Measuring inorganic cations and amines with ion chromatography mass spectrometry (IC-MS)

Two robust and sensitive analytical techniques in their own right – ion chromatography (IC) and mass spectrometry (MS) – can be combined to form an even more powerful technique: IC-MS. This multi-parameter method determines various analytes such as inorganic cations and amines in one run, unlike other analytical techniques.

A fully automated IC-MS system controlled by a single software guarantees reproducible and reliable results and assures data integrity for users. Conductivity and MS signals are recorded in parallel to obtain valuable information about the sample from two complementary detectors, making IC-MS an outstanding technique to quantify trace analytes in a variety of matrices. An additional advantage of using Metrohm

IC is that Metrohm Inline Sample Preparation options can be integrated to further reduce manual labor steps for better results.

This White Paper covers several IC-MS applications for the determination of inorganic cations (e.g., potassium, rubidium, strontium, barium) as well as ethanolamines, alkylamines, and biogenic amines (e.g., putrescine, cadaverine, histamine).

Ω **Metrohm**

INTRODUCTION

Ion chromatography is an analytical technique that can separate and quantify different ions and even different ionic forms of the same element (speciation). When using IC, matrix interferences can be reduced with proper sample preparation and via chromatographic separation of analytes from the matrix on the analytical column. Classical IC with conductivity detection can be complemented with mass selective detection to guarantee peak identity and reach even lower detection limits [1].

Inorganic cations in various water types, biogenic amines in foods and beverages, and even other amines (e.g., ethanolamines, methylamines) in matrices such as industrial process water are readily determined with ion chromatography mass spectrometry (IC-MS). The combination of these two techniques for such determinations offers several additional benefits to analysts beyond those already mentioned above.

Native IC drivers allow the control and operation of IC equipment and accessories in the same software as the mass spectrometer. Metrohm offers drivers for MS coupling including Waters™ Empower™ chromatography data software (CDS) and Agilent OpenLab™ CDS. Sample preparation steps remove interfering substances prior to injection on the IC, protecting the instrumentation and improving detection limits. These benefits are achieved with Metrohm Inline Sample Preparation (MISP), such as Inline Ultrafiltration or Inline Dialysis. This fully automated system controlled by a single software reduces manual labor, protects valuable assets, and guarantees reproducible and reliable results.

This White Paper highlights some applications for various amines and inorganic cations in different matrices with IC-MS.

AMINES IN COMPLEX MATRICES

Amines can be separated using cation exchange columns. They can be detected with either suppressed or non-suppressed conductivity depending on the analytical requirements. If increased sensitivity is necessary, a mass detector can help to further improve the detection limits and to confirm peak identity for amines in heavily loaded samples.

– MEASURING BIOGENIC AMINES IN FOODS AND BEVERAGES

Biogenic amines are created through the decarboxylation of amino acids (usually due to fermentation or protein decomposition). Because some of these compounds are toxic at higher concentrations, they are often used as indicators for food quality. For example, histamine, putrescine, and cadaverine are formed during the decomposition of fish protein by microorganisms [2]. During winemaking, certain amines can be released from fermentation processes thereby negatively influencing the taste and aroma of the final product [3]. Biogenic amines need to be monitored in many foods and beverages as they can indicate improper hygiene or poor manufacturing practices and even induce an allergic response in some people. IC or IC-MS are suitable techniques to determine their concentrations in these kinds of matrices.

Eight biogenic amines were separated on a Metrosep C Supp 1 column with a ternary gradient of varying concentrations of oxalic acid and methanol as the eluent (**Table 1**, **Figure 1**). Chemical suppression was used to reduce the background noise for a better signal-to-noise ratio. Conductivity and selected mass traces were recorded to detect the analytes down to a single µg/L concentration range. The method was found to be robust and repeatable with e.g., 2% RSD for six injections of 1 µg/L putrescine (based on peak area) (**Figure 2**).

Table 1. Eight biogenic amines were measured on the Metrosep C Supp 1 - 150/4.0 column (eluent gradient – A: 3 mmol/L oxalic acid, B: 3 mmol/L oxalic acid + 20% methanol, C: 10 mmol/L oxalic acid, flow rate 0.9 mL/min, column temperature 40 °C).

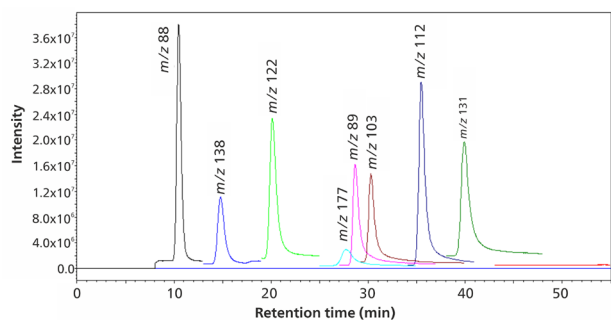| Compound	m/z	Retention time [min]
Isopentylamine	88	10.4
Tyramine	138	14.7
2-Phenylethylamine	122	20.0
Serotonin	177	27.6
Putrescine	89	28.5
Cadaverine	103	30.1
Histamine	112	35.5
Agmatine	131	40

Figure 1. Separation of eight biogenic amines (100 µg/L each, **Table 1**) on a Metrosep C Supp 1 - 150/4.0 column (eluent: oxalic acid/methanol gradient, flow rate 0.9 mL/min, column temperature 40 °C). The injection volume was 40 µL. The software used was Empower CDS.
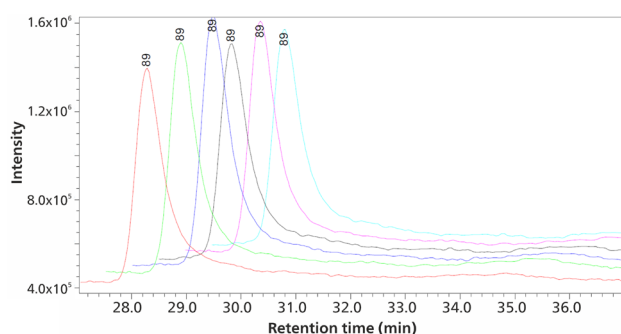

Figure 2. A repeatability study with six 200 µL injections of putrescine (1 µg/L) showed 2% RSD based on peak area. The software used was Empower CDS.

– ETHANOLAMINES AND METHYLAMINES IN PROCESS WATER

In many industries like petrochemical refining or natural gas production, gas scrubbing treatment is crucial to inhibit corrosion and prevent damage to the pipelines and costly equipment from acidic gases. Furthermore, monitoring of amines can ensure adherence to environmental protection laws. Scrubber solutions often contain amine mixtures (e.g., various ethanolamines). Being alkaline in nature, they neutralize harmful acidic gases such as H_2S and CO_2 and remove them from industrial processes—a process more commonly known as «gas sweetening» [**4**]. Additionally, such matrices are often very complex and can contain inorganic cations in higher concentrations, i.e., as heat stable salts.

Ethanolamines and methylamines are also used as raw materials for various production processes such as corrosion inhibitors, detergents, emulsifiers, polishes, chemical intermediates, and pharmaceuticals. Their determination is critical for optimal process performance including production, product quality, and protection.

In the following example, different ethanolamines were separated from alkali and alkaline earth metals (e.g., sodium, calcium) on a Metrosep C Supp 1 column. Detection was with suppressed conductivity and selected ion recording of the respective *m/z* signal. **Figure 3** shows the results of a repeatability study for determination of mono-, di-, and triethanolamine (10 µg/L, sample volume 20 µL). Ammonium was detected as an acetone adduct.
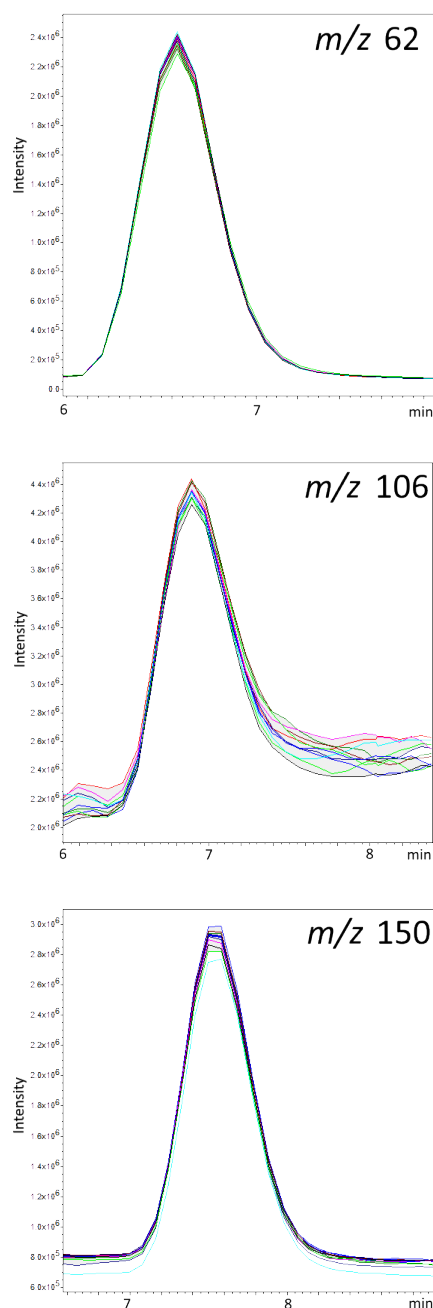

Figure 3. Mass signals of 10 µg/L mono-, di-, and triethanolamine (*m/z* 62, 106, and 150, respectively) on a Metrosep C Supp 1 - 150/4.0 column (eluent: 2.5 mmol/L oxalic acid, 1.2 mmol/L dipicolinic acid, and 8% (v/v) acetone; flow rate 0.9 mL/min, column temperature 40 °C). The sample volume was 20 µL. The software used was Empower CDS.

Non-suppressed cation determination is performed using a robust setup with minimal required instrument modules. Since the eluent is not suppressed, but reaches the MS, it is important to choose eluents that easily decompose in the ESI (electrospray ionization) source (e.g., oxalic acid which degrades to CO_2). This prevents salt precipitation and avoids corrosion that may occur when using mineral acid eluents.

As an example, 10 amines were injected on a short Metrosep C 4 - 50/4.0 column (**Table 2**). The analyte peaks were not completely separated and quantified using conductivity detection. However, by evaluating the mass specific traces, quantification is possible without impairing the results from partial coelution. Detection was accomplished in the single µg/L or even sub-µg/L range with a 5 µL sample volume (**Figure 4**). If a better separation was required, then a longer column (e.g., Metrosep C 4 - 250/4.0) would improve the peak resolution. Many other amines like diethyl-amine or triethylamine can be determined with the setup described in our Application Note **AN-M-005**.
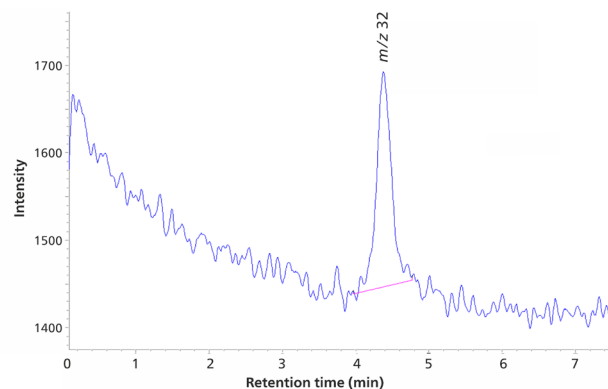

Figure 4. Mass signal of 7 µg/L methylamine (*m/z* 32) separated on a Metrosep C 4 - 50/4.0 column (eluent: 2.5 mmol/L oxalic acid, flow rate 0.5 mL/min, column temperature 30 °C). The sample volume was 5 µL. The software used was Agilent ChemStation®.

Table 2. Ten amines with corresponding *m/z* signals and retention times on a Metrosep C 4 - 50/4.0 column (eluent: 2.5 mmol/L oxalic acid, flow rate 0.5 mL/min, column temperature 30 °C).

Compound	*m/z*	Retention time [min]
Monomethylamine (MMA)	32	4.3
Ethylamine	46	5.0
Dimethylamine (DMA)	46	5.8
Trimethylamine (TMA)	60	9.8
Butylamine	74	9.6
Dimethylaminoethanol (DMAE)	90	8.2
Aniline	94	9.0
Cyclohexylamine	100	18.5
N,N-diethanolamine (DEA)	106	5.0
Triethanolamine (TEA)	150	6.2

INORGANIC CATIONS IN WATER

Ion chromatography with conductivity detection is a well-established technique for the multi-ion analysis of alkali and alkaline earth metals in their free cationic forms. Along with proper sample preparation, cations are determined with this method of choice in various matrices (e.g., foodstuffs, wastewater, pharmaceuticals, chemicals). In some cases, placing an MS detector in series after the conductivity detector can confirm peak identity and provide additional information about the compound.

ICP-MS (inductively coupled plasma mass spectrometry) systems are typically used for trace analysis of metals. However, the instrumentation is very expensive and needs experienced operators. A single quadrupole MS is less expensive and easier to operate. If the required detection limits are not too low and are in the µg/L range, single quadrupole MS is a suitable alternative to ICP-MS.

As mentioned in the previous section, in order to avoid corrosion inside the MS detector, eluents that flow to the MS must not contain mineral acids (e.g., nitric acid, sulfuric acid). With non-suppressed ion chromatography, eluents that decompose in the ESI chamber are favored. Oxalic acid eluents, for example, will form CO_2 which is then removed in the vacuum and does no harm to the MS detector.

With suppressed cation chromatography, the suppressor removes critical components from the eluent. The only risk here might be an exhaustion of the suppressor module. However, in this case the software can monitor the induced rise in the conductivity background and initialize the necessary steps to regenerate the suppressor.

– IC-MS DETERMINATION OF ALKALI AND ALKALINE EARTH METALS AS BARE CATIONS

In the following application example, three alkali metals (potassium, rubidium, cesium) and three alkaline earth metals (calcium, strontium, barium) were separated in one run on a Metrosep C Supp 1 column. A conductivity detector and a single quadrupole mass spectrometer with ESI and selected ion recording were set up in series to record the analyte signals.

The MS was optimized for the detection of small masses with rather harsh conditions to detect bare cations (**Table 3**). With this setting, masses above *m/z* 1080 were no longer resolved, but sensitivity was increased for masses below *m/z* 200.

With a 20 µL sample injection volume, 10 µg/L of alkali metals and 0.5 mg/L of alkaline earth metals were readily detected with suppressed conductivity (**Figure 5**), as well as with the MS (**Figure 6**).

Table 3. Selection of cation analytes and their respective *m/z* ratios.

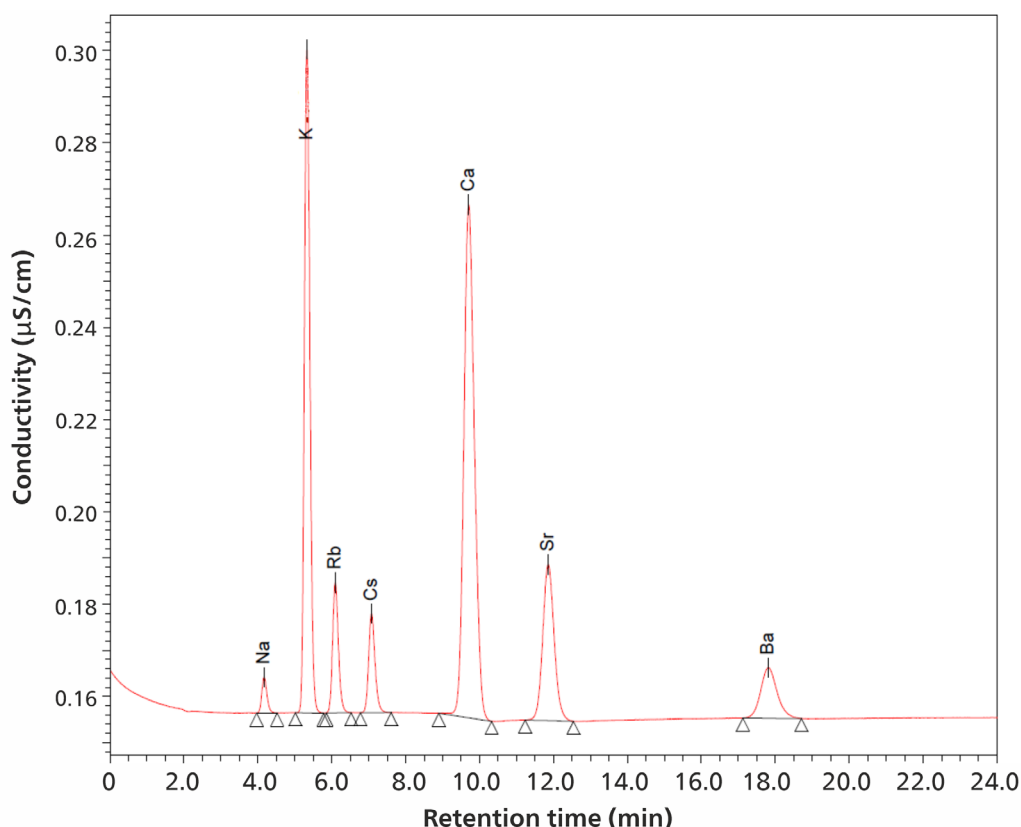| Analyte	Molecular mass [m]	Charge [z]	m/z
Potassium (K+)	39	1	39
Rubidium (Rb+)	85	1	85
Cesium (Cs+)	133	1	133
Calcium (Ca2+)	40	2	20
Strontium (Sr2+)	88	2	44
Barium (Ba2+)	137	2	69

Figure 5. Conductivity signal of a 20 µL injection of a 0.5 mg/L mixed cation standard separated on a Metrosep C Supp 1 - 150/4.0 column (eluent: 5 mmol/L oxalic acid, flow rate 0.9 mL/min, column temperature 30 °C). The software used was Empower CDS.
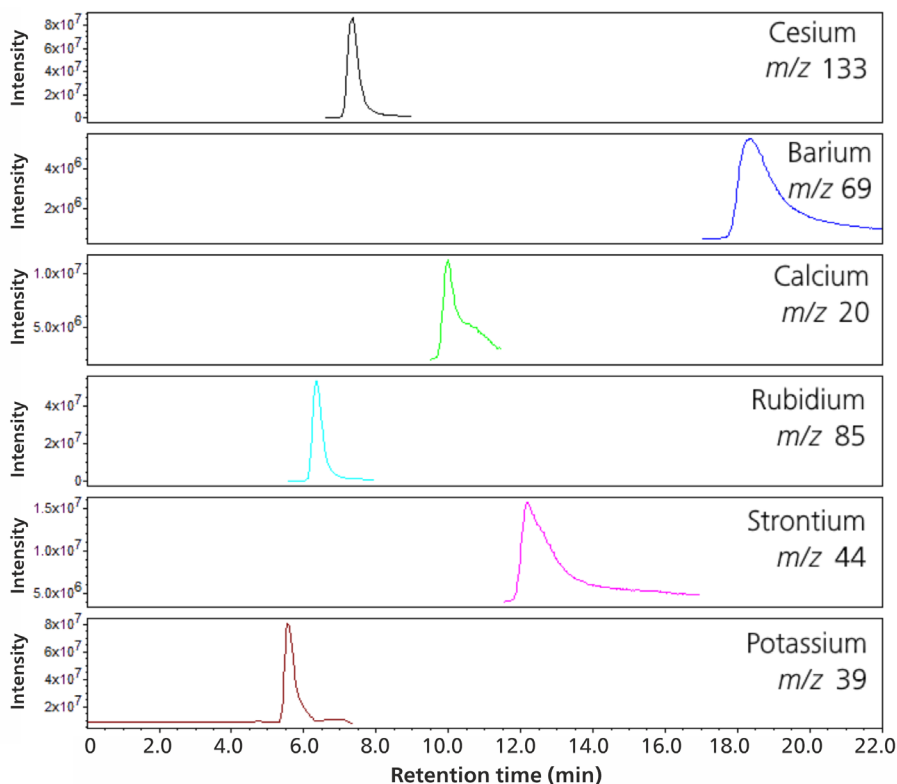
Figure 6. Corresponding mass signals of a 20 μL injection of a 0.5 mg/L mixed cation standard separated on a Metrosep C Supp 1 - 150/4.0 column (eluent: 5 mmol/L oxalic acid, flow rate 0.9 mL/min, column temperature 30 °C). Conductivity and mass signals were recorded simultaneously. The software used was Empower CDS.

– ALKALI AND ALKALINE EARTH METALS DETECTED AS ACETONE ADDUCTS

Several cations were separated on a Metrosep C Supp 1 column and detected with suppressed conductivity in this application example. By adding acetone to the eluent, the detection limits of alkali metals (e.g., lithium, sodium) and alkaline earth metals (e.g., calcium, magnesium) in a subsequent MS detector can be improved. These cations form acetone adducts which have higher mass-to-charge ratios than the single ions themselves. This acetone addition increases their sensitivity and enables detection down to a μg/L concentration range.

The MS used in this example was optimized for the detection of smaller masses. It was tuned by injecting a 1 mg/L solution of lithium, ammonium, potassium, and calcium in 10% acetone. As with the previous application example, masses above m/z 1080 were no longer resolved, but sensitivity was increased for lower masses (below m/z 200).

Signals for several acetone adducts were observed (between zero and three acetone molecules attached to the cations). The most intense signal was chosen for quantification. As shown in **Table 4**, calcium and magnesium adducts with three acetone molecules exhibited the most intense signal under the applied conditions. Lithium with two acetone molecules and sodium with one acetone molecule were the most intense signal generators. Potassium formed adducts with acetone, however, the signal of the single K$^+$ ions without acetone remained the most intense.

Table 4. Selected analytes and their most intense m/z signal with the responsible adduct.

Analyte	Retention time [min]	m/z	Adduct
Lithium	5.1	123	[Li + 2 acetone]$^+$
Sodium	6.0	81	[Na + 1 acetone]$^+$
Potassium	7.9	39	K$^+$
Calcium	12.5	107	[Ca + 3 acetone]$^{2+}$
Magnesium	14.7	99	[Mg + 3 acetone]$^{2+}$

This method is robust and sensitive, as shown in an overlay of 10 injections of 10 μg/L lithium (injected amount 0.2 ng, **Figure 7**).
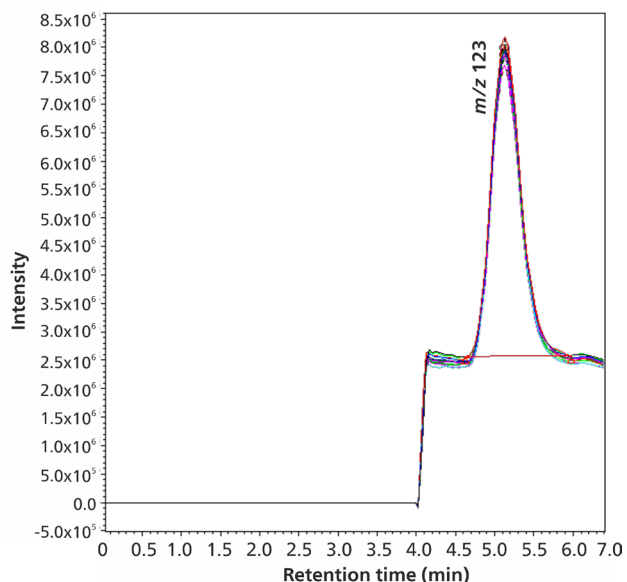
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Figure 7. Mass signal of 10 µg/L lithium (amount 0.2 ng) detected as its acetone adduct (*m/z* 123). Overlay of 10 injections, 20 µL each. The software used was Empower CDS.

Small amounts of alkali and alkaline earth metals are easily analyzed with suppressed cation chromatography and conductivity detection. This application is especially useful when a positive peak confirmation of these compounds is desired with a second independent detector.

CONCLUSION

Cations in various matrices are typically measured using either IC and conductivity detection, ICP-MS, ICP-OES (inductively coupled plasma optical emission spectrometry), or atomic absorption spectroscopy (AAS). Mass spectrometry is classically used for the detection of organic molecules. Its combination with high-performance liquid chromatography (HPLC) and gas chromatography (GC) is well-established.

IC-MS combines the benefits from both techniques by offering robust and repeatable measurements while saving time and effort for users. Multiple cations, including biogenic amines and other amine types, are sensitively and selectively determined in one determination. Single software operation, sample preparation, and automation possibilities simplify analysis even when analyzing low concentrations of analytes in difficult matrices.

References

[1] *Application of IC-MS and IC-ICP-MS in Environmental Research: Michalski/Application of IC-MS and IC-ICP-MS in Environmental Research*; Michalski, R., Ed.; John Wiley & Sons, Inc: Hoboken, NJ, USA, 2016. **DOI:10.1002/9781119085362**

[2] Sánchez, J.; Ruiz-Capillas, C. Application of the Simplex Method for Optimization of Chromatographic Analysis of Biogenic Amines in Fish. *European Food Research and Technology* **2011**, *234*, 285–294. **DOI:10.1007/s00217-011-1622-6**

[3] Buňka, F.; Ivičičová, B.; Buňková, L.; et al. Biogenic Amines Content in Selected Wines during Winemaking. *Journal of Microbiology, Biotechnology and Food Sciences* **2012**, *1* (4), 785–793.

[4] Dashti, S.; Shariati, A.; Khosravi-Nikou, M. R. Sensitivity Analysis for Selection of an Optimum Amine Gas Sweetening Process with Minimum Cost Requirement: Sensitivity Analysis of Amine Sweetening Process. *Asia-Pacific Journal of Chemical Engineering* **2015**, *10* (5), 709–715. **DOI:10.1002/apj.1907**

Further related Metrohm literature

An introduction to ion chromatography mass spectrometry (IC-MS). **WP-066**

Simple determination of haloacetic acids (HAAs) in potable water with ion chromatography hyphenated to mass spectrometry. **WP-075**

Coupling of ion chromatography and plasma mass spectrometry. **WP-008**

A strong combination – Coupling of Metrohm ion chromatography and mass spectrometry **8.000.5250**

Metrohm meets Empower 3 – Ion chromatography with the Chromatography Data Software (CDS) from Waters **8.102.5004**

IC Driver for Agilent OpenLab CDS – A perfect combination: Metrohm Ion Chromatography and OpenLab CDS Software **8.102.5007**

Sample Preparation Techniques for IC. **8.108.5070**

Metrohm Application Finder: Selection of IC-MS Applications

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