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# Direct coupling of supercritical fluid extraction to a gas phase atmospheric pressure chemical ionisation source ion trap mass spectrometer for fast extraction and analysis of food components

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**Abstract**

Supercritical fluid extraction (SFE) was coupled to a custom-built atmospheric pressure chemical ionization (APCI) source of an ion trap mass spectrometer (ITMS). This method was developed for the monitoring of static or dynamic carbon dioxide extraction of volatile aroma compounds in real time. The gas phase APCI source resulted in simple spectra where the extraction of individual compounds could be monitored. A classical mint extraction was used to demonstrate the possibilities of the method. Influence of cell loading and standard injection possibilities are described. Limit of detection of the system was 0.5 nl or lower for a series of test compounds. Prospect for a fast method for extraction and quantification was raised and discussed.


*Keywords:* Direct coupling; Supercritical fluid extraction; Food analysis

## 1. Introduction

Flavour extracts are conventionally produced by hydrodistillation, steam distillation, or solvent extraction. Supercritical fluid extraction (SFE) is, by comparison, a recent technique but offers several advantages over traditional techniques. $CO_2$ is the fluid of choice for SFE with food components because of its low critical constants, its low cost, non-toxic nature and ease of use. Supercritical $CO_2$ is also a remarkable tuneable solvent. By adjusting the pressure and temperature of extraction, properties of the solvent, and thus, the extraction efficiency can be varied. A simplistic approach is that solubility of most compounds generally increases with pressure, i.e. with increasing $CO_2$ density. On the contrary, a rise of temperature decreases $CO_2$ density and therefore reduces solubility. Pressure and temperature have to be adjusted together to find the optimum extraction conditions for a particular system.

Supercritical $CO_2$ has good solvent properties for non-polar compounds, but is not so satisfactory for polar compounds. The solvent properties of supercritical $CO_2$ can be modified by the addition of polar solvents. Care has to be taken in the choice of the modifier so that the new mixture is still in a supercritical state. In addition, the selectivity of the extraction may be reduced, resulting in the extraction of non-desired molecules. Methanol is the most widely used modifier. The main disadvantage to the use of modifier is the fact that the modifier is recovered together with the extract and may need a further step for its removal.

SFE can be accomplished by using either static, dynamic or static–dynamic mode [1]. The static mode uses a fixed amount of $CO_2$ to interact with the matrix in a sealed vessel for a period of time. This extraction mode minimises the amount of supercritical $CO_2$ used, but leads to partial extraction as partition between the sample and the supercritical fluid governs the degree of extraction. For dynamic extraction, fresh $CO_2$ is continuously pumped through the sample, which leads to more exhaustive extractions and is the strategy used in most cases. The static–dynamic mode starts with an initial static period followed by a dynamic one. This mode is

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used when the extraction process requires diffusion of $CO_2$ through the matrix.

After extraction, the extract is generally recovered in a cooled liquid solvent or by solid trapping and is analysed off-line via GC–MS, HPLC–MS or spectroscopic method [2].

SFE has been coupled on-line to a range of detection methods. Some of these systems focus on automation as the extract is trapped before analysis [3]. This is the case of chromatographic methods such as GC [4], LC [5] or Supercritical fluid chromatography (SFC) [6]. Dynamic on-line coupling systems have also been developed, mainly based on optical spectroscopic methods [1,7,8]. Among them, FT-IR is the most widely used method as it is the most powerful spectroscopic tool for the elucidation of molecular structure with quantitative analysis possible [9–11]. Another interesting coupling is with nuclear magnetic resonance (NMR) Spectroscopy, which allowed some selectivity to monitor extracted compounds. On-line coupling of SFE to NMR was applied to roasted coffee, black pepper and to differentiate isomers of Vitamin A acetate [12,13].

When operating on complex natural extracts, the selectivity of NMR and FT-IR are limited and result in complex spectra, which are difficult to interpret. This could be overcome, using direct mass spectrometry with a soft ionisation source. The direct coupling of supercritical fluid to mass spectrometry was pioneered by Smith et al. in 1983 and applied to mycotoxins [14]. A SFC device was coupled to an electron impact-chemical ionization source mass spectrometer via a direct fluid injection. The interface consisted of 35 cm $\times$ 0.1 mm i.d. platinum–iridium tube carrying between 2 and 30 μl/min of fluid toward the ionization source of the MS. Direct extraction analysis using a mass spectrometer was attempted in 1986 by Kalinoski et al. still with the direct fluid injection method to introduce sample in a chemical ionization source [15]. They worked on wheat samples doped with different mycotoxins. However, they suffered from high background noise and did not reach high sensitivity. These studies all focused on non-volatile analytes. However, highly volatile analytes are difficult to trap out of supercritical $CO_2$ and these compounds may be more readily analysed by direct mass spectrometry.

In this paper, attempts to couple SFE to a soft ionization mass spectrometer are presented. The detection system consists of a custom-built gas phase atmospheric pressure chemical ionisation (APCI) source linked to an ion trap mass spectrometer (ITMS). APCI-MS has already been used as a method for online analysis [16–18]. The soft ionisation of APCI-ITMS is potentially more selective than spectroscopic methods and can provide an individual monitoring of known compounds from a complex mixture [19]. Previous knowledge of the compounds present in the extract is however, necessary as the capacity of APCI-ITMS to identify unknown compounds is limited. SFE-APCI-ITMS is particularly suitable for the analysis of volatile compounds like aromas. As the extract is analysed on-line with no trapping device, all the volatiles extracted will be analysed.

SFE-APCI-ITMS was applied to study the extraction of volatile aroma compounds from mint to establish the feasibility of using this technique as a fast extraction-analysis device, which could find application as a rapid quality control method or for the on line monitoring of large scale extractions.

## 2. Experimental

### 2.1. SFE Apparatus and its coupling to MS

The scheme of the SFE apparatus and its coupling to the gas phase APCI-ITMS is given in Fig. 1. SFE grade $CO_2$ (Air Products, Nottingham, UK), at a nominal pressure of 95 bar, was pressurised, using a Jasco pump PU 1580, while the extraction cell (10 $cm^3$, Thar, Scientific and Medical Products Ltd., Cheadle, UK) was pre-warmed before extraction and maintained at a constant temperature in a GC oven. Valve 2 allowed $CO_2$ to enter the cell and isolate sections of the $CO_2$ delivery system. Valve 3, referred to later as the outflow valve, controlled the extract release and separated the cell from two deactivated fused silica capillary tubes, which acted as flow restrictors. The flow from these restrictors depended on the cell pressure, and was pre-determined by pressurizing an empty cell. The first restrictor (150 mm $\times$ 10 μm i.d.) allowed a low outflow of 6.5 ml/min (standard conditions) of gaseous $CO_2$ at a cell pressure of 95 bar. The second restrictor (10 cm $\times$ 50 μm i.d.) delivered a flow of 230 ml/min of gaseous $CO_2$ under the same conditions. These restrictors remained warm in the GC oven to minimise plugging problem [10].

A single restrictor was exposed below the APCI-ITMS sampling tube, nitrogen could be added below the extraction delivery if dilution of the sample was needed. Excess sample and nitrogen were vented into the laboratory air. Valve 5 was used to quickly remove $CO_2$ from the cell for cleaning or at the end of an extraction.

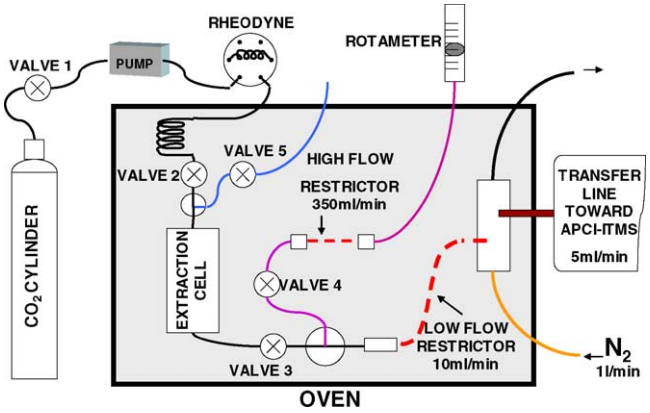


Fig. 1. Schematic of the SFE apparatus and its coupling to gas APCI-ITMS.

This combination of valves and restrictors allowed static or dynamic extraction to be performed, and controlled the signal intensity on the MS. To monitor a static extraction, Valve 4 was closed with only the low flow restrictor opened. The low flow restrictor, coupled alone to the extraction cell, lead to a flow rate in the extraction cell between 10 and 20 μl of supercritical $CO_2$ per minute, depending on the $CO_2$ density. In that case, extraction could be considered quasi static as the flow through the extraction cell was equivalent to 0.2% of the cell volume per minute and would not disturb the equilibrium in the cell. For dynamic extraction, both the low flow restrictor linked to the MS and the high flow restrictor were used. This resulted in a total flow of 240 ml/min of $CO_2$ gas out of the cell, which is equivalent to about 0.7 ml/min of supercritical $CO_2$ through the extraction cell. A rotameter was fixed at the end of the high flow restrictor to check that flow was stable.

### 2.2. Standard injection and limit of detection

A 7125 Model rheodyne was fitted prior to the extraction cell for injection of standard compounds (Fig. 1). Standard solutions were prepared in hexane and injected, using a 5 μl loop, just before the cell was pressurized. Hexane was selected because it is not readily ionized by APCI as its proton affinity is lower than that of water, and hence, would not form major ions. Injecting a solvent via the rheodyne can be seen as adding a modifier to supercritical $CO_2$. However, hexane shares similar solvation properties to supercritical $CO_2$ and would not be expected to substantially change the extraction process [20].

Standard injections were used to estimate the limit of detection of the system. In that case, the high flow restrictor was connected to the MS sampling tube, with no nitrogen flushing for maximum sensitivity. Standard solutions of α-damascone, 2,3,5-trimethylpyrazine, linalool, pyrrole and 1-octen-3-ol were prepared in hexane. Dilution series from 0.1 to 5 nl were injected into the empty cell, using the rheodyne.

### 2.3. Atmospheric pressure chemical ionization ion trap mass Spectrometer (APCI-ITMS)

A Thermo Finnigan LCQ Deca Xp ITMS was used with an APCI gas phase interface. The working principle of this source are similar to the APCI source developed by Linforth and Taylor [21]. The custom built APCI source formed the protonated molecular ion from the analysed compound with minor fragmentation and simplified spectral interpretation.

A scheme of the custom-built ionization source is given in Fig. 2. The extract was drawn into the source via a 0.53 mm i.d. deactivated fused silica capillary tube heated in a transfer line at 150 °C. Nitrogen (3 l/min) was introduced around the sampling capillary to create a venturi region at the end of the capillary and draw the sample through the capillary.

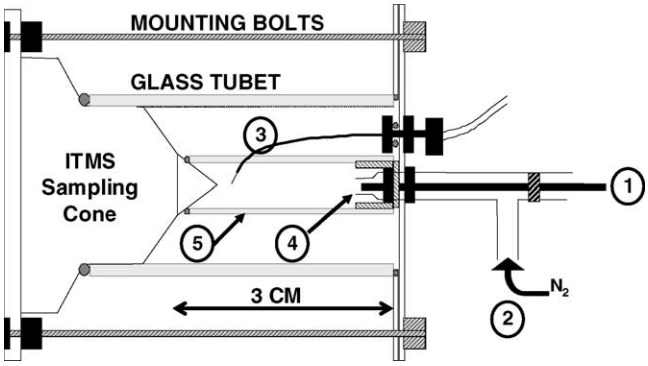


Fig. 2. Schematic of the gas phase APCI source. The sample is drawn in via a fused silica tube (1) by a venturi effect created by $N_2$ (2) in region (4), then is ionised in a inner chamber (5) by a corona pin (3) discharge before entering the ITMS sampling cone.

The sampling capillary tube ended in the ionisation chamber (a small glass tube mounted around the inlet of the mass spectrometer). The corona pin was brought through a hole in the side of the small glass tube, and terminated in the central position of the tube. The sampling flow rate of the MS was adjustable, and a value of 5 ml/min was used in the present work.

The ITMS was set up to work in full scan mode in the low mass range, from *m/z* 30 to 200. The multipole RF amplitude was decreased to 120 V to enhance sensitivity for low molecular weight ions. The ion-transfer tube was set at 3 V and 150 °C with the tube lens offset fixed at −20 V. Data points were averaged over 10 microscans, which corresponded to a data point every 1.5 s.

### 2.4. Sample and standard chemicals

A batch of 300 g dried mint from DBC Food Service (Welvyn Garden City, UK), with no information on the label, was used for these experiments.

R-(−)-Carvone, 2,3,5-trimethylpyrazine, linalool, pyrrole, 1-octen-3-ol, ethyl hexanoate, undecane and dodecane were supplied from Aldrich (Gillingham, UK). α-Damascone was supplied from Firmenich S.A. (Geneva, Switzerland).

### 2.5. Solvent extraction of mint

Mint (1 g) was extracted in triplicate in 20 ml dichloromethane for 90 min, with 30 min of sonication at regular intervals. The extract was then filtered, mixed (1:1) with an internal standard solution of undecane, dodecane and tridecane in dichloromethane (10 μl/ml) before injection onto a gas chromatograph–mass spectrometer (GC–MS) (Fisons GC800/MD800). The DB5 column (30 m × 0.25 mm, 1 μm film thickness, J&W) was maintained at 45 °C for 2.5 min, and then programmed at 15 °C/min to 160 °C, and then held for 10 min. The split injector was set at 200 °C. Compounds were identified, using authentic standards, on the basis of retention index and mass spectra.

## 3. Results and discussion

### 3.1. Preliminary analyses

Direct headspace analysis of mint, using APCI-ITMS, showed two major ions at *m*/*z* 151 and 155, which were interpreted as protonated molecular ion for carvone at mass 151 and 1,8-cineole for 155. These two compounds were the major components of the spearmint sample analysed by GC–MS [22].

In the first SFE-APCI-ITMS experiments performed, the signal intensity of carvone (*m*/*z* 151) was too high and saturated the mass spectrometer detector. This was overcome by minimizing the outflow from the extraction cell to 6.5 ml/min of $CO_2$ gas and diluting it (approximatively 100-fold) in nitrogen prior to the ITMS sample inlet to reach a signal size a decade below saturation. The carvone ion was used as a marker of the mint extraction and could be followed alone during the method development at *m*/*z* 151.

APCI is a soft ionisation method, which predominantly produces the protonated molecular ion with very little fragmentation, simplifying the spectral deconvolution. Furthermore, the $MS^n$ ability of ion trap may help to improve the separation of isobaric compounds depending on their fragmentation pattern. SFE-APCI-ITMS is a sensitive and potentially a more selective method to monitor the extraction of a mixture of compounds [19], compared with spectroscopic methods [9,12]

Carry over contamination was a second major problem encountered during SFE analysis. After extraction, a thorough cell cleaning was necessary to prevent any carry-over contamination from the previous extraction. It was observed that the frits and seals were trapping extracted compounds after the extraction. The frits and seals were immersed in hexane, sonicated for 15 min and then dried in an oven prior to further use. Before carrying out an extraction, the empty cell was pressurized with supercritical $CO_2$ and checked with APCI-ITMS to ensure that no carvone signal was detected.

APCI is particularly suitable for the ionization of volatiles extracted with $CO_2$. APCI ionization is performed via a proton exchange between protonated water in the gas phase and the analyte. Proton transfer occurs if the analyte has a proton affinity higher than water. This is true for almost all volatile organic compounds, with the notable exception of air constituents. Therefore, carbon dioxide is hardly ionized by APCI, and causes no interferences.

Preliminary extractions were performed at 95 bar and 60 °C, with the outflow Valve 3 closed for 2 min at the beginning of extraction to allow the extraction cell to reach its extraction pressure. Then the valve was opened, $CO_2$ flowed through both restrictors, resulting in a dynamic extraction. Identical mint extraction conditions gave reproducible results, with a coefficient of variation (100 × standard deviation/average) of about 10% for the maximum intensity of the carvone signal. This value was regarded as reasonable, considering the possible source of variation (temperature and pressure of extraction and flows from the restrictors as the most influential ones).

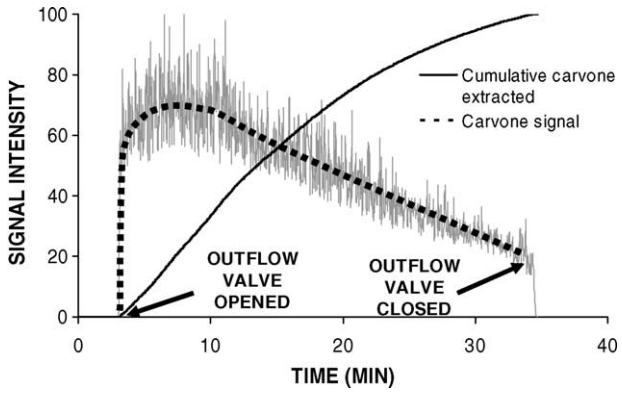


Fig. 3. Profile of dynamic carvone extraction from mint.

### 3.2. Extraction types

Static and dynamic extractions could be performed on the system (see Fig. 1). The carvone signal over time during a typical dynamic mint extraction is given in Fig. 3 (the dotted trend line is added to simplify the reading of the spiky raw data trace). Carvone was detected just after the outflow valve was opened and quickly reached a maximum plateau value, which persisted for a few minutes, then the curve decayed slowly with time. The initial high carvone signal is interpreted as a fast solubilization of easily accessible carvone into supercritical $CO_2$, while the decrease of the carvone signal is explained by the carvone concentration going down in the cell due to dilution with $CO_2$ combined with further extraction. The persisting plateau at the beginning of the extraction is a steady-state phase where carvone is further extracted from the mint, together with carvone leaving the cell with $CO_2$. It can be anticipated that the shape of this extraction profile will depend on the compound's solubility in supercritical $CO_2$ and the role of diffusivity in the extraction process.

The cumulative amount of carvone extracted was obtained by integrating the carvone signal over time. This showed an initial near-linear increase, which then declined over time resulting in the logarithmic shape curve typical of dynamic SFE extraction [3].

Fig. 4 shows the profile of carvone extraction over time during a static mint extraction. In this case, the low flow restrictor was used to deliver extracted volatile to the MS sampling tube, while Valve 4 remained closed. The appearance of the carvone signal on the MS was slightly delayed after opening the valve, the signal then increased quickly before showing a slower increase over time. The fast initial increase is interpreted again as the rapid solubilization of carvone in supercritical $CO_2$. The slower increase in the signal could have been due to a further extraction of carvone (increasing the concentration of carvone in the cell) or to a delay caused by the dead volume after the frits of the extraction cell. The flow rate through the cell was so low, that this dead volume

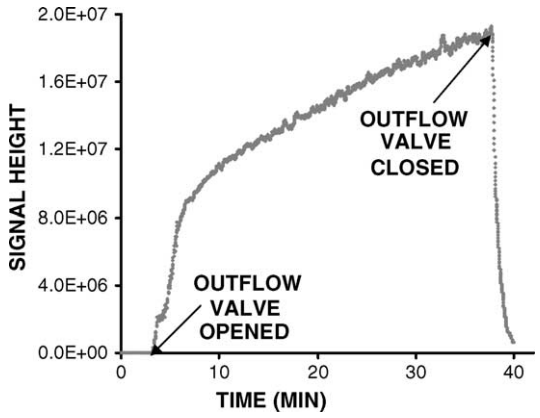


Fig. 4. Profile of static carvone extraction from mint.

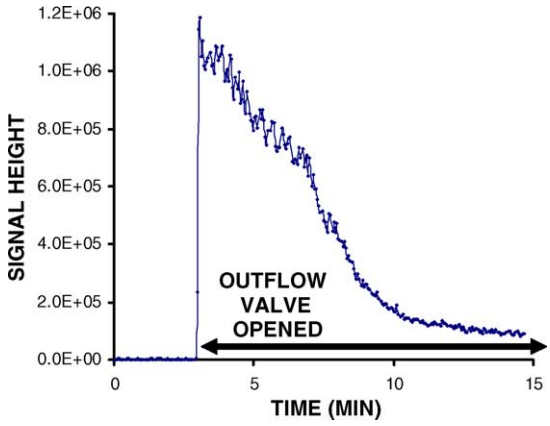


Fig. 6. Carvone standard injection vs. time.

may easily have delayed the signal, resulting in a difference between the actual concentration in the cell and what was detected by the MS.

The shape of the extraction curves can be used to estimate the kinetic of the extraction, find the optimum extraction conditions and decide when to stop the extraction.

### 3.3. Effect of cell loading on SFE

The 10 $cm^3$ extraction cell could hold a maximum of 2 g of dried mint. Different amounts of mint, from 0.2 to 2 g were extracted. Carvone's maximum signal height versus mint quantity in the extraction cell is presented in Fig. 5. Between 0.2 and 1 g, the relation between signal height and mint quantity was linear ($R^2$ = 0.999). Above 1 g of mint, the relationship was not linear and the signal increased less and less with additional mint. This was not due to reaching the saturation limit of the MS. The plateau in the signal was probably due to a change in the supercritical $CO_2$ to mint ratio. As mint quantity increased, there was not enough supercritical $CO_2$ available to extract carvone efficiently. For all the following extractions, 0.5 g mint was used, since this gave a readily detectable signal in the linear part of the signal versus sample amount curve (Fig. 5).

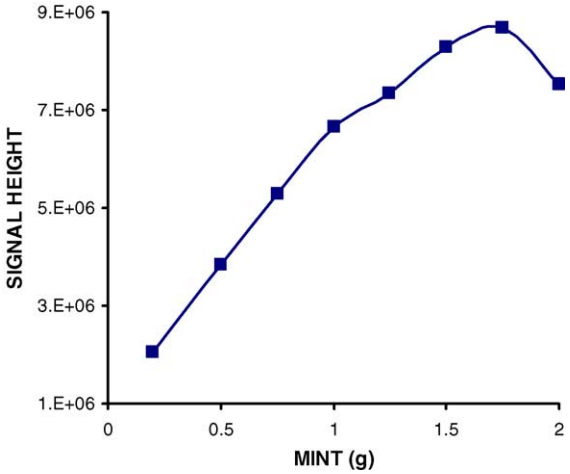


Fig. 5. Carvone signal vs. mint quantity in the cell for dynamic extraction.

### 3.4. Standard injection

Standard injections were performed with the rheodyne to calibrate, or find the limit of detection of the system. When injecting a standard via the rheodyne, the outflow Valve 3 was closed for 2 min to allow the standard to mix evenly in the cell with $CO_2$. The signal intensity over time for a carvone standard injected via the rheodyne is shown in Fig. 6. The curve profile started with a fast signal increase reaching a maximum, before decaying over time. Compared with the signal from an extraction, the signal from a standard did not stabilize at a maximum plateau and declined much faster. This is because, the behaviour of the standard depends on its distribution and solubilization in supercritical $CO_2$ as opposed to an extraction where other transport phenomena occur.

The relation between the maximum signal intensity and the carvone amount (80–875 nl) was linear ($R^2$ = 0.998) and reproducible as seen in the differences between replicates (Fig. 7). Standard injection was used to find the limit of detection of the system. In that case, the high flow restrictor was coupled to the MS, with no signal dilution by nitrogen,

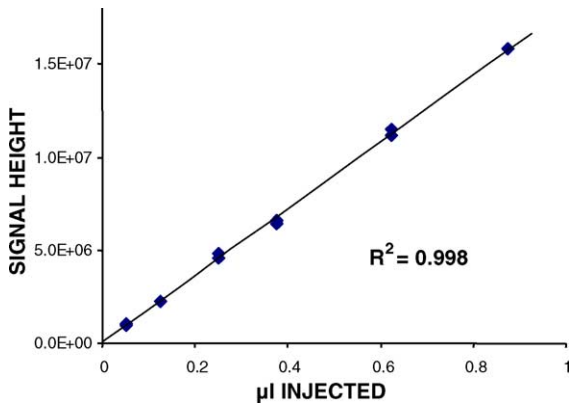


Fig. 7. Calibration curve for standard carvone injection.

Table 1
Variation of extraction parameters and their influence on the maximum signal height of carvone

| Pressure (bar) | Temperature (°C) | Static time (min) | Carvone |
|---|---|---|---|
| 95 | 40 | 2 | 1.9E + 06 |
| 125 | 40 | 2 | 1.5E + 06 |
| 95 | 40 | 30 | 2.9E + 06 |
| 125 | 40 | 30 | 2.2E + 06 |
| 95 | 80 | 2 | 4.2E + 6 |
| 125 | 80 | 2 | 3.4E + 06 |
| 95 | 80 | 30 | 3.2E + 06 |
| 125 | 80 | 30 | 4.0E + 06 |
| 110 | 60 | 16 | 3.9E + 06 |
| 110 | 60 | 16 | 4.1E + 06 |
| 110 | 60 | 16 | 4.1E + 06 |

for maximum sensitivity. The limit of detection was set at a signal-to-noise ratio of 3. The five standards used all displayed a limit of detection between 0.1 and 0.5 nl. This limit of detection is roughly equivalent to the amount in one gram of material containing 1 ppm of volatile.

### 3.5. Influence of extraction parameters

Optimization of three experimental variables was carried out in a two level factorial design with centre points. Pressure was varied between 95 and 125 bar, temperature ranged from 40 to 80 °C. An initial static extraction time was varied between 2 and 30 min. During the static time, the outflow Valve 3 remained close and was then opened (Valve 4 was already opened) for a dynamic extraction. This extraction was run to find an optimum value for pressure and temperature, while the static extraction time allowed studying the influence of diffusion. As different pressures were set up in the extraction cell, the flow out of the restrictors increased with higher pressure. This flow was corrected to standardize the results. The maximum signal height reached after the start of the dynamic mode was recorded, and the corrected results from the experimental design are shown in Table 1.

For carvone, the duration of the initial static time did not affect the maximum signal height of carvone. No further carvone was extracted with a longer static period. We interpreted this result as the fact that the partition of carvone between the matrix and the supercritical $CO_2$ was reaching an equilibrium, limiting further extraction. This result allows us to further interpret the static carvone extraction profile in Fig. 4. If no further carvone is extracted with a longer static time, this implies that diffusion was not governing the extraction. Therefore, the increase in signal seen in Fig. 4 may be more associated with an artefact due to dead volume, rather than a change in the actual concentration within the cell.

Pressure and temperature showed no major trends over the experimental conditions used. Temperature showed a slight effect, the extraction at 40 °C led to a poorer extraction compared with results obtained at 60 and 80 °C. Pressure seemed to have no effect on the carvone extraction in that case.

### 3.6. Quantification

Different strategies have been applied for on-line quantification. For SFE/FT-IR, the extract was trapped prior to its analysis [9]. Other methods like spectrophotometry [23], thermal lens spectrometry [24] or fluorometry [25] used the area obtained below the extraction curve for the quantification.

For quantitative SFE-APCI-ITMS, the signal area of the extracted compounds could be compared with the signal area of a standard injection. However, this could take a long time and the speed advantage of performing direct analysis would be lost.

The maximum signal height rather than the signal area showed clear linear relationships with sample and standard amounts (initial part of Figs. 5 and 7). The relationship between the maximum signal height and the signal area was consistent but different for both samples.

A preliminary estimation of carvone present in mint based on a 5 min long extraction was attempted by SFE-APCI-ITMS. Quantitative analysis of four replicates of mint samples gave an estimated carvone concentration of 1.2 mg (±0.1 mg) per g of mint based on signal height comparison. This value is of course an underestimation of the total carvone concentration in the mint given the area differences of standard and sample profiles. The difference in area between sample and standard profiles with the same height was a factor of 3, which would lead to an estimated carvone concentration of 3.6 mg/g mint. Quantification of carvone extracted by dichloromethane and analysed by GC–MS resulted in a total carvone concentration of 5.6 mg (±0.4 mg) per g mint.

Further work needs to be performed to validate the extraction-quantification process across a range of different food types with different extraction kinetics. The similarity of the results obtained by SFE-APCI-ITMS and GC–MS indicates that rapid quantitative analysis may be possible.

## 4. Conclusion

SFE-APCI-ITMS has proved a suitable method for a fast extraction and analysis method of volatile aroma compounds. The dynamic nature and the selectivity of the method make it ideal to study individual extraction kinetics, or monitor influences of various parameters on the extraction. Signal height correlated linearly to sample quantity and to standard injection and led to faster analysis for comparison between samples. Further work will investigate fast quantification possibilities, effect of modifier, and application to various food systems.

## Acknowledgments

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