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Technical Report

Profiling Trace Volatile Compounds in Blood by Gas Chromatograph Mass Spectrometry with Dynamic Headspace Extraction

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Abstract:

Various types of volatile substances are present in blood, and in addition to those that play roles in the formation of adducts such as proteins and nucleic acids, some are known to act as secondary messengers that regulate various biological functions. To learn more about these roles, the profiling of volatile components in blood has been attracting attention. Up to now, solid phase micro-extraction (SPME) and HS-SPME have been the primary methods used for analysis of volatile substances. The HS-SPME method is a static method in which a fiber coated with a solid (sorbent) extraction phase is exposed to the gas phase. Because extraction proceeds based on the equilibrium migration of volatile components, those volatile components that exhibit strong interaction with the extraction fiber present a strong profile. In this report, we focused on the dynamic headspace (DHS) method. The DHS method is a dynamic extraction method in which the gas phase is forcibly purged using an inert gas, and the volatile components are collected on the adsorbent. Since nearly all of the gas phase components can be collected, volatile components are efficiently collected, enabling a wider range of components to be analyzed by this method compared with conventional methods. Using a standard mixture of volatile substances, a comparison of the results of volatile substance profiling obtained using the HS-SPME and DHS methods showed that application of the DHS method permitted detection of all the volatile substances, including the alcohols, which were difficult to profile by HS-SPME. Furthermore, the results of validation of the DHS method confirmed the detection of all of the volatile components at ng levels. The results obtained applying this system with IL-10 knockout mice plasma confirmed the detection of 40 volatile compounds, in which a significant difference between samples was observed with respect to 15 compounds. High-sensitivity volatile substance profiling is possible using this system, and is expected to be applied in future clinical research.

Keywords: GC-MS, Metabolomics, Volatile, Dynamic Headspace Extraction

1. Introduction

Various types of volatile substances are present in blood, and some of the distinctive odors originating from blood have long been a means of distinguishing among diseases. For example, it is known that increased levels of ketones such as acetone in the blood of diabetic patients produce an apple-like sweet odor. It is thought that identification of these kinds of disease-specific volatile substances might permit the use of such volatile substances as biomarker candidates. For example, malondialdehyde and 4-hydroxy-2-nonenal are attracting attention as oxidative stress markers. In addition, the presence of such substances as hexanal and nonanal in the blood of lung cancer patients has also been reported.

In recent years, it has become clear that the confusion or mutagenesis that occurs in the intracellular signal transduction system is due to the formation of adducts such as proteins and nucleic acids, and such formation is caused by volatile components. These components are now known to be involved in the regulation of biological functions as secondary messengers. For example, it has been reported that they are involved in macrophage foam cell formation that occurs in the acceleration of gene expression and the onset of arteriosclerosis. Volatile components diffuse into breath and urine via the blood, so there is a reasonable expectation that early diagnosis, determination, and long-term monitoring of tissue disorders and diseases will become possible by analyzing the volatile components in blood.

Headspace microextraction, HS-SPME, has typically been applied in the measurement of volatile substances (Fig. 1). This method utilizes a piece of fiber that is chemically bonded or coated with a polymer or adsorbent. The liquid sample, which is sealed in the vial together with the coated fiber suspended above the liquid, is warmed to transfer the volatile components to the vapor phase, thereby exposing the vapor phase to the adsorbent-coated SPME fiber, and permitting extraction and concentration of the volatile components. Extraction is possible whether the sample is in solid, liquid or gas form, and because of this simple operation from extraction to analysis, this technique has been applied to various types of samples.

However, since the HS-SPME method is a static extraction method that is dependent on the partition coefficient of the volatile components and the coating phase, when the sample contains many contaminants, as in the case of blood, low recovery rates of volatile components has been a problem. Particularly in the case of volatile components having a hydroxyl group such as alcohols, reduced detection sensitivity has been a problem due to easy distribution in the liquid phase as a result of mutual interaction with water. Equilibration at a high temperature makes it possible to force volatile components into the gas phase, but since the extraction fiber is also exposed to a high temperature at this time, overall detection sensitivity is lowered, as has been reported. Thus, the profile of volatile components obtained using the HS-SPME method has a weakness in that volatile components that exhibit strong interaction with the extraction fiber present a strong profile.

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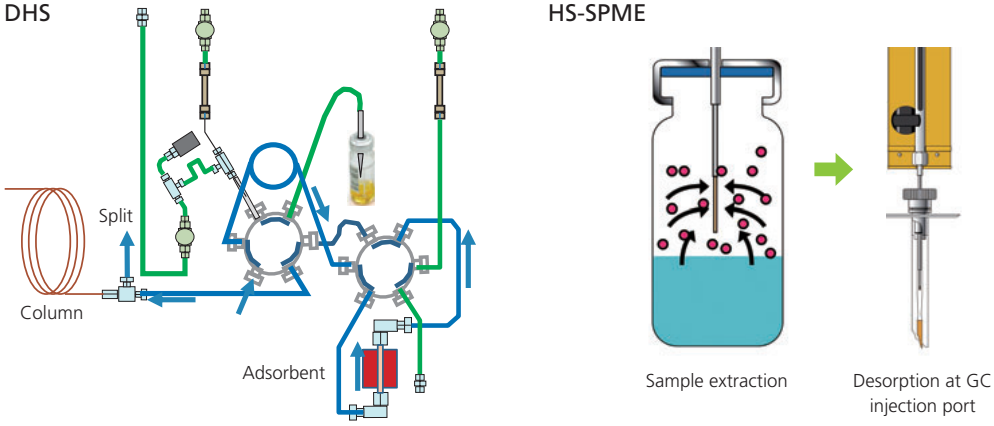
There is a dynamic extraction method for volatile substances referred to as the dynamic headspace (DHS) method (Fig.1). The DHS method is a dynamic extraction method in which volatile gas phase substances are forcibly purged using an inert gas, and the volatile substances are collected on an adsorbent. As the HS-SPME method is based on equilibrium migration in the liquid phase, gas phase and coating phase, the distribution equilibrium fluctuates due to changes in temperature or pressure. With the DHS method, nearly all of the gas phase portion can be collected in the adsorbent by purging the gas phase, thereby permitting efficient collection of the various volatile substances. Because the volatile substances contained in the blood vary widely and are present in extremely small quantities, the DHS method, which can efficiently collect a wide variety of volatile substances, is considered to be very suitable as a pretreatment method for comprehensive analysis of volatile substances in blood.

In this report, we compared the SPME and DHS methods using a standard sample of volatile components, and then conducted validation of the DHS method using a standard mixture of volatile components. Finally, we conducted analysis of the volatile components present in mouse serum using DHS-GC-MS.



Item	DHS	HS-SPME
Feature	Uniform concentration up to adsorbent breakthrough capacity from low to high boiling point	Non-uniform concentration rate due to adhesion competition
Concentration Rate	5 to 50-fold higher than the static HS method	2 to 5-fold higher than the static HS method

Fig. 1 Scheme of Principles of DHS and SPME Methods

2. Experiment

2-1. Reagents

A standard sample mixture consisting of 50 types of volatile substances was dissolved in acetone, and then adjusted to a concentration of 100 ng/µL. As an internal standard substance, 100 ng/µL of 1,1,1,3,3,3-hexafluoro-2-propanol was used. Mouse plasma was used for spike-and-recovery testing, and for actual sample analysis, IL-10 knockout mouse plasma was used. This is used as an age-related Crohn's disease chronic inflammation model, and blood plasma was collected from IL-10 knockout mice (N=6), consisting of a one 8-week old group with minor inflammation and a 16-week old group with significantly advanced inflammation. For the control group, 8-week old C57BL/6J wild-type mice were used.

2-2. Analytical Sample Preparation Method

For analysis of the standard mixture of volatile compounds, 1 mL of phosphate-buffered saline solution and 1.4 g of potassium carbonate were added to a 20-mL vial. Then, 1 µL each of the standard mixture of volatile compounds and the internal standard substance were added. In the mouse plasma analysis, 900 µL of phosphate buffer saline solution and 1.4 g of potassium carbonate were added to a 20 mL vial. Then, 100 µL of mouse plasma was added. To this, 1 µL of the internal standard solution was added. The prepared sample was immediately sealed with a vial crimp cap. For the septum, a 20-mm diameter silicone/PTFE high-temperature seal was used.

2-3. SPME, DHS-GC-MS Analytical Conditions

In the HS-SPME extraction, the vial was first warmed at 50 °C in a water bath for 10 minutes to equilibrate. Following equilibration, a DVB/CAR/PDMS fiber (2 cm 50/30 µm, Supelco) was exposed for 5 minutes to the gas phase in the vial for extraction of the volatile components. After the extraction operation, thermal desorption was conducted by exposing the fiber in the inlet for 2 minutes. The injection unit temperature was set to 280 °C for splitless injection. The DHS-GC-MS analytical conditions are shown in Table 1. For the scan/SIM method, the Smart SIM method optimization software feature was used to optimize the dwell time.

Table 1 Analytical Conditions

Headspace Sampler	: HS-20Trap
GC-MS	: GCMS-TQ8030

HS-20	
Mode	: Trap
Vial warming	: 50 °C
Vial stirring	: ON (3)
Vial pressurization time	: 2 min
Load time	: 1 min
Injection time	: 2 min
Needle flash time	: 5 min
Sample line temperature	: 150 °C
Trap tubing	: Tenax GR (50 mg, 60–80 mesh)
Warming time	: 10 min
Number of extractions	: 5
Pressure equilibration time	: 0.1 min
Load equilibration time	: 0.1 min
Thermal desorption temperature	: 280 °C
Transfer line temperature	: 150 °C
Trap cooling temperature	: –10 °C
Trap waiting temperature	: 25 °C
Dry purge time	: 10 min
GC cycle time	: 60 min

GC	
Column	: InertCap 5MS/NP (0.25 mm × 30 m, 1 µm) InertCap WAX-HT (0.25 mm × 30 m, 0.25 µm)
Column oven temperature	: 50 °C (3 min) → 5 °C /min → 230 °C (1 min)
Injection mode	: Split (1:10) High-pressure injection 360 kPa, 2 min
Carrier gas	: Helium gas
Control mode	: Linear velocity 30 cm/sec
APC1	: 100 kPa
APC3	: 65 kPa

MS	
Interface temperature	: 230 °C
Ion source temperature	: 230 °C
Measurement mode	: Scan/SIM
Scan event time	: 0.1 sec
Scan mass range	: *m/z* 35–300
SIM event time	: 0.2 sec

3. Results

3-1. Comparative Results Using SPME and DHS Methods

The HS-SPME method is a static extraction method based on the distribution equilibrium of each phase, and the profile of the volatile components that exhibit strong mutual interaction with the extraction fiber is emphasized. On the other hand, the DHS method relies on active purging of the gas phase, and because the volatile components are collected in the adsorbent, volatile components can be efficiently extracted and concentrated. To verify this, we compared the extraction methods using a mixed standard sample consisting of volatile substances, and examined the differences in the obtained volatile substance profiles. The analytical results are summarized in Fig. 2.

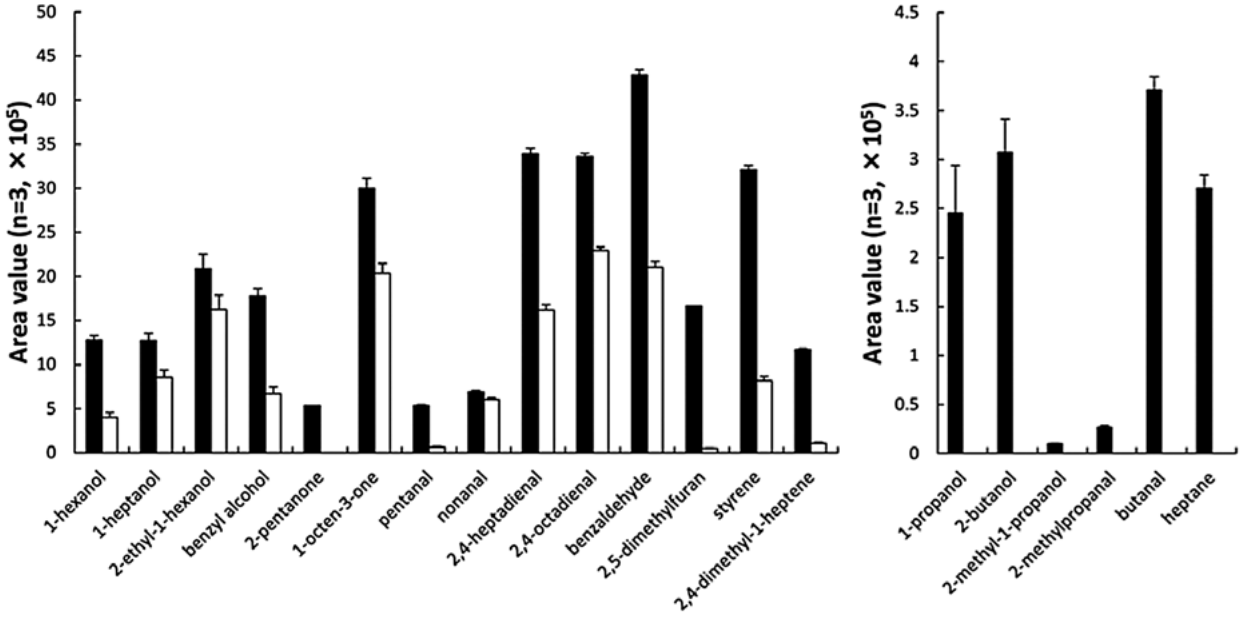


Fig. 2 Comparison of DHS and HS-SPME Methods
Black: DHS Method, White: HS-SPME Method

The analytical results indicate that all of the volatile components were detected by the DHS method, whereas by the HS-SPME method, 1-Propanol, 2-Butanol, 2-Methyl-1-propanol, 1-Penten-3-ol, 2-Pentanone, 2-Methylpropanal, 3-Methylbutanal, 2-Methylbutanal, and 2-Pentanal were not detected. Furthermore, the size of the area values for 3-Methyl-1-butanol, 4-Methyl-2-pentanol and 2-Penten-1-ol were about one-tenth those obtained using the DHS method. However, the area values for the volatile components including 2-Ethyl-1-hexanol and 1-Octen-3-one, etc. were comparable using the DHS and HS-SPME methods. A comparison of the mean RSD values using each method indicated 8 % for the DHS method and 20 % for the HS-SPME method.

Therefore, the overall results indicated that using the DHS method, a variety of volatile components, including alcohols, etc., which proved difficult to detect using the HS-SPME method, can be detected with high sensitivity.

3-2. Evaluation Results for DHS Method Using Standard Volatile Component Mixture

Next, we conducted validation of the DHS-GC-MS analysis using a volatile component standard mixture. For the validation, six criteria items were verified, including linearity, R2, LOD, RSD value near the LOD, intraday fluctuation, and spike-and-recovery testing. Generally, the LOD is specified as a concentration that provides an S/N ratio of 3, but using DHS-GC-MS, when a blank sample such as toluene was used, there were volatile substances for which an S/N ratio greater than 3 was obtained. Therefore, in this research, we used the calculation formula, LOD = 3.3 × SD/slope, based on the standard deviation of the quantitation values and the calibration curve slope, as stipulated by IUPAC. The RSD value was calculated based on the analytical results corresponding to the volatile component mixture standard concentration nearest the LOD among 0, 0.1, 0.5, 1, 10, 25, 50, and 100 ng/mL used to generate the calibration curve. The spike-and-recovery test was conducted by spiking mouse plasma with 100 µL of the volatile component standard mixture. The validation results are shown in Fig. 3 and Table 2.

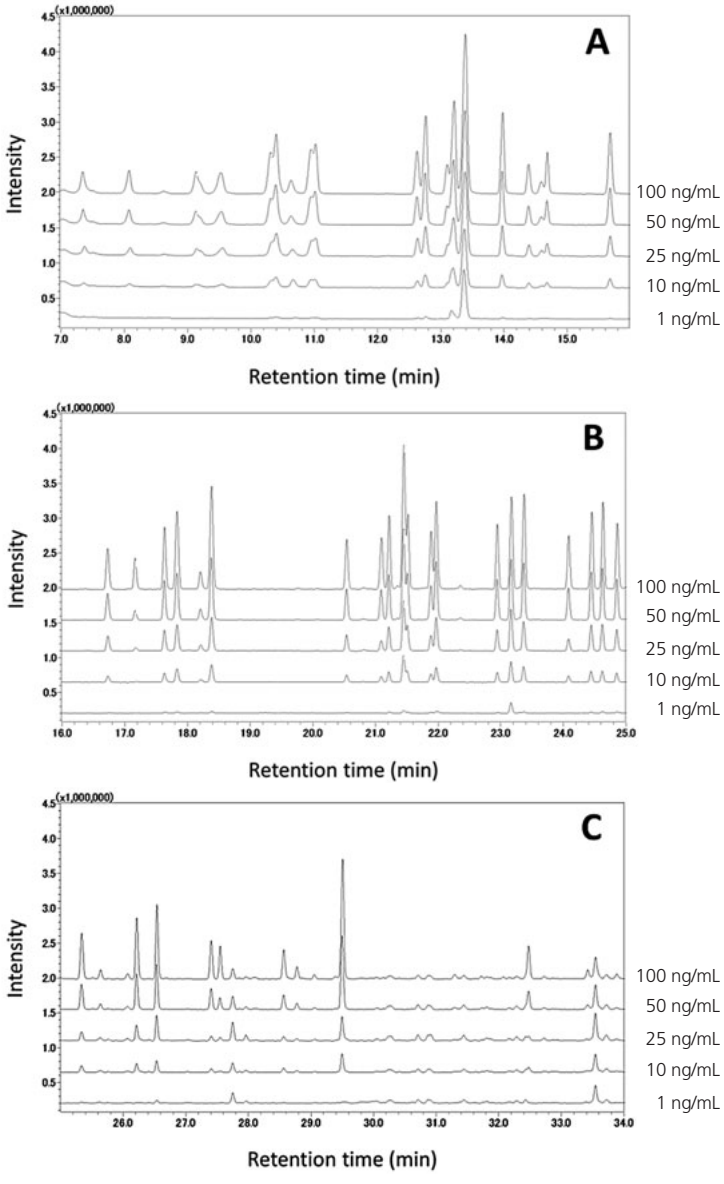


Fig. 3 Total Ion Current Chromatograms of Volatile Component Standard Mixture
A: 7 to 16 min, B: 16 to 25 min, C: 25 to 34 min

Table 2 DHS-GC-MS Validation Results

Compound	Target *m/z*	Slope	Intercept	R^2	Linear (ng/mL)	LOD (ng/mL)	RSD (%)*	RSD (50 ng/mL)	Recovery (25 ng/mL, n=3)	
								intraday (n=3)	Average (%)	RSD (%)
Alkanes										
Heptane	71	7353	2437	0.9997	0–10	0.14	3.0 b	3.1	105	6
2,4-Dimethyl-1-heptene	55	14292	8590	0.9991	0–100	0.08	14 a	1.6	98	1.4
Alcohols										
1-Propanol	59	2612	1743	0.9960	0–50	0.32	8.4 b	9.3	85	13
2-Butanol	45	3836	1531	0.9998	0–100	0.07	14 a	7.4	95	11
2-Methyl-1-propanol	41	115	34	0.9989	1–100	4.20	11 d	6.9	147	15
1-Butanol	41	13499	33574	0.9950	0–100	0.31	5.5 b	6.3	96	7.9
1-Penten-3-ol	57	41632	42049	0.9984	0–100	0.08	15 a	6.8	94	11
3-Methyl-1-butanol	55	16560	18299	0.9981	0–100	0.08	21 a	5.8	93	10
4-Methyl-2-pentanol	45	48338	67615	0.9969	0–100	0.06	12 a	5.5	98	9.4
1-Pentanol	55	28655	30427	0.9986	0–100	0.09	15 a	6.0	92	9.3
2-Penten-1-ol	57	12086	6758	0.9996	0–100	0.09	25 a	5.7	84	8.6
1-Octen-3-ol	57	28041	19704	0.9992	0–100	0.20	6.8 b	3.6	90	7.4
1-Hexanol	56	14910	14651	0.9990	0–100	0.15	5.0 b	4.5	90	8.6
1-Heptanol	55	14543	8829	0.9997	0–100	0.28	11 b	3.6	88	8.5
2-Ethyl-1-hexanol	57	21992	260285	0.9996	0–100	3.71	11 d	3.8	84	2.2
1-Nonen-4-ol	55	36095	8761	0.9997	0–100	0.08	19 a	3.7	87	8.3
1-Octanol	55	14541	7333	0.9997	0–100	0.51	20 b	3.5	89	9.1
2-Octen-1-ol	57	11441	281	0.9994	0–100	0.33	20 b	3.6	82	8.6
Benzyl alcohol	79	20360	62381	0.9994	0–100	0.58	8.0 b	3.8	77	6.0
Ketones										
2-Pentanone	43	6122	3925	0.9976	0–100	0.11	7.0 b	3.7	100	2.7
1-Octen-3-one	55	12077	–3209	0.9993	0–50	0.49	20 b	14	71	2.4
2-Octanone	58	24930	39841	0.9968	0–100	0.02	6.0 a	3.1	101	2.2
3-Octen-2-one	55	31667	14012	0.9980	0–100	0.02	1 a	3.3	93	2.0
Aldehydes										
2-Methylpropanal	57	172	200	0.9872	0–100	0.90	18 c	4.3	102	11
Butanal	43	4710	3421	0.9930	0–50	0.24	2.6 b	1.0	95	2.7
3-Methylbutanal	44	3182	3425	0.9980	0–100	0.07	15 a	2.4	112	4.1
2-Methylbutanal	41	5538	4103	0.9987	0–100	0.06	20 a	2.6	112	4.2
2-Butenal	41	6393	2700	0.9995	0–100	0.10	23 a	4.9	126	16
Pentanal	44	5352	13476	0.9958	0–100	1.03	10 c	0.7	128	3.1
2-Methyl-2-butenal	84	13361	18808	0.9963	0–100	0.04	12 a	2.0	119	2.9
2-Pentenal	83	10972	1341	0.9997	0–100	0.04	9.0 a	3.3	69	13
Hexanal	41	6864	7373	0.9984	0–100	0.20	13 b	3.2	121	4.0
2-Hexenal	41	6892	1113	0.9997	0–100	0.25	9.3 b	3.4	89	4.2
Heptanal	43	2025	3809	0.9976	0–100	0.86	3.1 c	4.2	116	5.3
2-Heptenal	41	6947	–5171	0.9983	0–100	0.11	17 b	5.4	81	7.0
Octanal	41	5533	–589	0.9968	0–100	0.27	5.4 b	13	112	5.3
2,4-Heptadienal	81	28487	–494	0.9994	0–100	0.04	10 a	7.3	91	9.0
2-Octenal	55	6626	–16090	0.9852	0–100	0.12	22 b	13	75	9.1
Nonanal	41	3877	–2753	0.9865	0–100	1.26	22 d	23	108	5.8
2,4-Octadienal	81	24419	–19659	0.9956	0–100	0.05	13 a	14	92	5.9
2-Nonenal	41	1671	–3695	0.9997	0.5–50	0.99	10 c	26	66	16
Decanal	67	2089	–1445	0.9683	0–100	1.97	24 d	35	94	9.2
2,4-Nonadienal	81	41974	–41813	0.9903	0–100	0.08	15 a	24	92	9.0
2,4-Decadienal	81	8695	–14893	0.9781	0–100	0.12	11 b	37	92	12
Benzaldehyde	105	34279	64892	0.9984	0–100	0.41	8.7 b	5.5	144	10

Compound	Target *m/z*	Slope	Intercept	R^2	Linear (ng/mL)	LOD (ng/mL)	RSD (%)*	RSD (50 ng/mL)	Recovery (25 ng/mL, n=3)	
								intraday (n=3)	Average (%)	RSD (%)
Others										
2,5-Dimethylfuran	96	19228	18172	0.9981	0–100	0.12	7.0 b	4.9	94	2.7
Toluene	91	103199	3000000	0.9980	0.5–100	5.64	4.4 d	3.7	95	3.2
2-*n*-Butylfuran	81	41227	46372	0.9973	0–100	0.01	6.6 a	2.9	101	2.4
2-Pentylfuran	81	29035	40791	0.9971	0–100	0.01	5.2 a	2.8	99	2.3
Styrene	104	35586	35963	0.9974	0–100	0.05	16 a	2.9	99	2.2

* RSD value of volatile standard solution substance mixture corresponding to LOD-closest concentration

a: 0.1 ng/mL, b: 0.5 ng/mL, c:1 ng/mL, d: 10 ng/mL

As shown in Fig. 3, by applying the DHS method, detection over a wide range was possible with a 1 ng/mL mixed standard solution of volatile substances. Also, by conducting SIM analysis of the target *m/z* of each of the volatile substances shown in Table 2, the detection sensitivity that was low for alcohols obtained using the HS-SPME method was elevated to sensitivity comparable to that obtained for aldehydes. Also, RSD values in the vicinity of the LOD yielded different results depending on the compound, suggesting the existence of volatile compounds with good detection repeatability notwithstanding a low LOD, as well as volatile compounds displaying low repeatability.

The intraday variation RSD values for the volatile substances were less than 10 % in all cases except for 2-Nonenal, Decadienal, 2,4-Nonadienal and 2,4-Decadienal, and in the spike-and-recovery test, except for 2-Methyl-1-propanol, good results were obtained, with RSD values at less than 10 %. Further, as for the average recovery, the effect of contaminants in the biological sample could not be confirmed.

The DHS method, unlike the HS-SPME method, permits the efficient migration of volatile components toward the adsorbent by forcibly purging the gas phase. Therefore, as volatile, low-molecular-weight components are also collected, overall detection sensitivity is improved. The results of this validation strongly suggest that a variety of volatile components can be detected with high sensitivity using the DHS-GC-MS method.

3-3. Blood Plasma Measurement Results using DHS

Lastly, we conducted DHS-GC-MS analysis of the volatile components in the blood plasma of IL-10 knockout mice as vivo samples. The IL-10 knockout mouse is a model mouse for Crohn's disease, a chronic inflammatory bowel disease that causes gastrointestinal inflammation. As samples, the plasmas of a mouse group with a mild degree and barely noticeable enteritis, and a mouse group with a significant degree of inflammation were used. (The inflammation degree was determined by dissection.) As a control, wild-type mouse plasma was used. The obtained results were determined as relative area values divided by the relative area value of the internal standard substance.

As for the analytical results, of the 40 volatile substances that were detected, 15 compounds showed a significant difference between samples (Table 3). Alcohols also were detected in the plasma samples, while 2,4-Dimethyl-1-heptene was detected only in the disease model. In addition, since both Scan analysis and SIM analysis can be conducted using Scan/SIM mode, qualitative analysis of the volatile components using the NIST library was also possible. From the above, it was demonstrated that a wide range of volatile blood components, including alcohols, can be analyzed by applying DHS-GC-MS.

Table 3 Volatile Components Present in IL-10 Knockout Mouse Plasma

Compound	Average relative area value ± SD (N=6)		
	Control	low inflammation, IL10	high inflammation, IL10
Butanal*	8.0 ± 2.9 × E-02	1.0 ± 0.4 × E-01	1.4 ± 0.8 × E-01
1-Propanol	3.6 ± 0.7 × E-01	3.5 ± 0.5 × E-01	4.0 ± 0.9 × E-01
2-Butanol*	3.2 ± 0.4 × E-01	4.6 ± 2.1 × E-01	4.4 ± 0.9 × E-01
2-Pentanone*	2.0 ± 1.2 × E-01	2.3 ± 0.6 × E-01	1.6 ± 0.5 × E-01
Heptane*	3.5 ± 0.4 × E-01	3.1 ± 0.5 × E-01	2.7 ± 0.3 × E-01
1-Butanol	1.3 ± 0.4 × E+00	1.5 ± 0.1 × E+00	1.5 ± 0.3 × E+00
Pentanal	3.5 ± 1.8 × E-01	2.8 ± 0.8 × E-01	2.9 ± 1.1 × E-01
1-Penten-3-ol	5.0 ± 3.4 × E-01	6.5 ± 1.8 × E-01	5.5 ± 2.9 × E-01
3-Methyl-1-butanol*	1.5 ± 0.6 × E-01	2.3 ± 0.6 × E-01	2.0 ± 0.4 × E-01
2-Pentenal	4.7 ± 3.4 × E-02	7.6 ± 2.7 × E-02	5.9 ± 1.8 × E-02
4-Methyl-2-pentanol	1.9 ± 2.7 × E-02	1.4 ± 3.2 × E-02	2.0 ± 2.1 × E-02
Toluene*	6.4 ± 0.7 × E+01	6.2 ± 0.5 × E+01	5.5 ± 0.5 × E+01
1-Pentanol	9.5 ± 4.4 × E-02	7.6 ± 1.1 × E-02	1.5 ± 0.8 × E-01

Compound	Average relative area value ± SD (N=6)		
	Control	low inflammation, IL10	high inflammation, IL10
Hexanal*	2.8 ± 6.2 × E-02	1.9 ± 1.2 × E-01	1.9 ± 1.3 × E-01
2-Penten-1-ol	0.5 ± 1.1 × E-02	1.2 ± 1.8 × E-01	1.4 ± 0.2 × E-01
2,4-Dimethyl-1-heptene*	0	4.0 ± 0.9 × E-02	3.7 ± 1.1 × E-01
1-Hexanol	1.2 ± 0.3 × E-01	1.1 ± 0.3 × E-01	1.4 ± 0.5 × E-01
2-*n*-Butylfuran*	0.6 ± 0.8 × E-02	0.6 ± 0.9 × E-02	1.6 ± 0.5 × E-02
Heptanal	0.5 ± 1.2 × E-02	1.3 ± 1.9 × E-02	2.0 ± 1.6 × E-02
Styrene	2.8 ± 1.2 × E-01	2.6 ± 1.1 × E-01	3.4 ± 1.6 × E-01
1-Octen-3-one	0.9 ± 0.6 × E-01	1.0 ± 0.6 × E-01	1.5 ± 0.7 × E-01
1-Heptanol	0.8 ± 0.7 × E-01	1.0 ± 0.5 × E-01	1.0 ± 0.7 × E-01
2-Pentylfuran	5.8 ± 1.1 × E-02	5.1 ± 0.7 × E-02	5.5 ± 1.5 × E-02
2-Octanone	1.5 ± 0.4 × E-01	1.4 ± 0.5 × E-01	1.4 ± 0.3 × E-01
Octanal	2.5 ± 1.0 × E-01	2.1 ± 1.0 × E-01	3.0 ± 1.3 × E-01
Benzaldehyde	1.4 ± 0.1 × E+01	1.3 ± 0.1 × E+01	1.4 ± 0.1 × E+01
2-Ethyl-1-hexanol	2.3 ± 0.6 × E+01	1.9 ± 0.5 × E+01	2.3 ± 0.7 × E+01
3-Octen-2-one	1.5 ± 2.0 × E-01	2.0 ± 1.1 × E-01	3.6 ± 2.8 × E-01
1-Octanol	2.2 ± 2.0 × E-01	1.8 ± 0.3 × E-01	1.9 ± 0.6 × E-01
2-Octen-1-ol	5.8 ± 1.5 × E-01	6.0 ± 2.1 × E-01	7.4 ± 2.6 × E-01
Nonanal	3.7 ± 0.8 × E-01	4.6 ± 3.0 × E-01	4.1 ± 0.9 × E-01
2,4-Octadienal*	1.6 ± 1.6 × E-02	2.4 ± 0.7 × E-02	3.0 ± 0.9 × E-02
Benzyl alcohol	1.2 ± 0.1 × E+03	1.1 ± 0.1 × E+03	1.3 ± 0.2 × E+03
Decanal	1.8 ± 0.7 × E-01	1.2 ± 0.3 × E-01	1.4 ± 0.9 × E-01
2,4-Nonadienal	9.6 ± 3.8 × E-02	8.3 ± 3.5 × E-02	1.1 ± 0.4 × E-01
Acetone_NIST*	2.1 ± 0.3 × E+02	1.7 ± 0.6 × E+02	1.5 ± 0.2 × E+02
2-Propanol_NIST*	9.1 ± 1.1 × E+03	8.7 ± 0.9 × E+03	7.5 ± 0.8 × E+03
3-Methyl-2-butanol_NIST*	2.0 ± 0.5 × E+00	2.3 ± 0.5 × E+00	1.5 ± 0.5 × E+00
2-Methyl-2-butanol_NIST*	5.1 ± 0.8 × E+03	4.9 ± 1.0 × E+03	3.8 ± 0.6 × E+03
Unknown_NIST*	8.0 ± 1.1 × E+01	8.0 ± 0.9 × E+01	6.7 ± 1.5 × E+01

* A significant difference ($p<0.05$) was confirmed in at least one set among the three groups using the t-test.

4. Summary

Use of DHS-GC-MS with the HS-20 trap enabled analysis of trace level blood components. Using a standard mixture of volatile components, results were compared with those obtained using the HS-SPME method. The use of DHS permits detection of a wide range of volatile components, including alcohols, with high sensitivity. Furthermore, the validation results demonstrated the detection of all the volatile compounds at ng levels. Also, the results of mouse plasma analysis indicated the detection of volatile components including alcohols, demonstrating that measurement of trace-level volatile components is possible. These results demonstrate that this system offers superior sensitivity to that obtained using SMPE in the measurement of volatile components. This technique is suggested for use in profiling volatile compounds in clinical research.

5. Acknowledgment

The IL-10 knockout mouse plasma was kindly provided by Associate Professor Masaru Yoshida and Lecturer Shin Nishiumi, Graduate School of Medicine, Kobe University.

References

Multi-Component Profiling of Trace Volatiles in Blood by Gas Chromatography/Mass Spectrometry with Dynamic Headspace Extraction

S Kakuta, T Yamashita, S Nishiumi, M Yoshida, E Fukusaki, T Bamba

Mass Spectrometry 2015 Vol.4 (1), A0034–A0034

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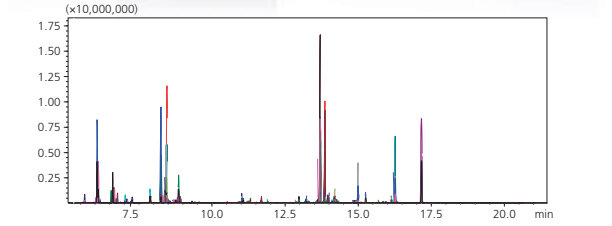
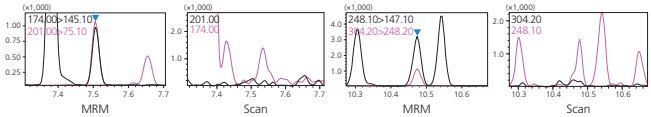


Total Ion Current Chromatogram (TIC) of MRM measurement for Metabolites in Standard Human Plasma



Comparison of MRM and Scan Mass Chromatograms for Metabolites in Standard Human Plasma

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