

Analysis of volatile organic compounds by direct infusion mass spectrometry (dims)

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Abstract

Volatile organic compounds (VOCs) exposure can have long term health effects. The accurate quantification of VOC metabolites is conducted, in this article, using direct infusion mass spectrometry (DIMS). The optimised DIMS method shows comparable classification and prediction capability to LC-MS and GC-MS but consumed only 5% of the analysis time, decreasing costs and improving productivity.

Introduction

Volatile organic compounds (VOCs)

VOCs are organic chemicals that have high vapor pressure at room temperature. Consequently, large numbers of molecules evaporate in the surrounding air.

VOCs are classified in naturally occurring chemical compounds and human-made derived substances. The first category comprises substances produced by plants for communication and scents.¹ According to their biosynthetic origin and chemical structure, plant volatiles can be grouped into isoprenoids or terpenoids, but also oxygenated VOCs (e.g. methanol (CH₄O), acetone (C₃H₆O), acetaldehyde (C₂H₄O), methyl-ethyl-ketone (MEK, C₄H₈O) and methyl-vinyl-ketone (MVK, C₄H₆O)), sulphur compounds and furanocoumarins.² Anthropogenic VOCs derive from the emissions of power and industrial plants, chemical production, petroleum refining and vehicle engines. Harmful VOCs are not usually acutely toxic, but can have long-term health effects. Long-term exposure to certain VOCs may increase the risk for cancer, birth defects, and neurocognitive impairment.

For example, acrolein is a substance ubiquitously present in cooked food and in the environment. It is formed from carbohydrates, vegetable oils, animal fats, and amino acids during heating, and by combustion of petroleum fuels and biodiesel. However, smoking of tobacco products is typically the largest source of acrolein exposure. Acrolein can induce necrotic and apoptotic cell death in humans.³ Acrylamide is formed during the heating of carbohydrate rich food and is

used for the production of polymers, formulation of cosmetics and body care products, and in the textile industry. It is carcinogenic and mutagenic.⁴ Acrylonitrile is a VOC widely used in the manufacture of plastics, acrylic fibres, and synthetic rubber. It is considered as a probable human carcinogen.⁵ Similarly, benzene, toluene, and xylene are known to be carcinogenic in humans.⁶ 1,3-butadiene is mainly used alone in the production of synthetic rubber, or as a copolymer with styrene. It is also found in automobile exhaust, exhaust from heating, and cigarette smoke. 1,3-butadiene is carcinogenic to humans by inhalation.⁷ N, N-dimethylformamide (DMF) is a solvent that is used in the production of electronic compounds, pharmaceutical products, textile coatings and in the manufacture of synthetic leather, polyurethane, and polyacrylonitrile fibres. It is found to be carcinogenic in humans.⁸ Styrene is one of the most important chemicals used worldwide to manufacture plastics, synthetic rubber and resins. It is also an environmental contaminant present in food, tobacco, and engine exhaust. It is classified as a possible carcinogenic to humans.⁹

Vinyl chloride exposure can cause angiosarcoma.¹⁰ Perchloroethylene, 1-bromopropane, and trichloroethene are constituents of tobacco smoke and are widely used in dry cleaning and metal degreasing solvents. They are a hazardous air pollutant and a common contaminant detected at waste sites.¹¹

VOC measurement challenges and commonly used methods

VOCs metabolites are useful biomarkers for assessing VOCs exposure. However, most of the VOCs are only in very low concentrations (ppt to ppb) in biological samples. Therefore, the accurate quantification demands a technique with great sensitivity, selective to the target VOC, reliable and user friendly. Originally VOCs measurements were made using Gas Chromatography with flame ionization detector (GC-FID) or mass detector (GC-MS). However, when conducting environmental analysis using a GC mass

spectrometer there are numerous inefficiencies, such as laborious and expensive sample preparation stages, and long chromatographic run times. As a result, liquid chromatography-mass spectrometry (LC-MS) solutions were introduced that are less time-consuming and have simpler sample preparation. Such methods are characterised by the direct injection of a water sample with no need for derivatisation, short chromatographic run times, and screening for a wider range of compounds in a single analysis.

Although being beneficial to comprehensive analysis, the chromatographic step of LC-MS limits the throughput, especially when the number of samples is large. Furthermore, there can be possible loss of some relevant analytical signals or the generation of artefacts by erratic retention time shift correction or background subtraction. Alternatively, direct infusion mass spectrometry (DIMS) provides a high throughput and more concise raw data than LC-MS by avoiding any chromatographic steps. Electrospray ionisation (ESI) is the most common method used for ionisation in the DIMS analysis of VOCs. The electrospray process ionization is accomplished by the loss or gain of a proton or other adducts, such as Cl⁻ ions in negative ion mode or K⁺ and Na⁺ in positive ion mode. The formation of such adducts is highly dependent on the salt content of the sample matrix. ESI produces minimal (usually no) fragmentation and the protonated or deprotonated analyte is referred to as the “pseudo molecular ion” of the parent molecule. This property means that DIMS analytical approaches using electrospray ionisation are able to directly predict m/z signal identity based on measured mass. The lack of extensive molecular fragmentation during electrospray ionisation results in reproducible ionization patterns for extracts representing similar biological matrices, and offers an experimental robustness suitable for larger scale investigations.¹²

Materials and method

Materials

VOCs standards were bought from Sigma Aldrich (Sigma-Aldrich S.R.L., Milan). acetonitrile, N-hexane and water were obtained from Carlo Erba (Carlo Erba reagents, Milan).

Sample preparation

VOCs characterised by strong lipophilicity are extracted from urinary and blood matrix by liquid-liquid extraction with N-hexane (ratio 1:2 matrix\N-hexane). While compounds with negative LogP are directly injected into the mass detector.

DIMS conditions

Sample are analysed with LCMS-8060 of Shimadzu (Shimadzu Italia S.R.L., Milan) using injection volume of 5µl. Mobile phase is acetonitrile (or n-hexane) for

organic compounds and formic acid in water 0.01% v/v for hydrophilic compounds. Capillary used for the infusion has internal diameter of 0.01 mm and length of 1 meter. Mass condition are summarised in table 1.

Nebulizing gas flow	2.9 L/min
Heating gas flow	10 L/min
Interface temperature	300°C
DL temperature	250°C
Heat block temperature	400°C
Drying gas flow	10 L/min

Table 1. Mass conditions

Results and discussion

Table 2 lists examples of used mass fragments for quantification.

Substance	m/z	ESI condition
Benzene	78	+
Methyl ethyl ketone	73	+
Acetone	59	+
Ethanol	47	+

Table 1. Mass conditions

Figure 1 shows the mass spectrum obtained for benzene.

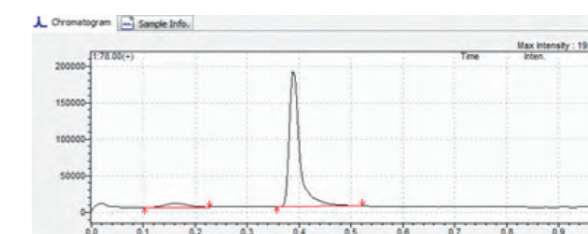


Figure 1. Mass spectrum of benzene by DIMS

The optimised methods permit analyses of VOCs in less than one minute with no need of derivatisation. DIMS has comparable classification and prediction capabilities to LC-MS but consumes only 5% of the analysis time, decreasing costs and improving productivity. However, matrix effects are inevitable because the samples are infused together without separation, which may result in reduced sensitivity and deteriorated capability for metabolite identification. In order to minimise such an effect,

the mobile phase should coincide with those used to extract the analyte from the biologic matrix.

Conclusion

A method using direct infusion mass spectrometry was developed to analyse VOCs. DIMS shows a similar classification and prediction capability to LC-MS and GC-MS but with the advantage of having a much higher throughput without chromatographic steps. DIMS can potentially be further developed as a fast-diagnostic method for VOCs exposition.



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References

1. Vivaldo G, Masi E, Taiti C, et al. (2017) The network of plants volatile organic compounds. *Scientific Reports* 7: 11050.
2. Agrawal AA (2011) Current trends in the evolutionary ecology of plant defence. *Functional Ecology* 25: 420-432.
3. Abraham K, Andres S, Palavinskas R, et al. (2011) Toxicology and risk assessment of acrolein in food. *Molecular Nutrition & Food Research* 55: 1277-1290.
4. Besaratinia A, Pfeifer GP (2004) Genotoxicity of Acrylamide and Glycidamide. *JNCI: Journal of the National Cancer Institute* 96: 1023-1029.
5. Koerselman W, van der Graaf M (1984) Acrylonitrile: a suspected human carcinogen. *Int Arch Occup Environ Health* 54: 317-324.
6. McMichael AJ (1988) Carcinogenicity of benzene, toluene and xylene: epidemiological and experimental evidence. *IARC Sci Publ*: 3-18.
7. Melnick RL, Shackelford CC, Huff J (1993) Carcinogenicity of 1,3-butadiene. *Environmental health perspectives* 100: 227-236.
8. Senoh H, Aiso S, Arito H, et al. (2004) Carcinogenicity and Chronic Toxicity after Inhalation Exposure of Rats and Mice to N,N -Dimethylformamide. *Journal of Occupational Health* 46: 429-439.
9. Huff J, Infante PF (2011) Styrene exposure and risk of cancer. *Mutagenesis* 26: 583-584.
10. Vianna NJ, Brady J, Harper P (1981) Angiosarcoma of the liver: a signal lesion of vinyl chloride exposure. *Environmental health perspectives* 41: 207-210.
11. Trevisan A, Macca I, Rui F, et al. (2000) Kidney and liver biomarkers in female dry-cleaning workers exposed to perchloroethylene. *Biomarkers* 5: 399-409.
12. Draper J, Lloyd AJ, Goodacre R, et al. (2013) Flow infusion electrospray ionisation mass spectrometry for high throughput, non-targeted metabolite fingerprinting: a review. *Metabolomics* 9: 4-29.

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