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DETERMINATION OF GLYBURID, GLIMEPIRID AND REPAGLINID IN WASTEWATER SAMPLES

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Introduction

To high grade antidiabetics consumption worldwide and to increasing number of prescriptions, these contaminants are founded in waste waters, rivers and ground waters. Effluents discharged from WWTP contaminates the rivers and thus, it is necessary to investigate the occurrence of antidiabetic compounds in waste waters. The aim of this work was to detect 3 antidiabetic (glyburide, glimepiride and repaglinide) contaminants in waste water treatment plant using SPE-LC/MS/MS method.

Materials and methods

Isolation of antidiabetics drugs from waste water was performed by solid phase extraction using Dionex Autotrace 280 automated solid phase extraction Strata C18 (500 mg, 6 mL). The pH of 250mL of effluent/influent was adjusted to 8.5 with NH₄OH 2% and the sample was filtered through 0.45 μm glass fiber filters. The Strata C18 (500mg/6mL) SPE sorbent was preconditioned with methanol and MilliQ with NH₄OH 0.2% at pH 8.5. The cartridge was air dried and eluted with MeOH. The eluate was evaporated to dryness in gentle nitrogen stream at 40°C and the analytes were reconstituted with 1mL of 60/40 acetonitrile/0.04% Acetic acid. Detection of compounds was performed on 1260 Agilent LC coupled with 6410 Mass Spectrometer. The analytes were separated on Eclipse C18 LC column at 30°C using an isocrat mobile phase of acetonitrile: 0.04% acetic acid (60/40, v/v %). The optimal flow rate was 0.2 ml/min and the injected volum was 10 μL. The contaminants were detected in negative electrospray (ESI) multiple reaction monitoring (MRM) mode. The LC-MS analysis time was 6 minute for all target antidiabetics. Retention times, MRM transitions, collision energies, fragmentor voltages, and other MS parameters are presented in Table 1. For each compound, two fragments of the de-protonated molecule [M-H] in negative ionization mode were monitored. Two MRM transitions were used, the most intense/abundant for quantitation (Quantifier) and the second most abundant for confirmation (qualifier).

Table 1. MRM transitions and MS/MS operating parameters selected for the analysis of target antidiabetic

Compound	Retention time	MRM Transition	Fragmentor voltage (V)	Collision energy (V)	Dwell time (msec)
Glyburid	3.57	492 → 170	140	45	60
		492 → 127	140	40	60
Glimepirid	4.04	489 → 364	140	40	60
		489 → 225	140	30	60
Repaglinid	5.22	451 → 379	160	20	60
		451 → 135	160	30	60

Results and conclusions

The SPE-LC/MS/MS method has been validated for waste water (effluent) in terms of: linearity, limits of quantification, intra-day and inter day-precision, accuracy. Linear regressions were obtained at 6 points in the range of 1 ng/mL – 100ng/mL with exception of repaglinid which presented a linear calibration range between 5 and 100 ng/mL. A good linearity was obtained for all compounds with determination coefficients R² higher than 0.99%. In fig. 1 are presented the MRM chromatogram of extracted ions obtained for a standard solution containing 20 ng/mL compounds and linear regression obtained for repaglinid.

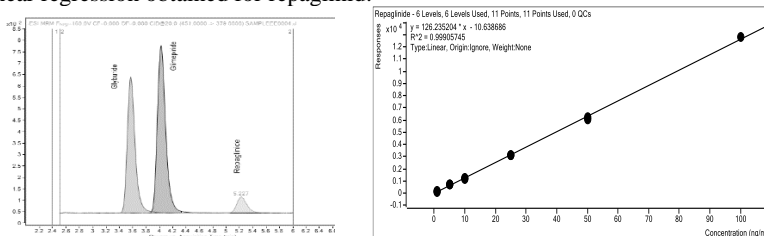


Figure 1. MRM chromatogram obtained for a solution containing antidiabetics 50ng/mL

Table 2. Performance parameters determined for antidiabetics in waste water samples

Compound	Calibration (ng/mL)	R ²	LOQ	Recovery rate (%)	Precision	
					Intra-day precision	Inter-day precision
Glyburid	1-100	0.9927	0.62	83.87	6.5	11.3
Glimepirid	1-100	0.9979	0.27	88.17	7.3	14.6
Repaglinid	5-100	0.9990	11.1	72.25	8.4	13.2

The method was successfully applied for detection of antidiabetic contaminants in waste water samples. Thus, for WWTP effluents were obtained concentrations in ranges 6.3-7.4ng/L for glyburide and 5.2-7.6 ng/L for glimepiride.

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