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Determination of carboxylic acids in water by gas chromatography–mass spectrometry after continuous extraction and derivatisation

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ABSTRACT

This paper describes a new approach for the determination of monocarboxylic, dicarboxylic and tricarboxylic acids (35 compounds) in water. The analytes, in acid medium (pH ~1.3), were sorbed on an 80 mg LiChrolut EN–Supelclean ENVI-18 (1:1) column and subsequently eluted with methanol. After evaporation of the extract to ~10 μL, the analytes were spiked with 60 μL of the derivatising reagent and derivatised in a household microwave oven for 3 min. Among the reagents tested (BF_3/1-butanol; acetyl chloride/1-butanol; isobutyl chloroformate/1-butanol; trimethylphenylammonium hydroxide, *N,O*-bis-(trimethylsilyl)acetamide, *N,O*-bis-(trimethylsilyl)trifluoroacetamide and trimethylchlorosilane), the best results in terms of reaction yield and stability of the derivatives were obtained with the mixture of 1% trimethylchlorosilane in *N,O*-bis-(trimethylsilyl)trifluoroacetamide. Microwave assisted derivatisation was used as an alternative heating approach for the rapid silylation of carboxylic acids. The proposed method proved to be a suitable analytical procedure for several types of carboxylic acids in water, with limits of detection within the range 0.6–15 ng L^{-1}, precision values from 4.0 to 6.0% (as within-day relative standard deviation) and recoveries from 93 to 101% for all the target analytes.

1. Introduction

Discussion on the health risks of chlorination by-products in drinking water has led to an increased interest in alternative disinfectants such as ozone, chloramine and chlorine dioxide. Although the above mentioned disinfectants are being used in many drinking water plants in the United States and Europe, few studies have been conducted to determine the identity and potential toxicological effects of the new byproducts originated (e.g. aldehydes, ketones, nitriles, carboxylic acids). In relation to carboxylic acids studies have been made on short-chain monocarboxylic acids and some dicarboxylic acids, which pass into finished drinking water, leading to a bacterial regrowth in distribution systems [1–5]. Carboxylic acids are also found in wastewater, rainwater and natural water due to biochemical process and anthropogenic emissions such as sewage sludge and exhaust fumes [6]. With each type of water, the concentration of these acids varies from a few μg L^{-1} to several hundred mg L^{-1}. Factors such as the type of carboxylic acid, its concentrations and sample matrix largely determine which analytical methods are suitable for a certain sample.

In most methods employed up to date carboxylic acids are previously extracted from natural matrices before quantification. Conventional liquid–liquid extraction consumes large amounts of organic solvents and it is labour intensive [6]. The quest for novel sample preparation procedures led to the development of fast and simple and solventless techniques such as solid-phase microextraction (SPME) [7,8], single-drop microextraction [9], dynamic headspace-needle trap extraction [10] and solid-phase extraction (SPE) [6,11–13]. The latter technique is advantageous for environmental monitoring because it can be readily automated via flow systems, thus large sample volumes can be processed with minimum sample manipulation [13,14]. Currently, methods used to determine carboxylic acids involve gas chromatography with mass spectrometric detection (GC–MS) [2–4,7–9,12,15–17], ion chromatography [18,19] and liquid chromatography [20–22]. Among these techniques, GC–MS is the most widely used due to its inherent advantages of high sensitivity, low cost, simplicity and resolving power.

Many carboxylic acids are thermostable and sufficiently volatile, thus fulfilling key requirements for GC measurements, although their high polarity makes it difficult to achieve satisfactory chromatograms with standard capillary columns. Polar stationary phases such as those based on polyethylene glycol or acids phases can be employed to enhance separation [23], but the maximum

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temperatures at which they can be operated preclude the analysis of compounds with high boiling points. Attempts to determine dicarboxylic and tricarboxylic acids using these columns resulted in poor chromatography [17,24], hence a derivatisation step (e.g. esterification, acylation and silylation) is mandatory. Esterification with alcohols using BF_3 or acetyl chloride as catalyst [16,17,25] and induced alkylchloroformate [26,27] are widely used procedures to determine dicarboxylic acids as well as short and long chain carboxylic acids. Intra-injector methylation of carboxylic acids with trimethylammonium hydroxide, trimethylanilinium hydroxide or trimethylphenylammonium hydroxide (TMPAH) is another alkylation process used [28,29]. In some cases silylation is the choice due to its inherent advantages such as an improvement in some GC characteristics (accuracy, reproducibility, sensitivity and resolution), by suppressing tailing and enhancing thermal stability and an enhancement in the mass spectrometric properties of the analytes by producing not only more favourable diagnostic fragmentation patterns but also characteristic ions for SIM in trace analysis [6,17,29,30]. *N,O*-bis-(trimethylsilyl)trifluoroacetamide (BSTFA) with 1% trimethylchlorosilane (TMCS) is an appropriate derivatising reagent, as it is sufficiently volatile to provide little interference with early eluting peaks. Other reagents such as *N,O*-bis-(trimethylsilyl)acetamide (BSA), unlike BSTFA, are known to produce a derivatisation by-product which can attack the initially formed ester to yield an artifact [30].

Conventional derivatisation methods may require considerable time at higher temperatures to reach conditions capable of completing the reaction. The combination of microwave assisted derivatisation (MAD) with silyl reagents can offer the ability to improve the derivatisation response while lowering overall analysis time compared to traditional methods. Thus, MAD has been successfully employed in the derivatisation of carboxylic acids [30], acidic herbicides [31] and steroids [32]. From these premises, the aims of this work were to: (1) study several reagents for derivatisation of a high number of carboxylic acids (35); (2) develop a continuous SPE unit for the extraction of carboxylic acids from water, and microwave-assisted derivatisation of the extract before determining the esters by GC–MS; and (3) evaluate the analytical performance and possible applications of the method on real water samples.

2. Experimental

2.1. Standards and reagents

Standards of the 35 carboxylic acids (>95% purity), listed in Table 1, were supplied from Sigma–Aldrich (Madrid, Spain). Stock solutions of the individual acids (10 g L^{-1}) were prepared in methanol or ethanol and working solutions prepared daily by diluting these stocks with water purified with a Milli-Q System (Millipore, Bedford, MA, USA). Methanol containing 2 mg L^{-1} of triphenylphosphate (TPP) as internal standard (IS) was used as eluent and also prepared on a daily basis. All these solutions were stored at 4 °C.

LiChrolut EN (particle size 40–120 μm), pyridine and chromatographic grade 1-butanol, methanol, ethanol, acetonitrile and ethyl acetate were purchased from Merck (Darmstadt, Germany). Silica-reverse phase sorbent with octadecyl functional groups (Supelclean ENVI-18) was supplied from Supelco (Madrid, Spain). TPP and the derivatising reagents, BF_3 (10% in 1-butanol), isobutylchloroformate (IBCF), TMPAH (0.5 M in methanol), acetyl chloride (5% in 1-butanol), BSA, BSTFA and TMCS were supplied by Fluka (Madrid, Spain). These reagents are toxics and were handled in accordance with the most current material safety data sheets.

2.2. Instruments and apparatus

Gas chromatographic analyses were carried out using a Focus GC instrument (Thermo Electron SA, Madrid, Spain) fitted with a split/splitless injector and a DSQ II mass spectrometer controlled by a computer running XCalibur software. Helium (purity 6.0) was used as the carrier gas at a flow rate of 1 mL min^{-1}. GC separations were conducted on a DB-5 MS fused-silica capillary column, 30 m × 0.25 mm i.d × 0.25 μm from J&W (Folson, CA, USA). The column temperature was initially set at 60 °C (held for 4 min) and then raised at 9 °C min^{-1} to 260 °C. All samples were injected in the split mode (1:20 ratio); the injector temperature was 280 °C. The MS operated in the electronic ionisation mode (70 eV), ion source and transfer line temperatures were 200 and 280 °C, respectively and the time for solvent delay was set at 4 min. The MS was operated in full scan detection mode for identification purposes (40–450 amu, scan time, 0.84 s), whereas the selected ion monitoring mode (SIM) was used to quantify the target analytes. For each silyl derivative, $M^{+\bullet}$, $[M-15]^+$, and other additional ions were monitored which are included along with the analytical figures of merit on the proposed method.

The continuous SPE system was assembled from a Gilson Minipuls-3 peristaltic pump (Villiers-le-Bel, France) fitted with poly (vinylchloride) tubes, two Rheodyne (Cotati, CA, USA) 5041 injection valves and a PTFE laboratory-made sorbent column containing 80 mg of the mixture LiChrolut EN/Supelclean ENVI-18 (1:1) sorbents. The sorbent column was conditioned with 1 mL of acetonitrile–methanol (1:1) and 1 mL of purified water. Under these conditions, the column remained serviceable for at least 1–2 months with no change in its properties.

2.3. Sampling procedure

Water samples were collected at several locations in precleaned amber glass bottles of 1 L. Sample bottles were filled without headspace and 20 mg L^{-1} of benzalkonium chloride was employed as preservative [33]. Samples were immediately placed into coolers with icepacks and transported to the laboratory, where they were refrigerated at 4 °C up to a week before analysis or frozen (−20 °C) up to 3 months. Samples containing visible solids (i.e., wastewaters) should be filtered prior to analysis through a 0.45 μm membrane filter (mixed cellulose esters, Millipore Ibérica, Spain) to prevent suspended particles from reaching the SPE unit. Raw and treated water samples were collected from two full-scale drinking water treatment plants located in Spain. City A (700,000 hab) employs ozone and chlorine for water disinfection whereas City B (60,000 hab) uses only chlorine.

2.4. Derivatisation procedures

Esterification with BF_3 or acetyl chloride was carried out by using methods described in the literature, slightly modified in relation to the volumes [16,17,25]. Fifty microliters of a standard solution containing 100 μg mL^{-1} of each carboxylic acid and 200 μg mL^{-1} of the IS, in 1-butanol were transferred into a small conical deactivated glass vial and 300 μL of solutions of BF_3 (10%) or acetyl chloride (5%) in 1-butanol were added. The vial was tightly sealed and heated for 60 min at 70 °C, and then cooled at room temperature. The butyl esters were manually extracted with 350 μL of n-hexane and 1 μL of the extract was injected into the GC–MS instrument. Derivatisation using IBCF was performed following a similar procedure described elsewhere [27]. Fifty microliters of the standard solution in 1-butanol, 260 μL of acetonitrile, 10 μL of pyridine and 30 μL of IBCF were transferred into the conical glass vial and after shaking in an ultra-sound bath for 5 min, the butyl esters were extracted as described above with 350 μL of n-hexane. For

Table 1
RRFs values of carboxylic acids after derivatisation with different reagents.

Carboxylic acid	BF_3/1-butanol	Acetyl chloride/1-butanol	IBCF/1-butanol	TMPAH	BSA	BSTFA	TMCS	1% TMCS in BSTFA
Acetic	0.51	0.59	0.64	0.67	0.78	0.85	0.59	0.98
Propionic	0.13	0.15	0.16	0.17	0.20	0.21	0.15	0.25
Butyric	0.19	0.22	0.24	0.25	0.29	0.32	0.22	0.37
2-Methylbutyric	0.51	0.59	0.64	0.67	0.78	0.85	0.59	1.01
Valeric	1.53	1.76	1.93	2.01	2.35	2.56	1.76	2.94
Isovaleric	1.53	1.76	1.93	2.01	2.35	2.56	1.76	2.95
Hexanoic	1.03	1.18	1.30	1.35	1.18	1.28	0.88	1.47
Octanoic	0.69	0.79	0.87	0.90	0.78	0.85	0.59	0.98
Nonanoic	0.41	0.47	0.52	0.54	0.47	0.51	0.35	0.59
Decanoic	0.50	0.49	0.57	0.60	0.50	0.59	0.51	0.61
Dodecanoic	2.06	2.37	2.60	2.71	2.35	2.56	1.76	2.96
Myristic	1.03	1.18	1.30	1.35	1.18	1.28	0.88	1.47
Palmitic	1.03	1.18	1.30	1.35	1.18	1.28	0.88	1.47
Heptadecanoic	0.69	0.79	0.87	0.90	0.78	0.85	0.59	0.99
Stearic	0.68	0.79	0.87	0.90	0.78	0.85	0.59	1.01
Oleic	0.51	0.59	0.65	0.68	0.59	0.64	0.44	0.74
Linoleic	0.41	0.47	0.52	0.54	0.47	0.51	0.35	0.59
Oxalic	0.15	0.17	0.19	0.19	0.29	0.32	0.22	0.37
Pyruvic	0.39	0.45	0.50	0.52	0.78	0.85	0.59	0.98
Glycolic	0.39	0.45	0.50	0.53	0.78	0.85	0.59	0.97
Succinic	0.08	0.09	0.10	0.10	0.16	0.17	0.12	0.20
Fumaric	0.10	0.11	0.12	0.13	0.20	0.21	0.15	0.25
Benzoic	0.74	0.85	2.68	3.01	3.92	4.26	2.94	4.90
o-Toluic	0.15	0.17	0.75	0.80	0.77	0.87	0.60	1.02
m-Toluic	0.22	0.25	1.10	1.15	1.18	1.28	0.88	1.47
p-Toluic	0.22	0.25	1.10	1.15	1.18	1.28	0.88	1.47
Phenylacetic	0.15	0.17	0.74	0.76	0.78	0.85	0.59	0.97
Salicylic	0.04	0.05	0.22	0.23	0.24	0.26	0.18	0.29
3-Hydroxybenzoic	0.11	0.13	0.55	0.57	0.59	0.64	0.44	0.74
2-Nitrobenzoic	0.11	0.13	0.55	0.57	0.59	0.64	0.44	0.74
3-Nitrobenzoic	0.07	0.08	0.37	0.38	0.39	0.43	0.29	0.49
4-Nitrobenzoic	0.07	0.08	0.37	0.38	0.39	0.43	0.29	0.49
3,4-Dihydroxybenzoic	0.03	0.03	0.15	0.15	0.16	0.17	0.16	0.20
Phthalic	0.09	0.10	0.44	0.46	0.47	0.51	0.47	0.59
1,2,3-Benzenetricarboxylic	0.03	0.04	0.17	0.18	0.19	0.20	0.19	0.23

methylation with TMPAH [28], 50 μL of the standard solution in methanol were mixed with 300 μL of TMPAH (0.1 M in methanol) and then 1 μL of the mixture was injected directly into the GC–MS instrument.

The silylation of the carboxylic acids using BSA, BSTFA, TMCS and the mixture of 1% TMCS in BSTFA [14] was performed as follows: 50 μL of the standard solution containing 100 μg mL^{-1} of each carboxylic acid and 200 μg mL^{-1} of the IS in ethyl acetate was transferred into a conical glass vial and mixed with 300 μL of the appropriate silylation reagent. The vials were tightly sealed and heated at 70 °C for 60 min. After cooling at room temperature, 1 μL aliquots were injected directly into the GC–MS for analysis.

2.5. Analytical procedure

A schematic diagram of the continuous SPE unit is shown in Fig. 1. A volume of 50 mL of standard solution or water sample with concentrations between 2 and 8000 ng L^{-1} of each carboxylic acid at pH ~1.3 (adjusted with 0.5 mL of 5 M HCl) was passed through the sorbent column (located in the loop of IV_1) at 4 mL min^{-1}. The retention of the target analytes was instantaneous and the sample matrix was sent to waste. An air stream (flow rate 3 mL min^{-1}) was used first to remove any residual water from the system and then as a carrier of the eluent (200 μL of methanol containing the IS) after IV_2 was switched. The organic extract was collected in a 1 mL amber glass vial and evaporated to a volume of ~10 μL under a gentle stream of ultrapure N_2. Potential errors in measuring the final extract volume were avoided by using the internal standard. Next, 60 μL of the mixture of 1% TMCS in BSTFA were added. After that the vial was tightly sealed and the analytes were derivatised using a household microwave oven for 3 min at 350 W. Finally, 1 μL aliquot of silylated derivatives was analysed by GC–MS in the SIM mode.

2.6. Calculation of detection limits

Limits of detection (LODs) were calculated by two different methods. Firstly, LODs were calculated as three times the standard deviation of residuals $S_{y/x}$, divided by the slope of each calibration graph. Secondly, the LODs were determined as the minimum detectable amount of analyte with a signal-to-noise ratio of 3:1 from different types of water samples (drinking, river and wastewater) spiked with the analytes at three concentrations levels (5, 20 and 50 ng L^{-1}).

3. Results and discussion

3.1. Optimisation of the derivatising reaction

In this work, we evaluate two types of reactions (esterification and silylation) for the simultaneous derivatisation of monocarboxylic, dicarboxylic and tricarboxylic acids. Each experiment was done in triplicate using 50 μL of standard solutions containing 100 μg mL^{-1} of each carboxylic acid and 200 μg mL^{-1} of the IS. The esterification reaction required a solvent extraction step to remove the excess of derivatising reagent, which would lead to GC column deterioration. For this reason, butyl ester derivatives (omitting the TMPAH experiment because the derivatisation was carried out into the heated GC-injector) were extracted with 350 μL of n-hexane. Identification of detected peaks was based both on retention times and on the MS spectra obtained. Fig. 2 shows the total ion chromatograms obtained after derivatisation with 10% BF_3 in 1-butanol (A), TMPAH (B) and 1% TMCS in BSTFA (C). In all cases (butyl, methyl

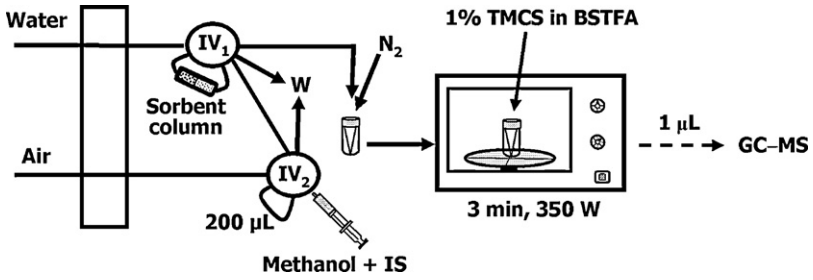

Fig. 1. Continuous flow unit for the SPE extraction of carboxylic acids in water and manual microwave assisted derivatisation. IV: injection valve; W: waste; IS: internal standard; TMCS: trimethylchlorosilane; BSTFA: *N*,*O*-bis-(trimethylsilyl)trifluoroacetamide; GC–MS: gas chromatograph–mass spectrometer.

and silyl esters), the derivative carboxylic acids were well-resolved on a commonly used DB-5 MS GC capillary column using the temperature program described in Section 2.2.

The effectiveness of each reagent for the derivatisation of the analytes was compared in terms of chromatographic relative response factors (RRFs), which were calculated by dividing the peak area of the derivative carboxylic acids by the peak area of an internal standard. Triphenylphosphate (TPP) was chosen as the internal standard on account of its inertness during derivatisation and the virtual constancy of its peak area throughout the experiments. The constant concentrations of the target compounds and internal standard, at the same GC–MS conditions (full scan mode, electron impact ionisation) enabled the effectiveness of the reactions to be compared using RRF: an increase in RRF indicated an increase in the derivatisation yield of esterification or silylation, taking into account the sensitivity of the detector to these compounds is different. In general, the sensitivity of the method obtained with silylation reagents was higher than that obtained with the butyl or methyl esters, probably due to a higher silylation yield or by the stability of the derivatives during analysis [32,34]. Thus, as can be observed in Table 1, the RRFs obtained with silylation reagents (columns 5–8, 0.12–4.90) were higher than those obtained with esterification reagents (columns 1–4, 0.03–3.01). In general, depending on the structures of the carboxylic acids, the reactivity of the different classes of acids towards esterification reagents was variable. RRF values for butyl and methyl ester derivatives of aliphatic acids (C_2–C_{18}; oxalic; pyruvic; glycolic; succinic and fumaric) were similar and comparable to the RRFs obtained with silylation reagents. For ester derivatives of aromatic acids, the lowest RRFs values were obtained when using BF_3 or acetyl chloride both in 1-butanol. TMPAH allow the possibility of performing the derivatisation of the analytes inside the GC injector, but some authors have observed that the highly basic characteristics of this reagent accelerate the damage to GC columns, which is a serious drawback [28,29]. For those reasons, the esterification reagents were discarded for further tests. Among the silylation reagents studied, the best results for the target analytes were obtained with the mixture of 1% TMCS in BSTFA, with RRFs ranging between 0.20 and 4.90, which was finally selected as derivatising reagent for the 35 carboxylic acids studied. Other advantages of the silyl reagent selected were: the excess of reagent does not interfere with the chromatographic peaks of the target analytes since it is volatilised with the solvent front, and the EI spectra of trimethylsilylated compounds yield structurally fragments ions which make identification highly reliable. These ion fragments can be used in SIM detection mode for a simpler and more selective chromatographic signal [17].

The derivatisation yield of carboxylic acids with TMCS in BSTFA depends on factors including the nature of the solvent in which the analytes are dissolved and the time/temperature reaction. To study the influence of the solvent sample medium, 50 μL of several solutions containing 100 μg mL^{-1} concentration of each carboxylic acid and 200 μg mL^{-1} of the IS in ethyl acetate, methanol, acetonitrile, ethanol or acetone were derivatised according to the procedure described in Section 2.4, and silyl esters were determined by GC–MS (SIM mode). The results obtained (see Electronic Supplementary Material, Fig. S1) showed that the derivatisation yield, in terms of RRFs, remains in consonance with the nature of the solvent; ethyl acetate provided the highest RRFs, in fact the values obtained for acetonitrile and the other solvents were 5–10 times lower. The influence of the amount of TMCS (the catalyst) in the derivatising reagent (BSTFA) was examined over the range 0–5% (v/v). The best results (see Electronic Supplementary Material, Fig. S2) were obtained by using proportions higher than 0.9% of TMCS prepared in BSTFA, so the concentration used till now was selected (1% TMCS in BSTFA). A considerable drawback of conventional derivatisation methods is the long time (viz. more than 50 min) and the high reaction temperature (viz. 70 °C) for the silylation reaction [6,17]. A promising strategy is the use of microwave assisted derivatisation (MAD), since it provides comparable reaction yields at lower times in the derivatisation of organic compounds when compared to those provided using traditional heating methods [30,32]. A comparative study about the derivatisation of carboxylic acids using microwave assisted or thermal energies was done (see Electronic Supplementary Material, Fig. S3). To this end, 200 μL of several standard solutions (100 μg mL^{-1} of each analyte with 200 μg mL^{-1} of IS in ethyl acetate) were mixed with 1.2 mL of 1% TMCS in BSTFA and heated into a water bath at 70 °C for 10, 30 and 60 min or introduced into a household microwave oven at variable power (70–500 W) and time (1–5 min). Regarding both energy systems, the best derivatisation yield (with similar RRFs) was achieved for 60 min using a water bath (70 °C) or microwave at 350 W for 3 min, which demonstrated the potential of microwave energy for the rapid derivatisation of carboxylic acids. Finally, the ratio between the volume of the standard solution and of the derivatising reagent added was studied in order to achieve the optimal reaction yield; the best results were obtained for a relation of volumes 1:6 (see Electronic Supplementary Material, Fig. S4).

3.2. Optimisation of the SPE unit

Carboxylic acids in drinking water and rainwater are usually present at μg L^{-1} levels, whereas inorganic anions have mg L^{-1} concentrations; thus, preconcentration and clean-up steps are usually required for their determination by chromatography. In a previous work, we developed a flow system for the preconcentration of aliphatic and aromatic carboxylic acids (that did not require derivatisation for determination by GC–MS) in water samples [13], in which the highest sorption efficiency was obtained with a mixture of LiChrolut EN/Supelclean ENVI-18 (1:1), using methanol as the eluent. When other solvents (ethyl acetate, acetonitrile, ethanol, 2-propanol, acetone, diethyl ether and dichloromethane) were used as eluent, the elution was ca. 1.5 times less effective. Therefore, a preliminary study of the effect of methanol on the silylation yield was conducted by using 200 μL of a standard solutions

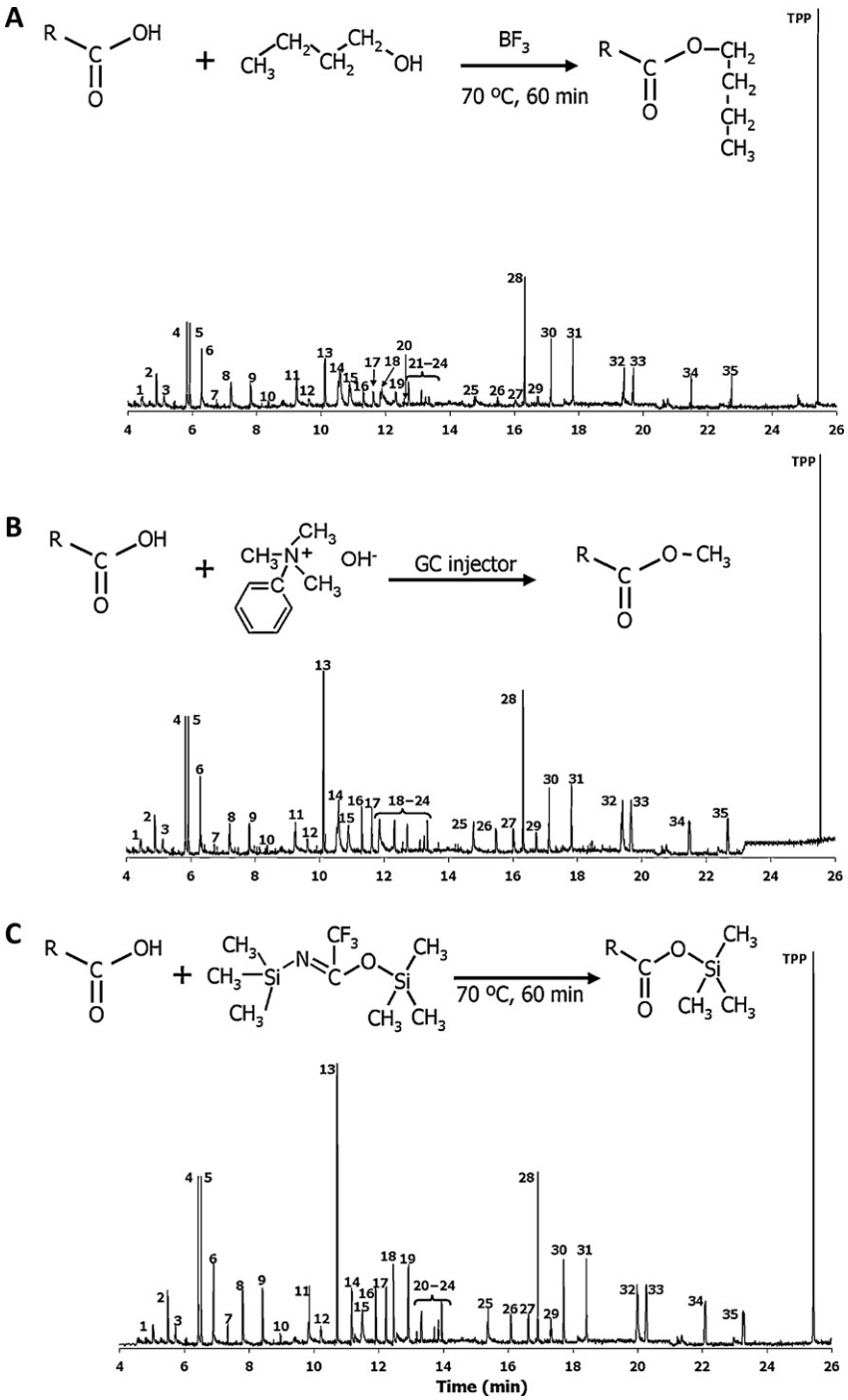

Fig. 2. GC–MS chromatograms (TIC mode) obtained after derivatisation of a standard solution of the 35 carboxylic acids with (A) 10% BF_3 in 1-butanol, (B) TMPAH (heated in the GC injector) and (C) 1% TMCS in BSTFA. 1: acetic; 2: propionic; 3: butyric; 4: valeric; 5: isovaleric; 6: hexanoic; 7: oxalic; 8: pyruvic; 9: glycolic; 10: 3,4-dihydroxybenzoic; 11: 2-methylbutyric; 12: 1,2,3-benzenetricarboxylic; 13: benzoic; 14: octanoic; 15: nonanoic; 16: phenylacetic; 17: o-toluic; 18: m-toluic; 19: p-toluic; 20: succinic; 21: decanoic; 22: fumaric; 23: salicylic; 24: 2-nitrobenzoic; 25: 3-hydroxybenzoic; 26: 3-nitrobenzoic; 27: 4-nitrobenzoic; 28: dodecanoic; 29: phthalic; 30: myristic; 31: palmitic; 32: heptadecanoic; 33: stearic; 34: oleic; 35: linoleic; TPP: triphenylphosphate (internal standard).

(100 $\mu g\,mL^{-1}$ of each analyte with 200 $\mu g\,mL^{-1}$ of IS in methanol) and 1.2 mL of 1% TMCS in BSTFA (1:6 volume ratio). Again it is verified that a low derivatisation yield (ca. 20%) was obtained in relation to that achieved when using ethyl acetate as sample medium. The behaviour of methanol in the derivatization reaction can be explained because the hydroxyl group also reacts with the derivatising reagent, decreasing the silylation yield. To avoid this problem, the resulting methanolic extract obtained after the pre-concentration/elution steps was reduced to a volume of ~10 μL and an excess of derivatising reagent is used. Thus, RRFs obtained in this case were similar to those obtained when the reaction was carried out in ethyl acetate medium. For this reason, it became necessary to carry out the evaporation of the methanolic extract; however, the methanolic extract only can be evaporated up to ca. 10 μL to avoid losses of the analytes. In these conditions (10 μL of the standards in methanol) and using 60 μL of the derivatising reagent (1:6 volume ratio), the efficiency of the derivatisation yield was similar to that achieved with ethyl acetate.

A previous continuous system optimized for the determination of some carboxylic acids in water was initially selected [13] but, as we expanded the number of analytes, a rigorous study was necessary in order to confirm that the chemical and flow variables that affect the preconcentration and elution process fell within the optimum ranges for the new analytes as well. As carboxylic acids require a pH value two units below their p*K*a values for adequate sorption as neutral compounds, the first chemical variable studied was the sample pH. The p*K*a values of the organic acids studied ranged between 3 and 5, therefore the water samples or aqueous standards solutions were adjusted at pH 1.3 by adding diluted HCl before their introduction in the continuous SPE system. Among the sorbents (Amberlites, Oasis HLB, LiChrolut EN, SupelClean-Envi 18, graphitised carbon black and fullerenes and derivatives), the best results were obtained with LiChrolut EN/Supelclean ENVI-18 (1:1) (see Electronic Supplementary Material, Table S1); 80 mg of the mixture were sufficient for complete retention of the 35 carboxylic acids tested. Complete elution of all acids was obtained with one injection of 200 μL of methanol. Flow variables were set as in the earlier system, samples and eluent flow rates of 4 and 3 mL min^{-1}, respectively, were chosen for further experiments. Finally, the breakthrough volume, which is directly related to the sensitivity of the method, was examined by using aqueous standard solutions at pH 1.3 containing 50 ng L^{-1} of each compound at different volumes (from 10 to 100 mL), for insertion into the SPE system. A sorption efficiency of ca. 100% was obtained with aqueous volumes up to 60 mL, above which it started to decrease because the capacity of the sorbent was over-loaded and/or the proper sample matrix eluted the acids. Accordingly, the 200 μL of methanolic extract from the SPE system was evaporated to ca. 10 μL and then derivatised as described above.

3.3. Analytical performance

Under the optimised conditions of the proposed method, calibration curves for aqueous standards solutions containing between 2 and 8000 ng L^{-1} of each 35 carboxylic acid were constructed by plotting the analyte to the internal standard peak area against the amount of analytes (12 points per curve). The results obtained are listed in Table 2. All target analytes showed good linearity with correlation coefficients greater than 0.996. The LODs, calculated on the basis of the standard deviation of residuals $S_{y/x}$, ranged from 0.6 to 15 ng L^{-1}. Additionally, the LODs were determined as the minimum detectable amount of analyte with a signal-to-noise ratio of 3:1 from different types of water samples (drinking, river and wastewater) spiked with the analytes at three concentrations levels (5, 20 and 50 ng L^{-1}). In both instances the LODs obtained for each acid were similar. The precision of the method, expressed as relative standard deviation (RSD) was evaluated by analysing 11 individual standard mixtures at three concentrations levels (100, 500 and 2000 ng L^{-1}) on the same day (within-day) and on three different days (between-day). The RSD obtained were found to be satisfactory with RSD lower than 6% (within-day precision) or 7% (between-day precision).

In order to check for possible matrix effects and investigate the applicability of the method to real water analysis, a recovery study was conducted. Taking into account that most waters contained carboxylic acids, their concentrations in the spiked samples were quantified and compared to those calculated as the sum of native concentration in unspiked samples and spiked concentrations. For this purpose, 50 mL of various types of water including drinking, pond, river, rain, well, swimming pool and wastewater were fortified at three different concentrations (100, 500 and 2000 ng L^{-1}) of each carboxylic acid and analysed in triplicate ($n = 3$). The mean recoveries for all analytes were in the range of 93–101%, which indicated that the method was reliable and can be used for the determination of carboxylic acids in water samples.

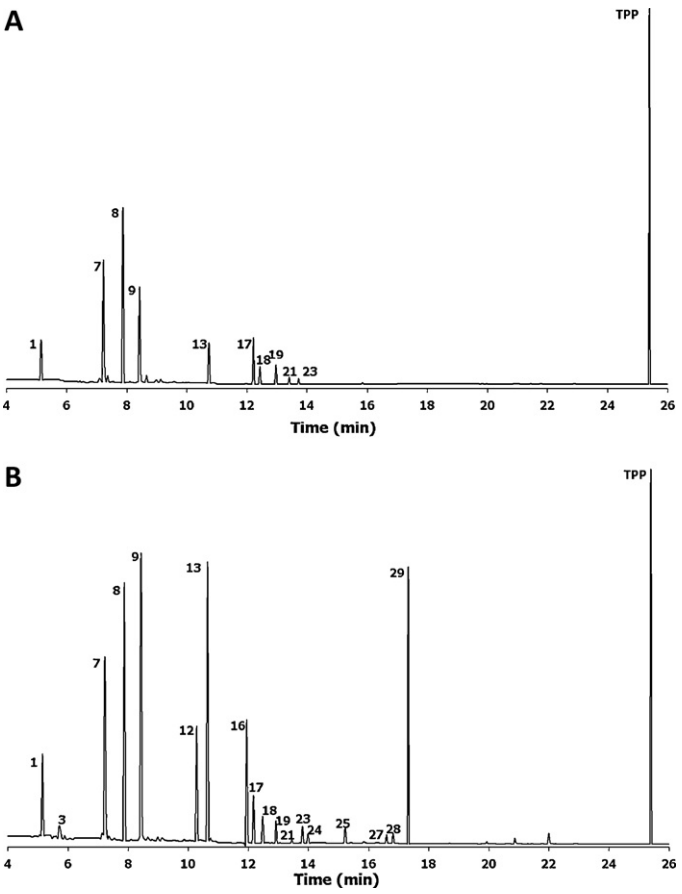

Fig. 3. GC–MS chromatograms (SIM mode) obtained in the analysis of 50 mL of (A) the raw water 1, diluted 2 times and (B) the same water, diluted 5 times, treated with ozone and chlorine (see Table 3). For peaks identification see Fig. 2.

3.4. Analysis of water

To examine the feasibility of the proposed sample treatment and GC–MS determination of carboxylic acids, over twenty water samples were analysed, including samples taken from different stages of two full scale drinking water treatment plants. The study allows discrimination between the production and removal of carboxylic acids in drinking water using two disinfectants (ozone and chlorine or chlorine alone). Samples were analysed in triplicate and when the concentration of some acids lay outside the linear range, the sample concerned was diluted with purified water to bring it within it. The results obtained from the analysis of water taken in the treatment plant that employed ozone and chlorine as disinfectant, showed that some carboxylic acids were found in the raw water samples although at a total concentration below 30 μg L^{-1} (see Table 3); the carboxylic acids can appear in raw water due to the degradation of natural organic matter or organic contaminants present in the water. Fig. 3A shows the chromatogram obtained for the analysis of 50 mL of a raw water sample. As can be observed, 10 carboxylic acids were found and only a few peaks from the matrix were detected, which did not disturb the determination of the analytes. After the ozonation and chlorination of the raw water 1 (see Fig. 3B), the acids appeared at higher concentrations than obtained without water treatment, and new acids (mainly aromatic) were produced. According to the literature, natural organic matter or pollutants in raw water are oxidized

Table 2
Linearity, limits of detection, precision and mass values used for detection of the 35 carboxylic acids.

Carboxylic acid	Linear range (ng L^{-1})	LODs (ng L^{-1})	RSD (%) (n = 11)[a]		m/z		
			Within-day	Between-day	$[M]^+$	$[M-15]^+$	Additional ion(s)[b]
Acetic	10–8000	3	4.5	5.1	132	**117**	115
Propionic	40–8000	12	5.6	6.0	146	**131**	118
Butyric	25–8000	8	6.0	6.5	160	**145**	117
2-Methylbutyric	10–8000	3	5.3	6.0	174	**159**	146
Valeric	3–8000	1	5.5	5.8	174	**159**	117
Isovaleric	3–8000	1	4.0	5.1	174	**159**	117
Hexanoic	7–8000	2	6.0	6.5	188	**173**	117, 132
Octanoic	10–8000	3	5.1	5.9	216	**201**	117
Nonanoic	16–8000	5	5.6	6.1	230	**215**	117
Decanoic	16–8000	5	4.7	5.1	244	**229**	117
Dodecanoic	4–8000	1	5.1	5.8	272	**257**	117, 132
Myristic	7–8000	2	5.8	6.5	300	285	**117**
Palmitic	7–8000	2	5.5	6.2	328	313	**117**
Heptadecanoic	10–8000	3	5.8	6.5	342	327	**117**, 132
Stearic	10–8000	3	5.6	6.4	356	341	**117**, 132
Oleic	15–8000	4	6.0	6.5	354	339	**117**, 132
Linoleic	17–8000	5	6.0	6.6	352	**337**	117, 132
Oxalic	25–8000	8	4.0	5.5	234	219	**147**
Pyruvic	10–8000	3	4.0	5.2	232	217	**147**, 190
Glycolic	10–8000	3	4.5	5.8	220	205	**147**, 177
Succinic	50–8000	15	5.7	6.9	262	247	**147**
Fumaric	40–8000	12	4.2	5.4	260	245	**147**
Benzoic	2–8000	0.6	5.4	6.8	194	179	**105**
o-Toluic	10–8000	3	5.8	6.7	193	178	91, **119**
m-Toluic	7–8000	2	5.0	6.2	193	178	91, **119**
p-Toluic	7–8000	2	5.4	6.7	193	178	91, **119**
Phenylacetic	10–8000	3	5.0	5.5	208	193	91, **163**
Salicylic	35–8000	10	4.7	5.4	282	**267**	146
3-Hydroxybenzoic	15–8000	4	4.0	5.2	282	**268**	193
2-Nitrobenzoic	15–8000	4	6.0	6.8	239	224	**165**
3-Nitrobenzoic	20–8000	6	5.0	5.9	239	224	**165**
4-Nitrobenzoic	20–8000	6	4.5	5.4	239	224	**165**
3,4-Dihydroxybenzoic	45–8000	15	4.0	5.2	370	355	**193**
Phthalic	17–8000	5	6.0	6.9	310	295	**147**
1,2,3-Benzenetricarboxylic	45–8000	13	4.7	5.5	426	411	**93**, 147, 249

[a] Relative standard deviation. Values obtained for samples fortified with 100 ng L^{-1} of each carboxylic acid.
[b] The peaks used for quantification are boldfaced; m/z for IS (triphenylphosphate): 77, 325, **326**.

during ozonation, leading to the formation of by-products dominated by organic acids and aldehydes [6]. The latter are easily oxidized to corresponding carboxylic acids (e.g. acetic, oxalic, pyruvic) [2]. Benzoic acids, which are formed from the ozonation of natural aromatic organics such as humic and fulvic substances, have been identified as both initiators and promotors of OH radical chain reactions at low pH and have been found in considerable concentrations in ozonated water containing fulvic acid [2,6]. This is consistent with the results obtained from the analysis of the treated water 1 and 2 (see Table 3), where the carboxylic acids produced in the largest amount were phthalic (35–70 μg L^{-1}), oxalic (37–50 μg L^{-1}) and 1,2,3-benzenetricarboxylic (36–42 μg L^{-1}) followed by glycolic (22–53 μg L^{-1}), pyruvic (20–40 μg L^{-1}) and phenylacetic (9.5–15 μg L^{-1}), and other acids at lower concentrations. According to the data listed in Table 3, chlorine forms similar types of carboxylic acids but at lower concentrations and in lower numbers. Thus, oxalic, glycolic, pyruvic and phenylacetic acid were found at concentrations between 1.2 and 9.9 μg L^{-1}, which were ~8 times lower than those obtained in ozonated and chlorinated waters. Also, acetic, decanoic, 4-nitrobenzoic, phthalic and 1,2,3-benzenetricarboxylic acids were only found in water samples treated with ozone and chlorine, which demonstrates that these compounds were formed by the ozone treatment.

The described procedure was also tested in environmental water samples (including pond, river, rain and well) and swimming pool and wastewater. The results obtained were listed in Table 4. Short-chain carboxylic acids (acetic, propionic, butyric and 2-methylbutyric), oxalic, pyruvic, glycolic, benzoic, o-toluic, m-toluic and p-toluic acids were found in pond, river and well samples probably due to biodegradation of organic contaminants. Some of these acids also appear in rainwater (0.05–6.5 μg L^{-1}) due to anthropogenic and natural emissions. The greatest number of acids was found in wastewaters (especially in the wastewater 1), where they can be found as products of the anaerobic fermentation of organic material.

4. Conclusions

An analytical method for the determination of 35 carboxylic acids in water was presented in this paper. Among the target compounds, there were some (dicarboxylic, tricarboxylic and nitrobenzoic acids) that cannot be determined directly by GC–MS because of their low volatility, and a comprehensive study of different derivatisation options was conducted. Among the derivatising reagents evaluated, the best results were obtained with BSTFA in the presence of TMCS. The derivatising reaction was simplified through the use of a microwave oven that substantially reduces the reaction time (ca. 3 min) compared to conventional alternatives (viz. more than 50 min) [6,16,17]. With the use of a continuous SPE unit a significant increase in the selectivity and sensitivity of the method was observed. In this way, the detection limits (0.6×10^{-3} to 15×10^{-3} μg L^{-1}) were very much lower than those obtained in other GC–MS methods (0.3–150 μg L^{-1}) [4,8] or liquid chromatography–MS alternatives (0.2–4.1 μg L^{-1}) [21].

The method mainly focused on evaluating the effect of different disinfection treatments in raw water (with ozone and chlorine or chlorine). The results showed that disinfection in the presence of ozone increased the concentration of some carboxylic acids

Table 3
Carboxylic acids found in water before and after ozonation and/or chlorination (±SD, μg L^{-1}, $n = 3$).

Carboxylic acid	Raw water 1[a]	Raw water 1 treated[b,c]	Raw water 2[d]	Raw water 2 treated[b,e]	Raw water 3[a]	Raw water 3 treated[a,f]	Raw water 4[a]	Raw water 4 treated[a,f]
Acetic	1.3 ± 0.1	6.5 ± 0.4	<0.003	8.0 ± 0.5	<0.003	<0.003	<0.003	<0.003
Propionic	<0.012	<0.012	2.9 ± 0.2	3.8 ± 0.2	0.40 ± 0.02	0.51 ± 0.03	<0.012	<0.012
Butyric	<0.008	2.7 ± 0.2	<0.008	3.6 ± 0.3	<0.008	0.93 ± 0.06	<0.008	0.57 ± 0.04
2-Methylbutyric	<0.003	<0.003	<0.003	<0.003	<0.003	2.9 ± 0.2	<0.003	1.5 ± 0.1
Hexanoic	<0.002	<0.002	<0.002	<0.002	3.0 ± 0.2	3.4 ± 0.2	2.7 ± 0.2	3.1 ± 0.2
Decanoic	0.17 ± 0.01	0.45 ± 0.03	<0.005	0.32 ± 0.02	<0.005	<0.005	<0.005	<0.005
Dodecanoic	<0.001	0.28 ± 0.02	<0.001	<0.001	15 ± 1	8.5 ± 0.5	<0.001	<0.001
Oleic	<0.004	<0.004	<0.004	<0.004	0.70 ± 0.05	0.14 ± 0.01	<0.004	<0.004
Oxalic	9.8 ± 0.6	37 ± 2	17 ± 1	50 ± 3	3.3 ± 0.2	2.8 ± 0.2	2.9 ± 0.2	3.1 ± 0.2
Pyruvic	5.4 ± 0.3	20 ± 1	4.2 ± 0.3	40 ± 2	15 ± 1	9.5 ± 0.5	15 ± 1	9.9 ± 0.6
Glycolic	3.0 ± 0.2	22 ± 1	2.7 ± 0.2	53 ± 3	9.3 ± 0.6	9.6 ± 0.6	15 ± 1	9.1 ± 0.6
Benzoic	0.25 ± 0.02	4.3 ± 0.3	4.3 ± 0.3	13 ± 1	1.5 ± 0.1	2.8 ± 0.2	1.4 ± 0.1	2.9 ± 0.2
o-Toluic	1.3 ± 0.1	3.9 ± 0.3	<0.003	2.6 ± 0.2	1.4 ± 0.1	3.1 ± 0.2	<0.003	<0.003
m-Toluic	0.35 ± 0.03	1.4 ± 0.1	0.28 ± 0.02	1.4 ± 0.1	0.50 ± 0.03	0.80 ± 0.05	<0.002	<0.002
p-Toluic	0.40 ± 0.03	1.3 ± 0.1	0.37 ± 0.03	0.86 ± 0.06	0.80 ± 0.05	1.2 ± 0.1	<0.002	<0.002
Phenylacetic	<0.003	9.5 ± 0.6	<0.003	15 ± 1	1.5 ± 0.1	1.4 ± 0.1	0.90 ± 0.06	1.2 ± 0.1
Salicylic	0.40 ± 0.03	3.4 ± 0.2	<0.010	3.1 ± 0.2	0.95 ± 0.06	1.3 ± 0.1	<0.010	<0.010
3-Hydroxybenzoic	<0.004	1.5 ± 0.1	<0.004	2.3 ± 0.1	<0.004	1.4 ± 0.1	<0.004	1.5 ± 0.1
2-Nitrobenzoic	<0.004	1.2 ± 0.1	<0.004	1.3 ± 0.1	<0.004	0.29 ± 0.02	<0.004	0.23 ± 0.02
4-Nitrobenzoic	<0.006	0.98 ± 0.06	<0.006	<0.006	<0.006	<0.006	<0.006	<0.006
Phthalic	<0.005	35 ± 3	<0.005	70 ± 5	<0.005	<0.005	<0.005	<0.005
1,2,3-Benzenetricarboxylic	<0.013	36 ± 2	<0.013	42 ± 2	<0.013	<0.013	<0.013	<0.013

[a] Sample diluted 2 times with purified water.
[b] Water treated with ozone and chlorine.
[c] Sample diluted 5 times with purified water.
[d] Sample diluted 3 times with purified water.
[e] Sample diluted 10 times with purified water.
[f] Water treated with chlorine.

Table 4
Analysis of environmental water samples by the proposed GC–MS method (±SD, μg L^{-1}, $n = 3$).

Carboxylic acid	Pond 1[a]	Pond 2[a]	River 1[a]	River 2[b]	Rain 1	Rain 2	Well 1	Well 2	Swimming pool	Waste 1[c]	Waste 2
Acetic	<0.003	8.4 ± 0.4	3.2 ± 0.2	2.5 ± 0.2	2.6 ± 0.1	1.3 ± 0.1	<0.003	<0.003	<0.003	20 ± 1	2.4 ± 0.2
Propionic	4.3 ± 0.3	5.4 ± 0.3	1.3 ± 0.1	1.3 ± 0.1	0.91 ± 0.06	<0.012	6.4 ± 0.4	1.3 ± 0.1	<0.012	9.2 ± 0.6	0.45 ± 0.04
Butyric	0.60 ± 0.04	0.15 ± 0.01	0.63 ± 0.04	<0.008	0.09 ± 0.01	<0.008	0.16 ± 0.01	<0.008	0.15 ± 0.01	0.45 ± 0.03	1.5 ± 0.1
2-Methylbutyric	3.1 ± 0.2	0.58 ± 0.04	<0.003	<0.003	<0.003	<0.003	<0.003	<0.003	2.6 ± 0.2	<0.003	0.91 ± 0.07
Hexanoic	3.1 ± 0.2	<0.002	2.1 ± 0.2	<0.002	<0.002	<0.002	<0.002	<0.002	0.80 ± 0.05	<0.002	0.30 ± 0.02
Dodecanoic	5.4 ± 0.3	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.15 ± 0.01	<0.001
Oleic	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	1.5 ± 0.1	<0.004
Linoleic	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	1.4 ± 0.1	<0.005
Oxalic	9.9 ± 0.6	3.1 ± 0.2	6.4 ± 0.4	17 ± 1	3.0 ± 0.2	3.3 ± 0.2	<0.008	<0.008	<0.008	16 ± 1	<0.008
Pyruvic	5.9 ± 0.3	5.7 ± 0.3	9.7 ± 0.5	6.4 ± 0.4	6.5 ± 0.4	5.9 ± 0.3	<0.003	<0.003	0.31 ± 0.02	18 ± 1	<0.003
Glycolic	9.1 ± 0.5	9.0 ± 0.5	15 ± 1	9.0 ± 0.5	0.31 ± 0.02	<0.003	<0.003	<0.003	0.90 ± 0.05	30 ± 2	<0.003
Benzoic	1.4 ± 0.1	7.9 ± 0.5	8.5 ± 0.5	<0.0006	<0.0006	<0.0006	<0.0006	<0.0006	<0.0006	0.84 ± 0.06	<0.0006
o-Toluic	1.3 ± 0.1	<0.003	0.35 ± 0.03	<0.003	<0.003	<0.003	<0.003	0.40 ± 0.03	<0.003	0.34 ± 0.02	<0.003
m-Toluic	1.6 ± 0.1	<0.002	<0.002	0.27 ± 0.02	<0.002	<0.002	<0.002	<0.002	0.42 ± 0.03	<0.002	0.31 ± 0.02
p-Toluic	0.50 ± 0.04	<0.002	<0.002	0.80 ± 0.06	<0.002	<0.002	0.75 ± 0.06	<0.002	0.14 ± 0.01	<0.002	<0.002
Phenylacetic	<0.003	<0.003	<0.003	<0.003	<0.003	<0.003	<0.003	<0.003	<0.003	2.6 ± 0.2	1.9 ± 0.1
3-Hydroxybenzoic	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	<0.004	0.80 ± 0.05	0.56 ± 0.04
4-Nitrobenzoic	<0.006	<0.006	<0.006	<0.006	<0.006	<0.006	<0.006	<0.006	<0.006	0.26 ± 0.02	<0.006

[a] Sample diluted 2 times with purified water.
[b] Sample diluted 3 times with purified water.
[c] Sample diluted 4 times with purified water.

significantly (mainly oxalic, pyruvic, glycolic, phthalic and 1,2,3-benzenetricarboxylic acids) with respect to their concentration in raw water samples. However, when the treatment was carried out only by chlorination, the concentrations of carboxylic acids remained almost constant with respect to untreated water. Furthermore some acids were only found in the water samples treated with ozone. We also examined environmental, swimming pool and waste water and surprisingly all types of samples contained carboxylic acids; the number of acids increased drastically in wastewaters as products of the anaerobic fermentation of organic material.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.talanta.2012.02.022.

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