Determination of tetrahydrofuran and ketones in urine by headspace technique

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Introduction and objectives

- Tetrahydrofuran (THF) is a compound widely used in industry as a solvent for resins and plastic material in the fabrication of dyes, paints, varnishes and adhesives
- Also, ketones -such as acetone, methyl ethyl ketone (MEK) and methyl isobutyl ketone (MIBK)- are used as solvents in the fabrication of the above mentioned preparations and, in some cases, appear together with tetrahydrofuran
- The analysis of unmetabolized solvents in urine is very useful for biological monitoring of this kind of compounds in occupational environment [1]; the development of analytical methods that allow the determination of unmetabolized ketones and THF in urine samples is very interesting as they are biomarkers of occupational exposition that have established biological limit values (VLB) [2]. In addition, THF can be absorbed by dermal via, so the measure of the environmental concentration may not be sufficient to quantify the overall exposition
- **The aim of this work has been to develop a method for the simultaneous determination of these compounds and to compare it with solid phase microextraction (SPME) [3]**

Experimental

PerkinElmer TurboMatrix 40 Trap,
- 2 ml sample volume
- Automatic headspace sampler. Constant mode, shaker on
- Oven time: 20 min
- Pressurization time: 1 min
- Injection: 20 psi, 0.01 min
- Oven temperature: 70 °C
- Needle temperature: 100 °C
- Transfer line temperature: 150 °C
- Column pressure: 16 psig

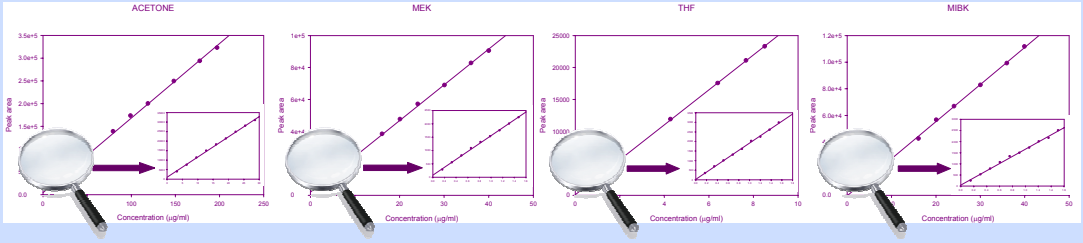
PerkinElmer Clarus 600 GC
- Oven program: 40 °C for 4 min then 20 °C/min to 90 °C
- Split Splitless Injector: 200 °C, Split flow: 20 ml/min
- D-Swafer: 15 psig He
- Column: HP-5MS, 30 m x 0.25 mm, 250 µm

PerkinElmer Clarus 600 T MS, source temperature: 180 °C, transfer line temperature: 200 °C
- Scan: m/z 40 – 300 Da (0.35s / 0.05is)
- SIR: (0.05d, 0.005ic) m/z 58 for AC (1.30 – 2.00 min), m/z 72 for MEK and THF (2.00 – 2.50 min) and m/z 100 for MIBK (2.50 – 4.00 min)

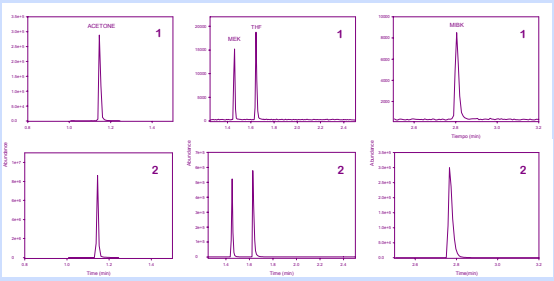
Results and discussion

Calibration curves, linear range of the calibration and limits of detection (LOD) for standard Acetone, MEK, THF and MIBK samples.

Compound	Correlation coefficient	LOD (µg/ml)	Linear range (µg/ml)
ACETONE	0.9995	0.88	3.2-197.13
MEK	0.9994	0.05	0.16-40.02
THF	0.9992	0.06	0.43-8.51
MIBK	0.9982	0.06	0.15-39.94



Precision of the method.



Chromatograms obtained from the determination of Acetone, MEK, THF and MIBK in urine with a concentration of 0.1 VLB (level 1) and 2 VLB (level 2).

Concentration (µg/ml)	Level 1	Level 2
ACETONE	3.20	94.60
MEK	0.16	4.86
THF	0.17	5.09
MIBK	0.15	4.48

Intra-day precision (% RSD), n = 10

RSD (%)	Level of Concentration 1	2
ACETONE	3.3	1.5
MEK	3.2	1.6
THF	4.4	3.4
MIBK	7.5	3.3

Comparison of the developed method with a certified method based on SPME technique using the paired-sample comparison analysis

SPME conditions

Sample volume	2.5 mL	Fibre 75 mm Carboxen/PDMS	
Equilibrium time	1 min	Headspace. Stirred	
Equilibrium temperature	50°C	Extraction temperature	50 °C
NaCl	0.9 g	Extraction time	20 min
		Desorption temperature	300°C
		Desorption time	4 min
		Inlet liner	0.75 mm

CG HP 6890A – MSD HP5973
He, 1.4 mL/min. Splitless
HP-1 60m x 0.25mm x 1µm
Oven: 4 min at 40°C, to 140°C at 20°C/min, held 2 min
SIM mode detecting *m/z* 43, 58 for AC, 43, 72 for MEK, 43, 58, 85 for MIBK and 42, 72 for THF

ACETONE		MEK		MIBK		THF	
HS	SPME	HS	SPME	HS	SPME	HS	SPME
16.9	21.1	2.5	3.6	2.1	2.7	0.9	1
16.2	14.7	2.3	3.5	2.1	2.6	0.8	1
79.7	80.3	15.3	16.2	7.4	7.3	3.4	4.4
78.5	69.8	14.6	15.1	7.1	6.2	3.4	3.6
31.9	34.1	8	8.2	15.5	13	0.9	0.7
106.8	109.1	17.9	17.3			6.7	7.8
78.9	72.2						

	ACETONE	MEK	MIBK	THF
t	0.59	-1.99	0.84	-1.87
P	0.58	0.10	0.45	0.12

Null hypothesis: mean of the paired differences = 0.0
Since the P-value for all the compounds is greater than or equal to 0.05, we cannot reject the null hypothesis at the 95.0% confidence level.

Intercomparison programme

Certificate for participating in the intercomparison programme 42 G-EQUAS for occupational medical-toxicological analysis. The method based on SPME technique has fulfilled the requirements for acetone, MEK, MIBK and THF in urine.

- There is a linear relationship between the amount of analyte extracted and the urinary concentration
- The relative standard deviation was below 10%
- The limits of detection were low enough to quantify ketones and THF in urine at occupational exposed levels
- There aren't statistically significant differences between the studied method results and the obtained with the certified method based on SPME
- The method can be used in biomonitoring routine of acetone, methylethyl ketone, methyl isobutyl ketone and tetrahydrofuran

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[3] C. Prado, P. Marín, J. Alcaraz, J.F. Periago. 12a Jornada de Análisis Instrumental. Expoquimia. Barcelona 2008.