

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

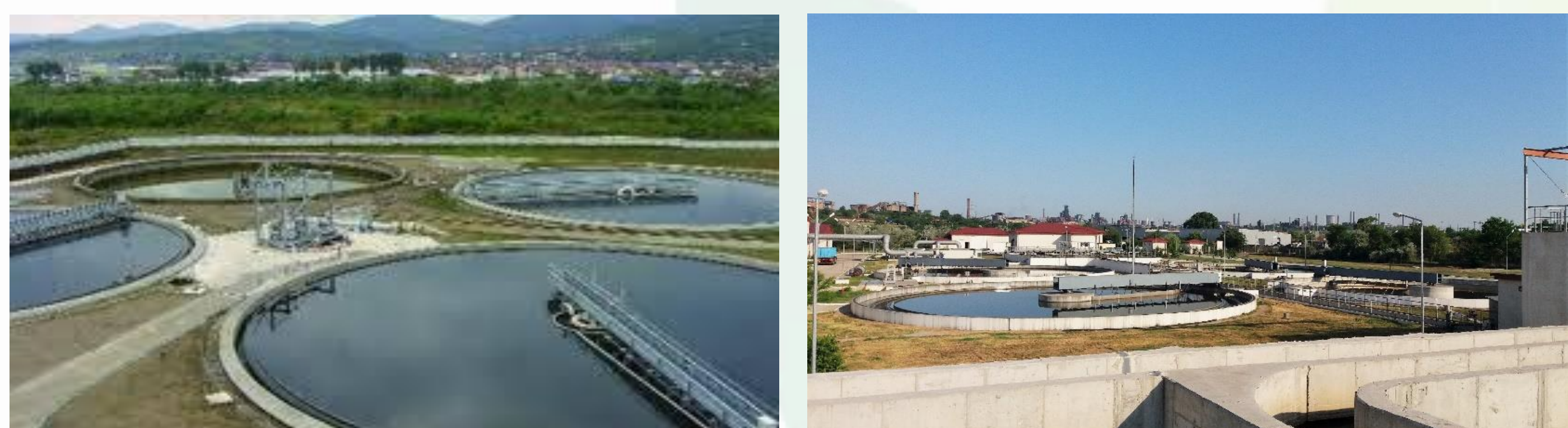
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### INTRODUCTION

Metformin is today the most prescribed drug in the world for the treatment of type 2 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), 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



Galati WWTP

Iasi WWTP

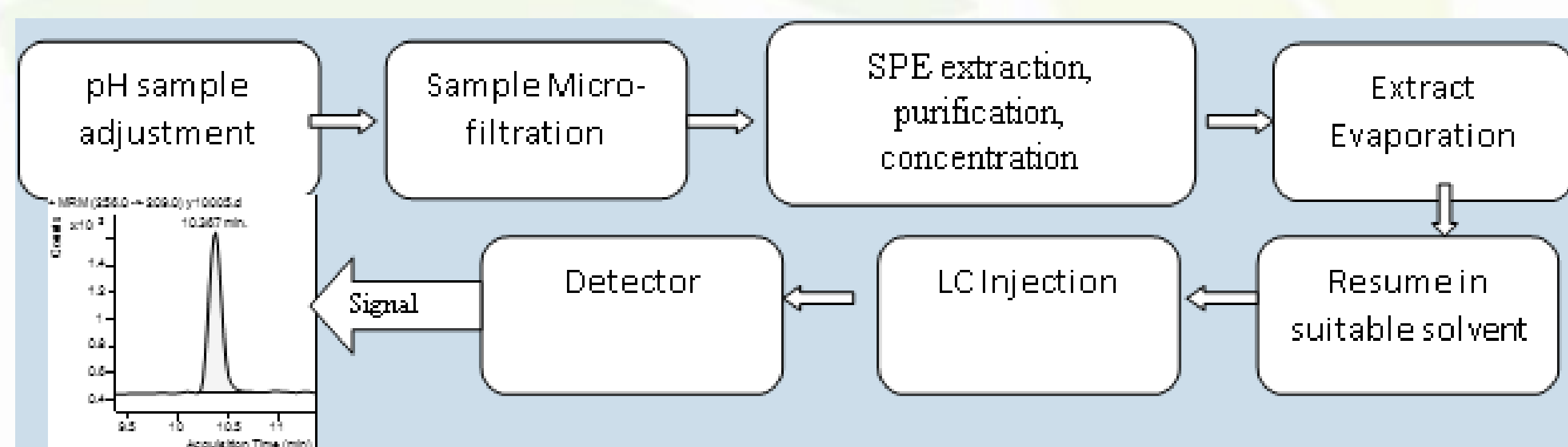
Influent and effluent samples were collected from the Iasi, Galati, Targoviste and Campulung-Muscel treatment plants.

### QQQ WORKING PARAMETERS FOR THE 6 ANTIDIABETICS

Compound	Time Segments (min)	MRM transitions (m/z)	Fragmentor voltage (V)	Collision energy (eV)	Dwell time (ms)
Metformin	0-4	130→71	80	25	40
		130→60	80	10	40
Guanil urea	0-4	103→60	80	15	40
		103→43	80	10	40
Glipizide	4-6	446→321	80	10	40
		446→167	80	20	40
Gliclazide	4-6	324→127	120	15	70
		324→110	120	20	70
Gliburide	6-9.5	494→369	100	15	40
		494→169	100	20	40
Glimperide	6-9.5	491→352	100	20	40
		491→126	100	10	40

### RESULTS AND DISCUSSION

#### The diagram of sample preparation



#### LC separation parameters and MS detection for anti-diabetics

Optimal separation parameters by liquid chromatography (LC Liquid chromatograph AGILENT 1260):  
Parameters of the quadrupole triple mass spectrometer (QQQ MS Triple quadrupole mass spectrometer Model 6410 Agilent) detector:

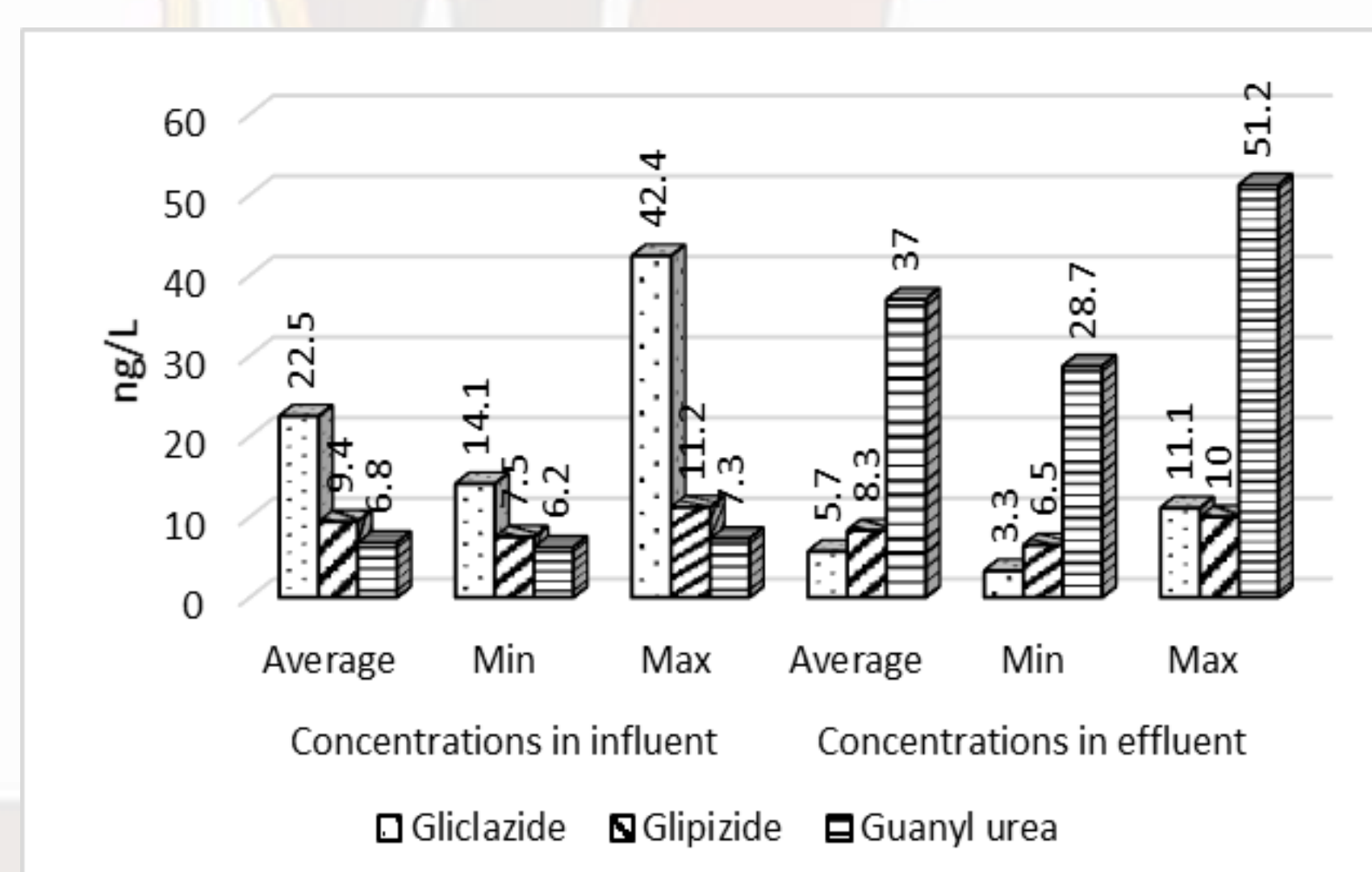
Column: Eclipse C18 100 mm x 2. mm and dp 3.4 μm	Ionization mode: ESI +
Column temperature: 30 °C	Gas temperature: 300 °C
Injected volume: 10 μl	Drying gas flow rate: 10 L/min
Mobile phase: 0.1 % formic acid/CAN 0-6 min 50% HCOOH, 6-9.5 min 50-40% HCOOH,	Gas pressure in Nebulizer: 50 psi
Mobile phase flow rate: 0.2 mL/min	Voltage applied to the capillary: 3000 V
Solvent samples: 0.1% formic/ACN: 50/50 (V/V)	Fragmentation voltage: 140-160 V
Sample run time 9 min	Collision energy: 20-45 V
	Cell acceleration voltage: 4 V

#### PERFORMANCE PARAMETERS DETERMINED FOR ANTIDIABETICS IN WASTE WATER SAMPLES

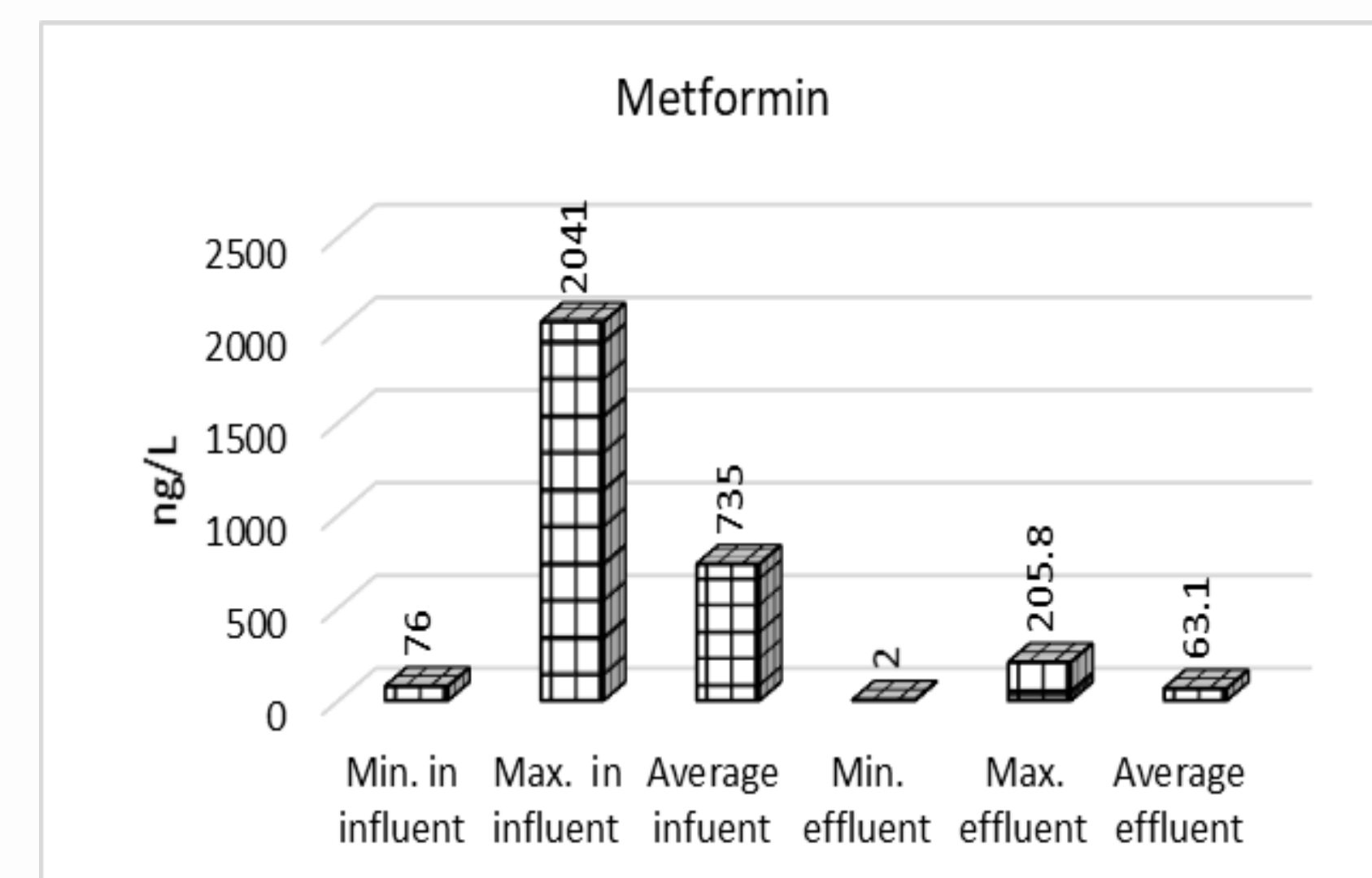
Compound	R2	Calibration range (ng/mL)	Regression equations	LOQ (ng/L)	Recovery rate (%)	Precision	
						Intra-day (% RSD <sub>r</sub> )	Inter-day (% RSD <sub>r</sub> )
Metformin	0.9904	1-100	5852x	0.4	64.4	8.4	13.6
Guanyl urea	0.9982	5-100	680x-1055	4.5	53.6	7.6	14.5
Glipizide	0.9974	1-100	1434x-1540	0.3	100.8	4.9	13.2
Gliclazide	0.9969	1-100	4338x-3203	0.2	104.4	7.9	12.4
Gliburide	0.9977	1-100	3321x-5534	0.4	116.8	6.5	11.3
Glimperide	0.9982	1-100	928x-2978	0.3	96.42	7.3	14.6

#### Elution gradient used to separate anti-diabetics from calibration solutions and water samples

Time (min)	0.1% Formic Acid (%)	Acetonitrile (%)	Flow rate (mL/min)
0	50	50	0.2
6	50	50	0.2
9.5	40	60	0.2
9.51	50	50	0.4
13.5	50	50	0.4
13.51	50	50	0.2



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



Metformin concentrations in influent and effluent samples of WWTP's

### CONCLUSION

The occurrence of hypoglycemic 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).

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