Article

Diallyldimethylammonium Chloride (DADMAC) in Water Treated with Poly-Diallyldimethylammonium Chloride (PDADMAC) by Reversed-Phase Ion-Pair Chromatography—Electrospray Ionization Mass Spectrometry

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Abstract: Poly-diallyldimethylammonium (PDADMAC) chloride is a flocculant agent extensively used in water clarification treatments. Commercial polyelectrolyte formulations often contain residual monomer (DADMAC), reaction by-products and other reactants as contaminants that could potentially affect human health. In the present study, we optimized an analytical method based on reversed-phase ion-pair chromatography coupled with mass spectrometry for quantifying ultra-trace levels of DADMAC, without preliminary treatments, in drinking water distributed by the Palermo aqueduct. The method was validated in terms of accuracy (recovery between 80 to 120%), precision (RSD < 10%), linearity range (from 0.5 to 15 µg/L), limit of quantification and limit of detection (LOQ 0.42 µg/L and LOD 0.12 µg/L). DADMAC was detected in all analysed water samples and the concentration ranged from 1.2 to 3.8 µg/L whit a mean value of 1.7 µg/L. To the best of our knowledge, this paper represents the first study concerning DADMAC concentration in water samples collected in Italy and, in this context, this paper can be considered very interesting when comparing future data on DADMAC monitoring in water. Moreover, this is one of a few cases where DADMAC was found in drinking water.

1. Introduction

Water is an essential element to life and is also considered the core of sustainable development, in order to improve several aspects, such as cultural, socio-economic and ecosystems and human health [1].

Indeed, water is vital for reducing the global burden of disease and improving the health, welfare and productivity of all people and, for these reasons, it is necessary to provide solutions to reduce or remove solid materials, chemical compounds and microorganisms (bacteria, viruses, etc.) to ensure the best quality conditions, not only for drinking water but for all necessary uses in human activities [2].

In this context, many biological, chemical and physical methods have been investigated and developed to improve water quality ang safety. For example, biological water treatment involves aerobic, anaerobic and anoxic process stages, each with different purposes [3]. During water treatments [4], different chemical or photochemical processes can be used, for example, Fenton or photo-Fenton reactions and physical mechanisms which generally involve separation procedures [5]. The initial stage (generally clarification) involves the use of coagulants and flocculants which accelerate the settling of suspended particles. In water

treatment, one of the most important physical procedures to reduce materials in suspension is flocculation and, in this context, one of most important chemical compounds used for this issue is poly-diallyldimethylammonium chloride (PDADMAC).

PDADMAC is one of the most important water-soluble synthetic polyelectrolytes, with a high cationic charge density and, generally, the best flocculation results when used in a concentration between 0.01 and 0.05%. Moreover, considering that PDADMAC is employed at approximatively neutral pH, only slight adjustments of this parameter may be needed during treatments. In detail, since the greater part of suspended and colloidal solids present in water is usually negatively charged [6], PDADMAC is extensively used as flocculant in water clarification treatments [7]. The flocculation processes carried out by PDADMAC are generally considered inexpensive, thanks to its relatively easy operation and the high quality of sludge produced [8]. One of the advantages of using PDADMAC in water treatment intended for human consumption is that, as already mentioned, it does not require a limited pH range, as is necessary in the case of using aluminum salts (or iron), for which it is necessary to adjust the pH of the water to be treated to favor the formation of aluminum hydroxide which, for non-optimal pH values, does not form; furthermore, the sludge produced during the treatments does not contain metal which could be solubilized by rainwater.

The use of this compound is very common in different states; indeed, the PDADMAC maximum concentration admitted for drinking water treatment has been regulated, and is generally in the range from 10 to 25 mg/L [9]. Unfortunately, the regulation limits are not unique; for example, the United State of America (USA), allows residue levels in drinking water below 50 µg/L [10]. On the other hand, up to now there is no regulation on the concentrations of the corresponding monomer, diallyldimethylammonium chloride (DADMAC), which could be present in drinking water, becoming a potential emerging contaminant that potentially effects human health [11]. In the treated water, the monomer can have various origins, for example, commercial polyelectrolyte formulations often contain monomers as residual, or monomers can be release as reaction by-products, along with other degradation reactions. For instance, poly-DADMAC residues in treated water are contaminants as they react with chlorine to produce a carcinogenic compound and, moreover, the polymer of PDADMAC can degraded by biological, chemical and photochemical reactions. In detail, PDADMAC can partially be oxidized to NO_3^- and, successively, NO_3^- can be degraded or transformed during the UV/chlorine treatment [12]. Besides, in the literature it was reported that polyamine polymer released simple amine molecules owing to the opening of the polyamine polymer ring and the separation of the $-N(CH_3)_2$ group during the UV/chlorine treatment [13]. Moreover, the literature also reports that commercial cationic polyelectrolytes [14] are constituted by the polymer and low levels of DADMAC (5%), which could react with the added chemicals (e.g., chlorine) and/or the organic compounds, forming new substances or by-products which can be more toxic or dangerous compared to the primary reagents [12,13] and, once in the environment, DADMAC is predicted to stay in water and soil for less than 60 days [14].

Several researchers supposed that DADMAC is a polymer resistant to chlorine; however, the American Water Works Association (AWWA) established that the concentration of monomer (DADMAC) in commercial polymer should be less than 5 ppm, while in the USA the maximum admitted concentration is 2 ppm [9].

Few data are reported in the literature regarding the toxicity of DADMAC [15], but since it is considered as an emerging contaminant of drinking water, it is necessary to monitor its concentration in water for human consumption, especially considering the constant exposure. In this regard, the main analytical methods for the determination of these compounds, such as direct determination by spectroscopy techniques, cannot be considered as appropriate methods due to their limited sensitivity. For instance, analytical methods to quantify cationic surfactants (i.e., quaternary ammonium compounds) generally use spectrophotometric techniques, that exploit the reaction of the analyte with an anionic dye [16]. However, these methods are inappropriate for monitoring DADMAC in drinking

water at trace levels (µg/L) and often spectrophotometric techniques are unreliable due to interfering substances. Other methods, that are based on indirect titration or back titration techniques [17], are not able to detect analyte at trace level, especially in the presence of interfering substances. Therefore, it is possible to assert that these methods show some limitations in terms of detection limits, reproducibility, precision, linearity and strength. Actually, a few studies report the determination of quaternary ammonium salts in different matrices by using hyphenated techniques [18–20]. In this regard, the use of hyphenated techniques, such as chromatography coupled with mass spectrometry, that are also able to remove or reduce interfering substances during analyte separation and determination, appear to be the appropriate analytical techniques for the determination of compounds at trace levels. Moreover, this type of hyphenated technique, thank to separation science, reducing the matrix effect, can be considered as very robust.

Although the use of selected hyphenated mass spectrometry techniques has been available for many years, research concerning the quantification of most of the chemical substances used for water purification and, more importantly, those formed during treatments, are not yet relevant.

However, in consideration of the ever more stringent regulations on substances and new emerging pollutants in water, such as the European watch list directive (EU WL FRAMEWARK), it is reasonable to suppose that methods and data relating to determination of these substances and by-products will have a relevant impact on science and the community. For example, several biocides such as Malachite Green dye, which is widely used in the aquaculture industry to control protozoan infections and fungal attacks, and is also used in textile industries and food, due to not being a regulated and monitored compound, was detected in ground and surface water due to the discharge of untreated wastewater from industry [21]. Moreover, for many years, there has been a growing concern over the fate of poly-DADMAC within the water treatment process and its presence in the environment at large, and one reason for this is its potential to form N-nitro-sodimethylamine (NDMA) [22].

In order to investigate the presence of DADMAC in drinking water, in the present study the authors optimized a reversed-phase ion-pair chromatography technique coupled with mass spectrometry (with electrospray ionization (ESI-MS)) method to quantify trace levels of DADMAC, without preliminary treatments, in drinking water distributed by a Palermo aqueduct company.

To the best of our knowledge, this paper represents the first study concerning DADMAC concentration in water samples collected in Italy.

2. Materials and Methods

Trace analysis presents critical issues due to analytical blank problems [23–25]. For this purpose, all the materials (instruments, glassware, etc.) used during the analysis were well washed with a solution (10%) of HNO_3 and, subsequently, rinsed with milli-Q water and RP grade acetone. Moreover, these were heated at 120 °C for one night. Different glassware and syringes were used to inject calibration samples and quality check solutions to avoid possible cross contamination.

Isotopically labelled compounds, used as internal standards (IS), were chosen according to the chemical properties and similar retention times of the analyte in order to choose a compound with similar chemical characteristics to the target compound. For this reason, Chlormequat—1,1,2,2-d4 chloride was elected as internal standard for this analysis.

Analyte standard of DADMAC and Chlormequat—1,1,2,2-d4 chloride (internal standard) were obtained from Sigma Aldrich (Milano, Italy). The purity grade of all standards was always above 95%. Stock standard solution of DADMAC (50 mg/L) was prepared in Milli Q water and the working solutions used for calibration (0.5, 1.0, 1.5, 2.0, 5.0,10.0, 15.0 µg/L) and quality check were daily prepared by serial dilutions using class A volumetric flasks. All solutions were stored at 4 °C. The molecular structures of DADMAC and Chlormequat are reported in Figure 1.
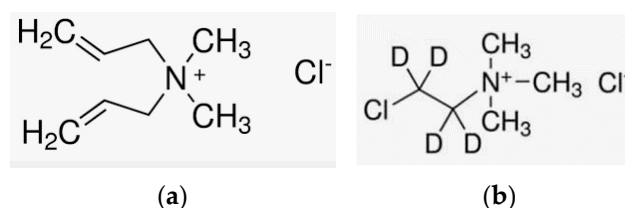
Figure 1. Molecular structures of diallyldimethylammonium chloride (**a**) and Chlormequat—1,1,2,2-d4 chloride (**b**).

HPLC grade acetonitrile and formic acid were purchased from J. T. Baker, and ammonium formate HPLC 99% grade was obtained from Alfa Aesar. Ultra-pure water was prepared using a Milli-Q Ultrapure System (NANO pure Diamond—Bearnstead). All the vessels and flasks were cleaned before use by rinsing three times with hot HNO_3 (2%) and rewashed three times with Milli Q water.

2.1. Method Validation, Quality Assurance/Quality Control (QA/QC)

The analytical method was validated referring to acceptance criteria according to UNI EN ISO17025 and the European SANTE guide [26,27].

Chlormequat—1,1,2,2-d4 chloride was added to all standard and samples, as internal standard, to monitor the analysis procedures and, moreover, procedural blanks were periodically analysed.

The linearity of the method was investigated by analyzing standard solutions at seven different concentration levels between 0.5 and 15 µg/L, and good linearity was observed (determination coefficient $R^2 > 0.997$ based on relative responses, analyte peak area/labelled internal standard peak area), indicating good performance of the analytical method optimized in this work.

Accuracy (expressed as percentage recovery) was evaluated by analyzing six replicate spiked samples at 10 µg/L and the recovery ranged from 80 to 120%.

Precision (expressed in terms of repeatability as relative standard deviation as a percentage) was evaluated by analyzing six spiked samples carried out on the same day to also determine the run-to-run instrumental analysis drifting. The relative standard deviation (RSD) was 6.6%. By considering low repeatability (<10%) and good accuracy, the matrix effect was considered negligible.

As reported in other research [28,29], the detection limit (LOD) and the quantification limit (LOQ) were determined as three times and ten times the noise level of the chromatogram in blank samples (IUPAC Criterion) with a result of 0.12 µg/L and 0.42 µg/L respectively.

Quality control samples and spiked samples, to study accuracy and repeatability, were subjected to the same procedures as the samples.

To evaluate the precision of each analysis, three analyses of the same sample were carried out. The relative standard deviations of the replicates were in the range 2–10%, which can be considered satisfactory for determinations at low concentrations (ppb or sub ppb level). The spiked samples were treated using a similar procedure to the other samples, in order to mimic the entire process. All analyses were performed by injecting a volume of 25 µL of sample or standard solutions by using a syringe of 50 µL in 20 µL of certified loop. Quality control solutions were analysed at the beginning, after every ten samples and at the end of the batch analyses. The entire method was subjected to validation and quality control procedures.

2.2. Instrumentation and Analyses

The analyses were developed by means of High Resolution Mass Spectrometry (HRMS) coupled with HPLC separation using a Thermo Q-extractive mass spectrometer and a Dionex Ultimate 3000 Chromatographic System. Considering the chemical-physical characteristics of the analyte, we opted for the H-ESI (Heated Ion-Electrospray) ion source.

The experimental operating conditions were optimized by standard infusion to detect the best ionization conditions and fragmentation. The final tuned source values and other instrumental parameters are briefly summarized in Table 1.

Table 1. HPLC-MS instrumental parameters.

Parameter	Detail
Column	Atlantis® dC18 100 mm × 2.1 mm × 3 μm
Column temperature (°C)	30
Eluent	45:55 acetonitrile/water formate buffer (pH 3.75)
Flow rate (mL/min)	0.4 (10 min)
Injected volume (μL)	20
Polarity	Positive
H-ESI Capillary Temperature (°C)	350
H-ESI capillary voltage (kV)	3.5
Ion transfer tube temperature (°C)	250
Sheath Gas flow (a.u.)	60
Auxiliary Gas flow (a.u.)	35
S-lens (eV)	70
Normalised collision energy NCE (eV)	65
Scan mass-range (m/z)	50–200

By considering data reported in the literature [15], the preliminary evaluation of the most appropriate chromatographic column for analyte separation led to the choice of an Atlantis dC18 100 mm × 2.1 mm × 3 μm column under the following chromatographic conditions: column temperature maintained at 30 °C, using an elution solvent mixture (isocratic) at 45:55 v/v% of acetonitrile/formic acid-ammonium formate (50 mM) aqueous solution (pH 3.75), at flow rate of 0.4 mL/min. In these conditions diallyldimethylammonium chloride (DADMAC) elutes at 0.87 min, while internal standard (Chlormequat—1,1,2,2-d$_4$ chloride) elutes at 0.57 min, as shown in the chromatogram reported in Figure 2.
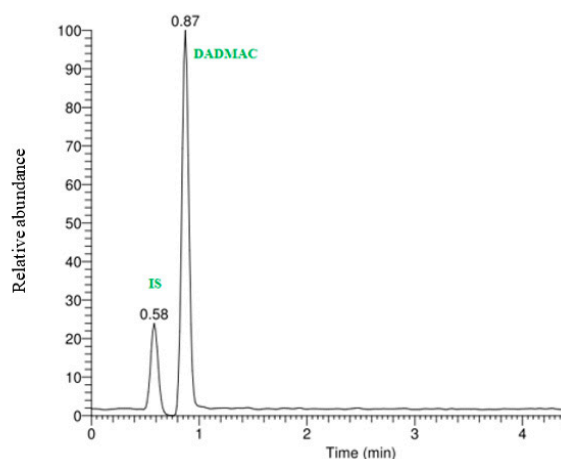

Figure 2. Total ion chromatogram of DADMAC and the internal standard (IS) Chlormequat—1,1,2,2-d4.

By considering the retention times of analyte, this analysis can be classified as fast in its detection of contaminant in treated drinking water.

In order to obtain most of the information and maximize both selectivity and sensitivity, the analysis was developed in MS/MS mode using the embedded HCD cell. This cell produces fragmentations in MS/MS mode with energies comparable to those accessible with a triple quadrupole, obtaining MS/MS spectra at high resolution (R = 70,000 and with high mass accuracy $\leq$ 5 ppm). This is a considerable advantage in ultra trace analysis. The parent ions' fragmentation of DADMAC (m/z 126.1278) and of the IS (m/z 126.0983) in the

mass range 20 m/z to 200 m/z were followed (Figure 3). Collision induced dissociation (CID) optimization led to a CID cell value of 65 eV, while for quantitative purposes the product ions selected were at m/z 84.0812 and m/z 70.0657 for DADMAC and m/z 67.0254 for IS.
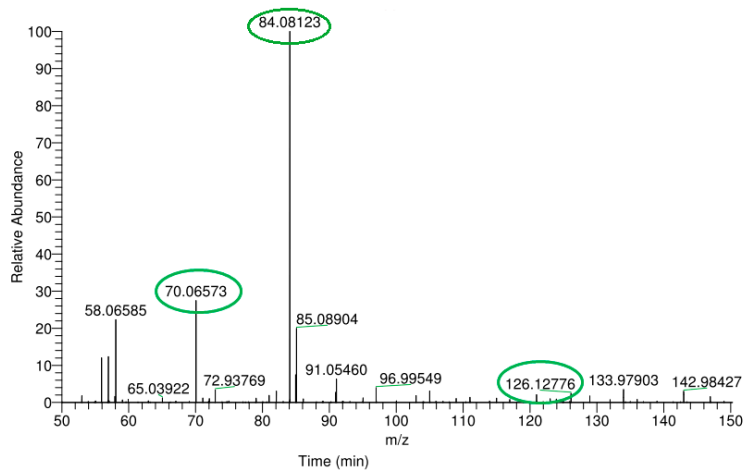

Figure 3. MS/MS spectra of DADMAC.

Analyte was identified both when comparing the retention times (RT) with standard RT and using double qualifier ions in accordance whit SANTE guidelines.

Figures 1 and 2 show the total ion chromatogram of DADMAC and of the internal standard (Chlormequat—1,1,2,2—d$_4$) and the MS/MS spectra for DADMAC, respectively.

Sample quantification was performed by means of isotope dilution in order to achieve a higher accuracy level. Sample concentration values were calculated by interpolation of the analytic signal on a calibration curve obtained from the linear regression of calibration point results in the range 0.5–15 µg/L. A representative graph of the calibration curve is shown in Figure 4.
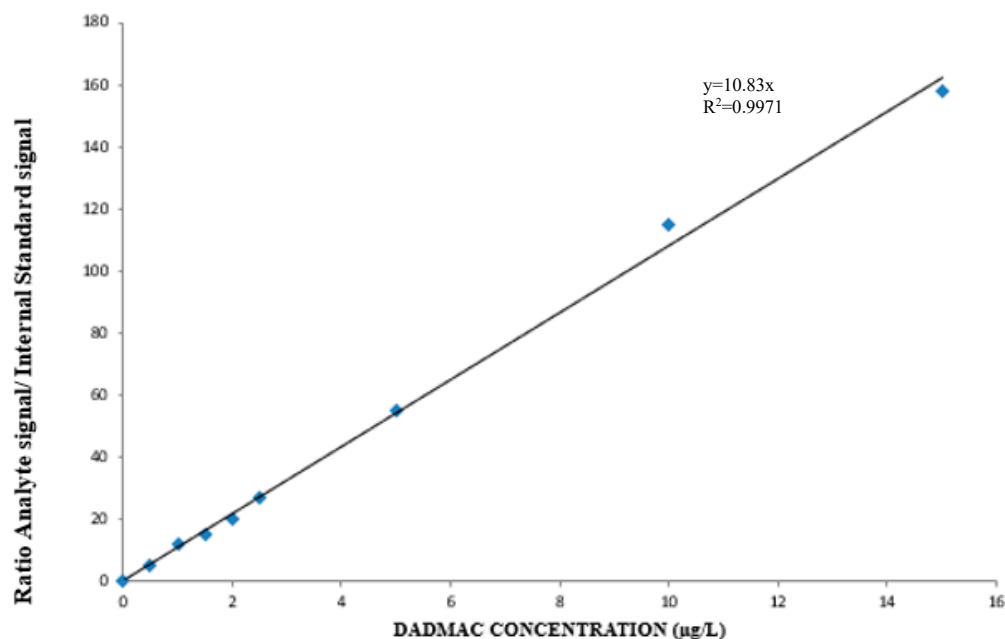

Figure 4. Calibration curve for DADMAC in the range from 0.5 to 15 µg/L.

2.3. Sample Collections

The water samples used in this research were provided by a waterworks company in Palermo (Italy) which manages the integrated water cycle. Samples were collected from the Risalaimi treatment plant that is the source of drinking water for the Sicilian area. Risalaimi is a rural area located near the municipality of Misilmeri, situated 15 km from Palermo city and, in this context, cross contamination can be considered.

The Palermo aqueduct is using PDADMAC in an experimental phase, in order to promote sludge dehydration, obtaining excellent results. The water derived from the sludge thickening process is added to the raw water to be treated and this could lead to the possible presence of monomer traces in the water supplied to the users. Sixteen water samples were collected in 0.250 L of polyethylene bottles and filtered through a 0.22 μm filter. Samples were collected during 16 consecutive days in the period between the end of January and the beginning of February with a sampling temperature ranging from 11.0 to 14.4 °C, with an average of 12.5 °C, and pH ranging from 7.4 to 8.0. After sampling, samples were immediately transported at a refrigerated temperature of 8 °C and, in order to avoid adsorption and degradation of the analyte, all samples were stored in pre-cleaned polyethylene bottles at 4 °C until analysis. Prior to injection to the HPLC, all samples and standard solutions were spiked with a known quantity of internal standard to carry out accurate quantitative analyses.

3. Results

In the present study, 16 drinking water samples obtained from the aqueduct of Palermo in Sicily were analyzed by means of High-Resolution Mass Spectrometry and a Heated Ion-Electrospray ion source to investigate the occurrence of DADMAC. Our findings show that the method developed allows the determination of trace levels (LOQ = 0.42 μg/L) of DADMAC in real water samples. DADMAC was detected in 100% of the analysed water samples (see Table 2) and the concentration ranged from 1.2 to 3.8 μg/L (average of three independent measurements) with a mean value of 1.7 μg/L.

Table 2. DADMAC concentrations (mean of three analyses) and average about water analyzed samples.

Sample N°	DADMAC (μg/L)
1	2.6
2	1.3
3	3.8
4	1.3
5	1.7
6	1.4
7	1.6
8	1.5
9	1.9
10	1.7
11	1.2
12	1.5
13	1.2
14	1.8
15	1.2
16	1.4
MEAN	1.7

In Table 2 the concentration and average value of DADMAC are reported for the 16 analysed samples.

In order to detect relevant statistical aspects, such as normal distribution of obtained results, a statistical analysis was performed. In this regard, free software for scientific data analysis, PAST 4.0, was used and in Table 3 results for the obtained data from the performed analyses are reported.

Table 3. Statistical summary concerning DADMAC concentration in water samples.

Parameter	Data
N	16
Min	1.2
Max	3.8
Sum	27.1
Mean	1.7
Std. error	0.17
Variance	0.44
Stand. dev	0.66
Median	1.5
25 prcntil	1.3
75 prcntil	1.775
Skewness	2.5
Kurtosis	6.9
Geom. mean	1.6
Coeff. var	39.2
95% conf. interval:	(1.3–2.0)

By considering data reported in Tables 2 and 3, it is possible to assert that DADMAC concentration does not show a normal Gaussian distribution, as reported by a ranged value of 95% confidence interval. In detail, DADMAC concentrations in three samples are minor than the lower limit of 1.3 ug/L, while two samples are more than the upper limit of the 2.0 ug/L for the confidence interval. By considering that, during water purification processes, the same concentrations of PDADMAC were added to water and, during flocculation procedures, climatic condition were similar, it possible to suppose that the DADMAC concentration released in water depends on several chemical physical properties that are not, however, the object of this study.

To try to identify the origin of DADMAC in the analyzed water samples, we had previously analyzed, after appropriate dilutions, the solution of the commercial polymer used in the treatment of the aforementioned waters, and, the concentration result for DADMAC in the polymer of PDADMAC was 150 µg/kg. Considering that the commercially used solution contains about 20% of PADADMAC, we can certainly state that the commercial product complies with current legislation (<5000 µg/kg) [30]. Taking into account the concentration of monomer and the active ingredient percentage in the commercial solution, and that in the water treatment phase the polymer was used at a concentration of 5.4 ppm (of active principle), if the monomer was not retained by the sludge its concentration in the waters should be around 4 µg/L. From the concentrations of DADMAC determined (meanly 1.7 µg/L) in the treated water, we can state that about 50% of the monomer of the commercial product is retained by the sludge, this also assuming that the polymer has not undergone decomposition.

From the analysis of the scarce literature data, we can state that the concentrations of DADMAC in the Palermo treated water are lower than those determined by Fen Jin et al. [15] in waters distributed in Tianjin in the north of China, and in the waters undergoing treatment in the USA, where the monomer residual amounted to around 50 µg/L. A very different case is represented by the treatment plant in Barcelona (Spain), in which the average concentration of DADMAC was 0.4 µg/L [31].

To the best of our knowledge, this is one of the few cases [15,31] where DADMAC was found in drinking water and, considering the extensive use of Poly-diallyldimethylammonium chloride (PDADMAC) for water treatment, it is important to investigate the concentration of Diallyldimethylammonium chloride in municipal water, especially for drinking water supplies.

Unfortunately, due to limited information on the toxicity of DADMAC and poly-DADMAC, a full chemical review of these chemicals is not possible. Indeed, in the literature, some papers report the determination of poly-DADMAC in different aqueous matrices,

such as river water [32] and drinking water [33], but unfortunately very few works are focused on the determination of the monomer.

However, by considering that, thanks to sensitive and selective of LC-MS/MS techniques, the DADMAC was detected in 100% of the analysed samples from the Palermo city water treatment plan, it is foreseen that determination of DADMAC in drinking water will become a very important issue.

4. Conclusions

An analytical method was developed to determine DADMAC in 16 water samples. The DADMAC proved to be effective in the field tests carried out by the Palermo Municipal Treatment Plant. By the proposed method, a low quantification limit was achieved for the determination of DADMAC by direct analysis without any pre-treatment, pre-concentration or clean-up step in the drinking of samples.

The liquid chromatography coupled with mass spectrometry used for the analysis of DADMAC in treated water showed a sufficient sensitivity and specificity to allow the quantification of the analyte at the concentrations compatible with human consumption of drinking water. The validated method was able to identify and quantify DADMAC at concentration levels ranging from 0.42 µg/L to 15.0 µg/L. This method is advantageous taking in to account reduced analysis time and the lack of water samples' clean-up/enrichment steps. The direct analysis of the samples limits the possibility of analyte loss and contamination.

The data obtained show that the concentration of DADMAC in Palermo drinking water is, on average, lower than those found in the literature, except in the case of the Barcelona drinking waters.

Although at present in the literature scarce data are reported to compare the levels of DADMAC in drinking water, it is to be hoped that several researchers will start reporting data on the concentration of this analyte in drinking water in order to provide data to the community to evaluate and compare analyses of drinking water in order to ensure a good quality standard level.

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