A POLY(METHACRYLIC ACID-ETHYLENE GLYCOL METHACRYLATE) MAGNETIC COMPOSITE FOR TRACE DETERMINATION OF TRICYCLIC ANTIDEPRESSANTS AND THEIR ACTIVE METABOLITES IN HUMAN URINE BY STIR BAR SORPTIVE DISPERSIVE MICROEXTRACTION

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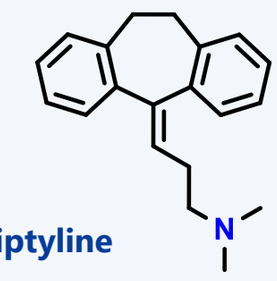
INTRODUCTION

- **Tricicyclic antidepresants (TCAs)** are widely used to treat depression, anxiety reaction and recently neuropathic pain
- Urine immunoassays are performed in cases of suspect overdose or pain management. These assays sometimes cause false-positive results and they do not have a high sensitivity
- The **aim** of this work is to develop a new method that provides analytical improvements in the determination of TCAs and their active metabolites

- **Stir bar sorptive dispersive microextraction (SBSDME)** [1] was born as a hybrid microextraction technique that combines the principles of stir bar sorptive extraction (SBSE) and dispersive solid-phase extraction (DSPE)
- In this technique, a magnetic material (in this case, **$CoFe_2O_4$@MAA-EGDMA polymer**), which is used as extraction phase, is dispersed by magnetic stirring and retrieved onto the NdFeB stir bar surface due to its magnetic properties
- The analytes can be desorbed by **liquid desorption** and subsequently injected to **LC-MS/MS**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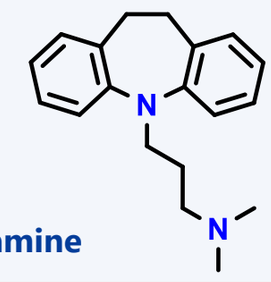
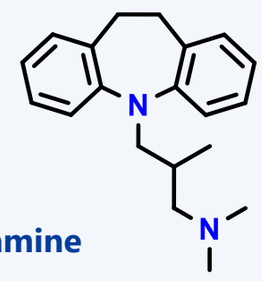
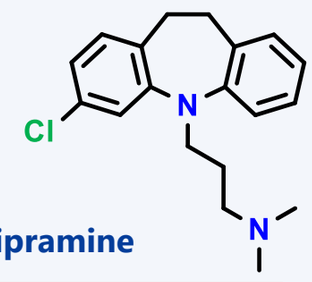
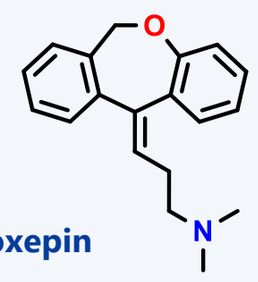

Imipramine

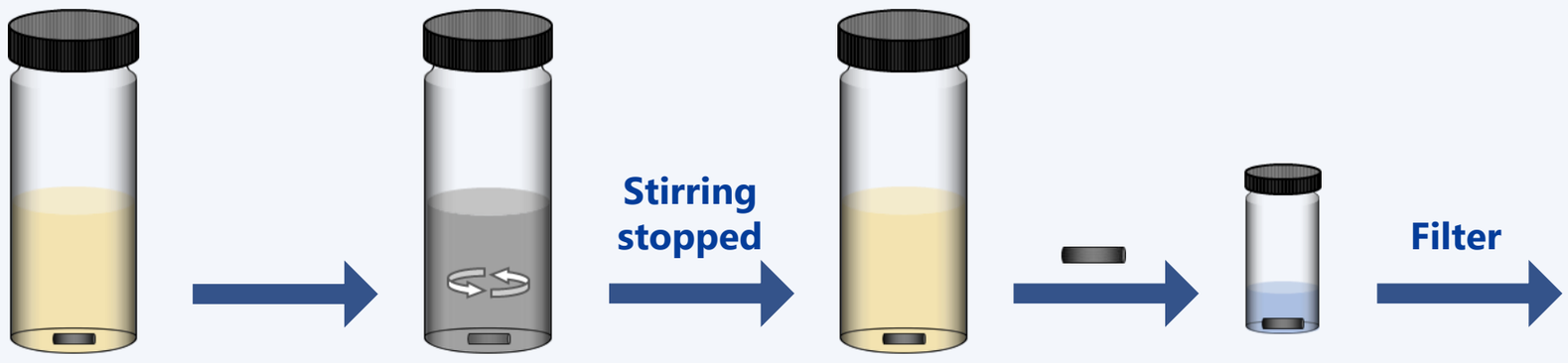

Trimipramine


Clomipramine


Doxepin

The target analytes of this work are the presented TCAs and their demethylated analogues

EXPERIMENTAL



25 mL urine
15 mg sorbent *
6.8% NaCl

5 min
High stirring

Liquid desorption
0.25 mL MeOH:H_2O:HAcO 6:3:1
5 min

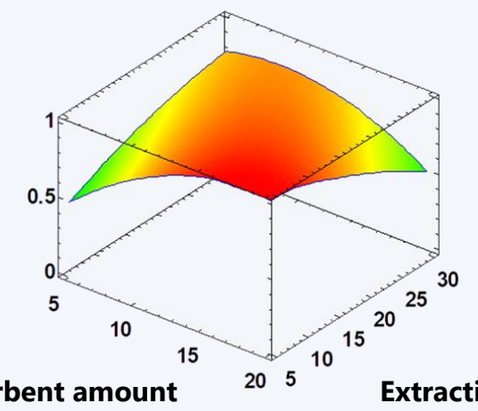
* $CoFe_2O_4$@MAA-EGDMA polymer

LC-MS/MS

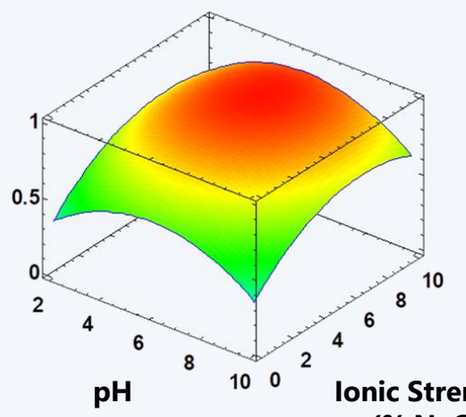
- **Injection volume:** 5 µL
- **Column temperature:** 35 ºC
- **Mobile phase:** MeOH (0.1% formic acid):H_2O (0.1% formic acid)
- **Elution mode:** Gradient
- **Flow:** 0.3 mL min^{-1}
- **Column:** Zorbax SB-C18 (50 mm length, 4 mm I.D., 1.8 µm)
- **Gas temperature:** 250 ºC
- **Gas flow:** 10 L min^{-1}
- **Nebulizer gas pressure**: 25 psi
- **Acquisition mode:** ESI^+ (MRM)
- **Capillary voltage:** +3000 V

RESULTS AND DISCUSSION

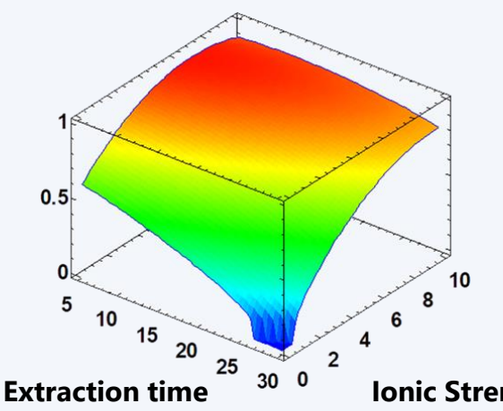
Selection of the experimental variables for the extraction procedure by the Response Surface Methodology



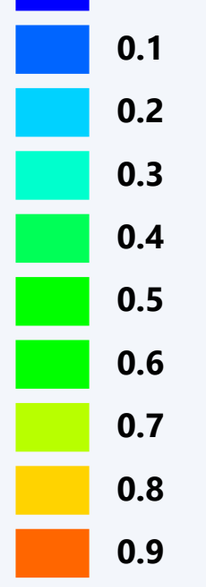
pH: 6.2
Ionic Strength: 6.8% NaCl



Sorbent amount: 15 mg
Extraction time: 5 min



Sorbent amount: 15 mg
pH: 6.2



Figures of merit

TCA	EF	LOD (ng L^{-1})	LOQ (ng L^{-1})	Repeatability (%RSD)					
				Intra-day			Inter-day		
				50 ng L^{-1}	250 ng L^{-1}	1000 ng L^{-1}	50 ng L^{-1}	250 ng L^{-1}	1000 ng L^{-1}
Doxepin	43	7.0	23.1	6.9	2.7	5.1	10.6	13.3	5.5
Nordoxepin	25	5.3	17.6	7.3	4.3	6.5	1.7	9.6	10.4
Imipramine	31	2.3	7.7	9.3	2.1	7.0	12.8	12.5	4.7
Desipramine	31	1.4	4.7	4.0	1.9	5.0	7.0	14.7	2.0
Amitriptyline	38	6.2	20.4	5.9	1.3	4.7	12.4	6.0	2.1
Trimipramine	34	2.7	8.9	4.2	1.0	5.3	14.7	14.2	6.1
Nortriptyline	36	2.2	7.3	2.2	2.0	5.3	12.9	9.1	1.4
Nortrimipramine	38	3.0	9.9	1.4	2.4	5.2	3.2	15.4	4.4
Clomipramine	41	2.5	8.3	9.8	2.7	5.3	17.9	14.1	12.5
Norclomipramine	41	2.0	6.6	3.3	3.4	3.0	6.8	8.5	7.6

- High level of linearity, that reached at least 10 ng mL^{-1}, was obtained for all compounds
- Low limits of detection (1.4 – 7.0 ng L^{-1}) and good values of precision (< 15 %) and enrichment factors (25 - 43) were achieved

CONCLUSIONS

- A fully optimized SBSDME-LC-MS/MS method that improves the sensitivity and selectivity of the determination of TCAs and their active metabolites in human urine at trace level has been presented
- The proposed method offers simplicity, rapid analysis time and satisfactory analytical features

[1] V. Vállez-Gomis, J. Grau, J.L. Benedé, D.L. Giokas, A. Chisvert, A. Salvador, Anal. Chim. Acta 1153 (2021) 338271

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