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TECHNICAL NOTE

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Fourier-Transformed Infrared Breath Testing After Ingestion of Technical Alcohol*

ABSTRACT: The study aim was to evaluate the feasibility of a Fourier-transformed infrared (FT-IR) analyzer for out-of-laboratory use by screening the exhalations of inebriated individuals, and to determine analysis quality using common breath components and solvents. Each of the 35 inebriated participants gave an acceptable sample. Because of the metabolism of 2-propanol, the subjects exhaled high concentrations of acetone in addition to ethanol. Other volatile ingredients of technical ethanol products (methyl ethyl ketone, methyl isobutyl ketone, and 2-propanol) were also detected. The lower limits of quantification for the analyzed components ranged from 1.7 to 12 μg/L in simulated breath samples. The bias was ±2% for ethanol and −11% for methanol. Within-day and between-day coefficients of variation were <1% for ethanol and <4% for methanol. The bias of ethanol and methanol analyses due to coexisting solvents ranged from −0.8 to +2.2% and from −5.6 to +2.9%, respectively. The FT-IR method proved suitable for use outside the laboratory and fulfilled the quality criteria for analysis of solvents in breath.

KEYWORDS: forensic science, forensic medicine, breath tests, ethanol, methanol, solvents, spectrophotometry, infrared, false-positive reactions

Denatured or contaminated ethanol products are sometimes ingested either accidentally or on purpose. In addition to black-market liquor, typical products that are misused include windshield washer fluids and cooker fuels (1). In addition to ethanol, these liquids may contain a low percentage of 2-propanol, methyl ethyl ketone, and methyl isobutyl ketone (http://www.lasol.fi/ktt_lasol/Marinol_100.pdf). Methanol-based car products are also easily available.

Symptoms even of lethal solvent poisonings are often nonspecific at the early stage. Especially in the case of methanol ingestion, the analysis method should be sufficiently sensitive and accurate to determine the presence of even small amounts of methanol from the mixture of ethanol and other less-toxic components. To speed up the diagnosis procedure conventionally based on blood tests, we earlier developed a portable low-resolution Fourier-transformed infrared (FT-IR) multicomponent point-of-care analyzer for exhaled breath (2).

The aim of this study was to evaluate the FT-IR analyzer's feasibility for out-of-laboratory use by screening the breath of inebriants, and to determine analysis quality in the presence of common breath components and solvents.

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Material and Methods

FT-IR Gas Analyzer

A portable FT-IR spectrometer (Gasmet DX2000™, Temet Instruments Oy, Helsinki, Finland) was equipped with a Temet Carousel Interferometer (Temet Instruments Oy, Helsinki, Finland) and a continuous-flow White-type multipass gas cell. The gas cell volume was 200 mL, the absorption path length 2.0 m, and temperature 50°C. The IR radiation source was silicon carbide. A Peltier-cooled mercury-cadmium-telluride (MCT) detector was operated in the wavenumber range of 4200 cm^{-1} to 900 cm^{-1}. All spectra were measured at an 8 cm^{-1} resolution at a rate of 10 scans/sec.

The reference library of the multicomponent analysis software (Calcmet™, Temet Instruments Oy, Helsinki, Finland) included IR spectra for ethanol, methanol, 1-propanol, 2-propanol, acetone, methyl ethyl ketone (MEK), methyl isobutyl ketone (MIBK), methyl tert-butyl ether (MTBE), ethyl acetate, toluene, butane, methane, nitrous oxide, carbon monoxide (CO), carbon dioxide (CO_2), and water (Fig. 1). The analyzer was inspected and calibrated before the study period in co-operation with the manufacturer. Certified gases and pro analysi (PA)-grade analytes were used for calibration. The calibration procedure has been previously described (2).

The analysis results were originally expressed in ppm or vol%. The conversion to mass concentration units was made assuming that the sample temperature was 34°C and pressure 1 atm Eqs. (1–6).

Screening of Participants' Breath

The breath of each participant was tested in a dormitory supported by the City of Helsinki. In this special residence, homeless men were allowed to stay even if they were drunk. It is very common among these men to drink low-priced denatured technical ethanol products, like windshield washer fluids and cooker fuels.

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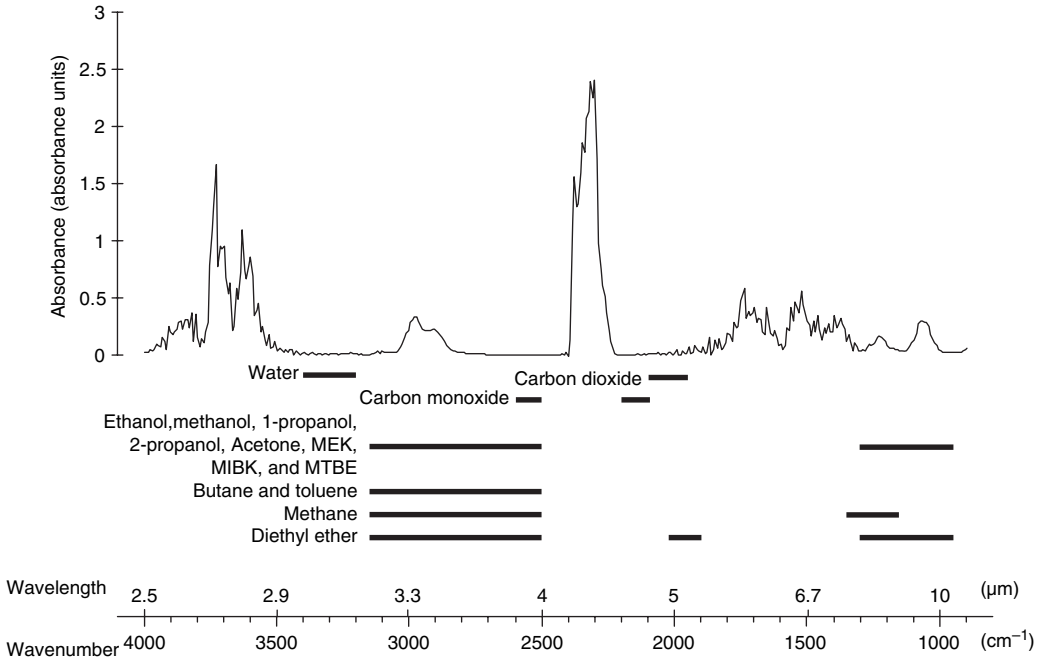

FIG. 1—*An FT-IR spectrum of a breath sample after ingestion of Marinol-100®. The bars under the spectrum represent the wave number range used in the analysis of the breath components.*

The purpose of the study was declared to the participants. The 35 men gave their informed consent and participated in the study without compensation. The participants were middle-aged men (median age 50 years; range 35–65 years), mostly of normal weight (median body mass index, 23; range 19–32). A total of 46 breath tests were done during five afternoons (three people participated three times and five participated twice).

The most common products ingested were Marinol-100® in 26 samples (cooker fuel, Berner Ltd., Helsinki, Finland) and Gambina™, in 16 samples (sweet Martini-cocktail, Altia Ltd., Rajamäki, Finland). Many of the men had drunk multiple products. Information about quality, quantity, and timing of consumption of ethanol-containing products was not exact because of the inebriation of the participants. Generally, 10 to 30 min had elapsed from the last exposure to breath testing.

Before each breath test, the measuring cell of the analyzer was flushed out with ambient air. Participants were asked to inhale deeply and then blow their entire lung volume through the analyzer's gas cell. The breath sample was trapped in the gas cell at the end of the expiration by closing the collecting system with a manual valve. A carbon dioxide (CO_2) concentration over 3% was used as a marker of an acceptable sample. Ethanol vaporizing from mouth mucous membranes because of prior drinking was considered by taking two or more breath samples. Rapid lowering of breath ethanol in subsequent measurements would have revealed a mouth alcohol effect. The analysis was performed immediately after sampling. The sample with the highest CO_2 was used in the final analysis.

Laboratory Tests

The possible deterioration in the analysis quality because of the matrix components earlier detected in the participants' breath was evaluated in laboratory tests. There is a general agreement that at least the following parameters should be evaluated for quantitative procedures: calibration model (linearity), limit of quantification, accuracy (bias, precision), selectivity, and stability (3).

The samples for laboratory tests on sensitivity, accuracy, and selectivity were made with the help of a breath simulator. The simulator design has been described earlier (4). The concentration of the main breath components in the simulated breath was: CO_2 5% and water 2.5%. Because of the volume of the simulator and the FT-IR gas cell, a few minutes were required for the system to stabilize after any change in settings. The stabilization was monitored by nonstop FT-IR analyses with 5-sec scanning time. Measurements with 1 min of scanning time were started only after the sample concentration had become constant.

The calibration model and linearity of the FT-IR analyzer is based on Beer's law. The linearity of the analyzer for ethanol and methanol in the range relevant for toxicology has been verified earlier (2).

The stability was evaluated by keeping a breath sample in the measuring cell for 3 h and analyzing it repeatedly. In addition to normal breath components, the samples contained 0.2–1.9 mg/L ethanol. During the test, the manual valve was closed and the sampling hose connected to the analyzer.

The lower limits of quantification (LLOQ) of components were determined in five different matrixes: pure nitrogen, simulated breath (2.5 vol% water vapor and 5.0 vol% CO_2 in N_2), simulated breath spiked with 910 μg/L ethanol or 630 μg/L methanol, and simulated breath spiked with 800 μg/L ethanol, 590 μg/L acetone, 97 μg/L 2-propanol, 150 μg/L MEK, and 96 μg/L MIBK. The latter mixture resembles exhaled breath after ingestion of Marinol-100®. Thirty samples of each mixture of components were analyzed. LLOQ was calculated for each of the components not present in the mixture Eq. (7).

Accuracy consists of random and systematic error components, i.e., bias and precision (5). The precision and bias of the ethanol and methanol analyses were investigated by analyzing simulated breath samples. The precision and bias were determined on ethanol levels of 0.27, 0.63, 1.1, 1.6, 2.1, and 3.2 mg/L and on methanol level of 63 μg/L. A total of four to 66 1-min measurements were done on each level. The nominal value for bias calculations was determined on the basis of the liquid injection rate and the gas flow

in the simulator. The precision was calculated according to Bookbinder (6) and divided into within-day and between-day repeatability Eqs. (8–12).

Selectivity. In addition to those substances detected earlier in the participants' breath, a few other general solvents that have IR structures in common with ethanol and methanol were tested as possibly interfering compounds. Many of these substances have previously been demonstrated to influence the analysis results of breath ethanol tests based on single-bandwidth IR-detection (7–9). The components selected for simulator testing were ethanol, methanol, 1-propanol, 2-propanol, acetone, MEK, MIBK, diethyl ether, and ethyl acetate.

The concentration of ethanol in the simulated breath was set to 0.27 mg/L to be close to the legal DUI (driving under the influence) limit enforced in Finland at that time (0.25 mg/L; drunken driving). The breath methanol concentration of 63 μg/L in the simulated breath corresponds to a subtoxic blood concentration of 0.18 g/L (5.7 mmol/L), if a blood:breath ratio of 2900 is applied (10,11). To maximize the interfering effect, the concentrations of the possibly interfering compounds tested were high and generally exceeded toxic levels.

The bias caused by the interferent in the matrix was calculated for each concentration level by comparing the analysis results of ethanol or methanol with the interferent to those without interferent (= nominal value, Eq. (8)). The procedure was performed twice for each interferent concentration level. Mean bias was calculated from the results of the six measurements. The overall effect of tested compounds was evaluated by calculating the average absolute bias Eq. (13).

Ethics

The Study Committee of the Social Services Department of City of Helsinki approved the research involving the human participants.

Statistics

Linear regression line equations and squared Pearson correlation coefficients (R^2) were calculated for the correlation of 2-propanol and acetone. Arithmetic mean and 95% confidence limits were calculated for the bias and the relative effects of the interfering solvents. One-way analysis of variance (ANOVA) was used for precision calculations. The statistics were calculated using SPSS for Windows 11.0 program (SPSS Inc., Chicago, IL).

Results

Acceptable samples were obtained from all participants. Acetone, 2-propanol, methyl ethyl ketone, and methyl isobutyl ketone were the most abundant solvents identified in addition to ethanol (Table 1). Breath acetone concentrations were very high and seemed to correlate with 2-propanol concentrations (Fig. 2). The concentrations of other solvents were toxicologically insignificant.

Twenty-four (69%) of the men were methane producers [methane >6.4 μg/L (10 ppm) in breath]. Ambient air methane was 2.5–3 μg/L. Breath carbon monoxide was over 4.5 μg/L (4 ppm) in 39 of the samples (85%), indicating a smoking habit (12).

The concentration of breath components decreased gradually during storage (Table 2). The relative decrease of each component was approximately equal regardless of the original concentration. Because the sample is blown directly to the sampling cell and analyzed immediately, the observed decrease of the sample component concentration during storage is not significant.

TABLE 1—*Breath test results.**

Component	Concentration	
	Median (μg/L)	Maximum (μg/L)
Ethanol	781	1677
Methanol	<LLOQ†	13
1-propanol	<LLOQ	31
2-propanol	43	134
Acetone	233	800
Methane	11	50
Butane	<LLOQ	14
MEK	80	253
MIBK	22	187
MTBE	6.6	19
Toluene	<LLOQ	8.0
Diethyl ether	<LLOQ	3.0
Ethyl acetate	2.4	9.1
CO	13	36
CO_2	4.1%	5.3%
H_2O	2.5%	3.4%

*Data from five breath testing sessions: 46 breath tests, 35 participants.
†<LLOQ, under the lower limit of quantification determined in simulated breath spiked with 900 μg/L EtOH.

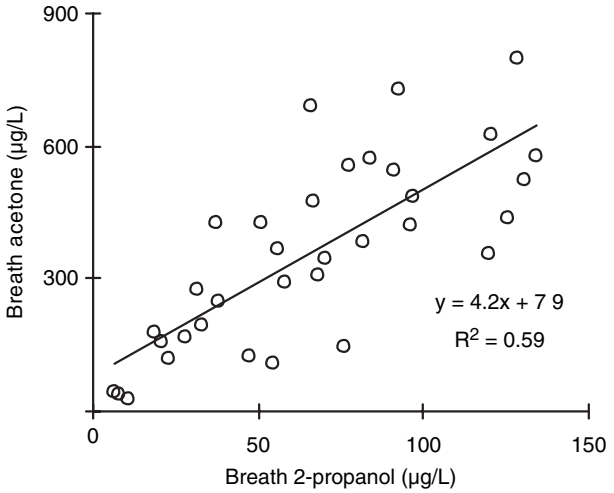

FIG. 2—*Correlation of acetone and 2-propanol concentrations in the 34 breath samples with values over the lower limit of quantification. Line represents linear regression.*

TABLE 2—*Sample stability.**

Time (min)	Sample concentration compared with original (%)		
	EtOH	CO_2	H_2O
15	98	98	96
30	96	97	92
60	92	95	87
120	86	91	79
180	81	86	72

*The means of the results of four test sessions are presented. The test samples contained 0.2–1.9 mg/L (100–1000 ppm) ethanol, in addition to normal breath components. During the test, the manual valve was closed and the sampling hose connected to the analyzer.

TABLE 3—*Lower limits of quantification (μg/L).*

Component	In N_2	In simulated breath spiked with*			
		None	Ethanol†	Methanol‡	Marinol§
Ethanol	8.0	11.9		12.7	
Methanol	2.2	6.6	3.0		3.3
1-propanol	9.6	10.3	10.2	17.5	8.2
2-propanol	7.0	11.3	6.0	9.3	
Acetone	2.8	5.0	2.9	3.8	
Methane	0.5	1.7	0.5	1.2	0.4
Butane	2.6	5.2	4.9	5.9	6.1
MEK	2.1	10.3	10.3	8.8	
MIBK	5.0	9.1	6.1	16.3	
MTBE	1.5	3.4	2.6	5.5	8.7
Toluene	2.5	4.8	4.3	5.8	4.2
Diethyl ether	1.2	1.8	1.3	2.0	3.7
Ethyl acetate	0.7	1.9	0.9	1.0	1.3
Carbon monoxide	1.4	1.7	1.9	3.1	1.8

*Simulated breath: carbon dioxide 5% and water 2.5% in nitrogen.
†Ethanol concentration 910 μg/L.
‡Methanol concentration 630 μg/L.
§Marinol: ethanol 800 μg/L, 2-propanol 97 μg/L, acetone 590 μg/L, MEK 150 μg/L, MIBK 96 μg/L.

The LLOQ for components in simulated breath ranged from 1.7 to 12 μg/L (0.5 to 6.5 ppm; Table 3). Adding water and carbon dioxide to the matrix caused marked elevation of the LLOQ when compared with the pure N_2 matrix.

TABLE 4—*Bias of analysis results in simulated breath.*

Component	Concentration (mg/L)	*N**	Mean bias (%)	95% confidence interval (%)
Methanol	0.063	45	−11.1	−12.1 to −10.2
Ethanol	0.27	66	−1.7	−2.0 to −1.5
	0.63	9	1.5	0.6 to 2.4
	1.1	8	0.5	0.2 to 0.9
	1.6	10	0.6	0.4 to 0.8
	2.1	4	0.6	0.5 to 0.7
	3.2	4	0.4	−0.7 to 1.5

*Number of measurements.

The bias of analysis results in simulated breath was ±2% for ethanol and −11% for methanol (Table 4). Within-day and between-day coefficients of variation were <1% for ethanol and <4% for methanol (Table 5).

Effects of various solvents on ethanol and methanol analyses are displayed in Tables 6 and 7. The absolute effect on ethanol and methanol readings ranged from −2.2 to + 6.0 μg/L (−1.2 to +3.3 ppm) and from −3.1 to +1.7 μg/L (−2.4 to +1.3 ppm), respectively. The bias of the analysis results caused by the interfering solvents ranged from −0.8 to + 2.2% for ethanol and from −5.6 to +3.2% for methanol. The average absolute bias was 0.8% for ethanol and 1.7% for methanol.

TABLE 6—*Effect of interferents on the breath ethanol reading.**

Interferent	Concentration (mg/L)	Mean effect on ethanol reading (%)	95% confidence interval for mean (%)
Methanol	0.19	0.4	0.1 to 0.7
	0.38	1.0	0.3 to 1.7
1-propanol	0.36	−0.3	−1.0 to 0.5
	0.72	0.1	−1.0 to 1.1
2-propanol	0.36	0.4	0.2 to 0.5
	0.72	0.4	−0.1 to 0.9
Acetone	0.35	0.8	0.2 to 1.3
	0.69	0.3	−0.4 to 1.0
	0.92	1.1	0.8 to 1.5
	1.8	1.5	0.5 to 2.5
MEK	0.43	0.6	0.2 to 0.9
	0.86	0.9	0.3 to 1.6
MIBK	0.60	0.8	0.4 to 1.2
	1.2	1.9	1.6 to 2.2
Diethyl ether	1.2	−0.7	−0.9 to −0.4
	2.4	0.0	−0.6 to 0.5
Ethyl acetate	0.52	1.4	0.8 to 2.1
	1.0	0.5	−0.5 to 1.4

*Ethanol concentration 0.27 mg/L.

Discussion

The actual human breath screenings confirmed the analyzer's feasibility in out-of-laboratory settings and revealed high concentrations of acetone in addition to ethanol and denaturants.

TABLE 7—*Effect of interferents on the breath methanol reading.**

Interferent	Concentration (mg/L)	Mean effect on methanol reading (%)	95% confidence limit for mean (%)
Ethanol	0.46	−0.1	−2.1 to 2.0
	0.91	−1.8	−4.6 to 1.0
2-propanol	0.36	−1.8	−3.4 to −0.3
	0.72	−1.1	−2.8 to 0.7
Acetone	0.92	−2.1	−3.1 to −1.0
	1.8	−4.0	−5.9 to −2.1
MEK	0.43	0.0	−2.5 to 2.6
	0.86	−0.6	−1.3 to 0.1
MIBK	0.60	2.0	0.1 to 3.8
	1.2	1.2	−1.0 to 3.4
Diethyl ether	1.2	−1.3	−2.8 to 0.3
	2.4	−2.1	−3.1 to −1.1
Ethyl acetate	0.52	−0.6	−2.0 to 0.8
	1.0	−2.9	−3.3 to −2.4

*Methanol concentration 63 μg/L.

The exhaled CO_2 concentration varied quite a lot among subsequent samples from the same individual participant. This variation was mainly the result of the inebriation of the participants. Nevertheless, even highly inebriated participants gave an acceptable sample. In this study, the sample with the highest carbon dioxide measurement was selected for analysis to obtain the best estimate

TABLE 5—*Summary of the analytical precision studies.*

Component	Nominal concentration (μg/L)	No. days	Analyses per day	Measured concentration (μg/L)	Within-day		Between-day		Total	
					SD^2	CV (%)	SD^2	CV (%)	SD^2	CV (%)
Ethanol	275	5	9	270	1.4	0.8	1.6	0.9	3.0	1.2
Methanol	63	3	12	57	2.4	3.5	0.5	1.6	2.9	3.8

SD^2, variation; CV, coefficient of variation.

of blood concentration of volatile components. To further improve analysis results, averaging two or three high-quality samples would be a good approach to lessen random error in analysis results.

The breath test results were not compared with blood concentrations. Blood tests were not performed in this study because controlling the solvent amount and time of drinking was not possible in the dormitory settings.

Most of the subjects tested in this study had drunk denatured ethanol products and had a variety of solvents in their breath. The most often misused product was the cooker fuel Marinol®. In addition to ethanol (over 80% w/w), it contains MEK (2% w/w), MIBK (2% w/w), and 2-propanol (1–5% w/w; http://www.lasol.fi/ktt_lasol/Marinol_100.pdf). All of these denaturants were detected in the exhaled breath of the participants, as expected.

According to the literature, the threshold concentration for acetone toxicity is 200–300 mg/L in human blood, corresponding to 0.6–0.9 mg/L in breath, if 330 is applied as blood:breath ratio (10,13). Four of the samples in this study were within the toxic range. High acetone concentrations measured in our study were most probably the result of metabolism of 2-propanol (Fig. 2). Similar relationship between acetone and 2-propanol in blood has been reported earlier (14). Measurable amounts of exhaled 2-propanol were detected in 33 out of the 46 samples. The concentrations were well below the toxic levels (0.4 g/L in blood, corresponding with 0.3 mg/L in breath, if 1426 is applied as blood:breath ratio (10,13)).

As expected, the analyzer was most sensitive when a single component was analyzed in pure nitrogen. Even though the overlapping compounds are taken into account in the analysis method, the strong absorptions of the matrix components in the simulated human breath increased the LLOQ. When ethanol, methanol, or even more components were added to the matrix, the LLOQ did not deteriorate further.

The bias was small for ethanol measurements in simulated breath. On the other hand, the methanol analysis results showed quite a large negative bias over the days of the study. The cause of the observed bias was not clear. Because we did not have a second analysis method, a bias attributable to the breath simulator could not be excluded. The bias did not affect the selectivity calculations because the nominal concentration (μ in the Eq. (8)) was determined before and after each interference measurement session. Effects of different solvents on ethanol and methanol analysis results were acceptably small.

Detection of breath methanol in the presence of other volatile components could be of vital importance because of its toxicity even at low concentrations; a blood methanol concentration over 0.2 g/L (6.2 mmol/L) is considered toxic (10). It would correspond to 69 μg/L (54 ppm) in breath, if blood-breath ratio of 2900 were used for conversion (11). The LLOQ for methanol in simulated breath spiked with 900 μg/L ethanol was 3 μg/L. Thus, the FT-IR method has a good safety margin in diagnosing or excluding toxic methanol exposure, even in the case of a low-quality sample resulting from poor cooperation. No methanol intoxication was detected during this study.

Conclusions

This portable FT-IR analyzer was suitable for out-of-laboratory use. Because of the multicomponent analysis software, the analyzer could rapidly quantify all of the detectable components in breath. High ethanol and acetone concentrations were measured in the participants' breath, as well as traces of other components of denatured ethanol. The FT-IR method was adequately selective, sensitive, and accurate in ethanol and methanol breath analysis even in the presence of high concentrations of other solvents. The calculated LLOQ for methanol was 10-fold below the toxic concentration.

Because of the simplicity of sampling and analysis procedure, nonlaboratory personnel, such as police officers or social workers, could also operate the analyzer for screening purposes.

Appendix

Equations

An example of converting volume/volume (e.g., ppm, vol%) units to mass/volume units (e.g., μg/L):

$$1\,\text{ppm} = \frac{10^{-6}\,\text{L}}{\text{L}} \tag{1}$$

$$1\,\text{vol}\,\% = \frac{10^{-2}\,\text{L}}{\text{L}} = 10{,}000\ \text{ppm} \tag{2}$$

$$pV = nRT \Leftrightarrow n = \frac{pV}{RT}\,(\text{ideal gas law}) \tag{3}$$

where p is the pressure (atm), V the volume (L), n the number of moles (mol), R the gas constant (0.08206 atm L/mol K) and T the temperature (K).

$$10^{-6}\,\text{L} \mathrel{\hat{=}} \frac{p \times 10^{-6}\,\text{L}}{RT} = \frac{1\,\text{atm} \times 10^{-6}\,\text{L}}{0.08206\,\text{atm L/mol K} \times 307.15\,\text{K}} = 3.97 \times 10^{-8}\,\text{mol} \tag{4}$$

where p = 1 atm, T = 34°C (307.15 K)

$$1\,\text{ppm} \mathrel{\hat{=}} 3.97 \times 10^{-8}\,\text{mol/L} \tag{5}$$

$$1\,\text{ppm ethanol} \mathrel{\hat{=}} 3.97 \times 10^{-8}\,\text{mol/L} \times 46.07\,\text{g/mol} = 1.83\,\mu\text{g/L} \tag{6}$$

Lower limit of quantification:

$$\text{LLOQ} = |C_0| + 10 \times \text{SD} \tag{7}$$

where $|C_0|$ is the absolute value of the mean of the analysis results and SD the standard deviation of analysis results.

$$\text{Bias}\ (\%) = \frac{\bar{x} - \mu}{\mu} \times 100 \tag{8}$$

where $\bar{x}$ is the mean of the measured values and μ the nominal value. Within-day variance:

$$\text{SD}^2_{\text{WD}} = \text{MS}_{\text{WG}} \tag{9}$$

Between-day variance:

$$\text{SD}^2_{\text{BD}} = \frac{\text{MS}_{\text{BG}} - \text{MS}_{\text{WG}}}{n} \tag{10}$$

Total variance:

$$\text{SD}^2_{\text{I(CT)}} = \text{SD}^2_{\text{BD}} + \text{SD}^2_{\text{WD}} \tag{11}$$

where MS_{WG} is within-groups mean squares value from the ANOVA results, MS_{BG} the between-groups mean squares value from the ANOVA results and n the number of measurements per day.

Coefficient of variation:

$$\mathrm{CV}(\%) = \frac{\sqrt{\mathrm{SD}_{xx}^2}}{\bar{x}} \times 100 \qquad (12)$$

where SD_{xx}^2 is within-day, between-day or total variance.

$$\text{Average absolute bias } (\%) = \frac{1}{n}\sum_{i=1}^{n} |\mathrm{Bias}(\%)_i| \qquad (13)$$

where Bias $(\%)i$ is the bias caused by the i-th interfering compound and n the number of interfering compounds tested.

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