

DOI: <http://doi.org/10.21698/simi.2023.ab33>

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

Vasile-Ion Iancu, Florinela Pirvu, Iuliana Paun, Marcela Antoneta Niculescu,
Gabriel Valentin Serban, Ionut Cristea, Florentina Laura Chiriac

National Research and Development Institute for Industrial Ecology – ECOIND Bucharest,
57-73 Drumul Podu Dambovitei Street, 060652, Bucharest, vasileiancu10@gmail.com,
Romania

Keywords: *pharmaceuticals residues, gastric antacids, contaminants, wastewater, SPE-LC-MS/MS*

Introduction

The increasing use of gastric antacids in the treatment of digestive tract disorders and their incomplete metabolism in the human body, in addition to the incomplete degradation of these molecules in sewage treatment plants, has led to the discharge of high concentrations of these substances into the aquatic environment. Thus, new studies regarding the presence, behavior and toxicity of these emerging contaminants in the environment are necessary. After consumption, proton inhibitor compounds (PPIs) are partially metabolized in the body, so that a part of the compound is eliminated in sewage treatment plants. The aim of this study was to investigate the occurrence of some antacid compounds (Omeprazole-OME, Rabeprazole-RAB, Pantoprazole-PAN, Lansoprazole-LAN, Famotidine-FAM, Cimetidine-CIM, Ranitidine -RAN, Nizatidine-NIZ), and their metabolites (5-hydroxy omeprazole: 5-OH-OME, 4-hydroxy omeprazole: 4-OH-OME, 5-hydroxy lansoprazole: 5-OH-LAN) 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 Liquid Chromatograph coupled with Mass Spectrometer (LC-MS/MS) system from Agilent Technologies (Waldbronn, Germany). The electrospray ionization (ESI) source was operated in positive mode. The injection volume was 5 μ L. Chromatographic separation of the compounds was done using a Luna Omega Polar C18 column (150 x 2.1 mm, 3 μ m) kept at 40°C. 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). The gradient program was as follows: 0÷1.5 min 70-20% A with 0.2 mL/min flow rate, 1.5÷3 min 20-5% A with 0.2 mL/min flow rate, 3÷8.5 min 5% A isocratic. Mass spectrometer working conditions were 300°C gas temperature, 4 V cell acceleration voltage, 10 mL/min nitrogen nebulizer gas flow rate, 4000 V capillary voltage, 40 psi nebulizer pressure. A 280 Auto Trace (Dionex- Thermo Scientific) automated solid phase extractor (SPE) was used to facilitate the sample preparation procedure and the extraction of antacid compounds from the wastewater samples. Before extraction, the pH of the samples was adjusted to 10 by adding a 2.0% ammonia solution. After adjusting the pH, the samples (500 mL surface water and

250 mL effluent/influent) were controlled contaminated with 1 mL of 50 µg/L internal standard (Famotidine-13C3). The analytes were extracted with Strata-C18 cartridges (500mg/6 mL, Phenomenex) using conditioning with methanol and ultrapure water pH 10. Twenty-four-hour flow proportional composite samples of influent (100 mL) and effluent (250 mL) samples were collected, during three consecutive days, from two urban Wastewater Treatment Plants (WWTPs) that serve the Ramnicu-Valcea (RV) and Galati (GL) municipalities.

Results and conclusions

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 1). Except for CIM, RAB, and 5-OH-OME, for which the concentration values were lower than limit of quantification (LOQ_{CIM} 0.59 ng/L; LOQ_{RAB} 0.21 ng/L; LOQ_{5-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. The target pharmaceutical residue and metabolites in the influents were dominated by 4-OH-OME for IF-GL, with a percentage of 29%. At the same time, RAN was the majority compound for IF-RV, with a percentage of 42%. 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 and up to 24% for WWTP-RV.

Table 1. Pharmaceutical residue concentration values determined in WWTPs (ng/L)

Compounds	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

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.

Acknowledgments. This work was carried out through the “Nucleu” Program within the National Research Development and Innovation Plan 2022-2027 with the support of Romanian Ministry of Research, Innovation and Digitalization, contract no. 3N/2022, Project code PN 23 22 01 01.