total Environ*, 1999, **225**, 109-118.

[8] C. G. Daughton, and T. A. Ternes, *Environ. Health Perspect.,* 1999, **107**, 907-938.

[9] D. R. Dietrich, S. F. Webb and T. Petry, *Toxicol. Lett*., 2002, **131**, 1-3

[10] B. Ferrari, N. Paxeux, R. L. Giudice, A. Pollio and J. Garric, *Ecotoxicol. Environ. Saf.,* 2003, **55**, 359-370.

[11] D. Ashton, M. Hilton and K. V. Thomas, *Sci. Total Environ.,* 2004, **333**, 167-184.

[12] B. Halling-Sorensen, S. N. Nielsen, P. F. Lanzky, F. Ingerslev, H. C. H Lutzhoft. and S. E. Jorgensen, *Chemosphere,* 1998, **36**, 357-394

[13] T. A. Ternes, *Water Res.* 1998, **32**, 3245-3260.

[14] T. Heberer, *Toxicol. Lett*., 2002, **131**, 5-17.

[15] D. V. Kolpin, E. T. Furlong, M. T. Meyer, S. D. Zaugg, L. B. Baber and H. T. Buxton, *Environ. Sci. Technol.,* 2002, **36**, 1202-1211.

[16] Alder A.C., Bruchet A., Carballa M., Clara M., Joss A., Löffler D., McArdell C.S., Miksch K., Omil F., Tuhkanen T., Ternes T.A., 2006. "Consumption and Occurrence" in Human Pharmaceuticals, Hormones and Fragrances: The challenge of micropollutants in urban water management. Edited by TA Ternes and A Joss. IWA Publishing, London, UK, ISBN: 1843390930 , pp15-54

[17] E. M. Golet, A. C. Alder and W. Giger,. *Environ. Sci. Technol.,* 2002, **36**, 3645-3651.

[18] G. R. Boyd, J. M. Palmery, Z. Zhang and D. A. Grimm, *Sci. Total Environ.,* **333**, 137-148.

[19] T. Scheytt, P. Mersmann, R. Lindstäd and T. Heberer, *Chemosphere*, 2005, **60**, 245-253.

[20] H. R. Buser, T. Poiger and M. D. Müller, *Environ. Sci. Technol.,* 1999, **33**, 2529-2535.

[21] T. A. Ternes, *Trends. Anal. Chem.,* 2001, **20**, 419-434.

[22] S. M. R. Wille, K. E. Maudens, C. H. Van Peteghem and W. E. E. Lambert, *J. Chromatogr., A,* 2005, **1098**, 19-29.

[23] M. Llompart, C. G. Jares, C. Salgado, M. Polo and R. Cela, *J. Chromatogr., A,* 2003, **999**, 185-193.

[24] P. Canosa, I. Rodriguez, E. Rubi and R. Cela, *J. Chromatogr., A,* 2005, **1072**, 107-115.

[25] H. B. Lee, T. E. Peart and M. L. Svoboda, *J. Chromatogr., A*, 2005, **1094**, 122-129.

[26] Z. Moldovan, *Chemosphere*, 2006, **64**, 1808-1817.

[27] S. Weigel, R. Kallenborn, and H. Huhnerfuss, *J. Chromatogr., A*, 2004, **1023**, 183-195

[28] L. Lissmore, C. Hao, P. Yang, P. K. Sibley, S. Mabury and K. R. Solomon, *Chemosphere*, 2006, **64**, 717-729.

[29] O. A. H. Jones, N. Voulvoulis and J. N. Lester, *Water Res,*. 2002, **36**, 5013-5022.

[30] A. Joss, E. Keller, A. C. Alder, A. Göbel, Christa S. McArdell, T. Ternes and H. Siegrist, *Water Research,* 2005, **39**, 3139-3152.

[31] M. Clara, B. Strenn, and N. Kreuzinger, *Water Res.* 2004, **38**, 947-954.

[32] T. Heberer, A. Mechlinski, B. Fanck, A. Knappe, G. Massmann, A. Pekdeger and B. Fritz, *Ground Water Monit. Remediat. 2004,* **24**, 70-77.

[33] I. J. Buerge, T. Poiger, M. D. Müller and H. R. Buser, Environ. Sci. Techn. 2003, **37**, 691-700

[34] T. Poiger, H. R. Buser, M. D. Müller, M. E. Balmer and I. J. Buerge, *Chimia*, 2003, **9**, 492-498.

[35] J. D. Cahill, E. T. Furlong, M. R. Burkhardt, D. Kolpin and L. G. Anderson, *J. Chromatogr. A,* **2004**, 1041, 171-180

[36] E. A. Goricano, J. L. M. Hermens and W. H. J. Vaes, *Water Res.*, 2003, **37**, 4377-4384.

[37] M. Caballa, F. Omil and J. M. Lema, *Water Res.*, 2005, **39**, 4790-4796.

[38] H. Fromme, T. Otto and K. Pilz**,** *Water Res. 2001,* **35***,* 359-370.

[39] D. Herren and J. D. Berset, *Chemosphere*, 2000, **40**, 565-574

[40] D. Herren and J. D. Berset, *Chemosphere*, 2000, **40**, 565-574.

[41] J D. Berset and T. Kupper, *Chemosphere*, 2004, **57**, 985-996.

[42] M. Ricking, J. Schwarzbauer and S. Franke, *Water Res.,* 2003, **37**, 2607-2617.

[43] H. Singer, S. Müller, C. Tixier and L. Pillonel, *Environ. Sci. Technol.,* 2002, **36**, 4998-5004.

[44] P. M. Thomas and G. D. Foster, *Environ. Toxicol. Chem.,* 2005, **24**, 25-30.

[45] C. Tixier, H. P. Singer, S. Canonica and S. R. Müller, *Environ. Sci. Technol.,* 2002, **36**, 3482-3489.