

PAPER

View Article Online
View Journal | View Issue



Cite this: *Environ. Sci.: Processes Impacts*, 2025, 27, 412

Mitigating matrix effects in oil and gas wastewater analysis: LC-MS/MS method for ethanolamines†

Glen Andrew D. de Vera,^a Loredana Caldiero,^b Giovanni Conte^b and Desirée L. Plata^a

The high salinity and organic content in oil and gas wastewaters can cause ion suppression during liquid chromatography mass spectrometry (LC/MS) analysis, diminishing the sensitivity and accuracy of measurements in available methods. This suppression is severe for low molecular weight organic compounds such as ethanolamines (e.g., monoethanolamine (MEA), diethanolamine (DEA), triethanolamine (TEA), *N*-methyldiethanolamine (MDEA), and *N,N*-ethyldiethanolamine (EDEA)). Here, we deployed solid phase extraction (SPE), mixed-mode LC, triple quadrupole MS with positive electrospray ionization (ESI), and a suite of stable isotope standards (*i.e.*, one per target compound) to correct for ion suppression by salts and organic matter, SPE losses, and instrument variability. The method was evaluated in produced water samples from Italy (NaCl salinity from 8110–18 100 mg L⁻¹; diesel range organic compounds ranging from 5.1–7.9 mg L⁻¹). After correcting for matrix effects, ethanolamines in produced water samples were quantified. The first batch of samples (March 2019) had 37–646 µg L⁻¹ total ethanolamines. The second batch of samples (September 2019) had greater ethanolamine content of 77–3976 µg L⁻¹ which was attributed to a reduced water cut during oil production, enhancing the proportionate abundance of these compounds in the aqueous phase. In all samples, DEA and MEA were the dominant ethanolamine species. Possible sources (e.g., corrosion inhibitor and biotransformation) and natural attenuation potential during storage (e.g., at different temperatures, acidification, and addition of sodium azide) were investigated. The developed analytical method enables further investigation of the fate of low molecular weight organic additives in oil and gas development and provides an enhanced ability to evaluate risks associated with chemical release to the environment.

Received 23rd November 2024
Accepted 24th December 2024

DOI: 10.1039/d4em00716f

rsc.li/espi

Environmental significance

Oil and gas wastewaters pose a threat to drinking water sources due to presence of hazardous chemicals. Of particular concern are ethanolamines, which are extensively used within the industry and have the potential for leaching into the environment. The lack of standardized methods for measuring ethanolamines exacerbates the challenge of assessing and mitigating these risks. This study developed a robust LCMS method for accurately quantifying ethanolamines in produced waters. It comprehensively addressed matrix interferences through the use of solid-phase extraction and compound-specific isotopes. Finally, this study highlights inaccuracies in semi-quantitative approaches that lack authentic standards and careful matrix analysis; this has broad implications to the field.

Introduction

Wastewaters from oil and gas industries including produced waters – water brought to the surface during extraction – pose a significant risk of contaminating drinking water sources due to the various chemicals involved throughout the extraction process. These chemicals, which include a complex mixture of

hydrocarbons, volatile organic compounds, and other halogenated byproducts, among others,^{1,2} can be released from spills from pipelines or during transport, leaks from wastewater storage ponds/facilities, or subsurface migration from fluids through failed well casings.³ Several compounds in this wastewater are mobile in the environment and capable of leaching into the ground and fresh water sources, negatively impacting water quality and ecosystems. Understanding and addressing potential drinking water contamination would require rigorous analysis and monitoring of oil and gas wastewaters, but several challenges impede comprehensive evaluation of these complex mixtures.

Quantitative analysis of individual organic compounds in oil and gas wastewaters are scarce due to instrumental limitations caused by the variable nature of the water samples and wide range of hydrogeochemical parameters. Particularly for liquid

^aMassachusetts Institute of Technology, Department of Civil and Environmental Engineering, Parsons Laboratory, 15 Vassar Street, Cambridge, Massachusetts 02139, USA. E-mail: gdevera@mit.edu

^bEni SpA – Upstream Technical Services, Via F. Maritano, 26 – 20097 San Donato M.se, MI, Italy

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d4em00716f>





Table 1 Compound-dependent parameters for analysis of 5 ethanolamines and 5 isotope-labelled standards by LC-MS/MS^a

Unlabelled (labelled) structure	Compound name	Precursor ion, <i>m/z</i>	Quantifier (qualifier) ion, <i>m/z</i>	<i>t_R</i> , min	Collision energy, eV	MDL, ^b µg L ⁻¹
	Ethanolamine (MEA) <i>d</i> ₄ -Ethanolamine (<i>d</i> ₄ -MEA)	62.1 66.1	45 (44.2) 48.1 (30.1)	5.4 5.4	9 (9) 9 (33)	0.1
	Diethanolamine (DEA) <i>d</i> ₈ -Diethanolamine (<i>d</i> ₈ -DEA)	106.1 114.14	88 (69.9) 95.9 (78)	4.6 4.6	9 (13) 9 (13)	0.1
	<i>N</i> -Methyldiethanolamine (MDEA) ¹³ C ₄ - <i>N</i> -Methyldiethanolamine (¹³ C ₄ -MDEA)	120.1 124.1	101.9 (58.1) 105.9 (60)	2.9 2.9	13 (21) 13 (21)	0.1
	<i>N,N</i> -Ethyldiethanolamine (EDEA) ¹³ C ₄ - <i>N</i> -Ethyldiethanolamine (¹³ C ₄ -EDEA)	134.1 138.12	115.9 (72, 44) 74 (46)	2.2 2.2	13 (21, 25) 17 (25)	0.2
	Triethanolamine (TEA) ¹³ C ₆ -Triethanolamine (¹³ C ₆ -TEA)	150.1 156.15	132 (88, 70) 138.1 (47.2)	3.3 3.3	13 (18, 21) 12 (28)	0.2

^a In parentheses are isotope labelled atoms, column: Acclaim Trinity P1. ^b MDL = standard deviation (*n* = 7, 1 µg L⁻¹) × Student's *t*-value at 99% confidence interval.

chromatography and mass spectrometry (LC-MS), the high salinity and organic matter content in oil and gas wastewaters can cause ion suppression with electrospray ionization. Such effect can be caused by a (a) decrease of the evaporation efficiency of the analyte due to increase in viscosity and surface tension of droplets caused by the sample matrix, (b) coprecipitation of analytes with non-volatile materials (*e.g.*, macromolecules), (c) competition between analytes and interfering compounds for ionization energy that impacts efficiency of the technique, and (d) neutralization in the gas phase.^{4,5} All of these can affect the amount of charged ion in the gas phase ultimately reaching the detector. The matrix components, especially salts, can also accumulate in the capillary, increasing electric resistance and preventing ions from transfer into the MS. These processes can diminish accuracy and sensitivity of the method (*e.g.*, non-detection of an analyte causing false negatives when ions are suppressed). Thus, a robust method that can correct for these matrix effects is needed for oil and gas wastewaters to be able to assess the risks of organic chemicals that can be inadvertently transported to groundwater sources.⁶ The method is particularly important for compounds that can partition easily from soil to water and readily transported to downstream drinking water sources.

Ethanolamines (Table 1) comprise a group of compounds that fall under this category. In oil and gas operations, these may be components of corrosion inhibitors, breakers, cross-linkers, or complexing agents of Zr(IV) to control the rate and timing of guar gum crosslinking,⁷ or components in the removal of acid gases (*e.g.*, H₂S)⁸ and CO₂ capture⁹ during refining. These compounds are miscible in water, not volatile (low vapor pressures of 0.4 torr (for monoethanolamine) and <0.01 torr at 20 °C for di- and tri-ethanolamine),¹⁰ and do not adsorb significantly in organic carbon in soil (low organic carbon/water partition coefficient, $K_{oc} = \log -0.2$ to -0.3 for monoethanolamine and diethanolamine).¹¹ These properties increase ethanolamines' likelihood of leaching and subsequent groundwater contamination. Considering the possible carcinogenic effects, as well as the potential for ethanolamine exposure to cause respiratory irritation, liver and kidney damage,^{12–14} it is important to have methods for accurate measurements of these compounds to better assess health and environmental risks. Ethanolamines can also act as precursors to other hazardous compounds, such as nitrosamines, which may form during water disinfection.^{15,16} As highlighted by the US Environmental Protection Agency,¹³ there is no standard method for ethanolamines despite their extensive use in the oil and gas industry. Methods that are available in the literature (*e.g.*, Dionex Thermo Fisher Note 271,¹⁷ ASTM D-7599 (ref. 18)) were developed using surface water samples and are not directly transferrable to oil and gas wastewater matrices. Matrix effects could result from the samples' high salinities (2000–30 000 mg L^{−1}), total suspended solids (TSS ~ 200 mg L^{−1}), petroleum hydrocarbon residues (around 60 mg L^{−1} on average, defined as nC_{10} – nC_{40} or "C10–C40" hydrocarbons), and production chemical additives (*e.g.*, corrosion inhibitors, scale inhibitors, and biocides). These matrix components could give rise to interferences leading to both false positive and false

negative results. The inaccurate determination of ethanolamine concentrations may then lead to misplaced regulatory actions if the method does not correct for matrix interferences.

This work presents a robust LC-MS/MS method that accurately measures ethanolamines such as monoethanolamine (MEA), diethanolamine (DEA), methyldiethanolamine (MDEA), ethyldiethanolamine (EDEA), and triethanolamine (TEA) in various produced waters from an Italian oil and gas extraction facility. We evaluated interferences across a range of real produced water chemistries and identified ways to correct for these interferences by desalting *via* solid-phase extraction and use of multiple compound-specific isotopic standards in both synthetic and real water samples. Using the method, matrix effects were negligible. The method in this study was compared to the method proposed by a regional authority for the analysis of ethanolamines (Eni SpA, personal communication, March 2019) to highlight the importance of accounting for matrix interferences in implementing methods that have regulatory implications.

Experimental methods

Reagents and materials

The reagents and materials used for sample preparation and LC-MS analysis are described in Text S1 (ESI†). Methanol, acetonitrile, ammonium formate, formic acid, sodium hydroxide, unlabeled and labelled ethanolamine standards and other chemicals used for extraction and matrix effects evaluation (salts, Aldrich humic acid) were of reagent grade or higher. Solutions were prepared using Milli-Q ultrapure water (18.2 MΩ cm, Millipore).

Water samples. Produced water samples were collected by Eni SpA at various locations (oil separator, stock tank, or water reinjection wells) to represent varied characteristics of produced waters in the plant (Text S2 and Table S1†). The produced water samples were collected in 250 mL amber bottles and shipped under cold storage to MIT in March 2019. These were referred to as PW1, PW2, PW3, and PW4 (PW-Mar samples) and were used for method development and assessment of matrix effects. Characterization of the water samples were done at MIT and Eni SpA. Major cations, anions and metals were analyzed by inductively coupled plasma mass spectrometry and ion chromatography (Dionex Integrion, Thermo Fisher Scientific). Diesel range organic (DRO) compounds were quantified using gas chromatography with flame ionization detection (Agilent 7890B) following liquid–liquid dichloromethane extraction.¹⁹ Another set of samples were collected in September 2019 to capture temporal variations of ethanolamines in the oil and gas facility.

Matrix effects investigation. The high salinity and bulk organic matter content in produced water samples can interfere with ethanolamine quantification. To systematically evaluate matrix interferences from inorganic salts and bulk organic matter, synthetic brine and humic acid solutions were prepared. The salinity of the synthetic brine was adjusted from 0–25 520 mg L^{−1} salinity (Table S2†) by diluting stock solutions of sodium chloride (50 000 mg L^{−1}), sodium bromide (2500 mg L^{−1}), sodium sulfate (5000 mg L^{−1}), and calcium carbonate (5000 mg L^{−1}). A humic acid solution (Aldrich, WI, USA) was prepared to achieve total organic carbon (TOC)



concentrations of 0–295 mg_C L⁻¹, simulating organic matter levels found in produced waters.²⁰ Each solution was spiked with ethanolamine mixture (20 µg L⁻¹ for each compound). Another set of samples was generated from the bulk organic matter extracted from PW-March samples (following solid-phase extraction, SPE). These extracts were spiked with isotopically labeled ethanolamines (10 µg L⁻¹ per compound) to assess suppression caused by co-extracted organic compounds (Table S3†).

Sample preservation. The stability of ethanolamines were investigated to determine appropriate storage conditions for samples (Table S4†) and examine the role of potential biodegradation. A closed bottle test (using 60 mL samples (PW1 and PW2 March samples) and spiked with 20 µg L⁻¹ ethanolamines) was conducted at different temperatures (20, 4, and -10 °C), lowered pH (pH 2), and with sodium azide (133 mg L⁻¹). No additional seed bacteria were added for this test. Thus, if ethanolamines decayed, it could be caused by indigenous bacteria that may be present in the samples and were not sterilized by temperature treatment or chemical additives. Samples (2.5 mL aliquot diluted to 10 mL with UV-treated ultrapure water) were taken for SPE and LC/MS analysis at 0, 7, 14, 28, and 56 days of storage. Multiple internal standards (10 µg L⁻¹) were then added to the sample aliquot prior to SPE. Pre-combusted glass containers were used for storage throughout the study. To further explore potential biodegradation in known ethanolamine sources like corrosion inhibitors, additional experiments were conducted using PW2-Mar as a source of naturally occurring microbial population and Versalis E-cori as corrosion inhibitor (1.7 mg mL⁻¹, provided by Eni Spa). Two milliliters of PW2-Mar were added to 60 mL of the Versalis E-cori solution, and ethanolamine concentrations were monitored at 20 °C over 56 days *via* SPE-LC/MS.

Extraction of ethanolamines. SPE was utilized for sample clean-up and desalting of produced water samples. SPE was done using a Visiprep vacuum manifold (Supelco 57030-U) connected to a benchtop vacuum pump (KNF Neuberger) (Fig. S2†). SPE columns were prepared by packing bulk sorbent in an empty glass SPE tube (Sigma Aldrich 504394) and packed with PTFE frits (20 µm porosity). The SPE procedure was optimized for SPE material (Oasis HLB and Agilent PPL) and elution solvent composition (methanol and 90/10 methanol/water with 2% formic acid). Prior to SPE, samples were filtered through combusted glass microfiber filters (GF/F, 25 mm, 0.7 µm, Whatman 1825025) assembled in a stainless steel microsyringe filter holder (Millipore XX3002500). Multiple isotopic standards (*i.e.*, one per compound; as *d*₄-MEA, *d*₈-DEA, ¹³C₆-TEA, ¹³C₄-EDEA, and ¹³C₄-MDEA; Cambridge Isotopes Laboratories, MA) were spiked to 10 mL filtered samples to correct for compound recovery differences attributed to distinct ethanolamine properties (*i.e.*, matrix interferences or ionization differences). The final procedure involved extraction using 1 g Bondesil PPL polymeric sorbents (Agilent, USA). The SPE cartridges were sequentially preconditioned using 6 mL of methanol and 6 mL of ultrapure water. The filtered sample (6 mL, pH 11) was loaded onto the cartridge at 1 mL min⁻¹, after which the cartridges were washed with 15 mL ultrapure water and then dried under

vacuum for 15 min at room temperature. The cartridges were eluted with 6 mL 2% formic acid in 90/10 methanol/water into pre-combusted glass vials.

Liquid chromatography and mass spectrometry. The extracts were analyzed using an Agilent 1290 Infinity II liquid chromatography system equipped with an Acclaim Trinity P1 column (2.1 × 100 mm, 3 µm). This column, as suggested in the Dionex 270 application note for ethanolamines, provides concurrent reversed-phase, cation-exchange and anion-exchange functionalities and was proposed for ethanolamines by a regional authority.¹⁷ The target compounds were separated *via* isocratic elution (90% acetonitrile; 10% 50 mM ammonium formate (pH 3.7)) at a flow rate of 0.5 mL min⁻¹ (analysis time = 7 min), injection volume of 10 µL, column temperature of 20 °C. Separate experiments based on the ASTM D7599 (ref. 18) with modifications by Lawrence Livermore National Laboratory²¹ were conducted using a Waters Atlantis HILIC column (Silica, 100 mm × 2.1 mm, 3 µm) and gradient elution involving ammonium acetate (15 mM) and 95/5 acetonitrile/15 mM ammonium acetate mobile phase (Table S5†). Between the two columns, better chromatographic resolution was achieved with the Acclaim Trinity P1 column (Fig. S3†). Thus, succeeding discussions will involve the use of Acclaim Trinity column.

Mass spectrometry was performed using an Agilent 6495 iFunnel triple quadrupole system in positive ESI mode, and spectral data were acquired by multiple reaction monitoring (Table 1). Analysis was done using optimized MS ion source conditions (capillary = 2000 V, ion funnel high pressure RF = 150 V, low pressure RF = 50 V, nebulizer pressure = 50 psi, nozzle voltage = 0 V, sheath gas heater = 330 °C, sheath gas flow = 11 L min⁻¹, drying gas temperature = 150 °C, drying gas flow = 18 L min⁻¹). MEA was the compound with the weakest response, and optimization of compound- and source-dependent parameters was performed to maximize sensitivity for this target molecule. The most abundant product ions (Text S3, Fig. S4†) were used for quantification and confirmation, and were similar to those reported in Dionex and ASTM methods.

The concentrations of ethanolamines were determined by the relative response of each target ethanolamine to its isotopically labelled internal standard. Qualifier ions (Table 1) were used for peak confirmation, with close retention times as a quantification criterion. A laboratory-fortified sample (15 µg L⁻¹ ethanolamine mixture spiked into LCMS-grade water) was analyzed during each SPE run to verify recovery, and sample matrix spikes were assessed during method development. To account for potential contamination, laboratory reagent blanks were included in every batch, and field blanks were analyzed alongside samples. Fresh calibration solutions were prepared for each analysis, and bracket standards were run after every 6–8 sample injections as part of quality control to ensure consistent system performance throughout the run.

Results and discussion

Method sensitivity, linearity, accuracy, and precision

The method detection limit (MDL) was determined by measuring ethanolamine concentrations in seven pure water



samples fortified with $1 \mu\text{g L}^{-1}$ authentic standards and $10 \mu\text{g L}^{-1}$ isotope standards. The MDL was calculated by multiplying the standard deviation of the replicate measurements by the student's *t*-value ($n - 1$ degrees of freedom).²² The MDLs (Table 1) ranged from $0.1 \mu\text{g L}^{-1}$ (MEA, DEA, MDEA) to $0.2 \mu\text{g L}^{-1}$ (EDEA, TEA). The reporting limit was chosen to be $1.0 \mu\text{g L}^{-1}$ (1.0 ppb , level 1 calibration standard), which is 5 to 10 times greater than the calculated MDL. At this concentration, all compounds had acceptable signal-to-noise ratios (>100), were resolved from one another, and clearly detectable. The LC/MS method was calibrated with each analyte at 1.0 – $40.0 \mu\text{g L}^{-1}$ concentrations and an isotopically labelled version of each analyte was added to each calibration point ($10.0 \mu\text{g L}^{-1}$) to generate a relative response ratio (Fig. S5†). Linear regression with $1/x$ weighting was used for all ethanolamines, where x is concentration, following the Dionex and ASTM methods.^{17,18} Coefficients of determination were required to be at least 0.990. In order to verify precision, replicate measurements of standard solutions were carried out. Precision was assessed in terms of

repeatability of concentration (expressed as percent relative standard deviation, % RSD) and accuracy was evaluated in terms of recovery. Calculated ethanolamine concentrations were found to be reproducible with RSD below 10% (Table S6†) and recoveries in ultrapure water of 92–107% were observed (Table 2).

Ion suppression and enhancement in ESI

Ion suppression can diminish accuracy and sensitivity of the method (*e.g.*, non-detection of an analyte causing false negatives when ions are suppressed). Critically, we note that matrix effects can lead to overestimation if the internal standard experiences more severe suppression, resulting in disproportionate signal enhancement of the analyte (Fig. 1). Dionex 271 and ASTM D7599 methods are susceptible to these effects as they rely on the use of only d_8 -DEA as an internal standard. In this study, we investigated the impact of produced water matrix on the sensitivity of the method by monitoring the peak areas of the added isotopically labeled ethanolamine standards (constant at $10 \mu\text{g L}^{-1}$ level) for each sample. Due to the variable characteristics of the samples, the extent of ion suppression or enhancement was highly variable and compound dependent (Fig. 1). For example, the signals of d_4 -MEA in all produced water samples decreased by more than 90% and were hardly detectable (Fig. S6†). Similarly, d_8 -DEA, the recommended standard in Dionex 271 and ASTM D7599 exhibited high degrees of ion suppression (up to 80%; Fig. 1a). These results are consistent with other studies²³ showing that smaller compounds (*e.g.*, d_4 -MEA and d_8 -DEA) were more susceptible to ion suppression due to possible ion–ion interaction with more massive and highly charged molecules (*e.g.*, bulk organic matter). Thus, without correcting for ion suppression, LC/MS

Table 2 Accuracy of the LC/MS method expressed as average % recovery of ethanolamines in pure water. In parenthesis are % relative standard deviation, $n = 3$

Level, $\mu\text{g L}^{-1}$	MEA	DEA	TEA	MDEA	EDEA
1	92 (2)	100 (7)	103 (8)	107 (2)	97 (3)
5	102 (2)	100 (4)	99 (3)	98 (2)	98 (2)
10	103 (3)	101 (5)	100 (3)	98 (2)	101 (2)
15	100 (3)	99 (2)	100 (4)	101 (3)	103 (5)
20	99 (2)	100 (2)	100 (9)	100 (6)	98 (0)
40	100 (1)	103 (9)	104 (4)	100 (3)	95 (2)

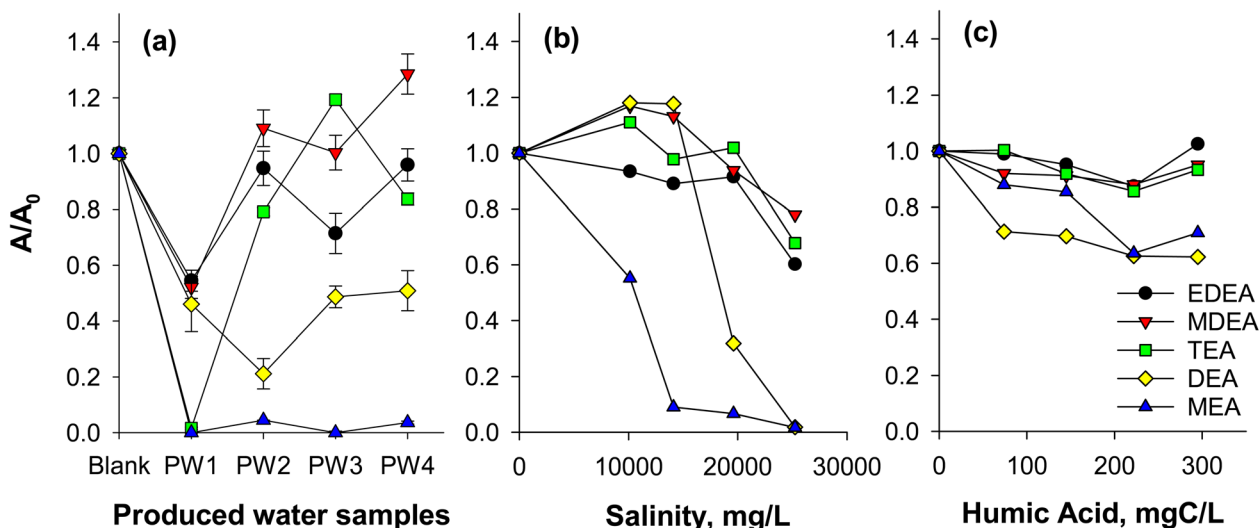


Fig. 1 Ion suppression in (a) produced water samples (PW–March), (b) synthetic brine solutions, and (c) humic acid solutions. A/A_0 corresponds to the area ratio of ethanolamines with matrix effects to ethanolamines without matrix effects (*e.g.*, in ultrapure water). Area ratios in (a) were obtained from isotopic standards ($10 \mu\text{g L}^{-1}$) of each ethanolamines, and are independent of unlabelled ethanolamines present in the sample. Error bars are standard errors ($n = 3$). For (b) and (c), area ratios were from unlabelled ethanolamines ($20 \mu\text{g L}^{-1}$) spiked to synthetic brine and humic acid-containing solutions. Note that lines are only used to guide the eyes.



analysis of ethanolamines in produced water samples could yield false negative results. Conversely, false positive results or overestimations would be obtained in the event that an internal standard used for other ethanolamines, such as d_8 -DEA, (*i.e.*, following the Dionex 271 (proposed by a regional authority) and ASTM D7599 recommendations) is impacted significantly by matrix effects. For example, signal enhancement in MDEA (added at $10 \mu\text{g L}^{-1}$ consistently) was observed in three of the four PW samples and in one sample for TEA (Fig. 1a) while DEA signals were dramatically suppressed in those same waters. Consequently, the relative abundance of MDEA would be augmented by both the enhanced MDEA sensitivity and the diminished DEA response, generating an overestimation of the real MDEA abundance. A strategy that relies on reducing the salt content of the sample through the use of SPE resins and leveraging compound-specific isotopically labeled authentic standards is proposed in this study, and utilization of this method could help eliminate the inaccurate determinations of ethanolamines provided by the Dionex 271 and related methods.

To further understand the effects of salts and bulk organic matter, experiments using ethanolamine-spiked synthetic brine and humic acid solutions were conducted (Fig. 1b and c). DEA and MEA experienced a high degree of ion suppression (up to more than 90%) at salinities of over $20\,000 \text{ mg L}^{-1}$ (Fig. 1b), confirming the contribution of salts for reduced analyte

response. In addition to diminished mass spectral sensitivity, salts also caused significant retention time shifts (Fig. S7†) using the Acclaim Trinity P1 column. Analytes eluted earlier as salt concentration was increased. For example, retention time for MEA changed from 5.2 min to 3.6 min when salinity was increased from 0 to $25\,250 \text{ mg L}^{-1}$, respectively (Fig. S8†). The shift in retention time was caused by the modified ion exchange properties of the column, where salts from the sample compete with ethanolamines for retention to the stationary phase. Large shifts in retention times are not acceptable, as they affect repeatability and may lead to non-detects (*i.e.*, false negatives) when quantification criteria require retention times consistent with the calibration standards. In some cases, false positives would also be possible if the retention time of an interfering compound shifted into the response window of the ethanolamine and produced an interfering diagnostic mass fragment ion.

To investigate the effect of bulk organic matter on ion suppression, synthetic humic acid solutions (0 – $295 \text{ mg}_\text{C} \text{ L}^{-1}$) were spiked with $15 \mu\text{g L}^{-1}$ ethanolamines. Note that the humic acid is representative of dissolved organic matter and may indicate an effect that could occur in the presence of hydrocarbons as well (*i.e.*, in produced water). These synthetic mixtures were directly injected to the LC/MS to observe organic matter-induced ion suppression. Bulk organic matter was also found to cause ion suppression (Fig. 1c). Consistent with earlier

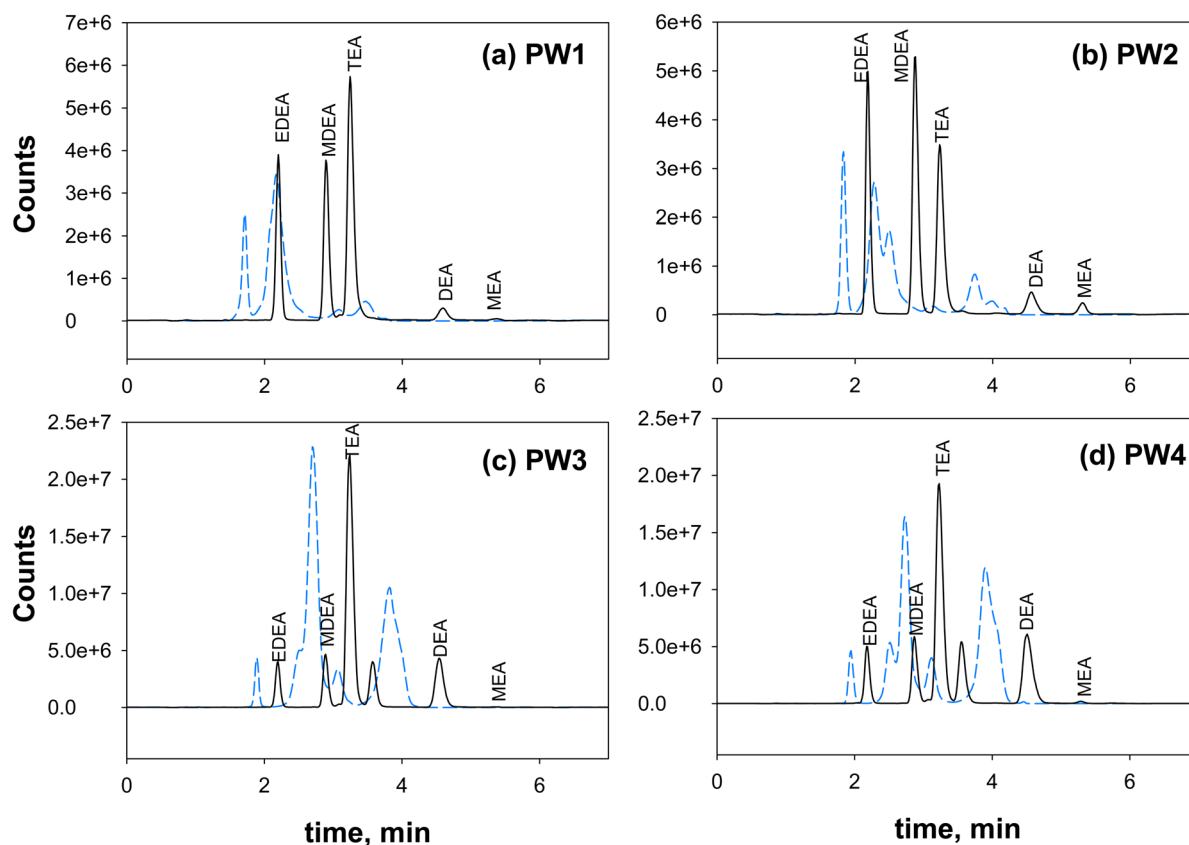


Fig. 2 Total ion chromatograms (TIC) of ethanolamines ($15 \mu\text{g L}^{-1}$) in PW-Mar samples ((a) PW1, (b) PW2, (c) PW3, (d) PW4) showing improved method sensitivity and peak resolution using the proposed SPE procedure. X-axis is time (min) and y-axis is counts/signal intensities. Peaks from left to right: EDEA, MDEA, TEA, DEA, MEA. Black line: chromatogram with SPE, Blue dashed line: chromatogram without SPE.



results, DEA and MEA were the most impacted ethanolamines, with suppression of 30–40% at 295 mg_C L⁻¹ humic acid.

Correction of matrix effects

Sample preparation procedures were next investigated to correct for ion suppression by salts and organic compounds, as well as retention time shifts caused by high salt content. Sample clean-up by SPE was tested for improved ethanolamine detection and quantitation. Optimization experiments involved determination of (a) appropriate SPE cartridge, (b) conditions for analyte retention, (c) eluent for enhanced recovery, and (d) correction of losses using isotope-labelled internal standards.

Solid-phase extraction

The SPE procedure was optimized by first evaluating appropriate SPE cartridge material and elution procedure. Oasis HLB and Agilent PPL cartridges were assessed since they were reported in previous studies for clean-up of produced water samples.^{24,25} For Oasis HLB, all ethanolamines except EDEA had poor adsorption (Fig. S9†). In contrast, Agilent PPL cartridge was able to retain most ethanolamines (Fig. S10†). The compounds were not observed in PPL's filtrate during loading and washing steps but were recovered during elution with methanol (bottom chromatogram in Fig. S10†). Therefore, the Agilent PPL cartridge was used to optimize the SPE method and no further experiments were conducted with the HLB cartridge.

Although the recoveries and precision of SPE demonstrated good consistency across the pH range of 2.6 to 11.0 (Fig. S11†), sample pH was adjusted to pH 11 prior to extraction. This step ensured that ethanolamines predominantly existed in their deprotonated form (>97%, Fig. S12†), while also standardizing the initial pH of all samples, regardless of their source and composition. The suspended particles and precipitates that form at this pH require filtration through glass fiber filters (0.7 µm, pre-combusted at 450 °C for 12 h) prior to SPE. Pre-combusted glass fiber filters are preferred due to possible contamination from binders in plastic syringe filters (Fig. S13†).

In addition to the type of cartridge, the eluent composition also significantly affected ethanolamine recoveries (Fig. S14†). Using only methanol as the eluent, ethanolamine recoveries were at 2–55%. This recovery increased to 80–113% when the eluent was acidified with 2% formic acid, likely due to the decreased affinity of ethanolamines with the SPE material when converted back to their charged state *via* pH-dependent protonation.

Overall, the final SPE procedure in this study employed the Agilent PPL cartridge and the following steps: conditioning with 3 mL of methanol twice (flow rate 2 mL min⁻¹), equilibration with 3 mL of pure water twice (flow rate 2 mL min⁻¹), loading of 3 mL of pH 11 samples twice (at 1 mL min⁻¹), washing/desalting with 3 mL of ultrapure water five times, 15 min cartridge drying under vacuum, and final elution with 3 mL of 2% formic acid in 90/10 methanol/water twice (flow rate 1 mL min⁻¹). This procedure was tested against a synthetic brine solution (salinity of 25250 mg L⁻¹, Fig. S15†) and the produced water samples (Fig. 2). The method was successful in desalting and

minimizing ion suppression. Note that there was no concentration factor applied in this procedure, as target concentrations were achievable even without a concentration step. If future analysis requires increased sensitivity (*e.g.*, below 1 µg L⁻¹ (1 ppb)), the SPE extracts can be rotary evaporated to obtain the desired concentration factor. The total ion chromatograms of ethanolamines after SPE of the brine solutions and samples resulted in improved peak shapes, sensitivity, resolution, and repeatability of retention times across samples (Fig. 2).

Use of compound-specific stable isotopes

While SPE results in improved detection capability, it still suffers from interferences from co-eluting organic matter from the sample matrix, ion suppression effects, as well as losses from the sample loading and elution procedures. Recovery of different ethanolamines vary by type of sample (Fig. S16†), and this can be attributed to the varying water quality. We consistently observed that isotopically labelled DEA and MEA in produced water samples have low recoveries (*e.g.*, less than 30% in produced water samples *versus* more than 50% in ultrapure water). This can be due to ion suppression caused by other matrix constituents (*e.g.*, organic matter) not removed during desalting by SPE.

The impact of the organic matter from produced waters was investigated by spiking isotopic standards to sample SPE extracts (Fig. S17†). This means that the samples have already been desalted, and SPE extracts only contained organic matter and ethanolamines from the sample. Compared to other ethanolamines, EDEA and MDEA were not significantly affected by the co-extracted organic matter. The opposite was observed for DEA and MEA. By comparing these results to samples spiked with isotopic standards followed by SPE, we could attribute the overall loss of ethanolamines from the SPE procedure and ion suppression caused by the bulk organic matter (Fig. S18†). Thus, to correct for these effects, isotope-labelled standards specific for each ethanolamine are required to accurately measure ethanolamine concentrations (Fig. S19†). Measuring concentrations of ethanolamines using only one internal standard (*e.g.*, *d*₈-DEA, *i.e.*, indicated in the Dionex and ASTM methods) will not provide accurate results due to varying degrees of ion suppression per analyte (Fig. 3). Indeed, under-recovery or suppression of *d*₈-DEA would lead to artificially enhanced other ethanolamine measurements in the absence of compound specific, isotopically labelled authentic standards.

Quantification of ethanolamines in produced water samples

Using the SPE procedure and multiple isotopic internal standards to correct for matrix effects, ethanolamines in produced water samples (PW-Mar, PW-Sept) were measured to prove practicality of the developed method in real applications. As previously discussed (Fig. 2), without SPE, ethanolamine peaks co-eluted at inconsistent retention times. With desalting by SPE, ethanolamines in produced waters were magnified with good resolution and eluted at repeatable retention times as the calibration standards resulting in more robust, sensitive, and accurate measurements. The addition of multiple isotopic



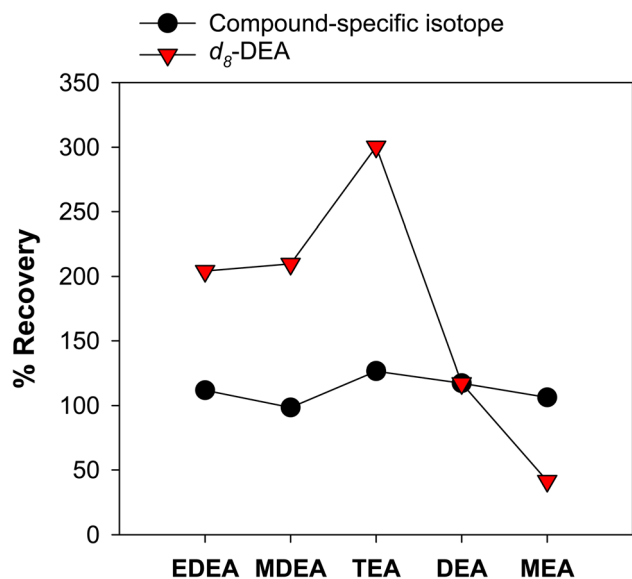


Fig. 3 Impact on accuracy of using a single (d_8 -DEA) and compound-specific internal standards. Black symbols are ethanolamine recoveries using compound-specific isotopic standards. Red symbols are ethanolamine recoveries determined using d_8 -DEA alone, as recommended in the Dionex (proposed by a regional authority) and ASTM methods. % Recovery = internal standard response ratios before SPE/internal standard response ratio after SPE; calculated from $20 \mu\text{g L}^{-1}$ ethanolamine standards spiked in pure water; response ratio refers to the peak area of the target ethanolamine/peak area of the internal standard.

Table 3 Average matrix spike recoveries ($n = 3$, spike level = $15 \mu\text{g L}^{-1}$) for ultrapure water, PW1 ($2\times$ diluted), PW2 ($10\times$ diluted), PW3 ($40\times$ diluted), and PW4 ($40\times$ diluted) March samples following the SPE-LC/MS method in this study. In parentheses are % relative standard deviation

Compound	Ultrapure water	PW1	PW2	PW3	PW4
MEA	103 (1)	133 (4)	97 (4)	130 (3)	111 (3)
DEA	105 (1)	108 (1)	105 (2)	110 (10)	108 (10)
MDEA	106 (2)	106 (2)	103 (1)	104 (2)	104 (2)
EDEA	108 (4)	109 (5)	107 (4)	107 (1)	108 (2)
TEA	103 (2)	109 (6)	107 (1)	107 (4)	107 (3)

internal standards further corrected for losses during the SPE procedure, instrument variability, and possible ion suppression from other matrix constituents. This study shows that the proposed method is applicable to water samples across a wide range of salinity and matrix compositions. Using this approach, matrix spike recoveries (spike level = $15 \mu\text{g L}^{-1}$) averaged ($\pm$ standard deviation) 118 (± 17) for MEA, 108% (± 2) for DEA, 104% (± 1) for MDEA, 108 (± 1) for EDEA, and 107% (± 1) for TEA across all PW samples (Table 3).

All produced water samples were found to contain some level of a variety of ethanolamines (Fig. 4). Among the samples, PW1 had the least amount of ethanolamines in both sampling events. In March 2019 samples, PW3 and PW4 had the highest total ethanolamine concentration, with DEA being the most abundant

compound ($432\text{--}465 \mu\text{g L}^{-1}$). PW3 and PW4 had relatively similar ethanolamine concentrations since both were collected from locations before reinjection to wells. PW4 was collected from a stock tank of all produced waters that were delivered to PW3 where reinjection occurs. On the other hand, PW1 and PW2 samples were taken from different oil separators. PW1 and PW2 samples (March 2019) had low ethanolamine content and were predominantly MEA ($26\text{--}153 \mu\text{g L}^{-1}$). When samples were collected in September 2019, the concentration of ethanolamines was notably different. PW3 and PW4 still had similar concentration profile, but with DEA reaching over $1000 \mu\text{g L}^{-1}$. For these samples, MEA also increased to more than double its initial concentration, while TEA was relatively consistent. The biggest jump in ethanolamine concentrations occurred with PW2, which can be explained by different sampling location and water cuts of the well in March and September 2019. "Water cut" refers to the mass percentage of water compared to the total liquids from an oil well. The March 2019 sample was taken with 40% water cut while the samples from September 2019 only had 20%. Since the water cut decreased, the abundance of DEA in the aqueous phase was enhanced (*i.e.*, DEA partitioned as it usually does, but into a smaller water volume). This resulted in a 1000-fold increase in DEA concentration, where PW2-Sept contained $3830 \mu\text{g L}^{-1}$ DEA. The proportional change in water cut did not correlate to the proportional change in ethanolamine concentrations, likely due to differences in composition of the produced waters over the hydrocarbon extraction that occurred in a 6 month time span or variations in utilized additives as well as transformations that may have transpired. In addition to changes in DEA, the shift to a lower water cut in PW2-Sept also led to the detection of MDEA ($12.5 \mu\text{g L}^{-1}$) compared to PW2-Mar (below $1 \mu\text{g L}^{-1}$).

Microbial transformations can significantly influence ethanolamine concentrations in produced waters. For example, DEA can be produced from ethoxylated fatty amines in surfactants. For ethoxylated fatty amines, microbial degradation can cleave the $\text{C}_{\text{alkyl}}\text{--N}$ bond through a hydrogenation reaction forming DEA as a breakdown product. A closed-bottle test by van Ginkel *et al.* (1993) reported that alkylbis(2-hydroxyethyl)amine was rapidly biodegradable *via* an initial oxidation of the alkyl chain.²⁶ The secondary amine byproducts did not biodegrade readily, contributing to the persistence of the amine byproducts. The same research group also reported that biodegradation of octadecylbis(2-hydroxyethyl)amine catalyzed by tertiary amine dehydrogenase could form DEA as one of the products.²⁷ Thus, long chain ethanolamines could serve as potential sources of DEA. In all PW samples, m/z 190 consistently appeared at about 1 min (Fig. S20†). Although preliminary, m/z of 190 may correspond to *N*-hexyldiethanolamine and its biodegradation could offer a potential route for DEA formation *via* a pathway described in Fig. S21.† Further studies are warranted to confirm if these biotransformation routes can contribute towards the abundance of DEA in produced waters.

It is important to note that concentrations discussed in this section were determined using multiple isotopic internal standards and not d_8 -DEA alone, as recommended in the Dionex and ASTM methods. Use of one compound-specific, isotopically labelled internal standard per compound is necessary for



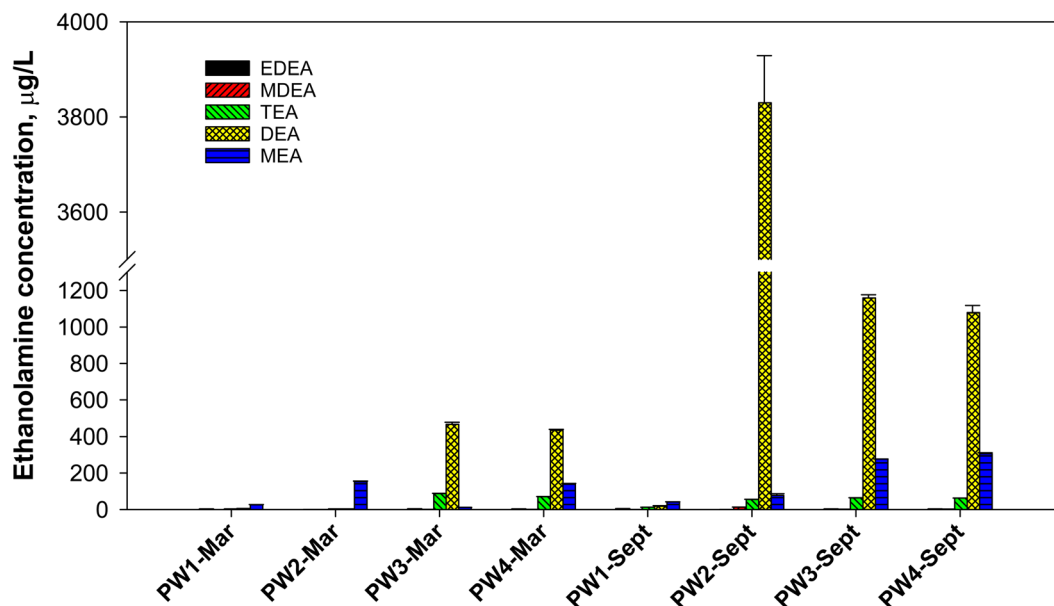


Fig. 4 Concentrations of ethanolamines in produced water (PW) samples quantified using the proposed analytical method that involves SPE and compound-specific isotopic internal standards. Field blanks $< 1 \mu\text{g L}^{-1}$ ethanolamines. Samples were diluted appropriately to fit the linear range. Error bars are standard deviation for PW-Mar, absolute deviation for PW-Sept.

accurate quantitation, as each ethanolamine can undergo ion suppression at varying degrees (Fig. 1). Critically, utilizing only d_8 -DEA as the internal standard can lead to overestimation of EDEA, MDEA, TEA *via* signal suppression of d_8 -DEA (*via* mechanisms described above) (Table S7†). MEA was underestimated when only d_8 -DEA was employed as a standard, as ion suppression for this compound was more severe compared to DEA. The use of a suite of internal standards and SPE extraction is necessary for accurate determination of ethanolamines.

Natural attenuation during storage and incubation

To check for formation or disappearance from biological or abiotic degradation pathways, several preservation techniques, such as acidification (pH 2), azide sterilization, freezing, and refrigeration were evaluated for 56 days. The spiked ethanolamines had varying trends when exposed to different storage conditions (Fig. S22†). EDEA and MDEA were relatively stable at all storage conditions (less than 20% decrease) while TEA and MEA decreased in 56 days. DEA was found to degrade by 50% after 7 days of storage and remained relatively at same concentration after a week. The decrease in DEA was accompanied by a slight increase in MEA which suggests possible biodegradation of DEA to MEA.²⁸ Note that the loss of DEA at all storage conditions indicates that the use of d_8 -DEA as an internal standard (as recommended by the Dionex 271 and ASTM D7599 methods) would lead to artificial enhancement of ethanolamine quantitation if the samples are not analysed in a timely fashion (*i.e.*, less than 7 days).

For MEA, a significant decrease (70%) was observed for PW2 samples stored at room temperature (20 °C), while that for PW1 remained unchanged. This suggests differences in abundance and characteristics of microbial population between samples. Since PW2 samples showed biological activity (as loss of MEA at

20 °C in Fig. S22†), this sample was used as source of seed bacteria to induce biodegradation of ethanolamines in dilute solution of Versalis E-cori corrosion inhibitor (1.7 mg mL⁻¹, contained 6.2 mg L⁻¹ MEA). A synthetic mixture of two mL of PW2 samples were added to the corrosion inhibitor solution (60 mL) and changes in ethanolamine concentrations were monitored at 20 °C (Fig. 5). MDEA and EDEA in this solution were below 1 µg L⁻¹ and remained so throughout the experiment. The results for DEA and TEA (over 75% and complete

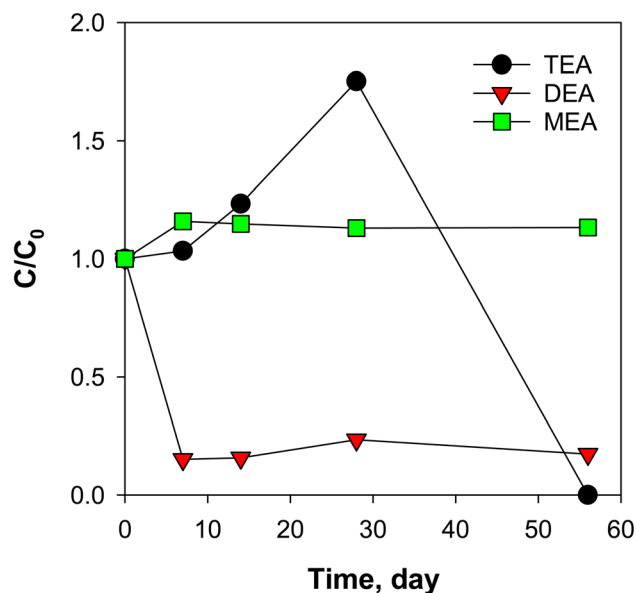


Fig. 5 Inoculation of Versalis E-cori corrosion inhibitor (1.7 mg mL⁻¹) with PW2-Mar sample (2 mL) suggesting microbial transformations of ethanolamines. EDEA and MDEA were below the quantification limit of 1 µg L⁻¹. Total volume = 60 mL, temperature = 21 °C.



mineralization, respectively, after 56 days) suggest that occurrence of biodegradation in corrosion inhibitors could occur in natural microbial populations in or derived from produced water. Thus, ethanolamine transformations should be an expected source of inter-well variability and sample preservation techniques must be carefully designed. Further studies could explore the use of recovery standards added in the field to determine the influence of this process on key ethanolamine analytes.

Overall, the results of these stability tests show that acidification and azide addition or low-temperature preservation (*i.e.*, freezing) can preserve the samples well. To minimize hazards associated with the use of acid and biocide, storing samples at cold conditions is strongly recommended. Freezing samples are preferred to limit biological activity even for long-term storage of samples (*e.g.*, 56 days).

Conclusions

This study presents a reliable analytical method for the accurate quantification of ethanolamines in highly saline and organic-rich produced waters from oil and gas operations. A detailed step-by-step procedure is outlined in Text S4 and Fig. S23.† By utilizing SPE with Bondesil PPL cartridges and compound-specific isotopic standards, followed by triple quadrupole LC/MS, this method offers a robust and adaptable approach for analyzing ethanolamines in a wide range of water types. It effectively accounts for varying matrix constituents, correcting for significant ion suppression caused by salts and organic compounds. The method demonstrated its reliability across different sample conditions, providing detailed insights into ethanolamine concentrations and their variation with operational parameters. DEA and MEA were the most prevalent species identified. Further research is necessary to identify other additives that could contribute to ethanolamines in oil and gas operations and to further investigate compounds that can be biotransformed to produce ethanolamines. Inter-laboratory studies are also warranted to allow for comparison of results and standardize this method for use in the energy sector.

This work emphasized that matrix effects should be rigorously evaluated in future LC/MS methods involving complex water chemistries, not only for ethanolamines but also for other low molecular weight compounds. The proposed method offers a valuable tool for further investigations into the environmental fate and risks of chemical additives in oil and gas production, contributing to improved environmental management and regulatory assessments.

Data availability

The data supporting this article have been included as part of the ESI.†

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by Eni SpA through the MIT Energy Initiative. The authors are grateful to Barathkumar Baskaran for reviewing the manuscript and the anonymous reviewers for the constructive comments.

References

- 1 G. J. Getzinger, M. P. O'Connor, K. Hoelzer, B. D. Drollette, O. Karatum, M. A. Deshusses, P. L. Ferguson, M. Elsner and D. L. Plata, Natural Gas Residual Fluids: Sources, Endpoints, and Organic Chemical Composition after Centralized Waste Treatment in Pennsylvania, *Environ. Sci. Technol.*, 2015, **49**(14), 8347–8355, DOI: [10.1021/acs.est.5b00471](https://doi.org/10.1021/acs.est.5b00471).
- 2 D. G. Abraham, H. K. Liberatore, Md. T. Aziz, D. B. Burnett, L. H. Cizmas and S. D. Richardson, Impacts of Hydraulic Fracturing Wastewater from Oil and Gas Industries on Drinking Water: Quantification of 69 Disinfection by-Products and Calculated Toxicity, *Sci. Total Environ.*, 2023, **882**, 163344, DOI: [10.1016/j.scitotenv.2023.163344](https://doi.org/10.1016/j.scitotenv.2023.163344).
- 3 L. Konkel, Salting the Earth: The Environmental Impact of Oil and Gas Wastewater Spills, *Environ. Health Perspect.*, 2016, **124**(12), A230–A235, DOI: [10.1289/ehp.124-A230](https://doi.org/10.1289/ehp.124-A230).
- 4 P. Panuwet, R. E. Hunter, P. E. D'Souza, X. Chen, S. A. Radford, J. R. Cohen, M. E. Marder, K. Kartavenka, P. B. Ryan and D. B. Barr, Biological Matrix Effects in Quantitative Tandem Mass Spectrometry-Based Analytical Methods: Advancing Biomonitoring, *Crit. Rev. Anal. Chem.*, 2016, **46**(2), 93–105, DOI: [10.1080/10408347.2014.980775](https://doi.org/10.1080/10408347.2014.980775).
- 5 J.-P. Antignac, K. de Wasch, F. Monteau, H. De Brabander, F. Andre and B. Le Bizec, The Ion Suppression Phenomenon in Liquid Chromatography–Mass Spectrometry and Its Consequences in the Field of Residue Analysis, *Anal. Chim. Acta*, 2005, **529**(1), 129–136, DOI: [10.1016/j.aca.2004.08.055](https://doi.org/10.1016/j.aca.2004.08.055).
- 6 US EPA and C. Ridley, Hydraulic Fracturing for Oil and Gas: Impacts from the Hydraulic Fracturing Water Cycle on Drinking Water Resources in the United States (Final Report), <https://cfpub.epa.gov/ncea/hfstudy/recordisplay.cfm?deid=332990>, accessed 2023-10-18.
- 7 M. Elsner and K. Hoelzer, Quantitative Survey and Structural Classification of Hydraulic Fracturing Chemicals Reported in Unconventional Gas Production, *Environ. Sci. Technol.*, 2016, **50**(7), 3290–3314, DOI: [10.1021/acs.est.5b02818](https://doi.org/10.1021/acs.est.5b02818).
- 8 U. Shoukat, D. D. D. Pinto and H. K. Knuutila, Study of Various Aqueous and Non-Aqueous Amine Blends for Hydrogen Sulfide Removal from Natural Gas, *Processes*, 2019, **7**(3), 160, DOI: [10.3390/pr7030160](https://doi.org/10.3390/pr7030160).
- 9 B. Lv, B. Guo, Z. Zhou and G. Jing, Mechanisms of CO₂ Capture into Monoethanolamine Solution with Different CO₂ Loading during the Absorption/Desorption Processes, *Environ. Sci. Technol.*, 2015, **49**(17), 10728–10735, DOI: [10.1021/acs.est.5b02356](https://doi.org/10.1021/acs.est.5b02356).
- 10 S. Kim, C. Yoon and D. Park, Vaporization and Conversion of Ethanolamines Used in Metalworking Operations, *Saf.*



- Health Work*, 2010, 1(2), 175–182, DOI: [10.5491/SHAW.2010.1.2.175](#).
- 11 Alberta Environment, Soil and Groundwater Remediation Guidelines for Monoethanolamine and Diethanolamine, 2010, <https://open.alberta.ca/dataset/94cc43cc-7840-495c-9b1f-df268a767206/resource/36db3e20-bafe-4db8-991f-2262705e681e/download/soilgroundwaterremguideethanolamine-2010.pdf>.
 - 12 H.-W. Leung, L. M. Kamendulis and W. T. Stott, Review of the Carcinogenic Activity of Diethanolamine and Evidence of Choline Deficiency as a Plausible Mode of Action, *Regul. Toxicol. Pharmacol.*, 2005, 43(3), 260–271, DOI: [10.1016/j.yrtph.2005.08.001](#).
 - 13 US EPA and J. Frithsen, Study of the Potential Impacts of Hydraulic Fracturing on Drinking Water Resources: Progress Report, (Dec 2012), <https://cfpub.epa.gov/ncea/hfstudy/recordisplay.cfm?deid=320611>, accessed 2023-10-18.
 - 14 CDC NIOSH, Ethanolamine National Institute for Occupational Safety and Health, 2011, <https://www.cdc.gov/niosh/Pel88/141-43.html>, accessed 10 Oct 2024.
 - 15 N. Dai, A. D. Shah, L. Hu, M. J. Plewa, B. McKague and W. A. Mitch, Measurement of Nitrosamine and Nitramine Formation from NO_x Reactions with Amines during Amine-Based Carbon Dioxide Capture for Postcombustion Carbon Sequestration, *Environ. Sci. Technol.*, 2012, 46(17), 9793–9801, DOI: [10.1021/es301867b](#).
 - 16 K. Yu, W. A. Mitch and N. Dai, Nitrosamines and Nitramines in Amine-Based Carbon Dioxide Capture Systems: Fundamentals, Engineering Implications, and Knowledge Gaps, *Environ. Sci. Technol.*, 2017, 51(20), 11522–11536, DOI: [10.1021/acs.est.7b02597](#).
 - 17 Thermo Fisher Scientific, Quantitative Analysis of Nitrogen Mustard Hydrolysis Products as Ethanolamines. Application Note 271, <https://assets.fishersci.com/TFS-Assets/CMD/Application-Notes/109792-AN271-IC-NitrogenMustard-Ethanolamines-19Jan2011-LPN2684.pdf>.
 - 18 ASTM, Standard Test Method for Determination of Diethanolamine, Triethanolamine, N-Methyldiethanolamine and N-Ethyldiethanolamine in Water by Single Reaction Monitoring Liquid Chromatography/Tandem Mass Spectrometry, <https://www.astm.org/d7599-16r17.html>, accessed 2023-10-19.
 - 19 B. Xiong, M. A. Soriano, K. M. Gutchess, N. Hoffman, C. J. Clark, H. J. Siegel, G. A. D. De Vera, Y. Li, R. J. Brenneis, A. J. Cox, E. C. Ryan, A. J. Sumner, N. C. Deziel, J. E. Saiers and D. L. Plata, Groundwaters in Northeastern Pennsylvania near Intense Hydraulic Fracturing Activities Exhibit Few Organic Chemical Impacts, *Environ. Sci.: Processes Impacts*, 2022, 24(2), 252–264, DOI: [10.1039/D1EM00124H](#).
 - 20 B. McDevitt, A. M. Jubb, M. S. Varonka, M. S. Blondes, M. A. Engle, T. J. Gallegos and J. L. Shelton, Dissolved Organic Matter within Oil and Gas Associated Wastewaters from U.S. Unconventional Petroleum Plays: Comparisons and Consequences for Disposal and Reuse, *Sci. Total Environ.*, 2022, 838, 156331, DOI: [10.1016/j.scitotenv.2022.156331](#).
 - 21 J. Owens, A. Vu and C. Koester, *Analysis of Ethanolamines: Validation of Semi-Volatile Analysis by HPLC-MS/MS by EPA Method MS888; LLNL-TR-408180, 945589*, 2008, p LLNL-TR-408180, 945589, DOI: [10.2172/945589](#).
 - 22 US EPA, Definition and Procedure for the Determination of the Method Detection Limit, Revision 2, <https://www.epa.gov/cwa-methods/procedures-detection-and-quantitation-documents>, accessed 2023-11-17.
 - 23 R. George, A. Haywood, S. Khan, M. Radovanovic, J. Simmonds and R. Norris, Enhancement and Suppression of Ionization in Drug Analysis U.: Therapeutic Drug Monitoring, *Ther. Drug Monit.*, 2018, 40, 1–8.
 - 24 J. L. Luek, P. Schmitt-Kopplin, P. J. Mouser, W. T. Petty, S. D. Richardson and M. Gonsior, Halogenated Organic Compounds Identified in Hydraulic Fracturing Wastewaters Using Ultrahigh Resolution Mass Spectrometry, *Environ. Sci. Technol.*, 2017, 51(10), 5377–5385, DOI: [10.1021/acs.est.6b06213](#).
 - 25 K. A. Sitterley, K. G. Linden, I. Ferrer and E. M. Thurman, Identification of Proprietary Amino Ethoxylates in Hydraulic Fracturing Wastewater Using Liquid Chromatography/Time-of-Flight Mass Spectrometry with Solid-Phase Extraction, *Anal. Chem.*, 2018, 90(18), 10927–10934, DOI: [10.1021/acs.analchem.8b02439](#).
 - 26 C. G. Van Ginkel, C. A. Stroo and A. G. M. Kroon, Biodegradability of Ethoxylated Fatty Amines: Detoxification through a Central Fission of These Surfactants, *Sci. Total Environ.*, 1993, 134, 689–697, DOI: [10.1016/S0048-9697\(05\)80072-5](#).
 - 27 C. G. Van Ginkel and A. G. M. Kroon, Metabolic Pathway for the Biodegradation of Octadecylbis(2-Hydroxyethyl)Amine, *Biodegradation*, 1992, 3(4), 435–443, DOI: [10.1007/BF00240365](#).
 - 28 S. Wyman, Triethanolamine Pathway, https://eawag-bbd.ethz.ch/tea/tea_map.html, accessed 2023-11-17.

