SPE-LC-MS/MS DETECTION OF PHARMACEUTICAL COMPOUNDS (GASTRIC ANTACIDES) IN WASTEWATER

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INTRODUCTION

There is rising proof that various pharmaceutic chemicals are persistent organic pollutants in natural freshwater ecosystems. These pharmaceuticals are appreciated as a fraction of emerging contaminants (ECs), which gain easy access to aquatic systems from varied starting points, such as human excretion through sewage systems, drain water, improper dumping, leeching from garbage dumps, or industries. Two of the most extensively used classes of pharmaceutical compounds world are proton pump inhibitors (PPIs) and histamine H2 receptor antagonists (HRAs). The aim of this study was to investigate the occurrence of some antacid compounds (Famotidine FAM, Cimetidine CIM, Ranitidine RAN, Nizatidine NIZ, Omeprazole OME, Rabeprazole RAB, Pantoprazole PAN, Lansoprazole LAN and the metabolites 5-OH-OME, 4-OH-OME), in two urban wastewater treatment plants (WWTP's) of Galati (GL) and Ramnicu-Valcea (RV),

MATERIALS AND METHODS

Analytical determinations were obtained with a 1260-6410B LC-MS/MS system from Agilent Technologies (Waldbronn, Germany). The electrospray ionization (ESI) source was used in positive mode. For the separation of analytes, a mobile phase gradient was used. The composition of the mobile phase was 10 mM ammonium acetate (A) and acetonitrile (B).

Optimized LC parameters were as follows:

- Chromatographic column: Luna Omega Polar C18 (2.1 x 150 mm, 3. µm);
- Column temperature: 40°C
- Injection volume: 5 µl
- Mobile phase: 10 mM ammonium acetate/ Acetonitrile
- Flow rate: 0.2 ml/min
- Elution: gradient (Table 1)
- Run-time : 13,5 min

Table 1. Gradient elution program of the mobile phase

Time (min)	10 mM ammonium acetate (A, %)	Acetonitrile (B, %)	Flow rate (mL/min)
0	70	30	0.2
1,5	20	80	0.2
3	5	95	0.2
8,5	5	95	0.2
Chromatographic column equilibration, 5 min			

Optimized triple qvadrupol mass spectrometer parameters:

- Ionization mode: Electrospray negativ ESI(+)
- Drying gas temperature: 300°C
- Drying gas flow: 10 L/min
- Nebulizer pressure: 40 psi
- Capillary voltage: 4000V
- MS tranzition: Multiple reaction monitoring/ MRM (Figure 1)

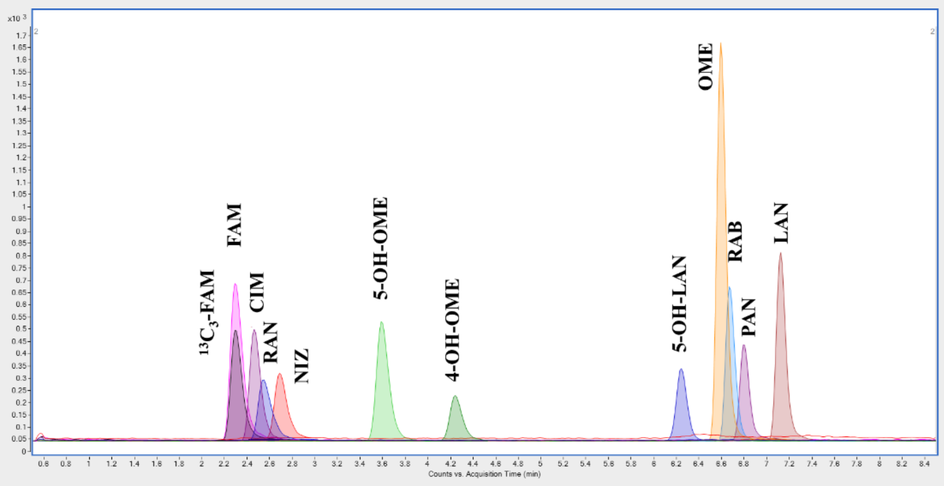

Figure 1. MRM chromatogram for the studied compounds (50 ng/mL)

RESULTS

Concentrations of pharmaceutical residues detected during sampling in influents and effluents ranged from 2.12 to 88.8 ng/L in GL influent and from 1.72 to 51.2 in GL effluent, from 5.95 to 374 ng/L in RV influent and from 3.92 to 52.8 ng/L in RV effluent (Table 2). Except for CIM, RAB, and 5-OH-OME, for which the concentration values were lower than limit of quantification (LOQCIM 0.59 ng/L; LOQRAB 0.21 ng/L; LOQ5-OH-OME 0.27 ng/L), all other compounds have been quantified in both influent and effluent samples. In most cases, pharmaceutical residue levels were higher in WWTP-RV than in WWTP-GL.

Table 2. Pharmaceutical residue concentration values determined in WWTPs (ng/L)

Compounds, ng/L	IF-GL	EF-GL	IF-RV	EF-RV
FAM	63.6 ± 3.3	10.1 ± 0.53	190 ± 9.9	47.2 ± 2.45
RAN	17.6 ± 1.0	13.2 ± 0.81	374 ± 22.1	30.7 ± 1.82
NIZ	11.8 ± 0.81	10.0 ± 0.62	55.2 ± 3.2	27.6 ± 1.57
4-OH-OME	88.8 ± 5.2	51.2 ± 2.9	128 ±10.4	52.8 ± 3.06
5-OH-LAN	2.68 ± 0.15	2.64 ± 0.11	6.80 ±0.35	3.92 ± 0.21
OME	51.6 ± 2.9	7.96 ± 0.47	25.6 ±1.49	20.6 ± 1.18
PAN	64.8 ± 4.1	16.8± 1.04	102 ± 6.32	29.2 ± 1.83
LAN	2.12 ± 0.15	1.72 ± 0.12	5.96 ± 0.43	5.72 ± 0.42

The target pharmaceutical residue and metabolites in the influents were dominated by 4-OH-OME for IF-GL, with a percentage of 29% (Figure 2). At the same time, RAN was the majority compound for IF-RV, with a percentage of 42% (Figures 2a and 2b). For WWTP-GL, PAN, and OME were determined in percentages up to 21% and respectively 17%, while for WWTP-RV, in influent samples, 4-OH-OME and PAN were also observed in higher percentages, 15% and 11%, respectively. For both WWTPs, 4-OH-OME was the dominant compound in the effluent samples, with percentage values up to 45% for WWTP-GL (Figure 2c) and up to 24% for WWTP-RV (Figure 2d).

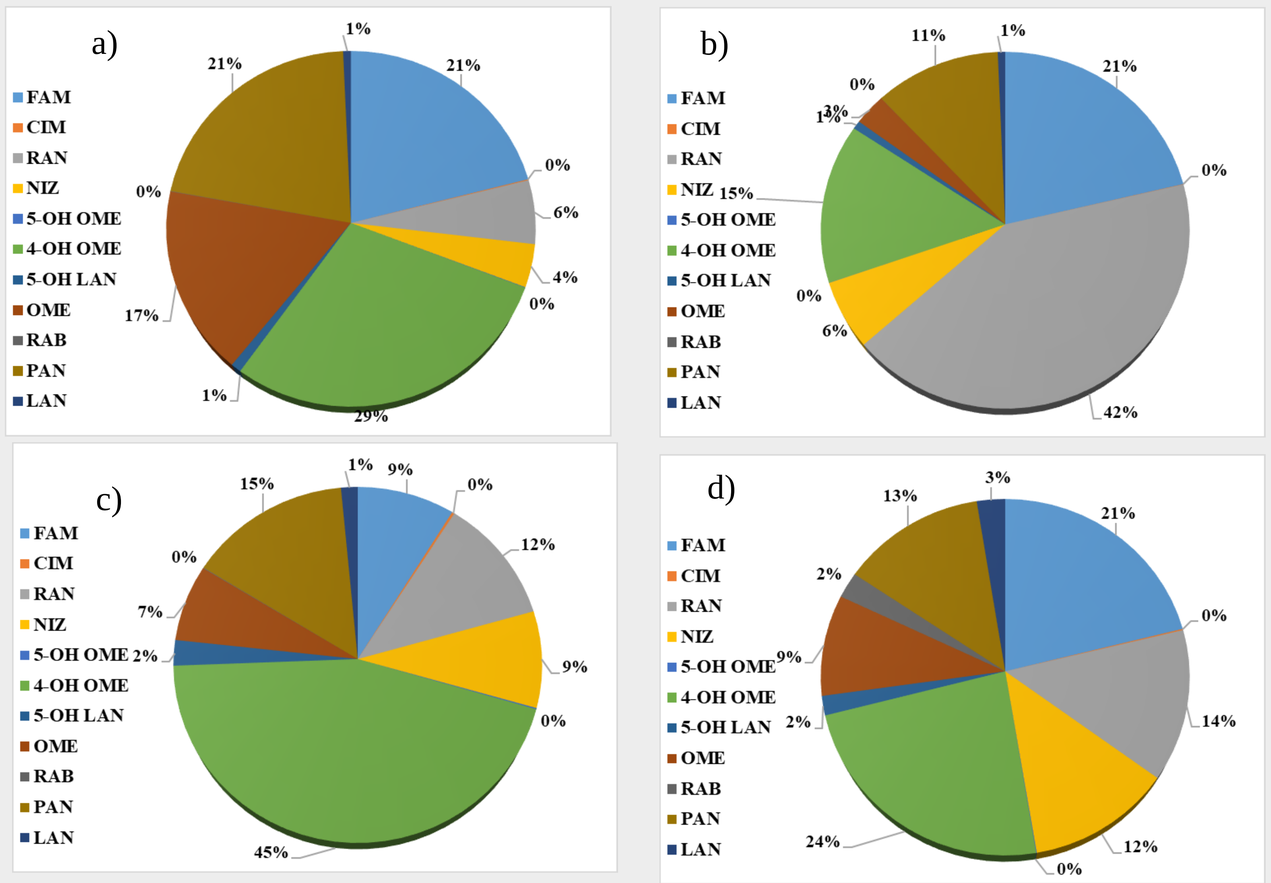

Fig. 2. Percentage distribution of the target analytes in (a) IF-GL, (b) IF-RV, (c) EF-GL and (d) EF-RV WWTPs

According to our data, the WWTP-RV presented better removal efficiency than WWTP-GL. For WWTP-GL, only 40% of the compounds RE > 50% values were recorded, while for WWTP-RV, 65% of the pharmaceutical compounds were removed in a percentage higher than 50% (Figure 3). Only the third part of the compounds tested presented RE higher than 70%. Thus, in WWTP-GL, the RE values determined for FAM, OME, and PAN were up to 84%, 85%, and 74%, respectively, while in WWTP-RV, for FAM, RAN, and PAN, the RE values were up to 75%, 92% and 71%, respectively.

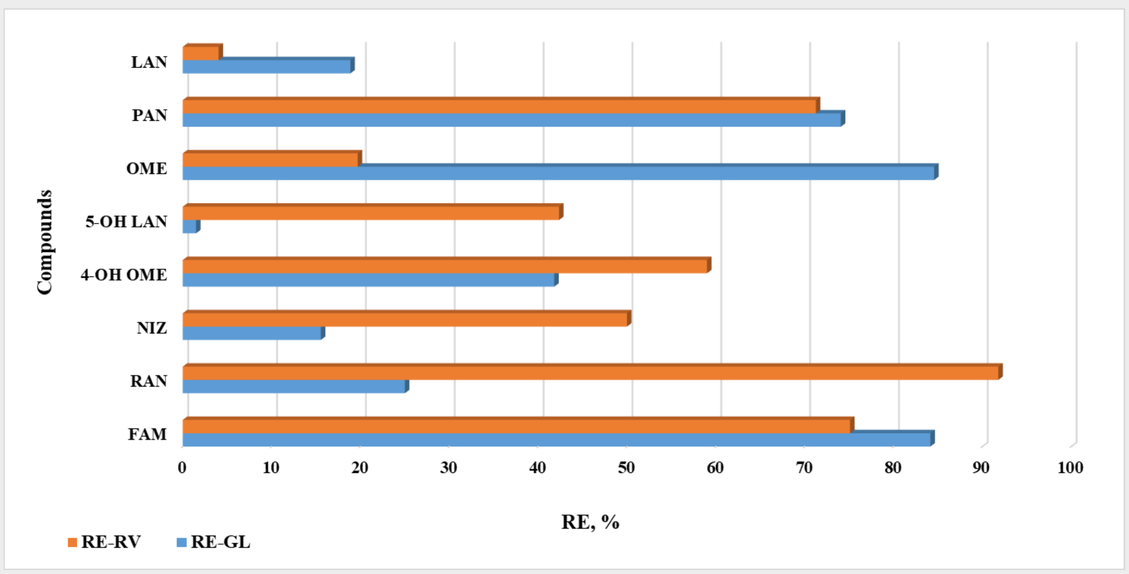

Fig. 3. Estimated removal efficiency of target pharmaceutical residue in both WWTPs

CONCLUSIONS

Pharmaceutical compounds were detected in all influent and effluent samples showing that contamination with antacid substances is real and can cause toxicity problems for aquatic organisms, through the effluent discharged into the receiving surface water.

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