10º Encontro da Divisão de Química Analítica da SPQ, ANALITICA2020

DEVELOPMENT AND VALIDATION OF AN INDIRECT GC-MS METHOD FOR THE QUANTIFICATION OF PSYCHOACTIVE SUBSTANCES IN SURFACE WATERS

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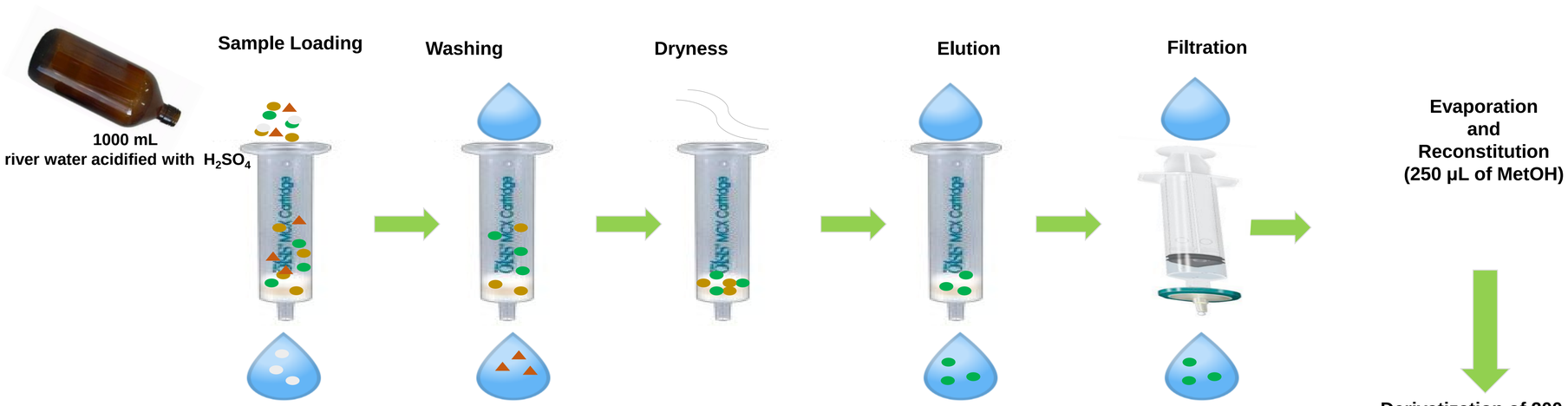
INTRODUCTION

The changes in the law to keep drug trafficking and consumption under control have boosted the synthesis and introduction of new psychoactive substances (PS) in the illegal market [1]. Many of this NPS are chiral and available as racemate or enantiomerically pure. These substances reach the environment through different ways such as direct disposal by industry, illegal discharges and as humans excretion products (of parent compounds and their metabolites) being a potential threat to non-target organisms [2, 3]. Occurrence of these substances in surface waters may also give insights about their consumption in a specific region.

The aim of this work is the development and validation of indirect method based on the application of solid phase extraction (SPE) followed by separation of the diastereomer using gas chromatography mass detector (GC-MS) for enantiomeric quantification of 8 PS (5 synthetic cathinones and 3 amphetamine like substances) based on the formation of diastereomers using (R) - (-) - α-methoxy-α- (trifluoromethyl) phenylacetyl chloride (*R*-MTPA-Cl) as chiral derivatization reagent. Two illicit piperazines (PP) were also included. PP were also derivatized with *R*-MTPA-Cl improving signal identification and detection. The optimized conditions allowed the quantification of the target PS (a total of 18 diastereomers and two PP) in less than 23.0 min.

METHOD

SOLID PHASE EXTRACTION - SPE



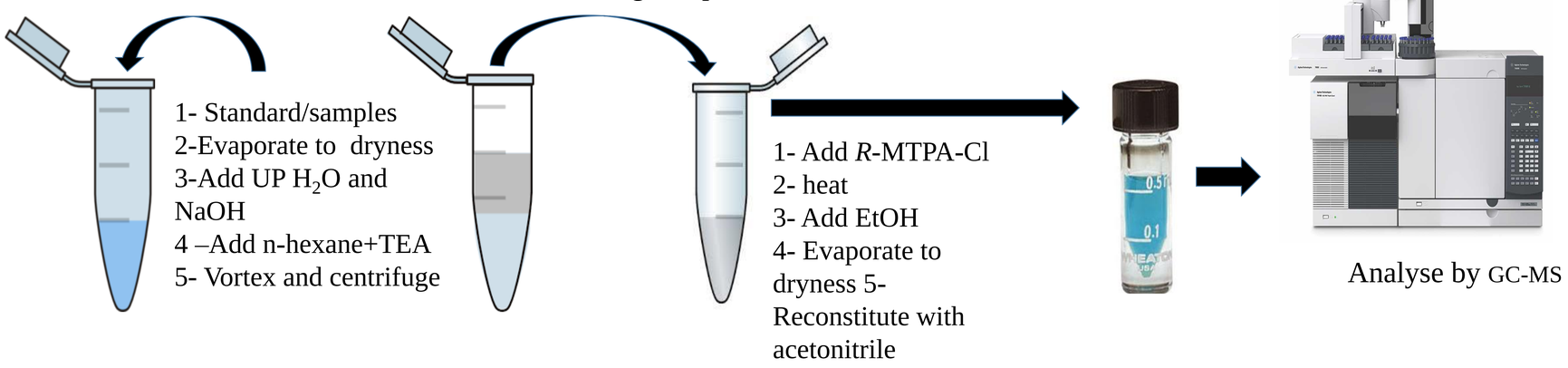
Upon arrival to the laboratory, all samples were immediately vacuum filtered and acidified to pH ≈ 3 with H_2SO_4. SPE was performed using OASIS® MCX cartridges without cartridge conditioning as described else were in [4, 5] and a mixture of ammonium hydroxide/ethanol were used as eluent.

For the formation of diastereomers the *R*-MTPA-Cl was used. The derivatization procedure established for amphetamines and derivatives was adapted and optimized for the inclusion of new classes of substances namely the synthetic cathinones and PP [5].

Analysis were performed using a GC-MS (Varian CP-3800 coupled with an ion trap mass spectrometer Saturn 2200 and an autosampler.

Chromatographic separation was performed using a Zebron (5% phenyl, 95% dimethylpolysiloxane) capillary column, 30 m x 0.25 mm I.D., 0.25 µm film thicknesses (Phenomenex, USA). The carrier gas was helium (99.999 % purity)

CHIRAL DERIVATIZATION (STANDARDS/SAMPLES)



RESULTADOS

Table 1: Target compounds, Quantification ion(s) (QI), retention time (RT) of the diastereoisomers (D1- first diastereomer to elute and D2- second diastereomer to elute),

Compound	QI(s)	Rt(min)	
		D1	D2
AM1	260, 234, 119	12.04	12.47
AM2	274, 200, 119	13.88	14.05
SCAT1	288	15.47	15.60
SCAT2	274	15.6	15.89
SCAT3	274, 200	17.18	17.50
AM3	274, 162	18.25	18.39
SCAT4	250, 206	18.75	19.16
SCAT5	288, 200	19.32	19.58
PP1	408	20.61	-
PP2	392, 146, 134	18.06	-

Table 1 show the ions used for the quantification of the diastereomers and the respective retention time. **Figures 1 and 2** represent the chromatograms showing the separation of the two diastereomers (AM3/1 and AM3/2).

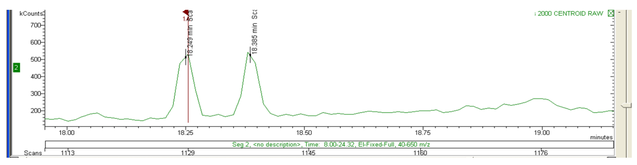


Figure 1: Chromatogram of the separation of AM3/1 diastereomers

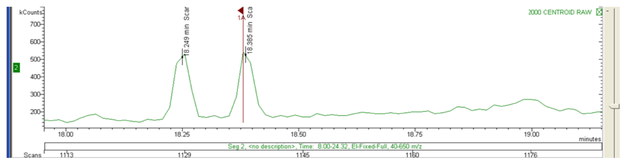


Figure 2: Chromatogram of the separation of AM3/2 diastereomers

The method was validated according to the International Conference on Harmonization and showed to be linear ($R^2 > 0.98$) (**table 2**). Limits of detection ranged from 17 to 100 ng/L and limit of quantification varied between 50 and 300 ng/L (**Table 2**).

Table 2: Target compounds, range of concentration (R), correlation coefficient (R^2), limit of detention (LOD) and limit of quantification (LOQ);

Compound	R (ng/L) Min	R (ng/L) Máx	R^2	LOD (ng/L)	LOQ (ng/L)
AM1/1	50	300	0,9891	31,8	50
AM1/2	50	300	0,9846	38	50
AM2/1	50	300	0,9968	18	50
AM2/2	50	300	0,9935	25	50
SCAT1/1	175	425	0,9916	52,2	175
SCAT1/2	175	425	0,9907	54,8	175
SCAT2/1	300	500	0,9855	62	300
SCAT2/2	300	500	0,9931	90	300
SCAT3/1	300	625	0,9906	81	300
SCAT3/2	250	625	0,9919	74	250
AM3/1	75	375	0,986	52	75
AM3/2	75	375	0,9926	38	75
AM4/1	75	375	0,9946	24	75
AM4/2	74	375	0,9886	34	75
SCAT5/1	75	375	0,9929	24,7	75
SCAT5/2	75	375	0,9964	17	75
PP1	250	625	0,9882	88	250
PP2	75	250	0,9928	29	75

CONCLUSÕES

Development of enantioselective methods is crucial for monitorization of chiral PS. This method will be used to evaluate the occurrence, spatial distribution, and the enantiomeric fraction of the PS in Portuguese surface waters in the Great Porto region. Data will allow to evaluate their environmental impact, determine/ verify the consumption of recreational drug by the population and their potential sources.

Acknowledgements

Projeto financiado pelo projeto: BIOENVIROM-CESPU-2019.

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