Evaluation and Application of Microextraction Techniques Coupled with Portable Analytical Instrumentation for On-site Analysis

by

Nathaly Reyes-Garcés

A thesis
presented to the University of Waterloo
in fulfillment of the
thesis requirement for the degree of
Master of Science
in
Chemistry

Waterloo, Ontario, Canada, 2012

Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

In recent years, on-site analysis has garnered increased interest from the scientific community. The development of smaller, more sophisticated analytical instruments, and the establishment of new environmental regulations have encouraged the application of new methodologies for field analysis. Prominent advantages of on-site analysis include elimination of error sources due to sample transportation and matrix modification, considerable reduction in analysis time, and more accurate and precise analytical results. Several techniques suitable for on-site analysis, which integrate sampling and sample preparation in one step, have demonstrated high versatility and throughput in field applications. This research was focused on the application and evaluation of three microextraction techniques: solid phase microextraction (SPME), needle trap devices (NTD) and membrane extraction with sorbent interface (MESI), which were then coupled with various portable instruments for on-site analysis of different systems. Additionally, the conducted project involved the development of an approach using ion mobility spectrometry detection (IMS) coupled with a miniaturized gas chromatograph (GC) as a powerful system for field analysis. This proposed GC-IMS exhibited satisfactory performance in terms of retention time (inter-day variation < 3%) and response stability (intra and inter-day relative standard deviations (RSDs) < 10 %). Moreover, when coupled with NTD, it showed limits of detection comparable to those provided by conventional benchtop instruments. Other portable GC instruments employed in this project included flame ionization and mass spectrometry detection. Three different sample systems were investigated using SPME and NTD together with these portable instruments: emissions of a pine branch, breath samples, and indoor pollutants in a polymer synthesis laboratory. Consequently, the feasibility of using SPME and NTD for determination of free and total concentrations was investigated. Finally, MESI was successfully

coupled with the newly proposed GC-IMS system, and its functionality was evaluated by analyzing acetone in breath samples.

Acknowledgements

I would like to take this opportunity to express my appreciation to all who have contributed to the completion of this project. First, I would like to thank my supervisor, Dr. Janusz Pawliszyn, for providing me with the opportunity to become part of his group and work on this challenging project. Second, I would like to thank my advisory committee members, Dr. Mario Gauthier and Dr. Michael Chong, for their advice and the time given to evaluate this research project, and for their constructive inputs.

I would like to thank Krunomir Dvorski from Science Technical Services (University of Waterloo) for being willing to help me every time I needed and for all the inputs he gave me regarding electronic assistance. I would also like to thank Torion Technologies and TeknoScan Systems Inc. for the technical support provided.

I would like to especially thank those group members that were constantly guiding and helping me throughout these two years: German Gómez, Érica Silva, Jiang Ruifen (Jennifer) and Erasmus Cudjoe. Thanks for your valuable advice, but most important, thanks for your sincere friendship. I would also like to thank Annabella Bai, Oana Goli, Emanuela Gionfriddo, Ezel Boyaci, David Donkor and Heide Flatt for their support during the completion of my Master degree.

I would like to acknowledge my beloved parents (Emilce and Henry) and my siblings (Henry Mauricio and Estefanía) for their constant support and understanding.

Dedication

I dedicate this thesis to German. Thanks for your sincere and pure love, your understanding and your constant support. Thanks for being my best friend and my life partner.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

BTEX	Benzene, toluene, ethylbenzene and xylene
CAR	Carboxen
DVB	Polydivinylbenzene
DI	Direct immersion
FID	Flame ionization detector
FPD	Flame photometry detector
GC	Gas chromatography
HS	Headspace
IMS	Ion mobility spectrometry
MESI	Membrane extraction with sorbent interface
MS	Mass spectrometry
NTD	Needle trap device
PAHs	Polycyclic aromatic compounds
PBPs	Persistent bioaccumulative pollutants
PDMS	Polydimethylsiloxane
PID	Photoionization detector
qMS	Quadrupole mass analyzer
QC	Quality control

SBSE	Stir-bar sorptive extraction
SPME	Solid phase microextraction
SVOCs	Semi-volatile organic compounds
TCD	Thermal conductivity detector
TMS	Toroidal ion trap mass analyzer
TOF	Time of flight
VOCs	Volatile organic compounds

Chapter 1: Introduction

In recent years, on-site analysis has garnered a wealth of interest from the scientific community.[1] The development of more sophisticated, smaller analytical instruments, as well as the establishment of new environmental regulations have encouraged the application of new methodologies for field analysis.[2,3] Advantages of on-site chemical analysis include elimination of error sources during sample transportation, a considerable reduction in analysis time, as well as added accuracy and precision in analytical results.[2,4] These important advantages found in on-site analysis make this approach often preferable over traditional analysis techniques. However, the performance of most common portable instruments is not sufficient in many circumstances, and traditional sample preparation techniques are unsuitable for application in field conditions.[3] For this reason, the development and implementation of miniaturized devices capable of integrating sampling and sample preparation into one step for rapid analysis is of substantial importance in analytical chemistry.[1]

In the current section, three different sample preparation approaches suitable for on-site analysis will be described: solid phase microextraction (SPME), needle trap devices (NTD) and membrane extraction with sorbent interface (MESI). New developments in portable instrumentation and miniaturization of gas chromatography will be also discussed. Particular attention will be dedicated to ion mobility spectrometry detection (IMS) for field analysis.

1.1. Sample Preparation techniques

1.1.1. Solid Phase Microextraction (SPME)

SPME is a widely accepted sample preparation technique developed by Pawliszyn and co-workers in 1990.[5] In this solvent-free technique, a fused silica fibre coated with a small amount of extracting phase is exposed to the sample[6] and only a small portion of the analyte proportional to the initial concentration in the sample matrix is removed during the extraction. Thus, the use of SPME makes it possible to quantify specific compounds when sampling conditions are controlled.[7]

In this microextraction technique, an equilibration process between different phases in the extraction system takes place.[8] Depending on the sampling approach used and the sample matrix being studied, different phases may affect the distribution of the analyte. When equilibrium in the extraction system is reached, the amount extracted is constant and independent of the extraction time (within the limits of experimental errors). At equilibrium conditions, the amount extracted by a SPME fibre is described as follows:[7]

$$n = \frac{K_{FS} V_F V_S C_o}{K_{FS} V_F + V_S} \qquad (1.1)$$

Where n is the number of moles extracted by the coating, K_{FS} is an extracting phase/sample matrix distribution constant, V_F is the fibre coating volume, V_s is the sample volume, and C_o is the initial concentration of the analyte in the sample. This equilibrium relation is limited to liquid polymeric phases such as polydimethylsiloxane (PDMS). However, in case of low analyte concentration, this analysis is analogous for solid sorbent coatings, assuming constant porosity of the sorbent.[6] Equation 1.1 considers only one homogeneous phase as the sample matrix.

Nonetheless, if more than one component is present in the extraction system, the expression can accordingly be modified by including volumes and distribution constants for each of the individual phases.[6]

Due to its simplicity, and the integration of sampling and pre-concentration in one step, SPME is a well suited sample preparation method for on-site applications. Today, various coating types able to extract analytes of different characteristics are commercially available, with PDMS coating being most commonly used. For analysis of volatile organic compounds (VOCs), fibre coatings that contain solid adsorbent material, such as Carboxen/PDMS (CAR/PDMS), PDMS/divinylbenzene (PDMS/DVB) and PDMS/DVB/CAR, have the best extraction efficiency. Several studies confirm the suitability of these coatings for the analysis of different VOCs, including low molecular weight analytes.[7,9] Since the mechanism involved in the extraction process using solid coatings is adsorption, competition between analytes for available adsorptive sites as well as possible displacement effects are two shortcomings that should be considered when these particular types of coatings are employed for quantitative purposes.[7]

Depending on the application process being implemented, different calibration approaches can be followed when on-site analysis is performed. External standard calibration is the most common calibration method, but can only be used when the sampling conditions are the same for both the standard solution and the real sample. Total control of sampling conditions is not always possible in field sampling however, and consequently, alternate calibration approaches are required.[7] In 2001, Koziel *et al.* introduced a new calibration model based on diffusion-controlled extraction of analytes on a solid SPME coating.[9] In this methodology, the SPME fibre is exposed to a gaseous sample under well-controlled convection conditions, and only for short extraction times so as to avoid competitive adsorption effects. Thus, under these conditions, the

SPME coating behaves as a perfect sink, where all analytes reaching the coating surface are irreversibly adsorbed. Koziel *et al*. first introduced a model which demonstrated that SPME calibration is possible without an external standard, by using the following equation:[9]

$$C_g = n\ ln\left(\frac{b+\delta}{b}\right)/2\pi D_g L t \qquad (1.2)$$

where C_g is the concentration of analyte, n is the amount of analyte extracted, which is determined from the detector response factor, b is the fibre radius, δ is the thickness of the effective static boundary layer, D_g is the analyte diffusion coefficient in air, L is the fibre length, and t is the sampling time. The diffusion coefficients in air can be estimated by using several models available in the literature. However, in normal air sampling conditions the Fuller-Schettler-Giddings is most convenient.[10]

$$Dg = \frac{0.001T^{1.75}\sqrt{\frac{1}{M_{air}}+\frac{1}{M_{VOC}}}}{p[(\sum V_{air})^{1/3}+(\sum V_{VOC})^{1/3}]^2} \qquad (1.3)$$

In Equation 1.3, T represents the absolute temperature, M_{air} is the apparent molecular weight of the air, M_{VOC} is the molecular weight of the analyte, p is the ambient pressure, V_{air} is the molar volume of the air, and V_{VOC} is the molar volume of the analyte. The thickness of the effective boundary layer δ can be calculated from the relation $\delta = 9.52b/Re^{0.62}Sc^{0.38}$, where Re is the Reynolds number ($Re = 2ub/v$; u is the linear velocity of the air, which can be measured with an anemometer, and v is the kinematic viscocity of the air), and Sc is the Schmidt number ($Sc = v/D_g$).

This interesting methodology was successfully evaluated using benzene, toluene, ethylbenzene and p-xylene (BTEX) in gas phase as the analytical model. The proposed model

compared well with experimental results obtained at very short extraction times and under controlled convection conditions. In addition, the humidity effect was found to be negligible at very short extraction times, which is convenient for on-site applications where humidity conditions cannot be controlled.[9] Analysis of biogenic volatile compounds[11] and quantification of aromatic hydrocarbons in indoor air[12] have been reported as applications of this SPME calibration approach.

1.1.2. Needle trap devices (NTD)

The needle trap device (NTD) is an exhaustive sample preparation technique wherein a sorbent bed immobilized in a needle retains analytes and/or small particles from a gaseous or liquid sample. The sample is introduced into the NTD using a pump or a gas-tight syringe. Once the analytes are extracted in the sorbent bed, the NTD is directly desorbed in the inlet of an analytical instrument. As in SPME, NTD integrates sampling, sample preparation and introduction in one step.[13]

The use of a packed needle for trapping organic compounds was first reported in 1970.[14] In this study, a large Tenax-filled needle was used for collecting fragrance compounds. Years after, in 1996, different sorbents, such as charcoal and silica gel, were used to pre-concentrate several organic compounds.[15] However, these two approaches involved a modified inlet system, and carrier gas flow was necessary to assist analyte desorption. In 2001, Pawliszyn and coworkers reported a practical needle trap, of 23 gauge and 40 mm in length, packed with glass wool (5 mm).[16,17] This device was used to trap different analytes by drawing a specific volume of air with a luer-lock gas-tight syringe, which were then desorbed in a gas chromatograph injection port

using 10 µL of carrier gas to aid the desorption. The results obtained showed the remarkable applicability of this device in the analysis of volatile compounds. Currently, various studies have been carried out using packed needles and similar approaches.[18-21]

Several features of needle trap devices, such as simple operation, rapid analysis and low cost, make this sample preparation technique an advantageous alternative for on-site sampling.[13,20] In addition, NTD is an exhaustive technique that can be easily calibrated by controlling the sampled volume (v) and determining the amount extracted (n) in an analytical instrument (Equation 1.4).

$$n = C_0 v, \text{ where } C_0 \text{ is the initial concentration of analyte} \qquad (1.4)$$

The breakthrough volume of a needle trap is a very important parameter, which describes the capacity of this type of sampling device. The amount of packed sorbent, concentration in the sample and affinity of the sorbent towards the analyte are all directly related to the breakthrough volume.[20] The sampling rate, on the contrary, is inversely proportional to this parameter. Other important variables that can affect the breakthrough volume are gas pressure, temperature, geometry of the bed, and humidity.[13,22]

Depending on the application, different types of sorbents can be chosen as NTD packing. CAR and DVB copolymers are probably most commonly used. Silica particles (bare and coated), Tenax, and cation exchange particles have also been reported as effective packing materials for NTD applications.[20,23-25] In order to immobilize the sorbent, a stainless spring stopper is located inside the needle at a specific distance from the tip, which determines the length of the sorbent bed. Next, the sorbent particles are aspirated inside the needle, one by one, until the desired length is reached; a guide wire is used to gently push the particles until the required position is

achieved. If the packing is loose, a small breakthrough volume is obtained, whereas, if the sorbent particles are very compact, there is flow restriction in the sorbent bed. In the following step, a small amount of epoxy glue is added in order to seal the tip of the needle while the aspirator is still on. Finally, the NTD is conditioned at 250 °C with nitrogen flowing through the sorbent bed.[20] Different types of sorbent beds, such as coated filaments, gold wires to trap mercury vapours, and also, the introduction of derivatization reagents, have extended the applicability of NTD to a wide spectrum of sample matrices.[26,27]

Different desorption schemes for NTD have been applied. The first desorption approach involved the use of 10 µL of air, used to facilitate the transfer of analytes from the sorbent bed into the column.[16] Similarly, desorption assisted by inert gases was studied. Thermal expansion desorption, addition of water to aid the release of analytes by water vapour, and use of solvent as a desorption approach have all been investigated as well.[13] Furthermore, modifications on the NTD design have been explored in order to facilitate desorption of analytes. For instance, by opening a side-hole above the sorbent bed, and using a special shaped liner with a restriction, the carrier gas is forced to pass through the sorbent bed, and consequently the desorption process is improved (Figure 1-1).[20]

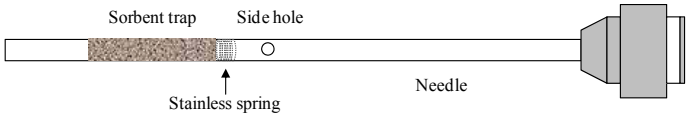


Figure 1-1. Side hole needle

Overall, NTD is a simple sample preparation approach that has demonstrated high versatility and practicality. One of the main advantages of this technique is its suitability in the analysis of total concentrations in systems where the presence of particulate matter is likely to occur. SPME,

in contrast, only permits the analysis of free analyte concentrations. The combination of both techniques can offer a more thorough idea of the composition of a sample matrix where both free analytes and particle-bound compounds can be found.[21] This idea will be further discussed in Chapter 3.

1.1.3. Membrane extraction with sorbent interface (MESI)

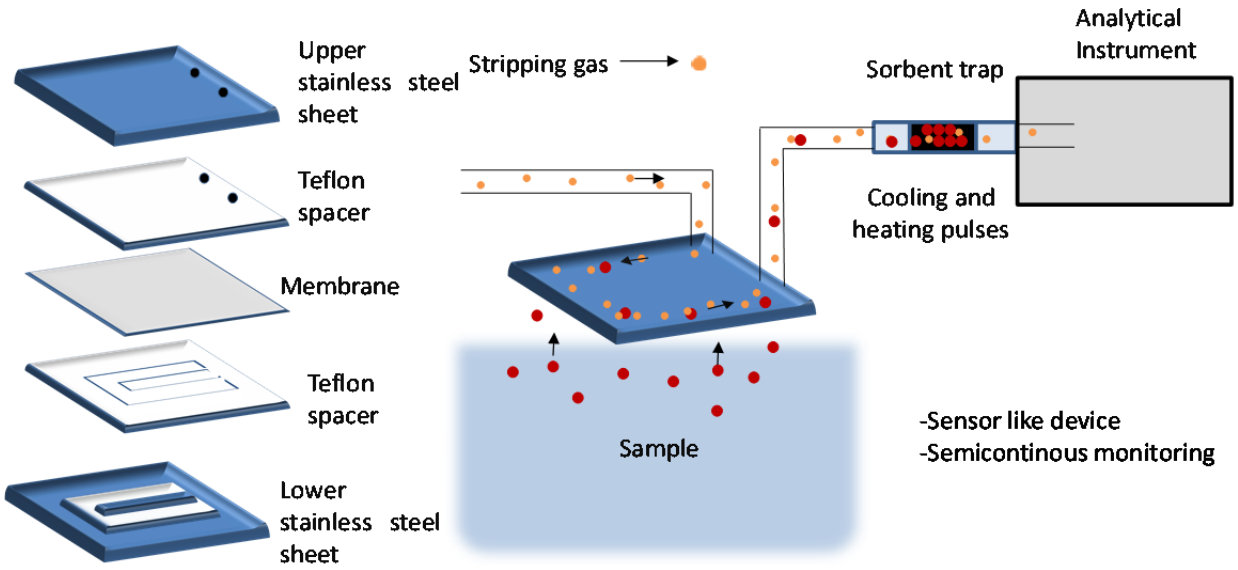


Figure 1-2. Schematic of the MESI system.

Membrane Extraction with Sorbent Interface (MESI) is another interesting sample preparation technique developed by Pawliszyn and coworkers.[28] A membrane housed in a special module, a sorbent trap, and an analytical instrument (which in most cases is a gas chromatograph), are the basic components of MESI.[29] This sample preparation technique permits semi-continuous monitoring of different analytes, while combining both sampling and pre-concentration steps in one.[28] Figure 1-2 illustrates the different parts contained in a MESI system.

First, the analytes permeate the membrane, which works as a selective barrier blocking the passage of water into the carrier gas.[30] Once the analytes have permeated the hydrophobic membrane, the stripping gas flowing on the other side of the membrane carries them to a sorbent bed, where they concentrate. The sorbent trap material is chosen depending on the target compounds. The use of Tenax, XAD-2 resin and carboxen have all been reported in MESI applications.[30,31] Alternatively, the sorbent trap capacity can be enhanced by using a Peltier cooler to decrease temperatures during the concentration process. This cooling system is constantly maintained on over time.

After the concentration step, trapped analytes are released from the sorbent bed either into the injection port, or directly in the GC column by thermal desorption (electric current pulses directly applied to the piece of tubing containing the sorbent bed).[30] When using a Peltier cooler, the cooling process is momentarily interrupted by the heating pulses applied for desorption. Once a heating pulse stops, the cooling system rapidly decreases the temperature in the sorbent bed recovering the initial extraction conditions. Under constant temperature conditions in the sampling medium, if a stable flow is maintained in the stripping medium and in the sample matrix, then diffusion of the compounds of interest through the membrane becomes the rate determining step of the extraction process, and Equation 1.5 can be applied.[32, 33]

$$C_s = \frac{bn}{B_2 A D_e K_{es} t} \tag{1.5}$$

where C_s is the concentration of the unknown, at steady state; b is the thickness of the membrane, n is the extraction amount, B_2 is a geometric factor defined by the shape of the membrane, A is the surface area of the membrane, D_e is the diffusion coefficient in the

membrane material, K_{es} is the membrane material/sample matrix distribution constant, and t is the extraction time.

Many parameters must be carefully considered when applying MESI. First of all, as in NTD, evaluation of the sorbent trap capacity is critical in order to avoid reaching breakthrough during sampling. Additionally, determination of the time required to reach a steady state in the system should be considered. The steady state can be defined as the time an analyte takes to permeate the membrane and reach the sorbent trap until a representative response of the sample concentration is obtained. Other important variables such as desorption time, trapping time, and temperature need to be evaluated as well.

1.2. Portable analytical instrumentation

1.2.1. Miniaturization of portable analytical instrumentation

The application of on-site analysis approaches substantially depends on the availability of portable analytical instrumentation and its performance.[2] In the last few years, significant attention has been dedicated to the development and implementation of miniaturized systems capable of providing reliable analytical data in field analysis.[34-36] Gas chromatography is one of the most powerful techniques in analytical chemistry; thus, its miniaturization represents a valuable tool in the development of such systems.[34,35] For instance, microchip-based GC, which consists of small channels fabricated on a silicon support to provide a separation medium, represents a clear advance in miniaturized gas chromatography, where a reduction in power consumption and fast analysis time are highly desirable.[34,37] Low thermal mass GC is another important approach towards GC miniaturization; in this approach, rather than using a bulky oven, resistive heating is applied to a capillary column using an electrically conductive material.

Thus, the use of capillary columns in portable instrumentation, combined with fast heating and low power consumption is possible.[38]

Significant development is being carried out on detection systems as well. Various types of detectors such as flame ionization (FID), flame photometry (FPD), thermal conductivity (TCD) and photoionization detectors (PID) have been installed in portable gas chromatographs.[35] However, these detection systems are not able to provide information about the identity of unknown substances present in matrices, a common occurrence in field analysis. For this reason, considerable effort has been placed on the development of mass spectrometry (MS) analyzers suitable for on-site analysis.[34,39] The miniaturization of different MS analyzers, such as time of flight (TOF),[40] quadrupoles,[41] ion traps,[34] and Fourier transform cyclotron resonance[42] have all been investigated. Particular attention has been focused on ion trap detectors, an analyzer with characteristics such as simplicity, less exigent optic element alignment and higher operation pressure, which, when compared to other analyzers, makes it quite suitable for miniaturization.[34] Moreover, possible effects due to a reduction in storage ion capacity of miniaturized ion traps can be overcome with the application of toroidal geometry. In the present investigation, a portable new version of a GC-MS developed by Torion Technologies (Tridion-9, Torion Technologies, American Fork, UT, USA) will be used for the first time as an approach for on-site quantitative analysis. This portable system, equipped with a carrier gas supply and a battery power source, consists of a low thermal mass injector, a low thermal mass GC, and a miniature toroidal ion trap mass analyzer (TMS).[34,43] Figure 1-3 presents a picture of this instrument.

The introduction of systems such as the one previously described represents an important step towards the evolution of analytical chemistry. Nevertheless, the application of these technologies is still in an incipient stage, and costs associated with these instruments can be

relatively high. Therefore, in cases where the analyst has prior knowledge of the identity of the analytes in the investigated system, inexpensive detection approaches such as IMS can be a valuable tool for fast field analysis. Further discussion about IMS detection is provided in Section 1.2.2.

Figure 1-3. New portable GC-TMS instrument (Tridion-9, Torion Technologies, American Fork, UT, USA).[43]

1.2.2. Ion mobility spectrometry

Ion mobility spectrometry is an analytical technique used to detect and identify ionized volatile or semi-volatile compounds by their mobilities in an electric field.[4] A general schematic of this technique is shown in Figure 1-4.

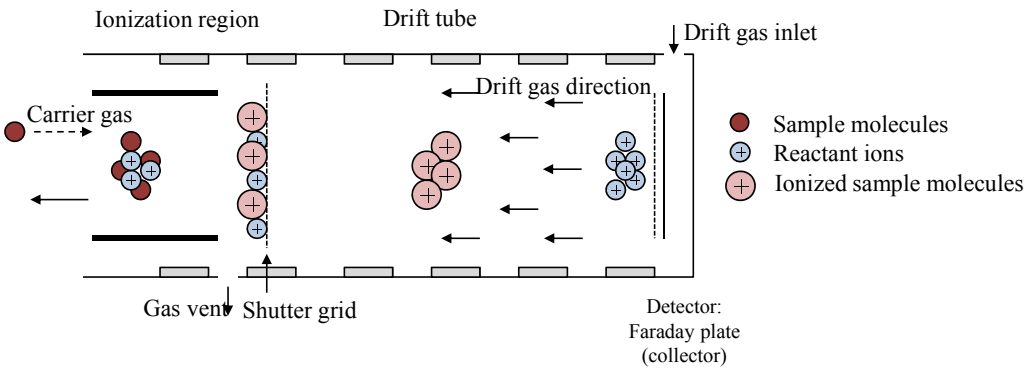


Figure 1-4. Schematic diagram of IMS.

In the first step, the vaporized sample is introduced into the system, and the compounds in the gaseous phase are ionized in the reaction region at atmospheric pressure. Different ionization sources can be applied in IMS, such as photodischarge, corona or partial discharge, lasers, electrospray ion sources, and others. However, most IMS analyzers are equipped with radioactive ionizing sources containing Nickel 63 (^{63}Ni).[4] The main advantages of using this type of ionizing sources rely on the stable production of reactant ions, low weight, low power requirements and simplicity. In the current section, particular emphasis will be placed on ^{63}Ni ionization sources.

Equation 1.6 represents the emission of high energy electrons, which is a spontaneous process, as well as the initial step in the production of ions.

$$^{63}_{28}Ni \rightarrow \beta^- + {}^{63}_{29}Cu \qquad (1.6)$$

The electrons emitted collide with gas molecules in the supporting atmosphere to form N_2^+ ions as shown in Equation 1.7.

$$N_2 + \beta^- \rightarrow N_2^+ + \beta' + e^- \qquad (1.7)$$

This reaction is followed by subsequent reactions, producing positive ions in ambient gas. These ions, named reactant ions, are used in the sample chemical ionization. The following equations represent the formation of reactant ions, which terminate in water clusters of a gas phase proton with the structure $(H_2O)_nH^+$:

$$N_2^+ + 2N_2 \rightarrow N_4^+ + N_2 \qquad (1.8)$$

$$N_4^+ + H_2O \rightarrow 2N_2 + H_2O^+ \qquad (1.9)$$

$$H_2O + H_2O^+ \rightarrow H_3O^+ + OH \quad (1.10)$$

$$H_3O^+ + H_2O + N_2 \rightarrow H^+(H_2O)_2 + N_2 \quad (1.11)$$

$$H^+(H_2O)_2 + H_2O + N_2 \rightarrow H^+(H_2O)_3 + N_2 \quad (1.12)$$

Temperature and level of humidity of the drift gas, which is air scrubbed over molecular sieves, determine the number of water molecules (n). Negative reactant ions are also formed from the attachment of an electron to molecular oxygen and the subsequent production of $(H_2O)_nO_2^-$.

As a result of the collision between sample molecules and positive reactant ions, the formation of an adduct ion ($MH^+(H_2O)_n$) can take place. Subsequently, stabilization of the adduct can occur by loss of water and formation of MH^+ as a product ion. Depending on the physical-chemical properties and the concentration of the sample, additional product ions such as dimers can be formed. On the other hand, negative reactant ions can originate negative product ions resulting from charge-transfer reactions.[4]

Once the product ions are formed, they are injected by a shutter grid into the drift region of the analyzer, where an electric field is applied. These ions travel through the drift region at different velocities and reach the collector electrode at specific drift times, a process dependant on its mass, charge and collision cross section. Thus, each ion swarm that arrives to the collector can be represented as a peak in the ion mobility spectrum.[4] The drift velocity of the ions (v_d) is proportional to the strength of the electric field (E), and the ratio between these parameters is equal to the ion mobility (K):

$$K = \frac{v_d}{E} \quad (1.13)$$

However, since ion mobility is affected by temperature and pressure, it is usually normalized and reported as reduced mobility(K_0), as follows:

$$K_0 = \left(\frac{d}{tE}\right)\left(\frac{P}{760}\right)\left(\frac{273}{T}\right) = cm^2/Vs \qquad (1.14)$$

Where d is the drift length (cm), t is the drift time (s), E is the field strength (V/cm), P is the pressure (torr) and T is the temperature (K).[4]

This analytical technique has mostly been used in military applications, in the detection of chemical weapons and explosives. Additionally, IMS analyzers have been utilized in other fields as well, including medical diagnosis, petrochemistry and environmental analysis. The main advantage of IMS is its suitability for field analysis due to the convenience of its technical requirements: low power requirements, small size, flexible operating conditions, and fast response.[4]

Despite the fact that IMS is an interesting analytical technique widely known and employed in several applications, particular situations during analysis need to be considered: first, in the analysis of complex matrices, competitive ionization is often likely to occur. Due to this effect, this technique as previously described can be only applied for quantification when the target compound has largely different ionization properties from those of the other constituents in the sample matrix.[4] A second important point to take into account is the concentration of the compound of interest. Ion mobility spectrometry using ^{63}Ni as ionizing source has shown very low detection limits for some substances, specifically for those with high proton affinities; however, when the concentration of the analyte is very high, saturation of the ionization source can take place, due to the depletion of reactant ions, and thus, no relationship between the

concentration and the peak area can be found.[4] Due to the above reasons, a wide investigation of the sample matrix and its effects is usually necessary before the IMS technique can be applied.

In order to improve the performance of the IMS analyzers, and take advantage of its benefits, several techniques have been hyphenated to this analytical technology. Gas chromatography coupled with IMS, for instance, has shown to be a useful alternative to overcome part of the limitations previously mentioned.[4,44] The pre-fractionation by GC allows the introduction of individual components into the system for detection and peak identification, avoiding competitive ionization among the different compounds in the sample. Despite the considerable improvements achieved in IMS performance by coupling it with a GC interface, it is important to point out that this modification cannot surpass restrictions in the analysis of high concentrations.[44]

Different applications of GC-IMS, such as analysis of terpenes from orange extracts,[45] determination of pesticides,[46] as well as other environmental monitoring approaches,[47,48] have demonstrated the potential of this system.

1.3. Investigated systems

1.3.1. Biogenic emissions

Volatile organic compounds emitted by plant life comprise the largest portion of global emissions; it has been estimated that isoprene represents about half of the total mass of those biogenic compounds.[49,50] The second most significant contribution to these emissions are monoterpenes, of which the two most abundant compounds are limonene and α-pinene.[51] Since monoterpenes are a highly reactive species, their role in atmospheric chemistry has been widely

investigated. Several studies have demonstrated that these compounds are able to rapidly react with OH radicals, and therefore influence the concentration of OH in the troposphere.[52] Furthermore, scientific evidence has shown that the oxidation of monoterpenes represents an important contribution to the formation of secondary organic aerosols (SOA).[53] Those oxidation products can either assist the formation of new particles, or condensate onto the existing particles, contributing to particle size and mass.[54] Based on this scientific evidence, it is possible to conclude that emission of these compounds affects the global oxidation chemistry, and the presence of particles resulting from oxidation of such compounds can influence radiation balance on a regional scale.[52,55]

When studying systems such as the one previously described, it is important to take into account both the high reactivity of the components, as well as the possible presence of particulate material. For this reason, the implementation of on-site approaches is highly important when aiming to avoid possible alteration of sample composition due to its reactivity. In addition, the plausible distribution of analytes not only in gas phase, but also onto the particles surface should be carefully accounted for, by using appropriate sample preparation techniques. Results obtained in the study of this interesting system will be described in Chapter 3.

1.3.2. Breath samples analysis

The composition of breath consists of ~78% nitrogen, 14 to 17 % oxygen, ~4% carbon dioxide, 0.96% argon and 6 % water vapor.[56,57] Additionally, the occurrence of different trace gases such as ammonia, ethanol, methanol, acetone, isoprene and other VOCs has been reported by several authors.[56,57] Characteristics typical of each individual, such as fitness, metabolism and diet, are determinant in the composition of breath samples.[57,58] For this reason, considerable

effort has been dedicated to the investigation of breath as a non-invasive diagnosis for the detection of different diseases.[59-61] Since acetone and isoprene are two of the most abundant compounds in breath, special attention has been placed on the investigation of metabolic processes related to their occurrence.[62] Acetone production has been associated with different metabolic pathways, with decarboxylation of acetoacetate and dehydrogenation of isopropanol being considered the two most important sources.[63] Various studies have revealed a strong relationship between acetone levels and diabetes.[63-65] Consequently, investigations of analysis methods that can facilitate the monitoring of this compound have gained considerable attention. Conversely, isoprene occurrence has been related to cholesterol biosynthesis;[66] however, high variability of isoprene levels, even in the same individual, has hindered its applicability as a non-invasive diagnosis tool. Recent studies have demonstrated that isoprene levels in breath are strongly dependent on physical activity due to changes in pulmonary gas exchange patterns.[66,67] As well as in acetone determination, methodologies employed for the analysis of this compound have been carefully studied.

Breath samples can be considered a complex system based on both the different metabolic processes involved, and the characteristics of the sample itself.[68] Respiration is comprised of various mechanisms of mass transfer, and hence, not only volatile compounds can be present in exhaled air, but nonvolatile substances have been found as well, in the form of aerosol droplets.[68,69] Thus, as in biogenic emissions, the distribution of volatile compounds in gas phase and in aerosol particles might be considered. In Chapter 3, interesting results obtained after analyzing breath samples using SPME and NTD will be discussed.

1.3.3. Analysis of indoors VOCs

Indoor air quality is an important indicator of health and safety in different locations, since people spend more than 80 % of their time in an indoor environment.[70,71] The occurrence of various indoor pollutants has been established as a result of ventilation system deficiencies, off-gassing from furniture and different materials, and even microbiological contamination.[72] Indeed, the monitoring of VOCs in environments where the manipulation of different chemicals or solvents is part of the daily routine is of particular interest. Quick assessment of the VOCs levels in a specific place can provide relevant information in terms of risk exposures during the performance of a given activity. In this research, the suitability and convenience of on-site analysis for these applications are discussed (refer to Chapter 3).

1.4. Thesis objective

On-site analysis offers well-known advantages, such as the reduction of analysis time and the possibility of obtaining more precise and accurate analytical results. More importantly, it offers the opportunity to draw prompt conclusions and take immediate action based on the collected data, thus providing a valuable tool over conventional methods. The availability of sample preparation techniques suitable for on-site analysis as well as developments on portable analytical instrumentation have paved the way for the implementation of protocols for in situ analytical determinations.

The objective of this project was to evaluate and apply SPME, NTD and MESI coupled with various portable instruments for on-site analysis. A new approach using IMS detection coupled with a miniaturized GC was proposed as a powerful configuration for field quantitative analysis.

Systems such as biogenic emissions, breath samples and a polymer synthesis laboratory were successfully analyzed using these portable systems. The feasibility of obtaining different information from the same system depending on the sample preparation technique employed was also discussed.

Chapter 2: Introduction of a miniaturized gas chromatograph into a modified handheld ion mobility spectrometry analyzer and evaluation of its performance using NTD.

2.1. Introduction

Advantages of IMS detection for on-site analysis, including low power consumption, fast analysis time, and flexible operating conditions, were already discussed in Chapter 1 (Section 1.2.2). However, when considering the implementation of this technology for field applications, the suitability of the sample preparation protocol to be used should be carefully evaluated. Typical approaches using IMS analyzers involve the direct introduction of gaseous samples into the system; sample introduction techniques include permeation tubes,[73] headspace samplers,[74] purge vessels[75] and membrane inlets.[76,77] In cases where analytes are present in liquid or solid matrices, evaporation and thermal desorption units have been successfully implemented.[78,79] Use of sampling swabs or membrane filters are the most common sample introduction approaches for direct sample collection and desorption, especially for qualitative analysis. By taking advantage of these desorption units, other sample preparation methods have been combined with IMS detection. For instance, stir-bar sorptive extraction (SBSE) was employed in the extraction of explosives from water samples before detection using a ^{63}Ni ionization source.[80] Similarly, fibre SPME exhibited a satisfactory performance when coupled with IMS detection. Applications of SPME-IMS include analysis of ephedrine in urine, cocaine and diazepam in aqueous solutions, terpenes in gas phase and tert-butyl ether in water.[81-83]

In this chapter, the coupling of NTD with a GC-IMS system is proposed for the first time. A miniaturized GC interface is coupled to a handheld IMS analyzer that was previously modified for SPME applications.[81] Thus, NTD joint with a GC-IMS system is proposed as an

advantageous, sensible protocol for quantitative on-site analysis. The versatility of the proposed system relies on the fact that both NTD and SPME sample preparation techniques can be coupled with this modified IMS analyzer. System performance is fully evaluated using α-pinene, limonene and acetone, all found in gas phase, as analytical models.

2.2. Experimental

2.2.1. Analytical reagents and supplies

α-Pinene (98 %) and (R)-(+)-limonene (97 %) were purchased from Sigma-Aldrich (Oakville, ON, Canada). Acetone (HPLC grade) was purchased from Caledon (Georgetown, ON, Canada). Nitrogen (5.0 ultra-high purity, 99.999%) was obtained from Praxair (Kitchener, ON, Canada). SPME fibres, (100 μm PDMS) were obtained from Supelco (Oakville, ON, Canada). New fibres were conditioned according to manufacturer instructions prior to their first use. Hypodermic stainless steel needles (22 gauge) were purchased from DynaMedical Corporation (London, ON, Canada). Carboxen 1000 (60/80 mesh) and DVB (100/120 mesh) were purchased from Sigma-Aldrich (Bellefonte, PA, USA), and from Ohio Valley (Marietta, OH, USA), respectively. A piece of silcosteel hydroguard (0.040" I.D., 1/16" O.D.) obtained from Restek (Bellefonte, PA, USA) was employed as a desorption line for SPME fibres and NTDs. Gas-tight syringes (1 and 5 mL) were purchased from Hamilton Company (Reno, NE, USA). A bi-directional syringe pump purchased from Kloehn (Las Vegas, NE, USA) was used for NTD sampling. To measure different flows, an ADM 1000 flow meter purchased from Agilent Technologies (Mississauga, ON, Canada) was employed.

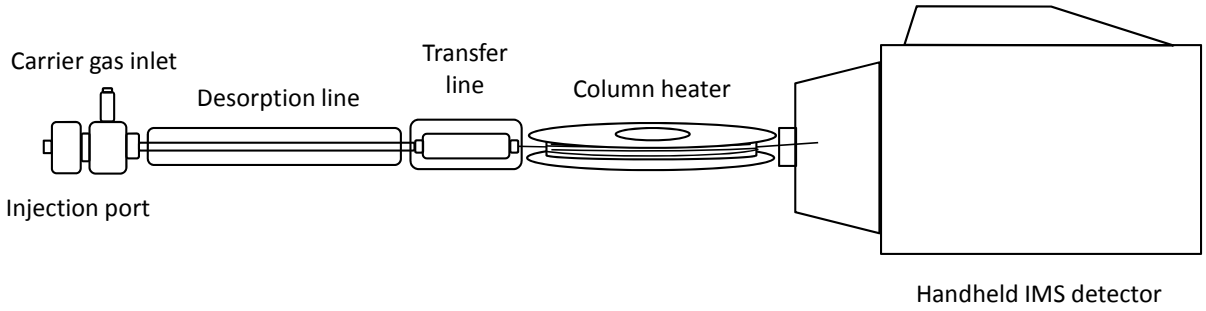
2.2.2. NTD construction

The original needles were cut to a total length of 9.5 mm. Subsequently, the empty needles were thoroughly washed with methanol (under sonication), and dried in an oven at 120 °C for two hours. The procedure used to pack a NTD is described elsewhere (refer to Section 1.1.2.).[20] A carboxen 1000 bed (10 mm) was initially packed in the needles, followed by a DVB layer of the same length. The sorbents were immobilized inside the needle by using a small spring plug at the beginning of the sorbent bed, and a small amount of epoxy glue at the end of the packing. The needles were conditioned at 250 °C under nitrogen flow for a minimum of two hours.

2.2.3. Instrumentation

A Sabre 2000 ion mobility spectrometer obtained from Smiths Detection (Mississauga, ON, Canada) was programmed in positive mode and employed. This IMS analyzer, equipped with ^{63}Ni ionization source, uses water as its calibrant/reactant ion (K_0= 2.300 $cm^2V^{-1}s^{-1}$) and operates at a positive high voltage of 1565 V. Purified air at 200 mL/min was used as the drift gas. The IMS was operated in vapor mode and the drift tube temperature was set at 111 °C. Spectra were collected after a 0.1 s delay, with a shutter grid width of 0.2 ms. The number of segments was set at 150 segments per analysis and, the number of co-added scans per segment was set at 100, with analysis duration of 300 s. A configuration schematic of the GC interface installed in front of a portable IMS analyzer is presented in Figure 2-1. A column heater taken from a Chrompack 2002 microGC was used to isothermally heat a piece of RTX-5 column (10 m; 0.25 mm I.D.; 0.25 μm) coiled around the heater. Silicosteel deactivated tubing (80 mm) was employed as a desorption line for SPME and NTD applications. Two ceramic resistors were used to heat both desorption and transfer lines. An internal reducing union (O.D. 1/16” to 1/32”) (Valco

Instruments Co. Inc., Houston, Texas, USA) was used as a transfer line between the desorption line and the column. All the heating units (desorption line, transfer line and column) were controlled by individual CN132 temperature controllers (Omega, Stamford, Connecticut, USA) installed in a custom made control box.



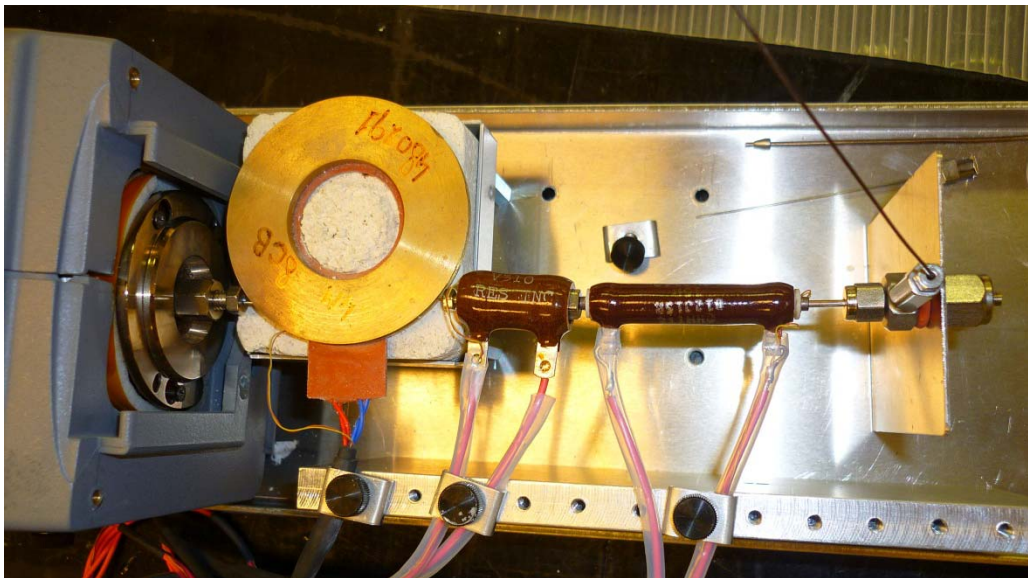


Figure 2-1. Schematic of the modified GC-IMS system (lateral view) (part A). Picture of the modified GC-IMS system (part B).

Nitrogen was used as carrier gas, and a Kofloc mass flow controller model 2203 (Kojima instruments inc., Kyoto, Japan) was employed to maintain a stable flow in the system.

Plasmagrams analysis was performed with software Instrument Manager 5.051 from Smiths Detection (Warren, NJ, USA). This software provides the greatest peak height in digital units (du) (maximum amplitude, MaxA), as well as the sum of all the maximum peak heights in the desorption process (cumulative amplitude, Cum A). Additionally, it displays the amplitude variation of plasmagrams throughout the analysis; the area resulting from the integration of the amplitude variation over time (du.s) was used as a response in all the experiments presented here. This software also enables use of a detection algorithm; depending on the compound, one or more ions can be formed at the operational conditions and defined as channels. Thus, detection of a specific substance can be subjected to monitoring of one or more channels.

2.2.4. Standard gases

A standard gas generator system was employed in the construction of the calibration curves. Individual standard permeation tubes were prepared by filling pre-cleaned Teflon tubing with a known mass of pure standards for each compound. Next, the tubes were placed in a permeation chamber at constant temperature and nitrogen flow. A diluting gas flow allowed low concentrations to be achieved in the sampling chamber. The concentrations of α-pinene and limonene exiting the standard gas generator were determined by extracting 120 mL of standard gas (at 2 mL/min) using a NTD. Subsequently, the NTD was injected in a GC-FID, where a calibration curve for liquid injections of standards was constructed to quantify amounts extracted by the NTD. Acetone concentration was determined by the difference in weight in the

permeation tube before and after placing it in the permeation chamber. For this purpose, the permeation rate of the tube was calculated by using the following equation: (initial weight of the tube - final weight)/time in the permeation chamber. Concentration was then calculated by dividing the permeation weight by the total nitrogen flow (flow passing through the permeation chamber + flow of the diluting gas).

2.2.5. Calibration

The GC-IMS system response was calibrated by means of amount extracted vs. detector response using a CAR/DVB NTD. Several volumes ranging from 5 to 120 mL were sampled from a known concentration set in the sampling chamber of the aforementioned gas generator system. Knowledge of the sampled volume and the concentration made it possible to determine the amount extracted onto the sorbent bed. The desorption of the NTD was carried out at 255 °C during 2 min, using 0.2 mL of nitrogen to assist the thermal desorption. Under these experimental conditions no carryover was observed.

Table 2-1. Equations for the analysis of variance.[84]

Source of variation	SS	Degrees of freedom	MS	F
Due to regression	$SS_{Reg} = \sum_i n_i(\hat{y}_i - \bar{y})^2$	1	MS_{REG}	$\frac{MS_{REG}}{MS_R}$
Variation of group means about the line = lack of fit	$SS_{LOF} = \sum_i n_i(\bar{y}_i - \hat{y}_i)^2$	k-2	MS_{LOF}	$\frac{MS_{LOF}}{MS_{PE}}$
Within the groups = pure error	$SS_{PE} = \sum_i \sum_j n_i(y_{ij} - \bar{y}_i)^2$	$\sum_i n_i - k$	MS_{PE}	
Total	$SS_T = \sum_i \sum_j n_i(y_{ij} - \bar{y})^2$	$\sum_i n_i - 1$		

At each x_i (i=1,..,k) there are $n_i$observations.

y_{ij}(j=1,…, n_i)
$\bar{y}_i$ is the mean value of replicates y_{ij}at concentration x_i
$\hat{y}_i$ is the value of y at x_i calculated by the calibration function.
MS=SS/df

Finally, an evaluation of the calibration data was carried using least-squares regression, as well as analysis of variance. Table 2-1 summarizes the equations required for the analysis of variance.

In Table 2-1, SS_T represents the variation of y values around the mean values. SS_T can be broken down into two components: SS_{Reg}, which accounts for variations in the fitted regression line, and SS_R ($SS_R = SS_{LOF} + SS_{PE}$), which contains the remaining variability around the regression line. The components of SS_R can be described as follows: SS_{PE} is the sum of squares due to purely experimental uncertainty (variability within each group of replicate measurements), and SS_{LOF} represents the variability of group averages about the regression line. This last parameter is an indicator of how well the data fits the chosen model.[84]

2.3. Results and discussion

2.3.1. GC-IMS performance

Limonene and α-pinene were selected to test the separation performance of the introduced GC interface. These compounds, as well as other monoterpenes, produce the same ion peak (monomer) when they undergo ionization using a ^{63}Ni source in positive mode and water as a reactant ion (Table 2-2). Therefore, the introduction of a separation step before IMS detection is critical, either for qualitative or quantitative analysis. Well resolved peaks of α-pinene and limonene were obtained at 76 °C and 140 mL/min (column conditions) within a short period of time (220 s). The connection between the desorption line and the column was maintained at 200

°C. Figure 2-2 presents the plasmagram amplitude variation throughout the analysis time for the selected channel. It is worth highlighting that in the proposed application, a single channel can be set for the detection of these monoterpenes.

Table 2-2. Parameters of the target analytes in the aforementioned GC-IMS system (retention times obtained at 76 °C and 140 mL/min in the GC column).

Compound	Retention time, s	Ion drift time, ms	K_0, $cm^2V^{-1}s^{-1}$
α-Pinene ($C_{10}H_{16}$)	131	12.95 ± 0.01	1.75 ± 0.01
Limonene ($C_{10}H_{16}$)	199		
Acetone (C_3H_6O)	55	11.85 ± 0.01	1.92 ± 0.01

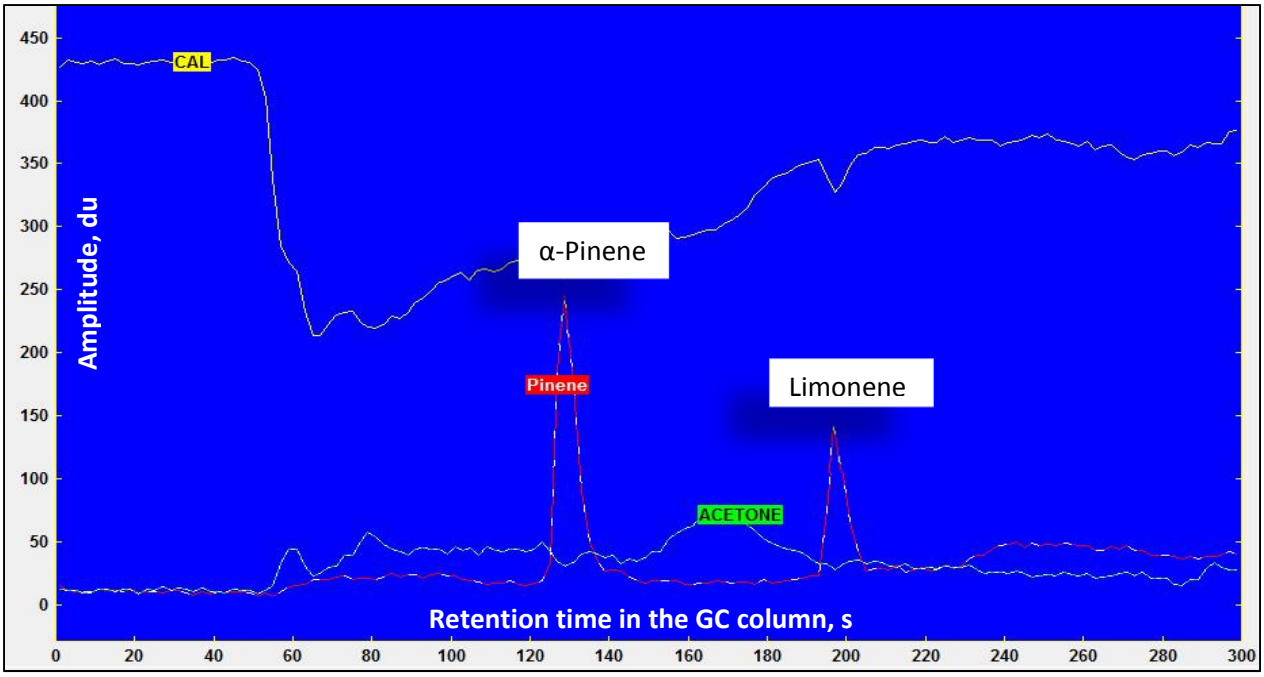


Figure 2-2. Plasmagram amplitude variation for α-pinene and limonene throughout analysis time.

In cases where both target compounds produce the same ion, the retention time of the analytes can be considered a crucial identification parameter. Consequently, good stability of

retention times is of significant importance in GC-IMS applications. In the current study, the retention time stability of the selected analytes was monitored at the described operational conditions. Intra-day repeatability of retention times for both compounds presented RSDs below 1 %, whereas the inter-day variation presented RSDs below 3 % during a 30-day period.

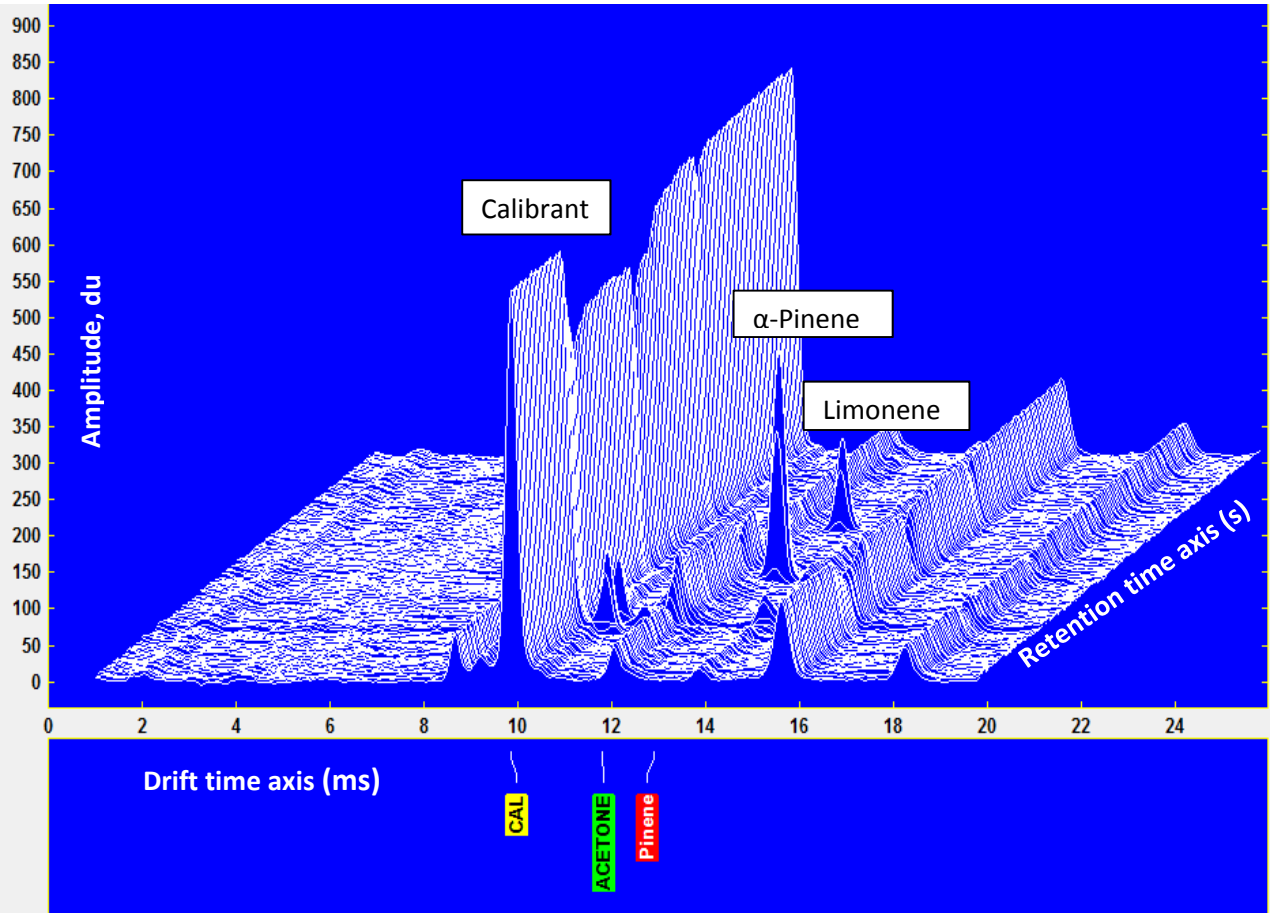


Figure 2-3. 3D plasmagram for α-pinene and limonene.

IMS detector response stability was also evaluated in the proposed set up. Quality control (QC) tests were run at least three times during every workday. The QC solution was comprised of 1.5 g of XAD-4 particles mixed with 3 g of pump oil spiked with the target analytes (2 µL of each compound per 32 g of pump oil) in a 20 mL vial.[85] The QC tests were performed by exposing a 100 µm PDMS fibre to QC vial headspace for 1 min at 30 °C without agitation. The

results obtained during seven consecutive days are plotted in Figure 2-4. Both intra and inter-day RSDs were below 10 % for both compounds.

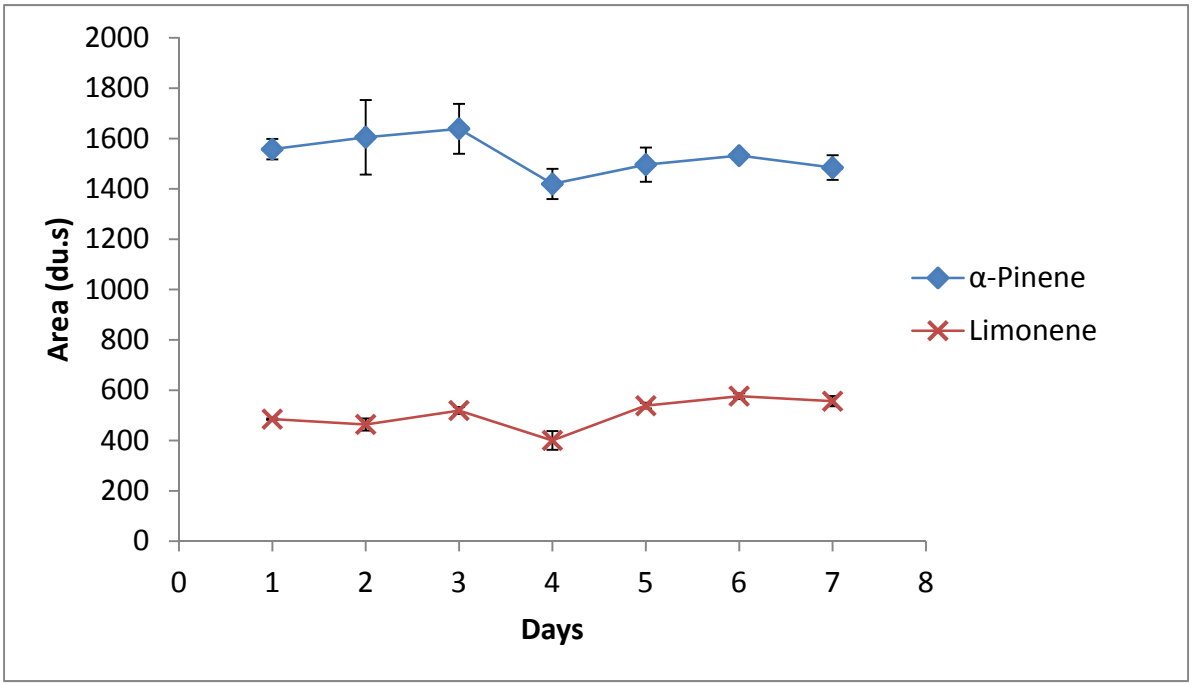


Figure 2-4. Stability of the GC-IMS response during seven consecutive days.

Typical RSD values for the responses of benchtop instruments are expected to be below 10%, and, depending on detector type, can sometimes be lower than 5%. It is known that one of the main limitations of using portable analytical equipment is its poorer performance when compared to conventional benchtop instruments. For this reason, it is worth emphasizing that the proposed GC-IMS system has exhibited satisfactory performance in terms of response and retention time stability. Furthermore, since IMS detection using ^{63}Ni is governed by the proton affinities of the target analytes, enhanced selectivity for trace analysis is also plausible by tuning the system to monitor specific ion mobilities (defined channels). Indeed, artifacts or interferences, which come either from the NTD sorbent or from the sample matrix, are considerably reduced as a result of their unsuitability to be ionized at the conditions employed in this study.

At this point, it is worth emphasizing that this system also allows for the combination of data in a 2D-matrix, as shown in Figure 2-3. The possibility of obtaining retention and drift time information in one single plot is an advantageous feature in a portable analytical instrument that can be coupled with a convenient sample preparation technique such as NTD. Thus, in cases of chromatographic co-elution, differences in the ion mobilities of the substances involved allow the user to monitor them by setting different channels.

2.3.2. Calibration of the GC-IMS system

Table 2-3 summarizes the set of conditions employed in the standard gas generator and the corresponding concentrations for each of the compounds.

Table 2-3. Conditions in the standard gas generator for each target compound.

Compound	Temperature in the permeation chamber, °C	Flow in the permeation chamber, mL/min	Flow of the diluting gas, mL/min	Concentration, ng/mL
α-Pinene	40	150	1460	0.11
Limonene	40	150	1460	0.05
Acetone	40	200	4520	0.18

As previously discussed in Chapter 1, one of the main disadvantages of IMS detection is its limitation in the analysis of high concentrations due to saturation of the ionizing source. Typical calibration profiles for IMS detection with ^{63}Ni ion sources exhibit a narrow linear dynamic range with a plateau response at higher concentration levels. Based on the advantages of linear calibration over other calibration models, only the linear region of the GC-IMS system response was taken into consideration in this work. In fact, since applications of this system discussed in future sections only comprise trace analysis of VOCs, considering only the linear dynamic range

for calibration is a valid approach.

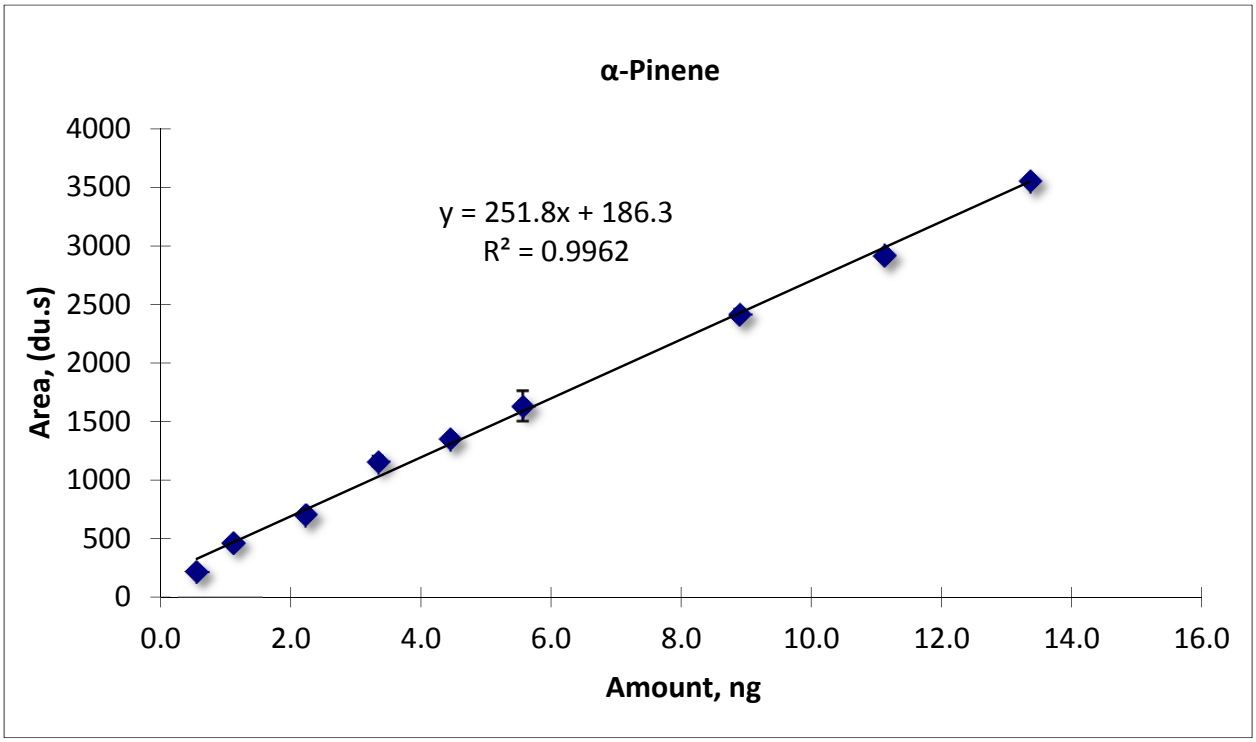


Figure 2-5. Linear response range for α-pinene using the described GC-IMS system.

Table 2-4 presents the calibration data corresponding to α-pinene, limonene and acetone in the GC-IMS system. At least seven calibration levels were evaluated for each of the compounds. The correlation coefficients obtained for the three target compounds reflect good linearity at the specified calibration range. However, to effectively confirm a linear relationship at the investigated conditions a linearity test using analysis of variance was performed (refer to Section 2.2.5.).

Table 2-5 contains the results obtained from the analysis of variance. The F-test values calculated for each of the analytes were lower than the critical value at a 95 % confidence level. These results confirm that a linear relationship exists between the instrument response and the amount of analyte introduced within the studied calibration range. Therefore, at this point it is

valid to state that the proposed analytical system is able to provide reliable analytical data at the specified conditions, and its further implementation in real applications is possible.

Table 2-4. Calibration data for the target analytes in the GC-IMS system.

Compound	Calibration range (ng)	Equation	R^2	LOD (ng)	LOQ (ng)	RSD, % (n=3)	Accuracy, % (n=4)
α-Pinene	0.6 – 13.4	y = 251.8x + 186.3	0.9962	0.20	0.65	7.8	95
Limonene	0.3 – 6.1	y = 318.4x + 15.7	0.9973	0.037	0.12	10.4	97
Acetone	0.2 – 9.0	y = 484.7x + 100.2	0.9962	0.12	0.38	15	95

Table 2-5. Testing the linearity of the regression model for α-pinene, limonene and acetone at a confidence level of 95 %.

Compound	Sum of squares				
	Residual (df)*	Pure error (df)	Lack-of-fit (df)	F-test estimated	F-test critic
α-Pinene	6.00×10^4 (14)	2.21×10^4 (8)	3.79×10^4 (6)	2.29	3.58
Limonene	3.93×10^4 (15)	2.08×10^4 (8)	1.85×10^4 (7)	1.01	3.50
Acetone	7.66×10^5 (15)	6.22×10^5 (10)	1.45×10^5 (5)	0.47	3.33

*Degrees of freedom in brackets.

Limits of detection and quantification for the target compounds were also investigated. For this purpose, eight replicates of 10 mL extractions from the standard gas generator were run in the GC-IMS system. Finally, LOD and LOQ were calculated according to the EPA procedure using the following equations: LOD = $t_{n-1,\ 1-\alpha=0.99}$ x SD and LOQ = 10 x sd where $t_{n-1,\ 1-\alpha=0.99}$ is the Student's t-value at 99 % of confidence, and SD is the standard deviation of the replicates. Taking into consideration the sampled volumes, the limits of quantification can be expressed in

terms of ng/mL as follows: 0.065 ng/mL for α-pinene, 0.012 ng/mL for limonene and 0.038 ng/mL for acetone. Based on our experience, these results are comparable with typical LODs achieved with conventional benchtop instruments, namely GC-qMS and GC-FID. Hence, this newly introduced analytical approach provides enhanced selectivity and satisfactory stability, as well as outstanding LODs, which are advantageous for trace VOCs analysis.

The accuracy of the proposed GC-IMS system coupled with NTD as an extraction technique was assessed by extracting 10 mL at 2 mL/min from gaseous standards prepared in 1 L glass bulbs. The concentrations of the three analytes in the gaseous standards were around 0.4 ng/mL. The calculated amount extracted was compared with the theoretical value. Accuracy data obtained one month after construction of the calibration curve can be found in Table 2-4. Results exhibited a good agreement between the calculated extracted amount and the theoretical spiked amount. For all analytes, recoveries higher than 95 % were obtained.

2.4. Conclusions

The coupling of NTD with GC-IMS was successfully evaluated using α-pinene, limonene and acetone as target analytes, and the potential of this configuration for on-site quantitative analysis was proved. Satisfactory stability and reproducibility results in terms of retention time and response were found. Furthermore, the proposed system exhibited LODs comparable to those provided by conventional benchtop instruments. A linear relationship at the evaluated calibration range was verified by least-squares regression and analysis of variance (F-test calculated<F-test critical at 95 % of confidence). Despite narrow linear dynamic ranges obtained for the studied analytes, the possibility of adjusting the sample preparation conditions, such as sampling smaller volumes with NTD or using shorter extraction times in SPME, is an alternative

to broaden the linear dynamic range of the system and extend its the applicability. Future directions should consider the introduction of a split valve to make this approach feasible to be used for the on-site analysis of higher concentrations. Finally, the introduction of a miniaturized GC before IMS detection was a simple way to considerably extend the scope of application of this analyzer while retaining its advantages.

Chapter 3: Coupling SPME and NTD with portable analytical instrumentation for on-site applications.

3.1. Introduction

SPME and NTD samplers have broadly demonstrated their suitability for analysis of VOCs, especially for on-site analytical applications. As emphasized previously, the advantages of these sampling approaches, such as reusability and integration of sampling and sample preparation in one step, make SPME and NTD superior over traditional sample preparation techniques employed for gas samples analysis. In addition, the use of SPME and NTD allow for discrimination between free and total concentrations in systems where aerosols or particulate matter are likely to occur.[21]

From the perspective of mass transfer processes theory, SPME is considered a particle-free sampling technique based on the significant difference between the diffusion coefficients of gaseous molecules and particles, from which analyte flux within the boundary layer can be determined.[86] Thus, the diffusion process that occurs in the boundary layer due to a concentration gradient is more pronounced for gaseous molecules than for particles, and consequently, the number of free molecules reaching the fiber surface is considerably greater than the number of particles being deposited on the fiber coating.[21] NTD, on the other hand, is an exhaustive extraction technique that enables compounds in gas phase, as well as particles present in the gaseous sample, to be trapped. Hence, the simultaneous application of SPME and NTD techniques for on-site quantitative analysis is shown to be a valuable method, which can be used to fully characterize a system.[21]

The role of portable analytical instrumentation in the implementation of on-site analysis strategies is also of paramount importance. For this reason, the application of these two sample preparation techniques, coupled with different portable instruments for the analysis of real samples, can provide valuable information regarding the capabilities of the whole integrated system, as well as evidence of possible limitations that can arise during field quantitative analysis.

In this section, SPME and NTD, together with different portable analytical instruments, are applied in the analysis of several systems. First, these techniques are employed in the analysis of biogenic compounds emitted by a pine branch using the GC-IMS system (described in Chapter 2). Furthermore, the analysis of breath samples using a portable GC-FID system coupled with SPME and NTD is described and discussed. Finally, a portable GC-TMS system coupled with SPME is employed for fast field air sampling in a polymer synthesis laboratory.

3.2. Experimental

3.2.1. Analytical reagents and supplies

α-Pinene (98 %), (R)-(+)-limonene (97 %) and isoprene (99 %) were purchased from Sigma-Aldrich (Oakville, ON, Canada). Acetone and toluene (HPLC grade) were purchased from Caledon (Georgetown, ON, Canada). Nitrogen, helium, and hydrogen (5.0 ultra-high purity, 99.999%) were obtained from Praxair (Kitchener, ON, Canada). SPME fibres (CAR/PDMS 85 μm and PDMS/DVB 65 μm) were obtained from Supelco (Oakville, ON, Canada). CAR/DVB NTDs were constructed as described in Section 2.2.2. Gas-tight syringes (1 and 5 mL) were

purchased from Hamilton Company (Reno, NE, USA). Glass bulbs (1 L) and Thermogreen LB2 septa were obtained from Supelco (Oakville, ON, Canada). For NTD sampling, a bi-directional syringe pump purchased from Kloehn (Las Vegas, NE, USA) and an AP-20 manual sampling pump from Komyo Ricagaku (Kanagawa, Japan) were used. To measure different flows, an ADM 1000 flow meter purchased from Agilent Technologies (Mississauga, ON, Canada) was employed. For the application of the diffusion based calibration method an HHF51 digital wire anemometer (Omega Engineering, Stamford, CT) was used to determine the air velocity. To maintain a constant convection during the SPME sampling of biogenic compounds, a mini-fan connected to a 12 V battery set was used. For on-site analysis of VOCs in a polymer synthesis lab, a portable device for rapid air sampling proposed by Augusto *et al.* was used.[12] Briefly, this device consists of a modified hair dryer (VS-513F, Helen of Troy, El Paso, TX, USA), with a reverted flow source and without a heating coil, which provides constant air flow to the SPME fibre. Figure 3-1 shows a schematic of the device.

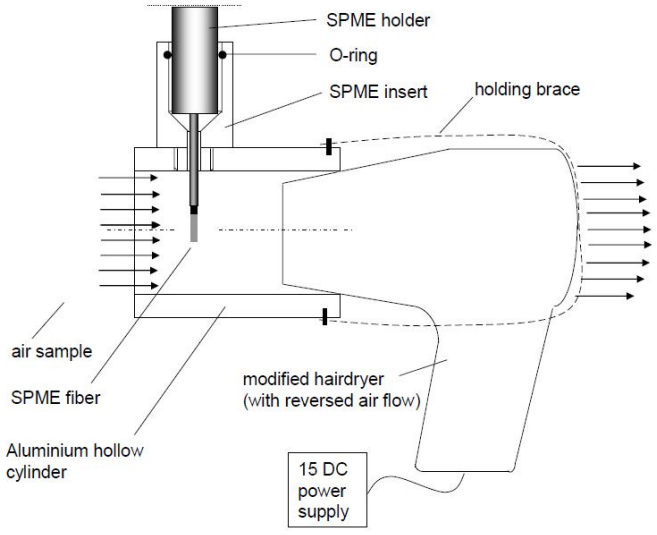


Figure 3-1. Portable dynamic air sampling device for SPME.[7]

3.2.2. Instrumentation

The GC-IMS system described in Chapter 2 was employed in biogenic compounds analysis.

For breath samples analysis, a portable GC-FID SRI 8610C (SRI instruments, Torrance, CA, USA) was used. A CP Porabond Q column (25 m x 0.32 mm x 5 μm) (Varian Inc., Middelburg, the Netherlands) was installed in the instrument, due to its suitability in retaining and separating compounds with high volatility. Since this system included its own air compressor, only hydrogen and helium needed to be provided. Oven temperature was programmed as follows: 90 °C for 2 min, 15 °C/min to 120 °C for 1 min, 10 °C/min to 140 °C for 7 min, 15 °C/min to 260 °C for 3 min. Helium (carrier gas), hydrogen and air were maintained at 15, 27 and 6 PSI, respectively. Detector temperature was set at 285 °C. Injection port temperature was kept at 250 °C for NTD desorption, and at 280 °C for SPME fibre desorption. For NTD analysis, 0.2 mL of helium was used to assist the thermal desorption. Desorption times for NTD and SPME fibres were 2 and 3 min, respectively.

For analysis of indoor contaminants in a polymer synthesis laboratory, a portable GC-TMS analyzer was used (Tridion^{TM}-9, Torion Technologies, American Fork, UT, USA). This instrument includes features to facilitate its portability, such as a set of lithium rechargeable batteries (30 V, 6.8 Ah), the capability to operate with 98 mL helium cartridges (2500 psi), and a low thermal mass GC system with a MXT-5 column (5 m x 0.1 mm x 0.4 μm). The column flow was maintained at 0.15 mL/min. Temperature programming was set at the following conditions: 50 °C for 10 s, 2 °C/s to 270 °C for 10 s, with a total run time of 130 s. The injection port temperature was set at 280 °C. This portable GC-TMS contains two split valves (a 10:1 and 50:1 split valve) than can be activated or deactivated throughout the running process. Thus, injections

were performed using the following split conditions: splitless mode for 2 s, 10:1 split valve on for 8 s, 10:1 split valve off and 50:1 split valve on for 30 s, and finally split valve 50:1 off. The detector voltage was set at -1475 V and the filament current was maintained at 1.08 A.

As a supporting instrument for some of the experiments, an Agilent 6890 gas chromatograph coupled with a 5973 MSD quadrupole mass spectrometer (GC-qMS) (Agilent Technologies, Mississauga, ON, Canada) was used. Chromatographic separation was performed using a Rxi®-624Sil MS (30 m x 0.32 mm x 1.80 μm) column from Restek, with helium as the carrier gas at a flow rate of 1.5 mL/min. The oven temperature was initially held at 40 ºC for 2 min, gradually increased to 55 ºC at a rate of 3 ºC/min, then to 250 ºC at a rate of 20 ºC/min, and then held for 3.25 min. During the analysis, the transfer line, MS Quad and MS source were set at 280 ºC, 150 ºC and 230 ºC, respectively, with the MS operating in electron ionization mode.

3.2.3. Standard gases

Standard gases for α-pinene, limonene and toluene were produced as described in Section 2.2.4. In the generation of toluene standard gas, the permeation chamber was maintained at 32 °C under a nitrogen flow of 150 mL/min; the diluting gas was maintained at 2000 mL/min.

For isoprene and acetone analysis, gaseous standards for SPME and NTD analysis were prepared by evaporating known volumes of pure compounds in a 1 L glass bulb. First, the glass bulb was thoroughly washed with methanol, dried overnight in an oven at 120 °C, purged with pure nitrogen for 1 hour, and then evacuated for approximately 30 min using a water aspirator. Next, volumes ranging from 1 to 5 μL of liquid compounds were spiked by means of a 10 μL syringe. Once complete evaporation of the standards was reached, the glass bulb was equilibrated using pure nitrogen. Different concentrations were obtained by transferring to other

glass bulbs specific volumes of this gas mixture, using a gas-tight syringe. Finally, the glass bulbs were equilibrated with pure nitrogen. When humidity in the gas standards was required the nitrogen flow was saturated with water, as shown in Figure 3-2.

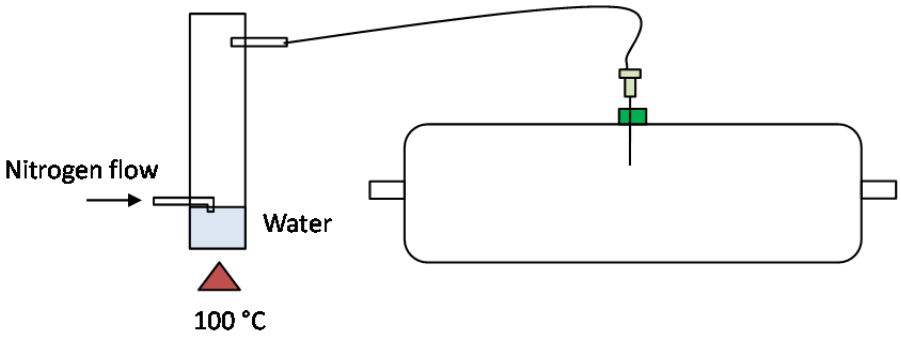


Figure 3-2. Apparatus for preparing gas standards with humidity.

3.2.4. Sampling methods

3.2.4.1. Sampling of biogenic compounds

On-site analysis of the compounds emitted by a pine branch was carried out using SPME and NTD samplers. For this purpose, the pine branch was enclosed in a silanized glass chamber (12 cm wide), as can be observed in Figure 3-3. A glass lid containing several holes with Thermogreen predrilled septa was used to close the system. A mini-fan was fixed to the chamber lid in order to supply constant air convection. Extractions using both sample preparation techniques were performed 20 min after enclosing the pine branch. Temperatures during every sampling period were recorded. SPME extractions were conducted using a 65 µm PDMS/DVB fibre and extraction times of 10 s. Desorption of SPME fibres was performed at 255 °C for 3 min. For NTD monitoring, volumes between 1 and 10 mL were sampled from the glass chamber. The desorption conditions were the same as described in Section 2.2.5. This procedure was repeated five different times during the same day, using the same branch. After every sampling

period, the branch was carefully removed from the container, and the sampling chamber was cleaned with methanol, dried in an oven at 120 °C and flushed with pure nitrogen.

Figure 3-3. Experimental setup for on-site sampling of biogenic emissions.

3.2.4.2. Sampling of breath samples

Analysis of breath samples was conducted by collecting exhaled gas in thoroughly cleaned glass bulbs. Before sample collection, the glass bulbs were cleaned and purged as described in Section 3.2.3. A volunteer was asked to exhale in the glass container while the stopcocks were opened. Before completing the exhalation process, the stopcocks were promptly closed, and the last 1000 mL of exhaled air were retained. As soon as the sample was collected, extractions using a CAR/DVB NTD and a CAR/PDMS SPME fibre were carried out from the same glass bulb. NTD extractions were performed by sampling 10 mL at 2 mL/min from the glass container. On the other hand, the extraction time for SPME analysis was fixed at 10 min. This process was repeated with breath samples obtained from five subjects.

3.2.4.3. Sampling of indoor pollutants

The on-site monitoring of contaminants in a polymer synthesis laboratory was accomplished by rapid field air sampling using an 85 μm CAR/PDMS fibre. For this purpose, various extractions were performed by exposing the SPME fibre for 30 s under constant air convection conditions. The air convection was controlled by using the portable air sampling device described in Section 3.2.1. This procedure was repeated at different times during the same day, and temperature of the room was registered before each sampling period.

3.3. Results and discussion

3.3.1. Analysis of biogenic compounds from a pine branch

3.3.1.1.Calibration

The calibration data presented in Chapter 2 (Section 2.3.2) was employed in this section. As emphasized previously (Chapter 1), no calibration curves are required when calibration of SPME is carried out using the diffusion-based model. In this calibration approach, only the amount extracted needs to be estimated from the detector response. Consequently, quantitative analysis using SPME and NTD can be conducted using the same calibration curve.

Table 3-1 lists the various parameters required to calculate concentrations using the diffusion-based SPME quantitative model (refer to Section 1.1.1. in Chapter 1). The values provided in this table (Table 3-1) correspond to the on-site determination of α-pinene emitted by a pine branch at 3 p.m. For this application, a 65 μm PDMS/DVB fibre was selected based on previous results, which reported a satisfactory performance of this type of coating for the extraction of biogenic compounds.[11]

Table 3-1. Different parameters involved in determining concentrations by SPME diffusion-based calibration. Values in this table correspond to on-site analysis of α-pinene (first replicate run at 3 p.m.).

Parameter	Values	Units
Amount of analyte extracted (n)	6.2	ng
Fibre radius (outside) (b) [a]	0.0135	cm
Fibre length (L)	1	cm
Sampling time (t)	10	s
Diffusion coefficient (Dg)[b]	0.059	cm^2/s
Temperature (T)	296.4	K
Pressure (P)	1	atm
M air	28.97	g/mole
V air	20.10	cm^3/mole
Mr (M air + M analyte)/(M air*M analyte)	0.04	mole/g
M analyte	136.2	g/mole
V analyte	196.7	cm^3/mole
Boundary layer thickness	0.02	cm
Reynolds number	10.06	
Linear velocity of the air (u)	55.9	cm/s
Air kinematic viscosity (v)	0.15	cm^2/s
Schmidt number	2.52	
Concentration (Cg)	**1.6**	**ng/mL**

[a]Value corresponding to a 65 µm PDMS/DVB fibre.
[b]Diffusion coefficient calculated using the Fuller-Schettler-Giddings model (Section 1.1.1.).

As can be observed in Figures 3-4 and 3-5, several peaks corresponding to the same channel were obtained from the analysis of the compounds emitted by a pine branch. These profiles suggest the presence of other monoterpenes able to produce the same ion under the selected ionization conditions. Based on this, the presence of α-pinene and limonene in the investigated system was determined by their retention times. These results support not only the importance of using a separation step before IMS detection, but also the necessity of a stable system that provides repeatable retention times.

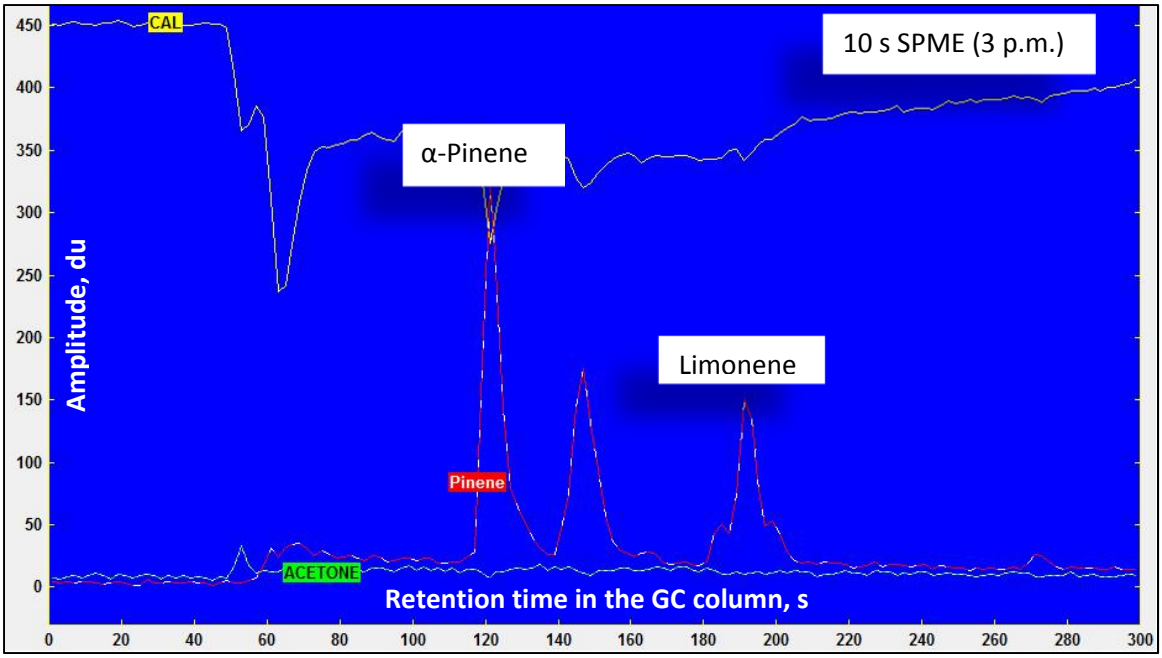


Figure 3-4. Plasmagram amplitude variation over the analysis time obtained after 10 s extraction from a pine branch using a PDMS/DVB SPME fibre and constant convection.

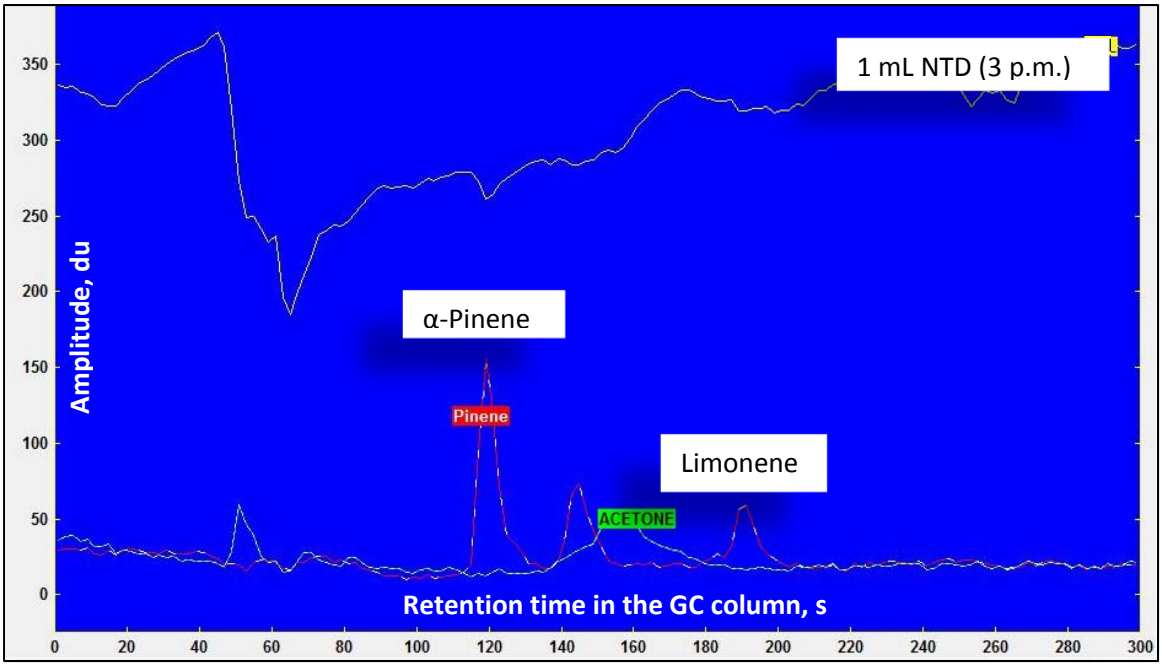


Figure 3-5. Plasmagram amplitude variation over the analysis time obtained after 1 mL extraction from a pine branch using a CAR/DVB NTD.

3.3.1.2. NTD and SPME sampling

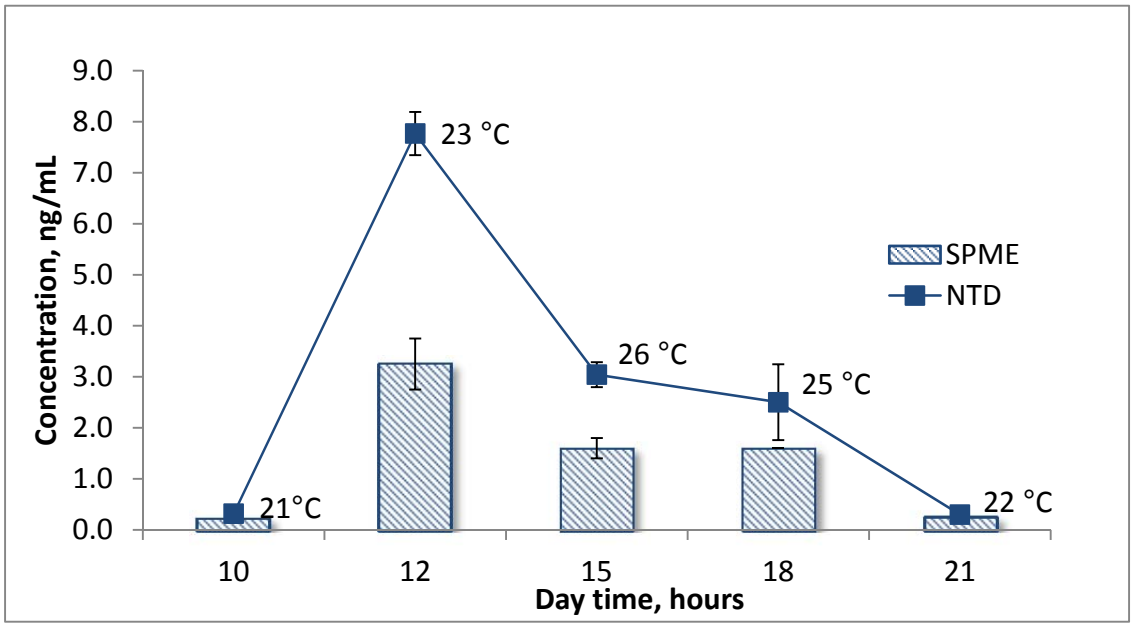


Figure 3-6. Concentrations of α-pinene at different times along the same day using SPME and NTD (n=2).

Figure 3-6 illustrates the plotted results corresponding to the quantification of α-pinene using SPME and NTD devices. Since baseline separation of limonene was not feasible at the selected experimental conditions for the GC-IMS system, only α-pinene concentrations were estimated. Due to the low detection limits that can be reached using this instrumental setup, relatively small volumes and considerably low extractions times are sufficient to obtain an adequate response with NTD and SPME samplers, respectively. A similar concentration trend was observed in the concentration profiles obtained with both sampling approaches along the same sampling day. These results were in agreement with findings previously reported by other authors where concentration maximums were found between 12 h and 15 h as a result of variations in temperature and illumination conditions.[11] At low concentration levels statistically equivalent concentrations where estimated using SPME and NTD. However, the results obtained at 12 and 15 hours revealed a significant difference in the concentration detected with both sampling

approaches.

These differences might be explained based on two possible reasons. First, in regards to terpenes analysis, it is worth emphasizing that these compounds are prone to undergo oxidation reactions. The contribution of these oxidation products to the formation of aerosols, or particle matter, has been well-documented in the literature by several authors.[87,88] Because α-pinene is the most common monoterpene present in biogenic emissions, the presence of particulate matter might affect its distribution in gas phase. Furthermore, different oxidation products of α-pinene, such as pinonaldehyde, pinic and pinonic acids, have been detected in aerosol particles[89,90]. Despite recent investigations demonstrating that α-pinene is a poor precursor for new particles formation,[90] the presence of its degradation products on particle matter strongly correlates this compound with the occurrence of aerosols. Based on the aforementioned reported findings, the presence of particulates in the investigated system is a possibility that should be considered. As was already mentioned in this document, SPME is a sample preparation technique that, based on its configuration, allows only for the determination of free concentrations. NTD, however, provides information about total analyte concentrations (free + bound). Thus, from this perspective, differences in SPME and NTD results might be attributed to the possible presence of particles where condensation of analytes might occur on their surface, affecting the distribution of the compounds in the investigated system. However, further studies are required in order to confirm this observation.

The possible second reason might be related to the fundamentals of the diffusion-based SPME calibration model. An essential condition for this type of calibration approach is the zero sink behavior of the fibre coating. Previous studies have demonstrated that PDMS/DVB fibres have a limited capacity of approximately 9 ng for benzene when this compound is present in a

BTEX mixture at similar concentrations (350 ppbv) for all the components.[9] In this case, the amount of α-pinene extracted at the aforementioned conditions was approximately 13 ng. Although benzene and α-pinene are compounds with different properties, since the investigated system is a complex mixture of various compounds, saturation effects might have occurred at high concentrations, affecting the application of this SPME calibration mode.

3.3.2. Analysis of acetone and isoprene in breath samples

Table 3-2 presents some physical-chemical properties corresponding to the target analytes in breath samples analysis.

Table 3-2. Physical-chemical properties of target analytes in breath samples.[91]

Compound	MW g/mol	Boiling point	Solubility in water	LogP	Henry constant (at 25 °C)
Isoprene	68.12	34 °C	642 mg/L (25°C)	2.347	7.67E-2 atm.m^3/mole
Acetone	58.08	56-57 °C	Miscible	-0.042	3.97E-5 atm.m^3/mole

3.3.2.1. NTD and SPME calibration for breath samples analysis

An 85 μm CAR/PDMS fibre was selected for breath samples analysis due to its well-known properties for the extraction of very volatile compounds.[7] Furthermore, various studies support the suitability of CAR/PDMS coating for breath sampling applications.[57,92,93]

For SPME quantitative analysis, an external calibration approach was chosen. Once the fibre coating is selected, the next step in SPME method development involves determination of extraction time. Figure 3-7 presents the extraction time profile constructed for acetone and

isoprene at 65 and 15 ng/mL, respectively. As can be seen, no displacement effects were observed between these two compounds, even when the selected concentrations were significantly higher than values found in the studied breath samples. Although, it was found that equilibrium for these analytes is reached after 20 min, since this time is too long for extraction and there is not a significant increase in the amount extracted, 10 min was chosen instead as the extraction time.

After selecting the extraction time, the calibration curve for SPME quantification was constructed. Figure 3-8 illustrates the calibration curves obtained for both target analytes.

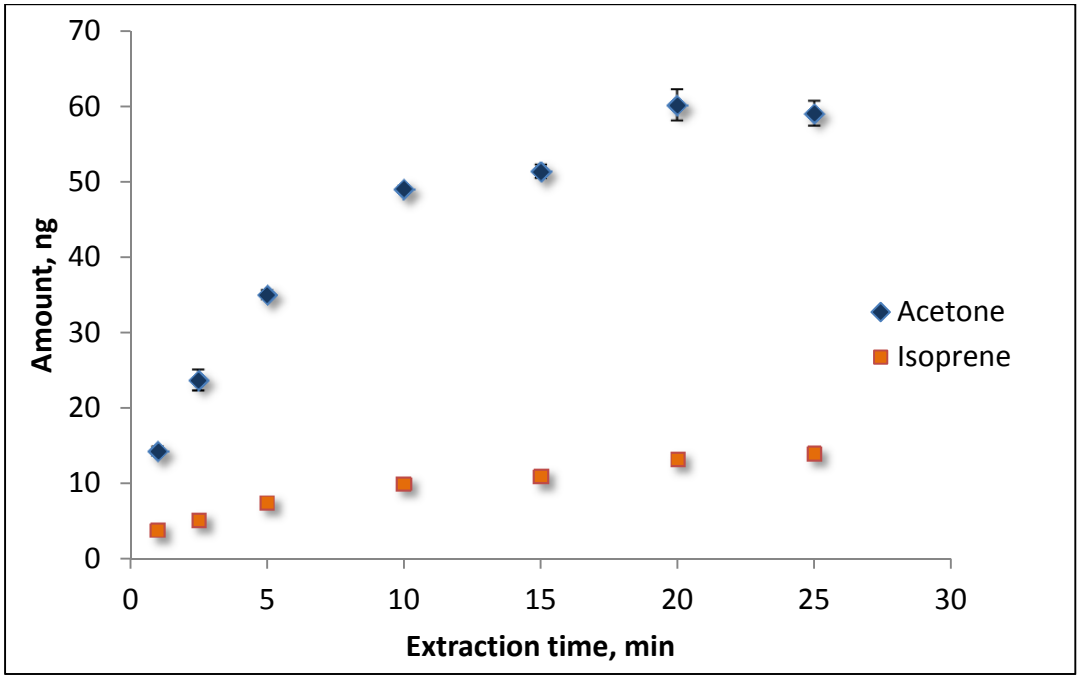


Figure 3-7. Extraction time profile for acetone (65 ng/mL) and isoprene (15 ng/mL) using a 85 µm SPME fibre (n=3).

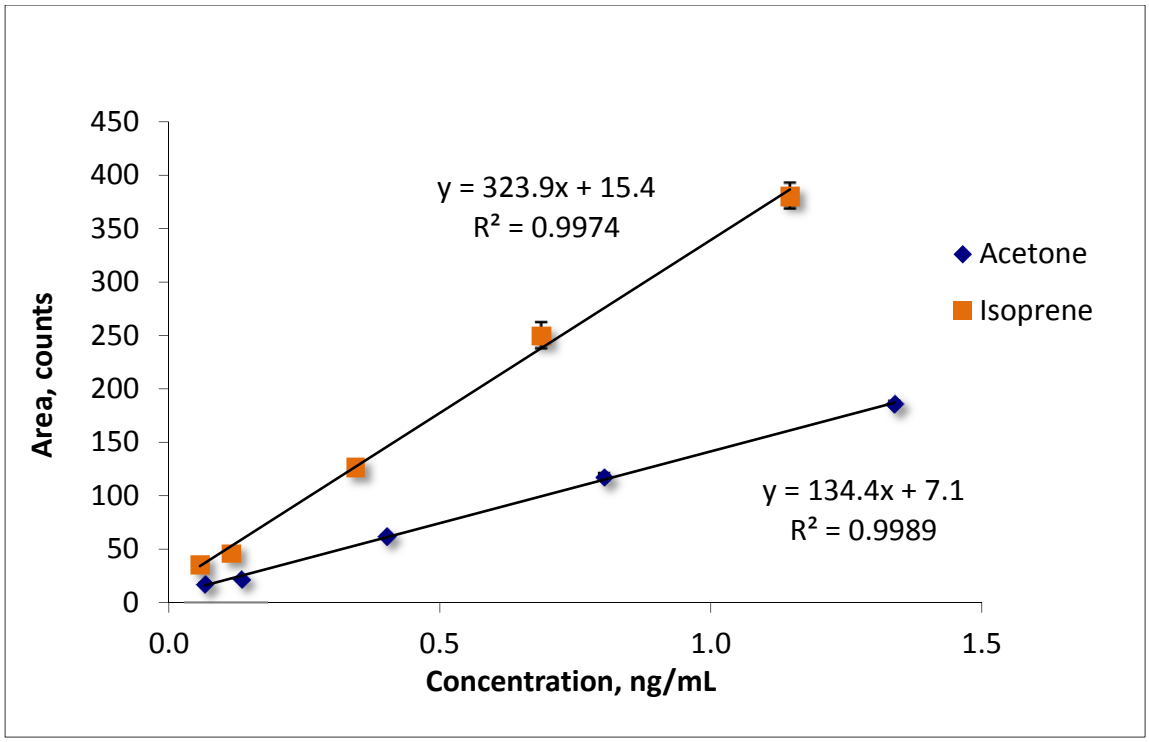


Figure 3-8. Calibration curves for acetone and isoprene constructed with a 85 µm SPME fibre (n=3).

To account for high humidity levels in breath samples, the standards for SPME calibration were prepared under 95 % humidity conditions, as described in Section 3.2.3. Since the sampling procedure employed for collecting breath samples involved only one or two exhalation cycles, concentrations lower than 1.5 ng/mL were obtained for both target compounds. Moreover, it is important to highlight that in the current study, mixed alveolar air (alveolar and dead space gas) was sampled. Therefore, the concentration levels presented here are not comparable with values reported in studies where the main goal is the determination of disease biomarkers, where the sampling of only alveolar air is a critical factor.

Table 3-3 summarizes the calibration data obtained using both sample preparation techniques. As can be seen, limits of detection and quantification for SPME were particularly low due to the coating affinity for highly volatile compounds. Alternatively, improved limits of

detection and quantification in NTD applications can be obtained by increasing the sampled volumes.

Table 3-3. Calibration data for SPME and NTD-GC-FID methods.

Sampling approach	Compound	Calibration range	Equation	R^2	LOD	LOQ	RSD, % (n=3)
SPME, ng/mL	Acetone	0.07 – 1.3	y = 134.4x + 7.1 ng/mL vs. area counts	0.9989	0.04	0.07	5.5
	Isoprene	0.06 – 1.2	y = 323.9x + 15.4 ng/mL vs. area counts	0.9974	0.04	0.06	7.1
NTD, ng (10 mL)	Acetone	4.0 – 148.1	y = 4.1x - 3.4 ng vs. area counts	0.9998	1.3 (0.13 ng/mL)	4.0 (0.4 ng/mL)	4.9
	Isoprene	3.4 – 126.8	y = 8.5x - 8.9 ng vs. area counts	0.9999	1.2 (0.12 ng/mL)	3.4 (0.34 ng/mL)	3.8

At this point, it is important to emphasize that the main objective of the current study is to determine possible differences between concentrations of acetone and isoprene when they are calculated using SPME and NTD sampling. Since high humidity levels are typically found in breath samples, evaluation of the humidity effect on both sampling techniques is an interesting aspect that must be considered. For this purpose, SPME and NTD techniques were both used in the sampling of standards prepared at the same concentrations, but at different humidity conditions. Figures 3-9 and 3-10 illustrate the results obtained for the humidity effect evaluation, in terms of amount extracted. As can be observed in Figure 3-9, the amount of acetone extracted with NTD was statistically the same in both humidity conditions. Similarly, the amount of isoprene extracted under high humidity levels was only slightly lower (less than 10 %) than the

result obtained from the standard gas prepared without moisture. On the other hand, results obtained using SPME were drastically affected by the presence of humidity: amounts of acetone and isoprene extracted under high humidity conditions were 30 and 40 % lower than amounts calculated in the absence of humidity, correspondingly.

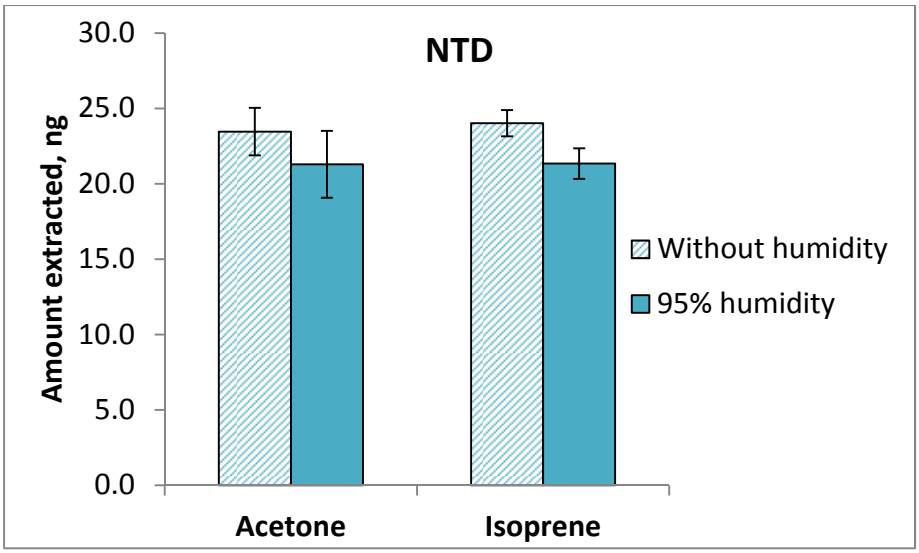


Figure 3-9. Differences in quantities of acetone and isoprene extracted using NTD to sample at different humidity conditions. The concentration in the standards gases were 2.7 and 2.3 ng/mL for acetone and isoprene, respectively. The sampled volume was 10 mL (at 2 mL/min) (n=5).

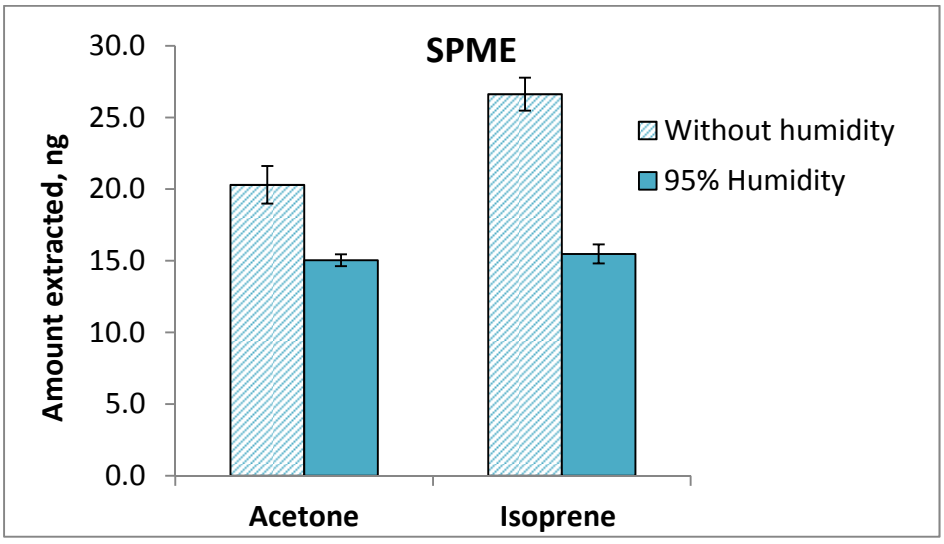


Figure 3-10. Differences in quantities of acetone and isoprene extracted using a 85 µm CAR/PDMS SPME fibre to sample at different humidity conditions. The concentration in the standards gases were 0.40 and 0.34 ng/mL for acetone and isoprene, respectively. The sampling time was 10 min (n=5).

As concluded by Koziel *et al.*, water molecules present in the sample matrix compete with analyte molecules for available active sites in solid SPME coatings where adsorption is the most important extraction mechanism.[9] Hence, a smaller number of active sites in the sorbent are occupied by acetone and isoprene molecules, and consequently, lower amounts of analytes are extracted on the fibre. This effect is particularly pronounced when long extraction times are used. Similar results were reported for analysis of perchlorethylene in a dry cleaning shop using carboxen fibres for passive sampling[94] and for analysis of sulphur compounds in breath samples.[95] This scientific evidence supports the importance of preparing gaseous standards for SPME external calibration under appropriate humidity conditions, particularly in cases where high humidity levels are present in the studied samples. Moreover, these results reflect the relevance of considering matrix effects when applying SPME and NTD simultaneously in the determination of both free and total concentrations.

As was previously introduced, the idea of using SPME and NTD as a simple approach in obtaining information related to free and total concentrations in gas samples has been proposed. Experimental data has demonstrated the feasibility of simultaneously using these sample preparation techniques to analyze systems such as barbecues, cigarette smoke and NaCl aerosols.[21] Since aerosols are defined as a suspension of solid particles or liquid droplets in gas, breath samples are undoubtedly classified as an aerosol form. In light of the results discussed in this section, special attention should be paid to calibration conditions, since both sampling approaches are affected differently by humidity. Due to this effect, incorrect concentrations could be calculated, allowing mistaken conclusions to be drawn regarding the analyte distribution in a given system.

3.3.2.2. Analysis of breath samples using SPME and NTD

Based on the results reported in the previous section, analysis of breath samples from different subjects was performed. Figure 3-11 illustrates the concentrations that were determined using SPME and NTD techniques in the collected breath samples.

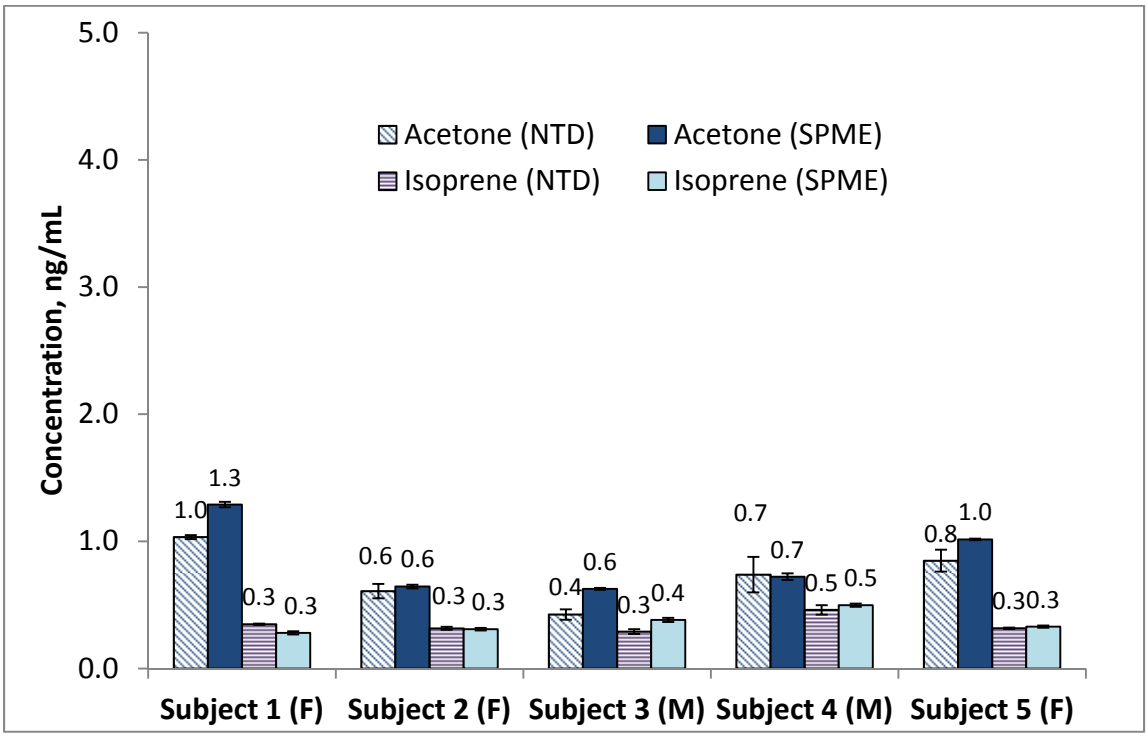


Figure 3-11. Concentrations of acetone and isoprene detected with SPME and NTD samplers in different breath samples (n=2). The volume extracted using NTD was 10 mL (at 2 mL/min). The extraction time in SPME sampling was 10 min (85 µm CAR/PDMS fibre).

As shown in Figure 3-11, concentrations obtained using SPME and NTD were equivalent to each other for the studied analytes. Minor differences observed between SPME and NTD measurements can be attributed to experimental error. These results are in agreement with the expected behavior of these compounds according to their physical-chemical properties. Indeed, isoprene is a highly volatile and hydrophobic compound (LogP=2.32), so its partition in water is not expected under the described experimental conditions. Similarly, acetone exhibits high

volatility at room temperature, although its Henry's constant is lower than the value reported for isoprene. Due to the more hydrophilic characteristics of acetone, one might expect a possible partition of this compound in the water droplets. However, since the volume of the aqueous phase is significantly lower than the volume of the breath gas, most of the acetone is expected to be found in the gas phase.

In this particular case, the studied analytes were found only in the gaseous phase of the sample matrix. Due to the limitations of using GC-FID, it was not possible to explore the occurrence of other analytes in different samples. However, future considerations should involve the use of this powerful sampling approach combined with mass spectrometry when analyzing less volatile compounds that are more likely to be distributed in particle phase.

3.3.3. Analysis of contaminants in a polymer synthesis lab

3.3.3.1. Calibration

An 85 μm CAR/PDMS fibre was chosen for this application due to its high affinity towards very volatile compounds and behavior as a zero sink under a wider range of conditions.[9] For on-site analysis, the same calibration approach applied in Section 3.3.1. was used to quantify toluene at different times throughout the same day.

In the present section, only SPME was employed as a sample preparation technique due to limitations related to the current configuration of the instrument, specifically its injection port. The instrument employed in this particular experiment (Tridion-9) is a recently introduced version of the portable GC-TMS developed by Torion Technologies. The injection port included in this piece of equipment only allows the use of a Merlin microseal septum, which is exclusively designed for usage with 23 gauge probes. Therefore, to avoid possible leaks,

applications are limited to the use of needles of same specified diameter. Currently, hardware modifications are being implemented by the manufacturer in order to make this system functional for both SPME and NTD applications.

Based on the reasons mentioned above, calibration of the portable GC-TMS was accomplished by exposing a SPME fibre for different durations (from 5 s to 6 min) to a constant concentration of toluene produced in a standard gas generator (refer to Section 3.2.3.). The amount of toluene loaded on the fibre at each extraction time was estimated by repeating the extractions at the same conditions, and performing the injections in a benchtop GC-MS, where a liquid calibration curve was previously run. Figure 3-12 depicts the calibration results obtained for toluene in the portable GC-TMS. Total ion current (TIC) was used as signal response, since ion quantification features are not included in the new portable GC-TMS software.

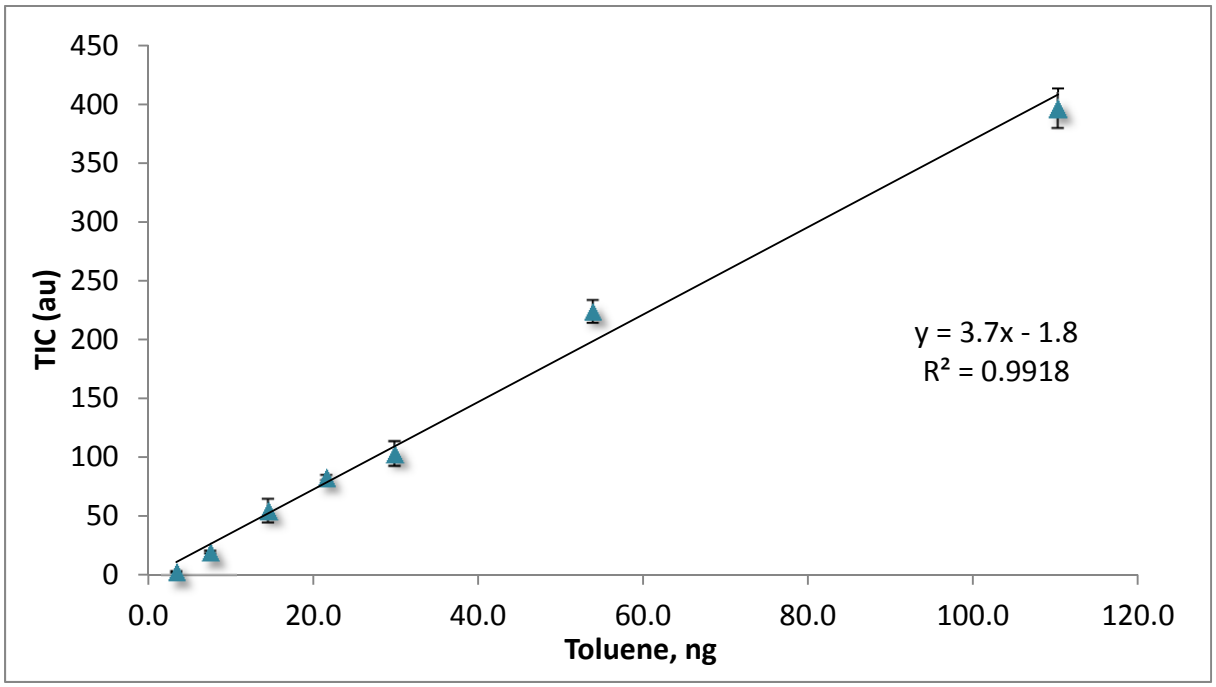


Figure 3-12. Portable GC-TMS response for toluene (n=3) (Total ion current arbitrary units vs. ng).

Good linearity was observed in the range of 3.4 and 110.3 ng of toluene, which is in agreement with the limited linear range typical for ion trap detectors. Intra and inter-day RSD values were between 7 and 20 %, which are considered acceptable for quantitative analysis using portable instrumentation.

Table 3-4 summarizes the parameters involved in the calculation of toluene concentrations during the on-site analysis. As in Section 3.3.1., the temperature was constantly monitored throughout the sampling process.

Table 3-4. Different parameters involved in determining concentrations by SPME diffusion-based calibration. Values in this table correspond to on-site analysis of toluene in a polymer synthesis lab.

Parameter	**Values**	**Units**
Amount of analyte extracted (n)	46.4	ng
Fibre radius (outside) (b) [a]	0.0145	cm
Fibre length (L)	1	cm
Sampling time (t)	30	s
Diffusion coefficient (Dg)[b]	0.079	cm^2/s
Temperature (T)	295.9	K
Pressure (P)	1	atm
M air	28.97	g/mole
V air	20.10	cm^3/mole
Mr (M air + M analyte)/(M air*M analyte)	0.045	mole/g
M analyte	92.14	g/mole
V analyte	111.14	cm^3/mole
Boundary layer thickness	0.014	cm
Reynolds number	28.3	
Linear velocity of the air (u)	150	cm/s
Air kinematic viscosity (v)	0.15	cm^2/s
Schmidt number	1.93	
Concentration (Cg)	**2.0**	**ng/mL**

[a]Value corresponding to a 85 µm CAR/PDMS fibre.
[b]Diffusion coefficient calculated using the Fuller-Schettler-Giddings model (Section 1.1.1.).

3.3.3.2. On-site analysis results

Interesting results were obtained from the on-site analysis of VOCs carried out in the polymer synthesis laboratory. First, it was possible to easily spot the occurrence of various solvents in the studied site. Tetrahydrofuran and isopropyl alcohol, as well as toluene, were successfully identified by matching their spectra with the instrument database information.

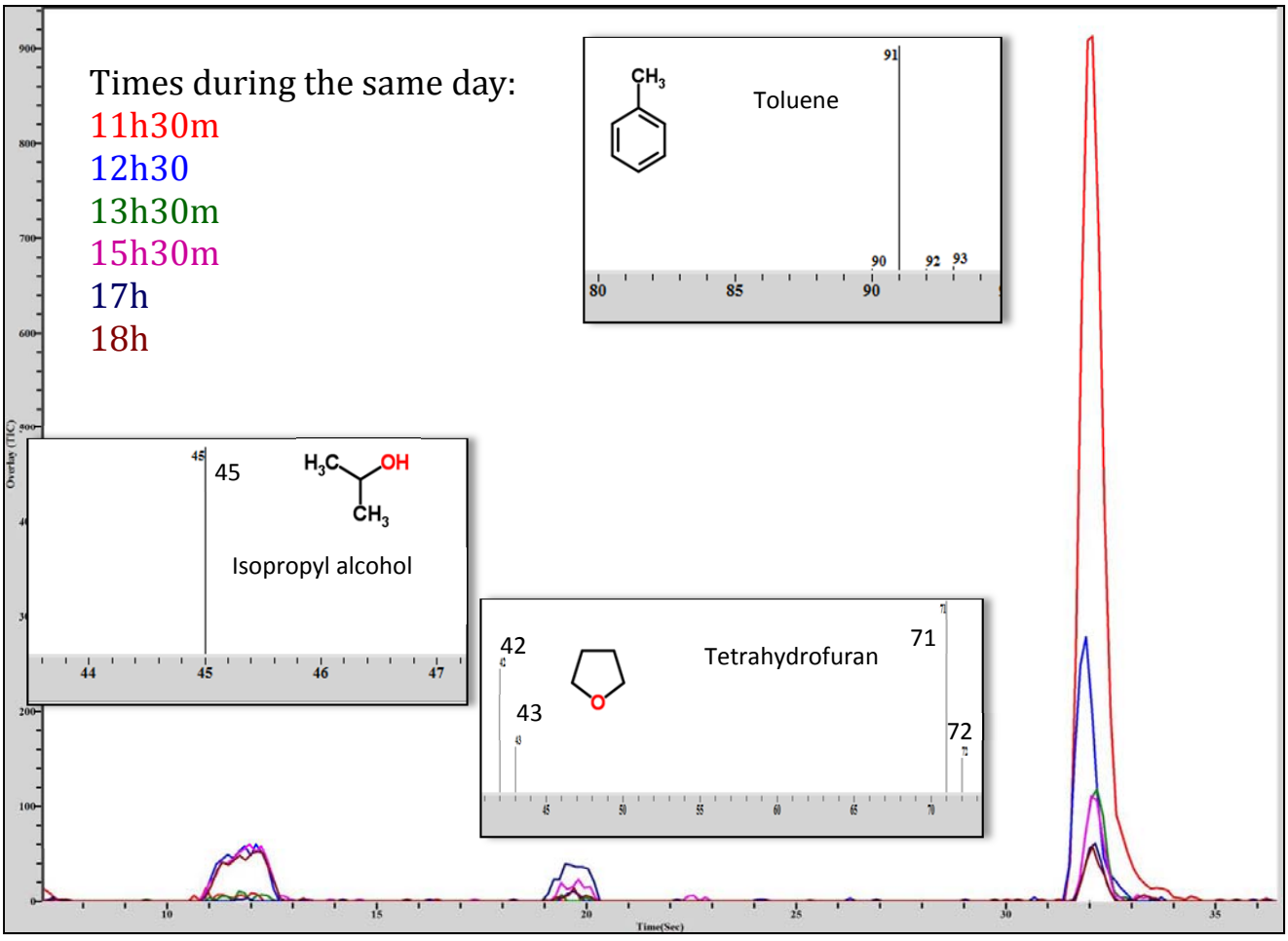


Figure 3-13. Chromatographic profiles obtained at different times during the same day.

Regarding quantification using the portable GC-TMS, Table 3-5 presents the results obtained from the quantitative analysis of toluene at the aforementioned conditions. In addition to these results, Table 3-5 registers concentrations determined in a conventional benchtop quadrupole, which were obtained from extractions conducted parallel to the on-site analysis.

Table 3-5. Concentrations of toluene determined with SPME rapid field air sampling coupled with a portable GC-TMS system and a conventional benchtop quadrupole.

Time of the day	Temperature, °C	Concentration of toluene	
		Using a conventional GC-MS, ng/mL±EE* (n=1)	Using a portable GC-TMS, ng/mL±SD (n=3)
11 h 30 m	22.9	2.2±0.1	3.0±1.0
12h 30 m	22.6	0.50±0.03	0.6±0.2
13 h 30 m	23.2	0.30±0.02	0.20±0.01
15 h 30 m	23.0	0.20±0.01	0.30±0.02*
17 h	22.5	0.10±0.01	0.20±0.01
18 h	22.2	0.10±0.01	0.20±0.05

*Assuming 5 % experimental error (related to instrument response drift and SPME method typical RSDs).

As can be seen in Table 3-5, good agreement was found in the results obtained with both gas chromatographs at 11h30m and 12h30m. Variations at low concentration levels are related to the short extraction time selected (30 s) that allows the analyst to estimate the concentration at a very specific time of the day (slight changes in concentration between extractions could occur). Due to the longer run time set in the conventional GC-MS (20 min) compared to the one in the portable GC-TMS (130 s), analysis in the benchtop GC-MS was carried out by doing only a single extraction at each turn; conversely, three replicates were run in the portable GC-TMS per turn. Since total analysis time is a parameter of paramount importance in field analytical applications, it is noteworthy to mention that the combination of SPME with this portable GC-TMS provides a valuable tool for fast field quantitative sampling (analysis accomplished in 200 s), even when non-target analysis is conducted. Also, it is important to highlight that since this

method estimates concentration in a considerably short period of time, changes in activities in the sampling location, such as opening a solvent bottle or turning on a rotary evaporator, could drastically affect the results obtained.

3.4. Conclusions

SPME and NTD were effectively coupled with different portable instruments, and the suitability of these approaches in the application of quantitative analysis of various systems was demonstrated.

First, the GC-IMS system introduced in Chapter 2 was successfully coupled with SPME and NTD samplers for on-site analysis of biogenic compounds emitted by a pine branch. Quantitative analysis was satisfactorily accomplished in a significantly short period of time by virtue of the low detection limits that IMS detection provides. Interesting results were found with each of the sample preparation techniques employed, suggesting the presence of particles in the investigated system. Although further investigation is required in order to confirm the presence of aerosols in this specific system, it is important to emphasize that the proposed setup can be used for the investigation of both free and total concentrations in samples where the presence of particles have been already determined. The importance of GC as a separation step before IMS detection was confirmed in this particular case, where several compounds able to produce the same ion at the specified conditions were found. This simple sampling protocol can be easily followed when performing on-site analysis of other substances of environmental, forensic, and medical interest.

In addition to the application of SPME and NTD in the analysis of biogenic compounds emitted by a pine branch, these techniques were used in the analysis of breath samples. Equivalent concentrations of acetone and isoprene were calculated using both sample preparation

techniques. Results were explained based on the physical-chemical properties typical of each target compound. Also, the effect of humidity on these sample preparation techniques was examined; based on the experimental findings presented here, it can be concluded that humidity is an important variable that should be considered when applying SPME and NTD in the determination of both free and total concentrations in aerosols such as breath. Unlike NTD, SPME is highly affected by the presence of humidity in gas samples. Hence, accounting for this matrix effect is of paramount importance in SPME analysis. Else, inaccurate results regarding analyte distribution in a given system may be reported when this variable is unaccounted for.

Finally, the convenience and feasibility of using a portable GC-TMS coupled with SPME for on-site analysis of contaminants in a polymer synthesis laboratory was demonstrated. This analytical approach exhibited a satisfactory performance when compared with a conventional GC-qMS system at the aforementioned conditions. As a result of the considerable reduction in analysis time, coupling SPME with this portable GC-TMS system gives the user the opportunity to make decisions in the sampling place, as well as collect more information in a shorter period of time. The well-known advantages of mass spectrometry detectors available in this portable configuration are a powerful tool for non-target analysis, especially in on-site applications, where occurrence of various unknown compounds is likely to occur. This approach can potentially be used to conduct workplace safety assessments, especially in cases where immediate information is required in order to ensure that workers are not being exposed to a harmful environment.

Chapter 4: Membrane extraction with sorbent interface (MESI) coupled with GC-IMS for on-site semi-continuous monitoring

4.1. Introduction

When monitoring VOCs in systems where either single or multiple processes are involved, it is important to consider possible changes in target analytes concentration over time. Used for monitoring purposes, MESI (refer to Section 1.1.3.) has demonstrated its feasibility to easily monitor VOCs in a semi-continuous mode for long intervals of time. In this sample preparation approach, the membrane module acts as a sensor-like device that is continuously exposed to the investigated system.[28] Once a steady state between membrane and sample under study is reached, quantification of analytes becomes possible. Since a sorbent trap is used as a medium in the pre-concentration of analytes that permeate the membrane, different extraction times can be selected, provided that trap capacity is not exceeded. Thus, for every period of time that the sorbent trap is desorbed, a response proportional to the actual analyte concentration can be obtained.

MESI has been used for on-site analyses of different systems. Some applications of MESI include monitoring the thermal degradation products of polystyrene[96] and polyacrylonitrile,[97] analysis of biogenic emissions,[31] on-site environmental monitoring of BTEX and chloroform,[30] and semi-continuous analysis of breath samples.[29,98,99] Furthermore, various detector types have been coupled with this sample preparation technology.[30,98,99] In this section, the coupling of MESI with a portable GC-IMS system is proposed for the first time. The advantages of IMS detection for on-site analysis, when they are combined with the particular features of MESI,

result in an interesting configuration for field sample investigation. Monitoring of acetone in breath samples was chosen as a model for the evaluation of the proposed system.

4.2. Experimental

4.2.1. Analytical reagents and supplies

Acetone (HPLC grade) was purchased from Caledon (Georgetown, ON, Canada). Nitrogen (5.0 ultra-high purity, 99.999%) was obtained from Praxair (Kitchener, ON, Canada). Hydroguard MXT guard columns (0.28 and 0.53 mm I.D.) obtained from Restek (Bellefonte, PA, USA) were used as transfer lines and in the construction of the sorbent trap for MESI. A flat sheet PDMS membrane (SSP-M823, 0.005") was obtained from Silicone Specialty Products Inc. (Ballston Spa, NY, US). A 600 mL glass chamber was used to hold the membrane module during the sampling procedure (refer to Figure 4-1). Glass bulbs (1 L) obtained from Supelco (Oakville, ON, Canada) were employed to prepare standard gases.

4.2.2. Instrumentation

For the MESI experimental setup, a piece of PDMS membrane (3.8 cm x 2.6 cm) was mounted into a special module, as shown in the Figure 1-2 (Chapter 1). To check for leaks, the membrane device was immersed in de-ionized water and purged with nitrogen. For the sorbent interface construction, a piece of 55 mm of MXT guard column (0.53 mm I.D.) was packed with carboxen 1000 (60/80 mesh) (15 mm sorbent bed length), following the same procedure as in NTD packing (Section 2.2.2.). This sorbent interface was housed in a custom-made control unit where both a Peltier cooler, as well as the application of heating pulses, facilitated enrichment of the analytes and subsequent desorption into the column. A mini-fan was used to ensure a homogenous convection in the sampling chamber, as shown in Figure 4-1.

The IMS analyzer previously described in Chapter 2 was employed in the current section at the same operational conditions. To couple the MESI system with the GC-IMS system, desorption and transfer lines used for SPME and NTD applications were removed. A schematic representation of the entire system is illustrated in Figure 4-1.

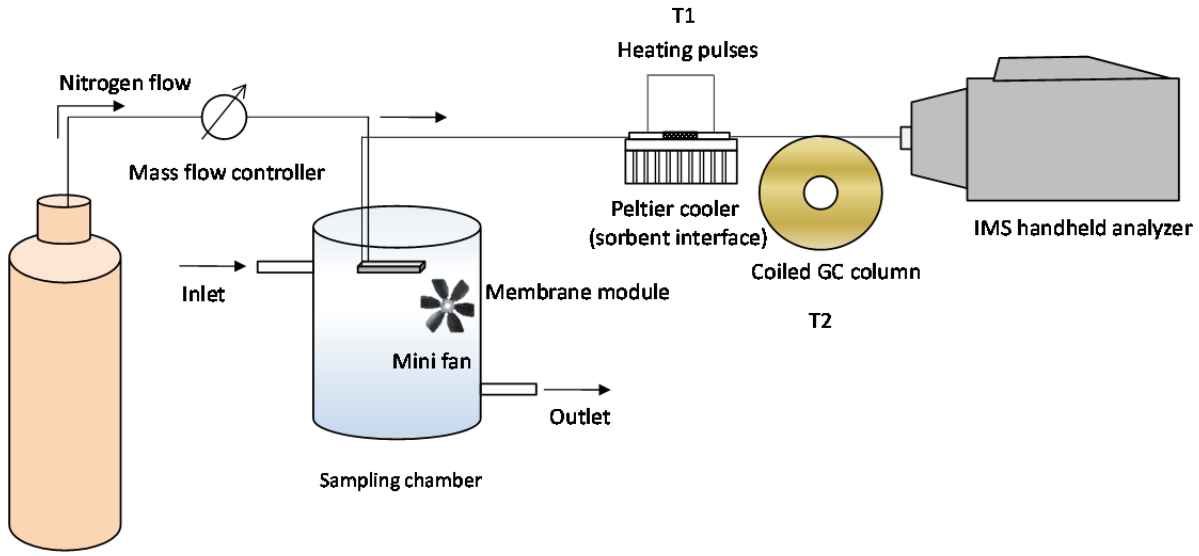


Figure 4-1. MESI-GC-IMS setup.

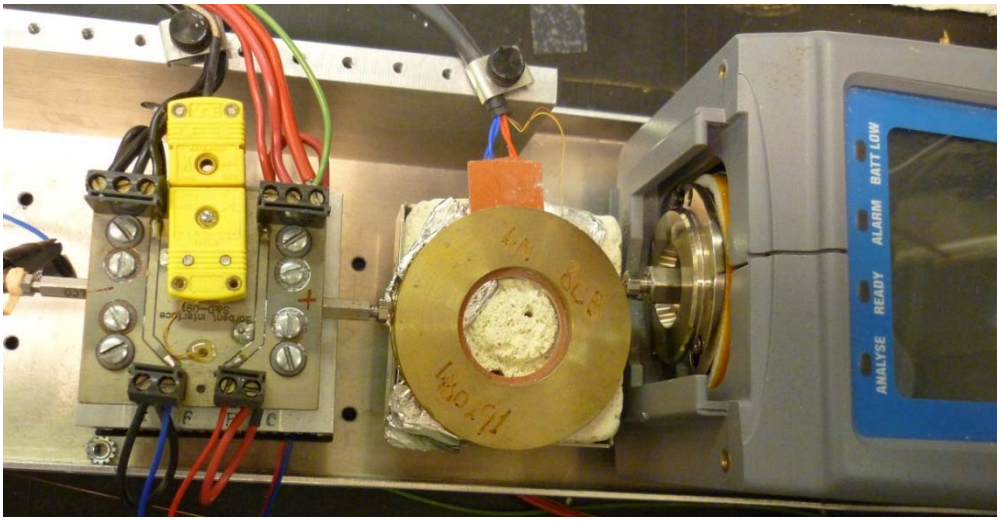


Figure 4-2. Connection between the sorbent interface control unit and the GC-IMS system.

4.2.3. Standard gases

An initial acetone standard gas was prepared as described in Section 3.2.3. Different concentrations were then obtained by transferring specific volumes of this standard gas by means of a gas-tight syringe into the chamber used for MESI sampling. To calculate the final concentration of acetone, the volume of the glass chamber (600 mL) was taken into account. The standard gas generator system described in Section 2.2.4 was also used for part of the experiment. A permeation tube containing pure acetone was placed in the permeation chamber at 30 °C, with a constant nitrogen flow of 150 mL/min. The diluting gas flow was modified in order to obtain different concentrations.

4.3. Results and discussion

4.3.1. Conditions and stability of the MESI-GC-IMS system

The operational conditions for the MESI system are presented in Table 4-1.

Table 4-1. Operational parameters for the MESI-GC-IMS system.

Operational parameter	Value
Desorption temperature	200 °C
Extraction temperature	6 °C
Desorption pulses	10 s
Column temperature	40 °C
Column flow	100 mL/min

Similarly to SPME, in MESI it is important to take into account the effect of the boundary layer on the extraction rate. Since a permeation process from the sampling medium to the stripping phase is constantly occurring, boundary layers in the inner and outer parts of the membrane should be considered.[98] Therefore, convection conditions in the stripping and feeding phases are critical factors to be controlled in order to enhance the mass transport of analytes through the membrane material. In this study, 100 mL/min was selected as the stripping gas flow, since it maintains good convection in the inner side of the membrane, and provides good stability in the IMS detection system, avoiding easy saturation of the detector. Convection in the outer side of the membrane was also taken into account, by keeping a mini-fan turned on during the experiments.

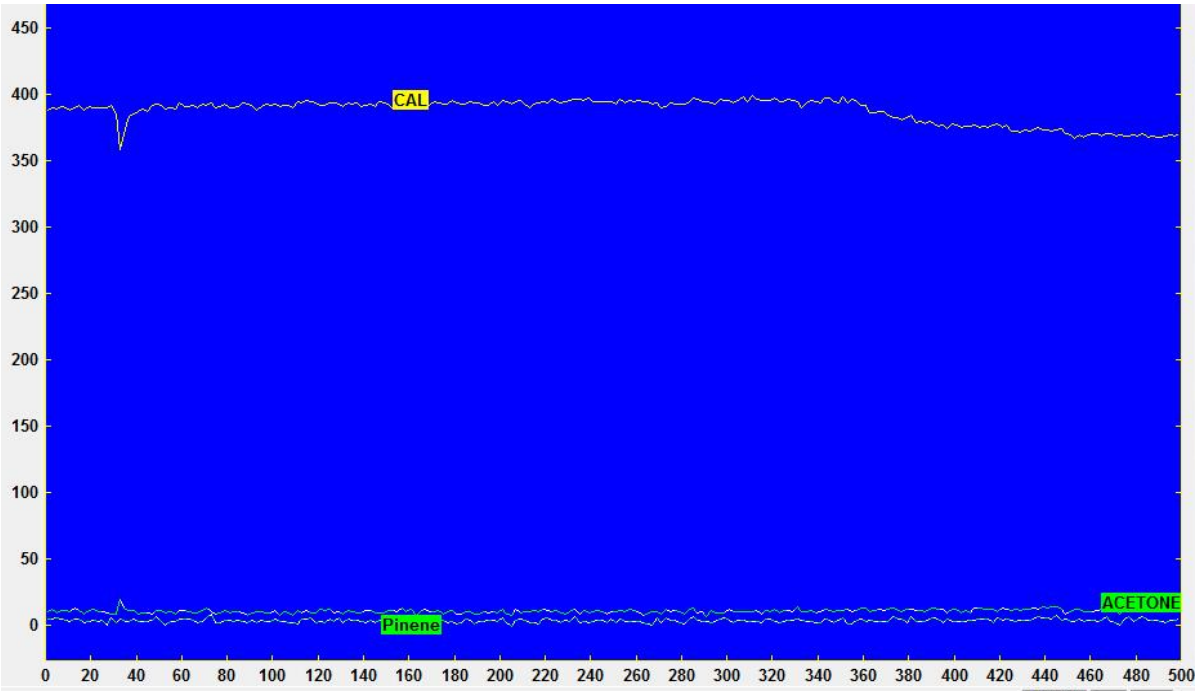


Figure 4-3. Background signal obtained from the MESI-GC-IMS system.

Once the entire MESI-GC-IMS system was set up, blank runs were performed at the specified conditions. Figure 4-3 presents a plasmagram amplitude profile corresponding to a blank run: as demonstrated, no significant background interferences related to the trap were observed. It is important to emphasize that a clean response that is relative free of background interferences is crucial in this form of application, where considerably low concentration levels are usually handled. As was previously discussed in Chapter 3, the selectivity of IMS detection towards only those analytes with high proton affinity can be beneficial, since possible interferences coming either from the sample matrix, or from the sorbent itself, are not always detectable at these mild ionization conditions.

Once a clear, stable baseline was obtained, the gas generator outlet was connected to the sampling chamber of the MESI system. Figures 4-4 and 4-5 exhibit plasmagram amplitude profiles corresponding to 1 and 2 min trapping periods, respectively. As can be seen, good performance of MESI coupled with the modified GC-IMS system was found.

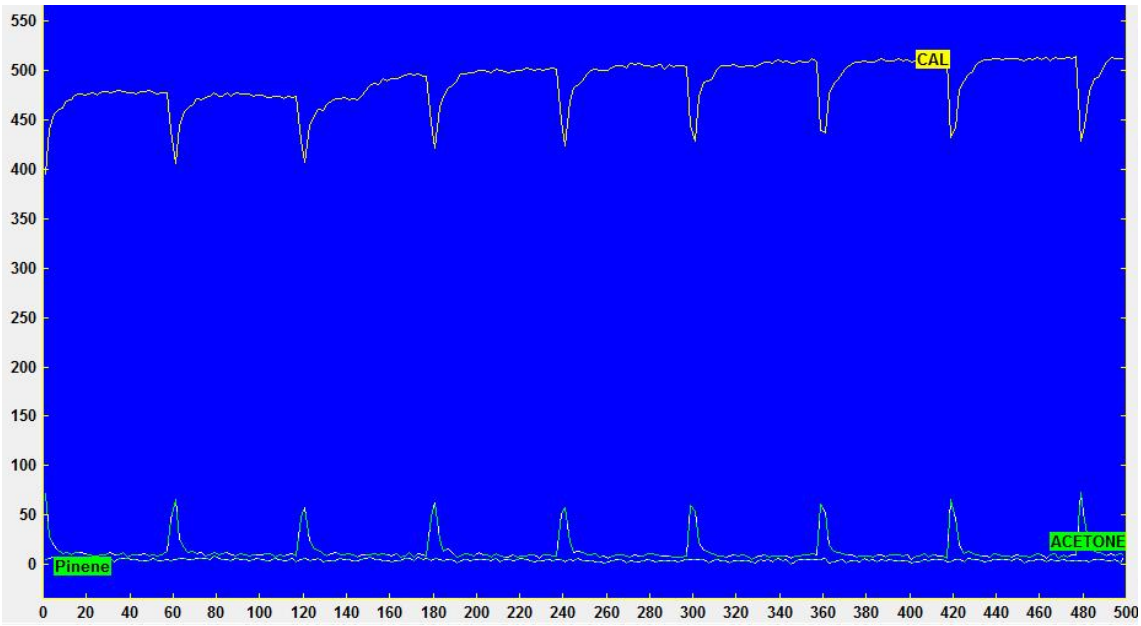


Figure 4-4. Plasmagram amplitude profile obtained for 1 min trapping time (acetone 1.1 ng/mL).

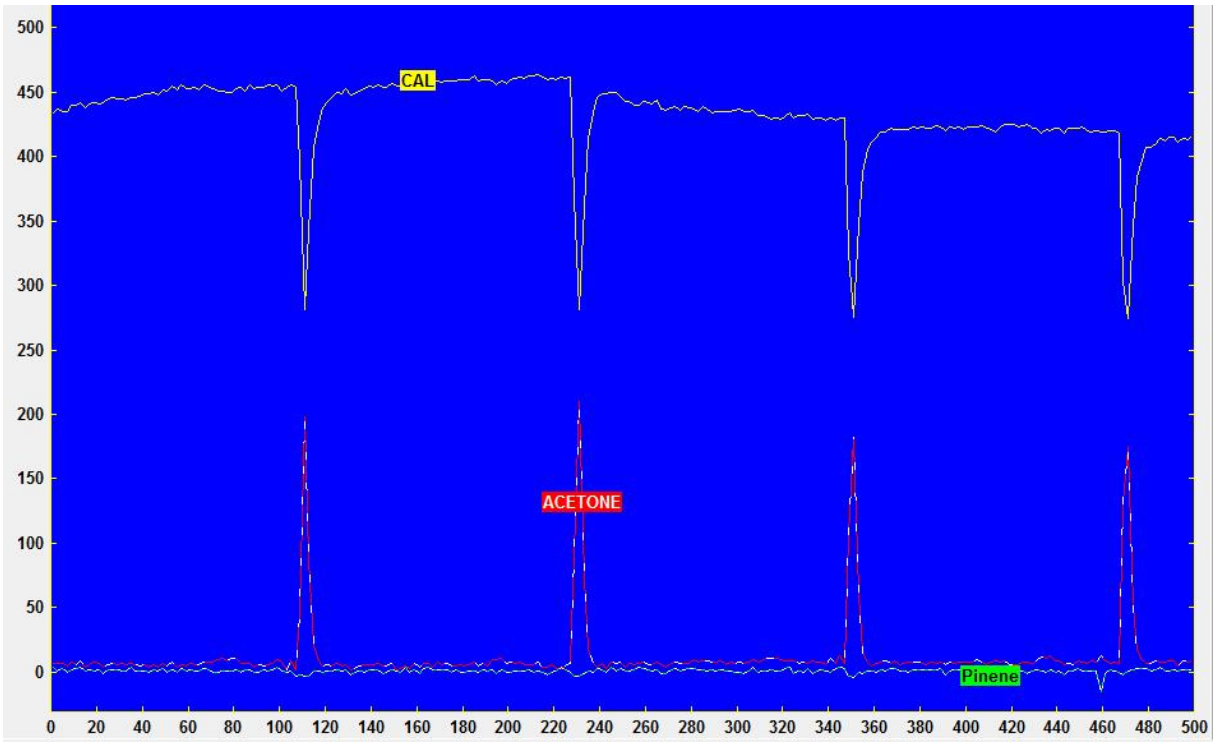


Figure 4-5. Plasmagram amplitude profile obtained at 2 min trapping time (acetone 1.1 ng/mL).

A critical factor to be considered in MESI applications is how fast the heating pulse is produced. High desorption effectiveness in a short period of time ensures a sharp injection band; as a result, a clear instrument response in terms of peak shape is reached. Due to the high quantity of power consumption required to fulfill this condition, on-site applications of MESI might be hindered.

4.3.2. Determination of the steady state

The steady state is an important parameter to be considered in this membrane extraction technique. Once the MESI system is in contact with the sample, a certain amount of time is

required for the extraction system to equilibrate. Thus, only peaks registered after reaching the steady state can be considered representative of the investigated system.

Figure 4-6 shows the variation of the instrument response, from the moment the membrane module was exposed to a breath sample collected in the sampling chamber, until a constant response was obtained.

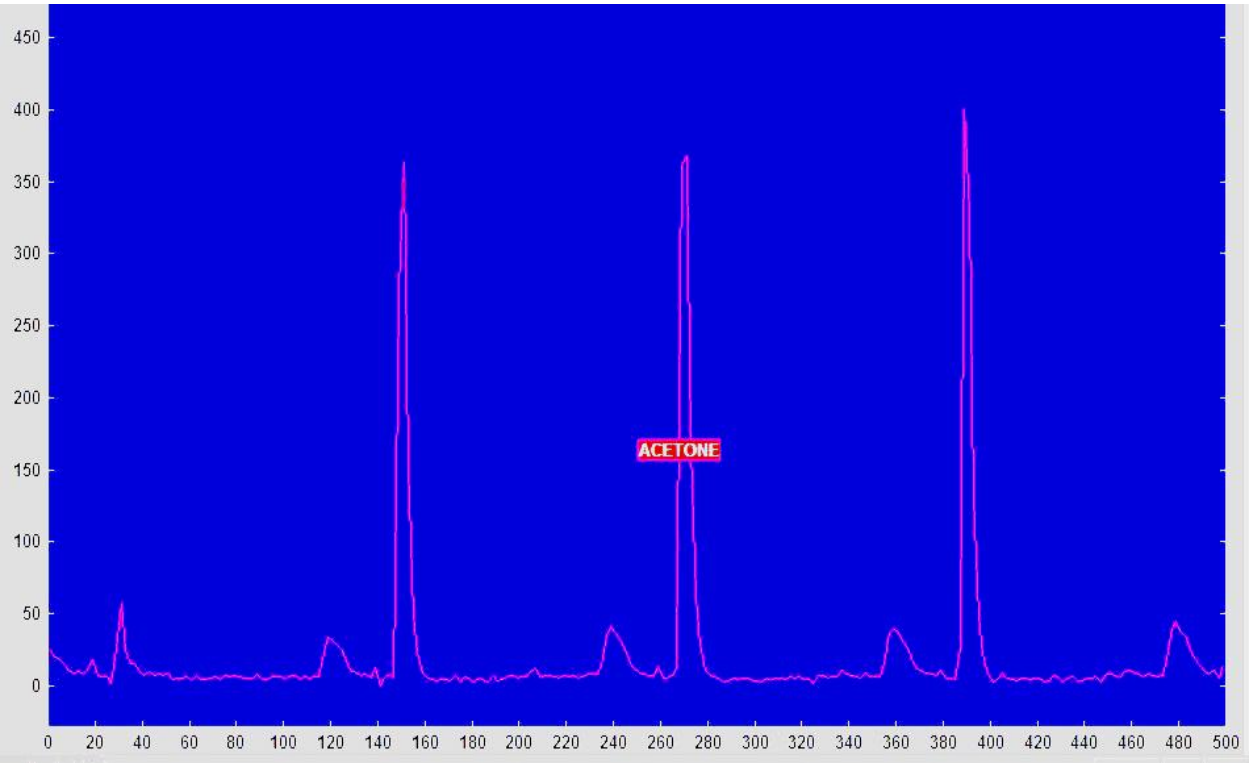


Figure 4-6. Detector response variation from first contact between a breath sample and the membrane, until constant peak areas were obtained. The sampling cycle was set at 2 min.

Due to the high flow set in the stripping phase of the MESI system (100 mL/min), it was possible to obtain a constant response only a few minutes after starting the sampling cycle. It is worth emphasizing that the convection on the sample side was constantly controlled by a mini-fan in the chamber. As was previously stated by Liu *et al.*, the flow rate in the stripping phase should be properly optimized in order to enhance the mass transfer of analytes without causing a

high degree of sample dilution.[100] Since IMS detection is capable of detecting concentrations in the low ng/mL levels, even at high flows, a considerable increase in flow rate can be applied without affecting the sensitivity of the system.

4.3.3. Evaluation of the trap capacity

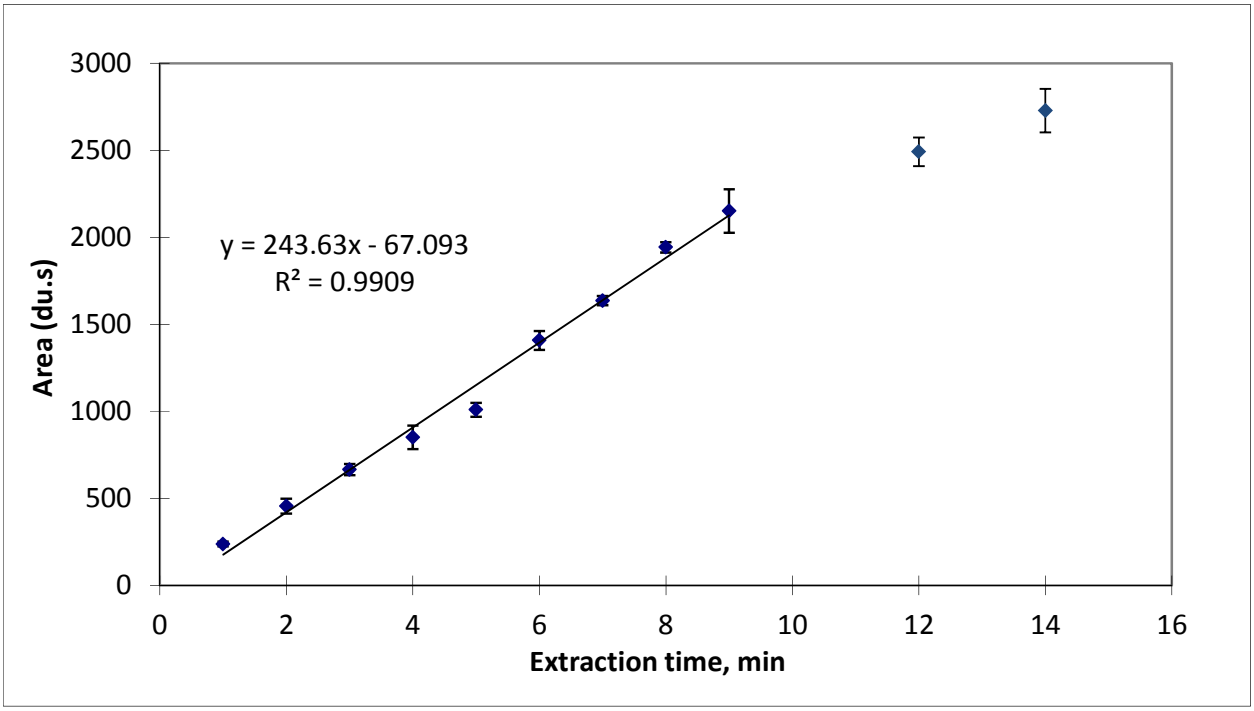


Figure 4-7. Evaluation of the trap capacity at different extraction times (concentration of acetone =2.3ng/mL, n=3).

The capacity of the sorbent trap was evaluated at the above conditions. For this section of the experiment, the connection between the trap and the column was modified, allowing a split so that the detector saturation could not be reached before observing breakthrough in the sorbent interface. Different extraction times were tested in order to determine when breakthrough was observed. As can be seen in Figure 4-7, a linear relationship was found between 1 and 9 min trapping times. At 12 and 14 min extraction times, a substantial deviation from linearity was observed. These findings were expected, based on the considerably high flow rate set in this

study. Although high flow rates can be chosen to accelerate the mass transfer process in MESI applications, breakthrough can occur in shorter times due to the probability of analytes being stripped from the sorbent bed under high flow conditions. Based on these findings, and by virtue of the low detection limits achievable with IMS detection, 2 min was selected as the trapping time for this application. Previous studies done on the analysis of acetone in breath samples with MESI have reported longer extraction times varying from 5 to 20 min,[29,98,99] with lower flows in the stripping phase used in these cases (<5 mL/min). Furthermore, the IMS detection unit used in this study is unable to perform runs longer than 500 s, due to the configuration limitations of the instrument itself. Therefore, by selecting 2 min as the extraction time, it was possible to obtain at least four peaks in each run.

4.3.4. Calibration and analysis of breath samples

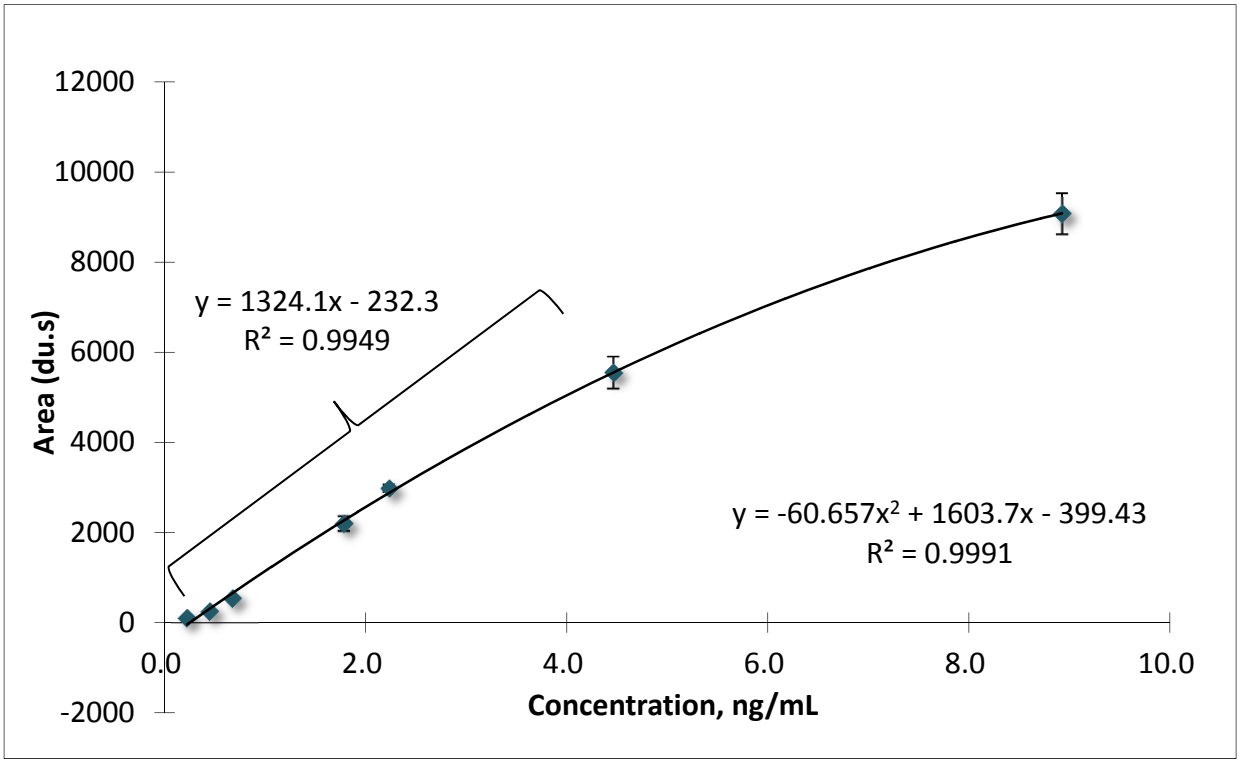


Figure 4-8. Calibration curve for acetone using the MESI-GC-IMS system (n=4).

For this MESI application, an external standard calibration approach was followed, since all the experiments were performed under the same conditions. However, it is important to mention that variations both in temperature and convection influence analyte permeation, and consequently may affect MESI calibration. The calibration curve was constructed by exposing the membrane module to standard gases of acetone prepared as described in Section 4.2.3. After running each calibration point, the sampling chamber was purged with nitrogen until a clean baseline was reached. Calibration results are plotted in Figure 4-8.

As previously emphasized in Chapter 2, IMS detection using a radioactive ionizing source is characterized by narrow linear dynamic ranges, due to depletion of the reactant ions at high concentrations. This situation is clearly reflected in Figure 4-8 for acetone detection. As a result of the distinctive high proton affinity of acetone (812 kJ/mole), ^{63}Ni IMS detection exhibits a superior sensitivity towards this compound.[4] Although a substantial deviation of the linearity is observed at high concentrations, a different model, such as a second-order polynomial function, can be applied to fit the calibration data.[4,101] As shown in Figure 4-8, a second-order calibration equation was found to be appropriate to fit the instrument response as a function of acetone concentration using MESI (R^2=0.9991). The linear portion of this specific application was also indicated in Figure 4-8.

At this point it is important to highlight the importance of selecting an appropriate calibration model for IMS detection. Typical analytical applications are characterized by linear relationships between analyte concentration and instrument response. Nonetheless, in some cases a different calibration model should be employed in order to accurately represent a calibration function.

Once the described system was calibrated, the instrumental setup was tested with breath samples provided by three subjects. Ideally in breath sample analysis, parameters such as CO_2 levels and exhalation patterns should be considered in order to account for variations among volunteers.[59] In this work, the breath sampling procedure was not optimized, since the main objective here is demonstrating the feasibility of the MESI-GC-IMS coupling as a practical approach for on-site semi-continuous monitoring.

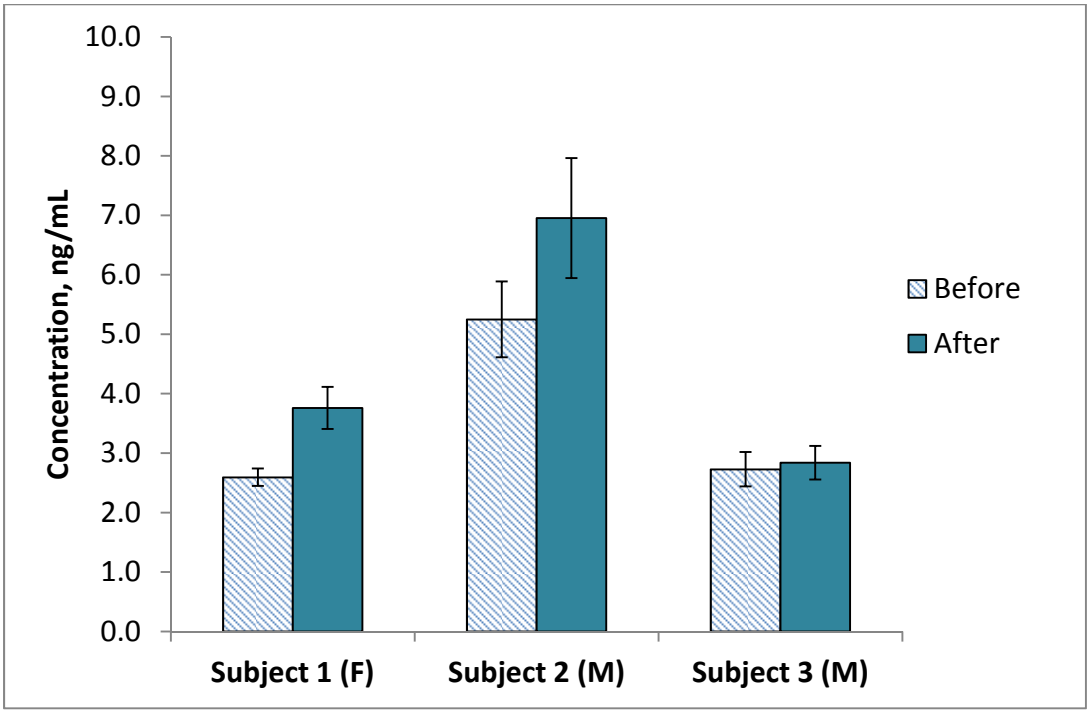


Figure 4-9. Concentrations of acetone in breath samples from three volunteers before and after lunch (n=4).

Figure 4-9 presents the results obtained from the analysis of breath samples. Concentrations of acetone were in the range of 2 to 7 ng/mL. Since only two exhalation cycles were considered during the sampling procedure and, as mentioned before, a strict breath sampling protocol was not followed, the estimated concentrations were below those values reported in the literature.[63,64]

Several studies have reported a decrease in breath acetone concentrations after food ingestion.[62,63] However, the results found here corresponding to acetone levels before and after lunch were not conclusive. The reasons given above regarding the employed sampling methodology is the most probable explanation for these findings.

Difficulties encountered during the real breath sample analysis are mainly associated with the sampling protocol rather than to the instrumental approach itself. Due to the complexity of the breathing process and the typical physiological differences among subjects, tremendous effort has been dedicated to the standardization of breath sampling procedures. Therefore, the applicability of the proposed system in breath analysis is strongly correlated to the use of proper sample collection approaches.

4.4. Conclusions

The suitability of coupling MESI with a GC-IMS detection system was demonstrated, and hence the capability of performing semi-continuous monitoring with this instrument is introduced as an additional feature. Thus, SPME and NTD can be employed as sampling techniques for spot on-site analysis, and MESI can provide a valuable tool to monitor concentration changes over time.

Once again, low detection limits of IMS were advantageous, since an enhanced mass transfer process was possible by using a high flow rate (100 mL/min) without sacrificing the sensitivity of the technique, and short trapping times (2 min) were sufficient to register a representative response from the investigated system. Although a considerable deviation from linearity was observed at acetone concentrations above 4 ng/mL, a second-order calibration equation exhibited good correlation with the calibration data.

The potential of the proposed MESI-GC-IMS system was tested by analyzing acetone present in breath samples. This integrated system can be used in a variety of applications where monitoring of highly volatile compounds is intended, although sufficiently high proton affinities are a requirement for IMS detection with ^{63}Ni ionizing source.

Chapter 5: Summary

SPME, NTD and MESI were successfully coupled with portable analytical instrumentation for the quantitative analysis of various systems. Portable equipment employed in this project included GC-FID, GC-TMS and GC-IMS systems. The latter instrument was the result of coupling a miniaturized GC interface and a desorption unit with a handheld IMS analyzer. This proposed GC-IMS system exhibited satisfactory performance in terms of retention time (inter-day variation < 3%) and response stability (intra and inter-day relative standard deviations (RSDs) < 10 %). When this system was coupled with NTD, it yielded limits of quantification comparable to those provided by conventional benchtop instruments (0.065 ng/mL for α-pinene, 0.012 ng/mL for limonene and 0.038 ng/mL for acetone).

Three different systems, namely emissions of a pine branch, breath samples and indoor pollutants in a polymer synthesis laboratory, were investigated using SPME and NTD together with portable instrumentation. In the analysis of biogenic compounds emitted by a pine branch, quantitative analysis was satisfactorily accomplished in a significant short period of time by virtue of the low detection limits that IMS detection provides. In addition, results obtained using SPME and NTD suggested the possible presence of particles that are likely to be produced during the oxidation of different biogenic compounds. On the other hand, in the analysis of breath samples, equivalent concentrations of acetone and isoprene were calculated using both sample preparation techniques. The effect of humidity in both SPME and NTD sampling techniques was studied, and results revealed that both techniques were differently affected by the presence of moisture in a sample matrix. These experimental findings support the relevance of proper calibration conditions in order to accurately characterize systems such as aerosols in

terms of free and total concentrations. Finally, the convenience and feasibility of using a portable GC-TMS coupled with SPME for on-site analysis of contaminants in a polymer synthesis lab was demonstrated. This analytical approach exhibited a satisfactory performance when compared with a conventional GC-qMS system, as well as a considerable reduction of the analysis time.

Lastly, the suitability of coupling MESI with a GC-IMS detection system was verified. Based on the outstanding detection limits provided by IMS detection, it was possible to select a high flow rate of 100 mL/min and a short trapping period (2 min) for the analysis of acetone in breath samples. Thus, by using the same analytical instrument, it is plausible to use SPME and NTD for spot on-site analysis, while the use of MESI can provide a valuable tool to monitor concentration changes over time.

References

1. J. Pawliszyn, Anal. Chem., 75 (2003) 2543-2558.

2. J. Pawliszyn, Trends Anal. Chem., 25 (2006) 633-634.

3. X. Liu, J. Pawliszyn, Int. J. Environ. Anal. Chem., 85 (2005) 1189-1200.

4. H. Borsdorf, G.A. Eiceman, Appl. Spectros. Rev., 41 (2006) 323-375.

5. C.L. Arthur, J. Pawliszyn, Anal. Chem., 62 (1990) 2145-2148.

6. H. Lord, J. Pawliszyn, J. Chromatogr. A, 885 (2000) 153-193.

7. J. Pawliszyn, Handbook of Solid Phase Microextraction (2009).

8. J. Pawliszyn, J. Chromatogr. Sci., 38 (2000) 270-278.

9. J. Koziel, M. Jia, J. Pawliszyn, Anal. Chem., 72 (2000) 5178-5186.

10. W.J. Lyman, W.F. Reehl, D.H. Rosenblatt, Handbook of Chemical Property Estimation Methods (1990).

11. C.A. Zini, F. Augusto, E. Christensen, B.P. Smith, E.B. Caramão, J. Pawliszyn, Anal. Chem., 73 (2001) 4729-4735.

12. F. Augusto, J. Koziel, J. Pawliszyn, Anal. Chem., 73 (2001) 481-486.

13. H.L. Lord, W. Zhan, J. Pawliszyn, Anal. Chim. Acta, 677 (2010) 3-18.

14. F. Raschdorf, Chimia, 32 (1978) 478-483.

15. T. Qin, X. Xu, T. Polak, V. Pacakova, K. Stulik, L. Jech, Talanta, 44 (1997) 1683-1690.

16. J.A. Koziel, M. Odziemkowski, J. Pawliszyn, Anal. Chem., 73 (2001) 47-54.

17. J. Pawliszyn, "Needle Trap" US Pat. 6,481,301 (issued November 19, 2002).

18. D.-. Lou, X. Lee, J. Pawliszyn, J. Chromatogr. A, 1201 (2008) 228-234.

19. Y. Gong, I.-. Eom, D.-. Lou, D. Hein, J. Pawliszyn, Anal. Chem., 80 (2008) 7275-7282.

20. A. Wang, F. Fang, J. Pawliszyn, J. Chromatogr. A, 1072 (2005) 127-135.

21. X. Li, G. Ouyang, H. Lord, J. Pawliszyn, Anal. Chem., 82 (2010) 9521-9527.

22. M. Harper, Ann. Occup. Hyg., 37 (1993) 65-88.

23. L.G. Blomberg, Anal. Bioanal. Chem, 393 (2009) 797-807.

24. H. Jurdáková, R. Kubinec, M. Jurčišinová, Z. Krkošová, J. Blaško, I. Ostrovský, L. Soják, V.G. Berezkin, J. Chromatogr. A, 1194 (2008) 161-164.

25. M. Mieth, S. Kischkel, J.K. Schubert, D. Hein, W. Miekisch, Anal. Chem., 81 (2009) 5851-5857.

26. J. Cai, G. Ouyang, Y. Gong, J. Pawliszyn, J. Chromatogr. A, 1213 (2008) 19-24.

27. Y. Saito, I. Ueta, M. Ogawa, K. Jinno, Anal. Bioanal. Chem, 386 (2006) 725-732.

28. M.J. Yang, S. Harms, Y.Z. Luo, J. Pawliszyn, Anal. Chem., 66 (1994) 1339-1346.

29. H. Lord, Y. Yu, A. Segal, J. Pawliszyn, Anal. Chem., 74 (2002) 5650-5657.

30. A. Segal, T. Górecki, P. Mussche, J. Lips, J. Pawliszyn, J. Chromatogr. A, 873 (2000) 13-27.

31. X. Liu, R. Pawliszyn, L. Wang, J. Pawliszyn, Analyst, 129 (2004) 55-62.

32. J. Pawliszyn, In Comprehensive Analytical Chemistry, Sampling and Sample Preparation for Field and Laboratory; Barcelo, D., Pawliszyn, J., EDS.; Elsevier: Amsterdem, 2002; Vol. 37, pp 253 – 278.

33. Y.Z. Luo, J. Pawliszyn, Anal. Chem., 72 (2000) 1064-1071.

34. J.A. Contreras, J.A. Murray, S.E. Tolley, J.L. Oliphant, H.D. Tolley, S.A. Lammert, E.D. Lee, D.W. Later, M.L. Lee, J. Am. Soc. Mass Spectrom., 19 (2008) 1425-1434.

35. Y.I. Yashin, A.Y. Yashin, J. Anal. Chem., 56 (2001) 794-805.

36. A. Keil, H. Hernandez-Soto, R.J. Noll, M. Fico, L. Gao, Z. Ouyang, R.G. Cooks, Anal. Chem., 80 (2008) 734-741.

37. G. Lambertus, A. Elstro, K. Sensenig, J. Potkay, M. Agah, S. Scheuering, K. Wise, F. Dorman, R. Sacks, Anal. Chem., 76 (2004) 2629-2637.

38. A. Wang, H.D. Tolley, M.L. Lee, J. Chromatogr. A, 1261 (2012) 46-57.

39. B.A. Eckenrode, J. Am. Soc. Mass Spectrom., 12 (2001) 683-693.

40. J.A. Syage, M.A. Hanning-Lee, K.A. Hanold, Field Anal. Chem. Tech, 4 (2000) 204-215.

41. Microsaic Systems. www.microsaic.com

42. W.V. Rimkus, D.V. Davis, K. Gallaher, In Proceedings of the 4th Workshop on Harsh-Environment MS, St Petesburgh Beach, FL, 2003.

43. Torion Technologies. http://www.torion.com/

44. A.B. Kanu, H.H. Hill Jr., J. Chromatogr. A, 1177 (2008) 12-27.

45. M.A. Baim, F.J. Schuetze, J.M. Frame, H.H. Hill, Am. Lab., 31 (1982) 59.

46. M.A. Baim, H.H. Hill Jr., HRC & CC. J. High Res. Chrom, 6 (1983) 4-10.

47. H. Borsdorf, A. Rämmler, J. Chromatogr. A, 1072 (2005) 45-54.

48. J.I. Baumbach, S. Sielemann, Z. Xie, H. Schmidt, Anal. Chem., 75 (2003) 1483-1490.

49. J.-. Muller, J. Geophys. Res., 97 (1992) 3787-3804.

50. A. Guenther, J. Geophys. Res., 100 (1995) 8873-8892.

51. M. Kanakidou, J.H. Seinfeld, S.N. Pandis, I. Barnes, F.J. Dentener, M.C. Facchini, R. Van Dingenen, B. Ervens, A. Nenes, C.J. Nielsen, E. Swietlicki, J.P. Putaud, Y. Balkanski, S. Fuzzi, J. Horth, G.K. Moortgat, R. Winterhalter, C.E.L. Myhre, K. Tsigaridis, E. Vignati, E.G. Stephanou, J. Wilson, Atmos. Chem. Phys., 5 (2005) 1053-1123.

52. R. Atkinson, J. Arey, Atmos. Environ., 37 (2003) S197-S219.

53. R.J. Griffin, D.R. Cocker III, J.H. Seinfeld, D. Dabdub, Geophys. Res. Lett., 26 (1999) 2721-2724.

54. M. Kulmala, Science, 302 (2003) 1000-1001.

55. N. Yassaa, J. Williams, Atmos. Environ., 39 (2005) 4875-4884.

56. Comroe J H 1965 Physiology of Respiration 2nd edn (Chicago, IL: Year Book Medical Publishers)

57. T. Ligor, M. Ligor, A. Amann, C. Ager, M. Bachler, A. Dzien, B. Buszewski, J. Breath Res., 2 (2008) .

58. Lumb A 2005 Nunn's Applied Respiratory Physiology (Oxford: Butterworth-Heinemann)

59. Amann A and Smith D (ed) 2005 Breath Analysis for Clinical Diagnosis and Therapeutic Monitoring (Singapore: World Scientific)

60. D. Smith, P. Španěl, Mass Spectrom. Rev., 24 (2005) 661-700.

61. W. Miekisch, J.K. Schubert, G.F.E. Noeldge-Schomburg, Clin. Chim. Acta, 347 (2004) 25-39.

62. C. Turner, P. Španěl, D. Smith, Physiol. Meas., 27 (2006) 321-337.

63. M.P. Kalapos, Biochimica et Biophysica Acta - General Subjects, 1621 (2003) 122-139.

64. C. Deng, J. Zhang, X. Yu, W. Zhang, X. Zhang, J. Chromatogr., B: Anal. Technol. Biomed. Life Sci., 810 (2004) 269-275.

65. C.N. Tassopoulos, D. Barnett, T.R. Fraser, Lancet, 1 (1969) 1282-1286.

66. T. Karl, P. Prazeller, D. Mayr, A. Jordan, J. Rieder, R. Fall, W. Lindinger, J. Appl. Physiol., 91 (2001) 762-770.

67. J. King, A. Kupferthaler, K. Unterkofler, H. Koc, S. Teschl, G. Teschl, W. Miekisch, J. Schubert, H. Hinterhuber, A. Amann, J. Breath Res., 3 (2009) .

68. G.R. Johnson, L. Morawska, Journal of Aerosol Medicine and Pulmonary Drug Delivery, 22 (2009) 229-237.

69. I. Horváth, J. Hunt, P.J. Barnes, K. Alving, A. Antczak, E. Baraldi, G. Becher, W.J.C. van Beurden, M. Corradi, R. Dekhuijzen, R.A. Dweik, T. Dwyer, R. Effros, S. Erzurum, B. Gaston, C. Gessner, A. Greening, L.P. Ho, J.M. Hohlfeld, Q. Jöbsis, D. Laskowski, S. Loukides, D. Marlin, P. Montuschi, A.-. Olin, A.E. Redington, P. Reinhold, E.L.J. van Rensen, I. Rubinstein, P. Silkoff, K. Toren, G. Vass, C. Vogelberg, H. Wirtz, B. Balint, A. Blomberg, J. Freels, M. Goldman, J. Hunt, S.A. Kharitonov, F. Kelly, C. Lehmann, A. Lindstrom, R. Robbins, M. Rothe, H.-. Smith, W.R. Steinhaeusser, W.G. Teague, J. Vaughan, Eur. Respir. J., 26 (2005) 523-548.

70. M. Maroni, B. Seifert, T. Lindvall, Indoor Air Quality - A Comprehensive Reference Book (1995).

71. V. Larroque, V. Desauziers, P. Mocho, Anal. Bioanal. Chem, 386 (2006) 1457-1464.

72. P. Bocchini, D. Dello Monaco, R. Pozzi, F. Pinelli, G.C. Galletti, Microchimica Acta, 165 (2009) 271-278.

73. H. Borsdorf, H. Schelhorn, J. Flachowsky, H.-. Döring, J. Stach, Anal. Chim. Acta, 403 (2000) 235-242.

74. Z. Karpas, Anal. Chem., 61 (1989) 684-689.

75. H. Borsdorf, A. Rämmler, D. Schulze, K.O. Boadu, B. Feist, H. Weiß, Anal. Chim. Acta, 440 (2001) 63-70.

76. T. Kotiaho, F.R. Lauritsen, H. Degn, H. Paakkanen, Anal. Chim. Acta, 309 (1995) 317-325.

77. A.R.M. Przybylko, C.L.P. Thomas, P.J. Anstice, P.R. Fielden, J. Brokenshire, F. Irons, Anal. Chim. Acta, 311 (1995) 77-83.

78. K. Tuovinen, H. Paakkanen, O. Hänninen, Anal. Chim. Acta, 404 (2000) 7-17.

79. G.M. Bota, P.B. Harrington, Talanta, 68 (2006) 629-635.

80. E. Baltussen, P. Sandra, F. David, C. Cramers, J. Microcolumn Sep., 11 (1999) 737-747.

81. X. Liu, S. Nacson, A. Grigoriev, P. Lynds, J. Pawliszyn, Anal. Chim. Acta, 559 (2006) 159-165.

82. J.K. Lokhnauth, N.H. Snow, J. Sep. Sci., 28 (2005) 612-618.

83. M. Nousiainen, S. Holopainen, J. Puton, M. Sillanpää, Talanta, 84 (2011) 738-744.

84. D.L. Massart, B.G.M. Vandeginste, S.N. Deming, Y. Michotte, L. Kaufman, Chemometrics: A Textbook (1988)

85. G.A. Gómez, MSc thesis, University of Waterloo (2012).

86. J. Pawliszyn, Solid Phase Microextraction: Theory and Practice (1997).

87. M.O. Andreae, P.J. Crutzen, Science, 276 (1997) 1052-1058.

88. J.D. Fuentes, M. Lerdau, R. Atkinson, D. Baldocchi, J.W. Bottenheim, P. Ciccioli, B. Lamb, C. Geron, L. Gu, A. Guenther, T.D. Sharkey, W. Stockwell, Bull. Am. Meteorol. Soc., 81 (2000) 1537-1575.

89. V. Librando, G. Tringali, J. Environ. Manage., 75 (2005) 275-282.

90. H. Saathoff, K.-. Naumann, O. Möhler, Å.M. Jonsson, M. Hallquist, A. Kiendler-Scharr, T.F. Mentel, R. Tillmann, U. Schurath, Atmos. Chem. Phys., 9 (2009) 1551-1577.

91. ChemSpider, (accessed 26.10.2012) http://www.chemspider.com/

92. A. Ulanowska, T. Kowalkowski, E. Trawińska, B. Buszewski, J. Breath Res., 5 (2011).

93. M. Ligor, T. Ligor, A. Bajtarevic, C. Ager, M. Pienz, M. Klieber, H. Denz, M. Fiegl, W. Hilbe, W. Weiss, P. Lukas, H. Jamnig, M. Hackl, B. Buszewski, W. Miekisch, J. Schubert, A. Amann, Clin. Chem Lab Med., 47 (2009) 550-560

94. M.J. Zare Sakhvidi, A.R. Bahrami, A. Ghiasvand, H. Mahjub, L. Tuduri, Environ. Monit. Assess. (2012) 1-9.

95. P. Mochalski, B. Wzorek, I. Śliwka, A. Amann, J. Chromatogr., B: Anal. Technol. Biomed. Life Sci., 877 (2009) 1856-1866.

96. I. Ciucanu, M. Kaykhaii, L. Montero, J. Pawliszyn, J. Szubra, J. Chromatogr. Sci., 40 (2002) 350-354.

97. M. Kaykhaii, A. Sarafraz-Yazdi, M. Chamsaz, J. Pawliszyn, Analyst, 127 (2002) 912-916.

98. W. Ma, X. Liu, J. Pawliszyn, Anal. Bioanal. Chem, 385 (2006) 1398-1408.

99. Y. Yu, J. Pawliszyn, J. Chromatogr. A, 1056 (2004) 35-41.

100. X. Liu, J. Pawliszyn, J. Membr. Sci., 268 (2006) 65-73.

101. C. Zscheppank, U. Telgheder, K. Molt, Int. J. Ion Mobil. Spec., (2012) 1-8.