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## ANALYTICAL DETECTION OF THE ANTIDIABETIC PHARMACEUTICALS IN WASTEWATER TREATMENT PLANTS

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### **Introduction**

Metformin (MET) is today the most prescribed drug in the world for the treatment of type two diabetes, but also it is used as an anti-cancer agent and as a treatment for polycystic ovary syndrome. Due to its high consumption, low octanol-water partition coefficient ( $K_{ow}$  -2.6), and high aqueous mobility, MET is expected to be present in surface waters once released in the environment through the wastewater effluent discharge. This study was conducted to evaluate the presence and behaviour of antidiabetic compounds in urban wastewater treatment plants.

### **Materials and methods**

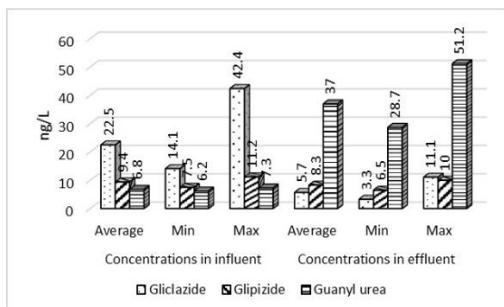
Influent and effluent samples were collected from the Iasi, Galati, Targoviste and Campulung-Muscel treatment plants. The method of analysis was based on solid phase extraction of contaminants from wastewater samples using SPE Strata X cartridges (500mg/6mL, Phenomenex) containing polymeric styrene divinylbenzene adsorbent. The analytes were chromatographically separated and quantified with a UHPLC-MS/MS (Agilent Technologies) 1260/6410B system on an Eclipse C18 column (100 x 2 mm, 3.4  $\mu$ m). The mobile phase used was a mixture of 0.1% formic acid and acetonitrile with elution in gradient: 0-6 min 50% HCOOH, 6-9.5 min 50-40% HCOOH, with a flow rate of 0.2 mL/min and injection volume 10  $\mu$ L at 30C. The compounds were determined based on MRM (Multiple reaction monitoring) transitions between the protonated precursor ion  $[MH]^+$  and the first 2 most abundant product ions.

The selective extraction of the compounds was based on a concentration of water samples of 250 and the use of Strata X cartridges (500mg/6mL, Phenomenex). The 250 mL volume sample was filtered onto the 0.45  $\mu$ m glass membrane and then brought to pH 10 with 0.2%  $NH_4OH$ . The adsorbent was conditioned with methanol and pure water, after which the prepared sample was eluted by cartridge followed by a washing of the matrix with pure water. Then the analytes were eluted with methanol and the extract was evaporated and resumed with 1 ml mobile phase (50/50, 0.1% HCOOH / acetonitrile).

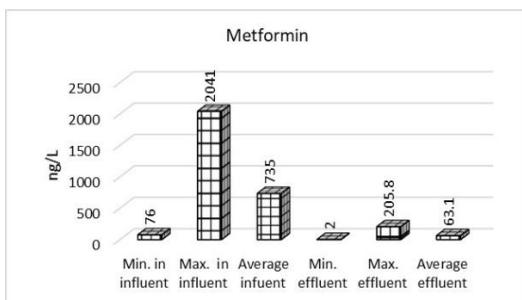
### **Results and conclusions**

During the monitoring period, it was observed that the *influent samples* were contaminated with the following antidiabetics, in decreasing order of concentration values, metformin ( $76 \div 2,041$  ng/L, average 735 ng/L), gliclazide ( $22.5 \div 14.1$  ng/L, average of 42.4 ng/L), glipizide ( $9.4 \div 7.5$  ng/L, average 11.2 ng/L), guanlyl urea ( $6.8 \div 6.2$  ng/L, average 6.8 ng/L), according to figures 1 and 2. The effluents samples

were polluted with next antidiabetics: metformin ( $2 \div 206$  ng/L, mean 63.1 ng/L), guanyl urea ( $8.3 \div 21.3$  ng/L, mean 22.7 ng/L), gliclazide ( $3.3 \div 19.1$  ng/L, mean 9.6 ng/L), glipizide ( $6.5 \div 10.0$  ng/L, average 8.3 ng/L).



**Figure 1.** Antidiabetics' concentrations (minimum, maximum, average) in influent and effluent samples of WWTP's



**Figure 2.** Metformin concentrations in influent and effluent samples of WWTP's

The occurrence of hypoglycaemic agents in the influent and the effluent is probably due to the large amounts of prescribed and consumed antidiabetic drugs but also due to their incomplete metabolism. The data regarding the presence of metformin suggest the consumption model, the elimination efficiencies of the studied stations but not the number of populations served by each treatment plant. Metformin and gliclazide were ubiquitous being determined in all influent and effluent samples at the highest concentration levels (MET 2041 ng/L in influent and 206 ng/L in effluent). The elimination efficiencies of antidiabetic compounds detected in influent are high for metformin ( $67.6\% \div 98.5\%$ ), gliclazide ( $72.9 \div 76.6\%$ ), and low for glipizide ( $10.7 \div 13.3\%$ ).

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