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Validation of a gas chromatography–mass spectrometry isotope dilution method for the determination of 2-butoxyethanol and other common glycol ethers in consumer products

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ABSTRACT

A gas chromatography–mass spectrometry isotope dilution (GC–MS ID) method was developed and tested for the determination of 14 common glycol ethers in consumer products. Stable isotope labelled standards, 2-methoxyethanol-D_7 and 2-butoxyethanol-$^{13}C_2$ (CDN isotopes) were employed to enhance the accuracy and precision of the glycol ethers determination. A 1000-fold sample dilution with methanol was applied to avoid column overload and contamination. At this dilution matrix effects were in most cases negligible and did not interfere with the analysis. The instrument detection limit (IDL) for analysed compounds varied from 0.01 to 1 μg/mL; while the estimated limit of quantification (LoQ) varied between different glycol ethers from 0.02 to 3.4 μg/mL. Calibration was tested in the range of 0.1–200 μg/mL and showed that the linear fit is upheld from 0.1 to 10 μg/mL, and extends beyond this range for some of the analytes. Recoveries of glycol ethers from products with different matrices were similar. The recoveries varied from 87% to 116% between the analysed compounds, while measurements precision varied between 2% and 14%. The method is applicable to products with glycol ether concentrations above 0.002–0.2% (w/w). The concentration range can be extended below the specified limits by decreasing the dilution factor; however, with lower dilution the sample matrix effect is expected to be stronger. Products with very high concentrations of glycol ether (>20%) may need to be further diluted prior to injection to avoid column overload. The method can be used for testing liquid and aerosol products designed for household use, such as cleaners, paints, solvents and paint stripers, for compliance and enforcement of regulations which limit glycol ethers content.

1. Introduction

Most glycol ethers are colorless, moderately volatile compounds with the combined characteristics of both ethers and alcohols. Their unique properties make them soluble in water as well as in many organic solvents. As they leave no residue and evaporate relatively quickly they are sought after components of a wide range of products for both industrial and domestic use [1]. More than 30 glycol ethers are currently synthesized by the chemical industry and their usage is increasing, partly due to the growing popularity of water based coatings and paints. Other consumer products such as varnishes, dyes, adhesives, cosmetics, diluents and even pesticides also contain glycol ethers [2] making them widespread in today's household environment. 2-Butoxyethanol (2-BE) is a common ingredient used in paints, cleaning products (mostly general purpose cleaners and window cleaners), in printing inks, as well as in some pesticides and hydraulic fluids. 2-Methoxyethanol (2-ME) is used as an anti-icing agent for jet fuels in the aircraft industry. To a lesser extent it is used as a chemical intermediate, in specialty coatings and pharmaceutical and electronics manufacturing. The production and use of glycol ethers unavoidably leads to their release into the environment where they are destroyed by light and aerobic biodegradation [3,4]. Being relatively short lived they do not accumulate in the environment; however, because they are widespread, exposure to them at the "point of use" is common. They easily enter a body through the skin and inhalation and prolonged exposure may cause numerous negative health effects [5]. As the concern about the negative heath impact of glycol ether grows, industry is forced to look for alternatives which are not easy to find; and more often than not, the alternative is another compound from the same family.

The toxicity of glycol ethers differs between ethylene (E-series) and propylene (P-series) glycol ether chains, and depends on their molecular weight and the metabolites generated by breakdown processes [6]. The E-series are suspected of disrupting reproductive systems, testicular atrophy, teratogenicity and bone marrow depression. In addition 2-BE appears to have some carcinogenic

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Table 1
Analysed glycol ethers, their abbreviations, monitored ions (target/quantification ion followed by confirmation ions), expected retention times (RT) in minutes, and MSD acquisition windows (*W*).

Glycol ether	Abbreviations	Ions	RT	*W*
2-Methoxyethanol (ethylene glycol methyl ether)	2-ME (EGME)	45, 76, 58	11.8	1
1-Methoxy-2-propanol (propylene glycol methyl ether)	PGME	45, 47, 75	12.8	1
2-Ethoxyethanol (ethylene glycol ethyl ether)	2-EE (EGEE)	59, 45, 72	14.1	2
1-Propoxy-2-propanol (propylene glycol propyl ether)	PGPE	45, 73, 59	18.1	2
2-Butoxyethanol (ethylene glycol butyl ether)	2-BE (EGBE)	45, 87, 57	20.3	3
1-Butoxy-2-propanol (propylene glycol butyl ether)	PGBE	57, 45, 87	21.0	3
2-(2-Methoxyethoxy)ethanol (diethylene glycol methyl ether)	MEE (DEGME)	45, 59, 90	21.4	3
Dipropylene glycol methyl ether[a]	DPGME	59, 73, 103	22.6	4
2-(2-Ethoxyethoxy)ethanol (diethylene glycol ethyl ether)	EEE (DEGEE)	45, 59, 72	22.9	4
2-Hexyloxyethanol	2-HE	85, 43, 63	24.8	5
2-(2-Butoxyethoxy)ethanol (diethylene glycol butyl ether)	BEE (DEGBE)	45, 57, 75	26.3	5
2-Phenoxyethanol	2-PE	100, 43, 30	27.3	6
Tripropylene glycol methyl ether	TPGME	59, 73, 45	28.0	6
2-(2-Hexyloxyethoxy)ethanol	HEE	43, 45, 85	29.1	7
2-Methoxyethanol-D_7 (recovery standard)	D_7-ME	50, 49, 83	11.7	1
2-Buthoxyethanol-$^{13}C_2$ (surrogate standard)	$^{13}C_2$-BE	47, 88, 45	20.3	3

[a] DPGME standard was a mixture of 3 isomers: CAS 20324327 (RT 22.57 min), CAS 34590948 (RT 22.64 min) and CAS 13429077 (RT 22.94 min). The latter may interfere with EEE analysis at very low concentrations.

effects in certain animals. Propylene glycol ethers with the alkoxy group at the primary position are considered less toxic as none of the effects associated with shorter chain ethylene glycol ethers have been reported for them, however, toxicity towards the liver and kidney has been observed. In addition, some teratogenic effects have been reported when the primary position is occupied by a hydroxyl group as in propylene glycol 2-methyl ether (PGME β-isomer) and its acetate [6,7]. Based on the results of toxicological studies many governments are taking actions to regulate the concentrations of glycol ethers in products designed for consumer use. As a result of these health concerns, Environment Canada decided to restrict the concentration of 2-BE in some consumer products [8]. While industry is forced to comply with the regulation it searches for alternative substitutes; the use of 2-BE and other E-series glycol ethers will inevitably decline but, at the same time uses of P-series is expected to grow. A robust method for the analysis of common glycol ethers in commercial products of different matrices is necessary to support the enforcement of the existing regulations as well as these foreseen in the near future. The above work was undertaken to fill this requirement. It focuses on the measurement of 2-buthoxyethanol (2-BE), 2-methoxyethanol (2-ME) and 12 other common glycol ethers (Table 1) in commercial products, mainly household cleaners, paints, paint stripers and solvents. It provides information about the instrumentation, the sample treatment and the methodology necessary to obtain accurate and reproducible results. The methodology was thoroughly tested in our laboratory with a variety of commercial products including aerosols.

2. Materials and methods

2.1. Instrumentation

Samples were analysed using an Agilent 5973N Mass Selective Detector (MSD) coupled to an Agilent 6890 Gas Chromatograph equipped with a Gerstel Multi-Purpose Sampler (MPS 2). Separation was achieved on a DB-624 (6% cyanopropylphenyl-94% dimethylpolysiloxane) capillary column (60 m × 0.32 mm ID, 1.80 μm film thickness) using splitless injection (1 μL) and constant carrier gas flow (He, 1.5 mL/min). The injector was kept at 260 °C and after the initial 3 min purged with 30 mL/min helium flow to avoid a build-up of contamination and sample residue. The GC temperature program started at 40 °C, held for 2 min, followed by a 6 °C/min raise up to 140 °C before ramping at 12 °C/min to 250 °C. At this temperature the column was baked for 2.17 min before cooling back to 40 °C. Overall run time was 30 min.

The GC–MS interface was held at 290 °C, MS quads at 150 °C, and ion source at 230 °C. The MSD worked in combined FS-SIM EI mode (70 eV). Full scanning (FS) was used for compounds identification while selected ion monitoring mode (SIM) was used for quantification. Acquisition started after a 10 min solvent delay followed by 7 time windows. Compounds retention times, their monitoring ions and acquisition windows are given in Table 1.

2.2. Calibration and control

While a "round robin" and an inter-laboratory validation studies were not available at the time of the project, we made every effort to ensure the quality of the results. Certified standards of each of glycol ether (98% pure or better) were purchased from AccuStandard Inc. The purity of the standards was confirmed by GC–MS full scan analysis of each compound. Standard stock solution (1000 μg/mL) was prepared by diluting weighed amounts of glycol ethers in methanol (OmniSolv, HPLC grade). All standards stock solutions were checked on monthly basis against newly prepared standards. When stored in septum sealed glass vials in the dark at 4 °C these solutions were found to be stable for several months. Standard working solutions (1–200 ng/μL) were prepared daily by diluting the stock solution with methanol.

Calibration curves for each of the analytes were constructed using average values of duplicate analyses at each calibration level (0.1–200 ng/μL, 14 levels). Calibration controls at concentrations below and above expected experimental range were processed at the beginning and at the end of each batch of 8–10 samples. Blank (solvent) samples were run before and after each standard injection, and after each 4–5 product samples to make sure that there was no carryover and that the system is free from interferences. A control sample spiked with known amount of native glycol ethers was processed daily.

The isotope dilution method was used to aid quantification of glycol ethers. The relative response factors (RRF's) of target analytes to ^{13}C labelled 2-buthoxyethanol surrogate ($^{13}C_2$-BE, CAS No. 163127-01-3) and D-labelled 2-methoxyethanol recovery standard (D_7-ME, CAS No. 108152-85-8) were used to correct for instrument drift and sample volume differences to ensure method accuracy and precision. These standards were included in each of the samples analysed. The percentage of surrogate recovery was monitored to make sure that it remains in the acceptable range (Section 3.6). Surrogate recoveries had to fall within 80–120% range, samples that fail to meet this criterion were reanalysed.

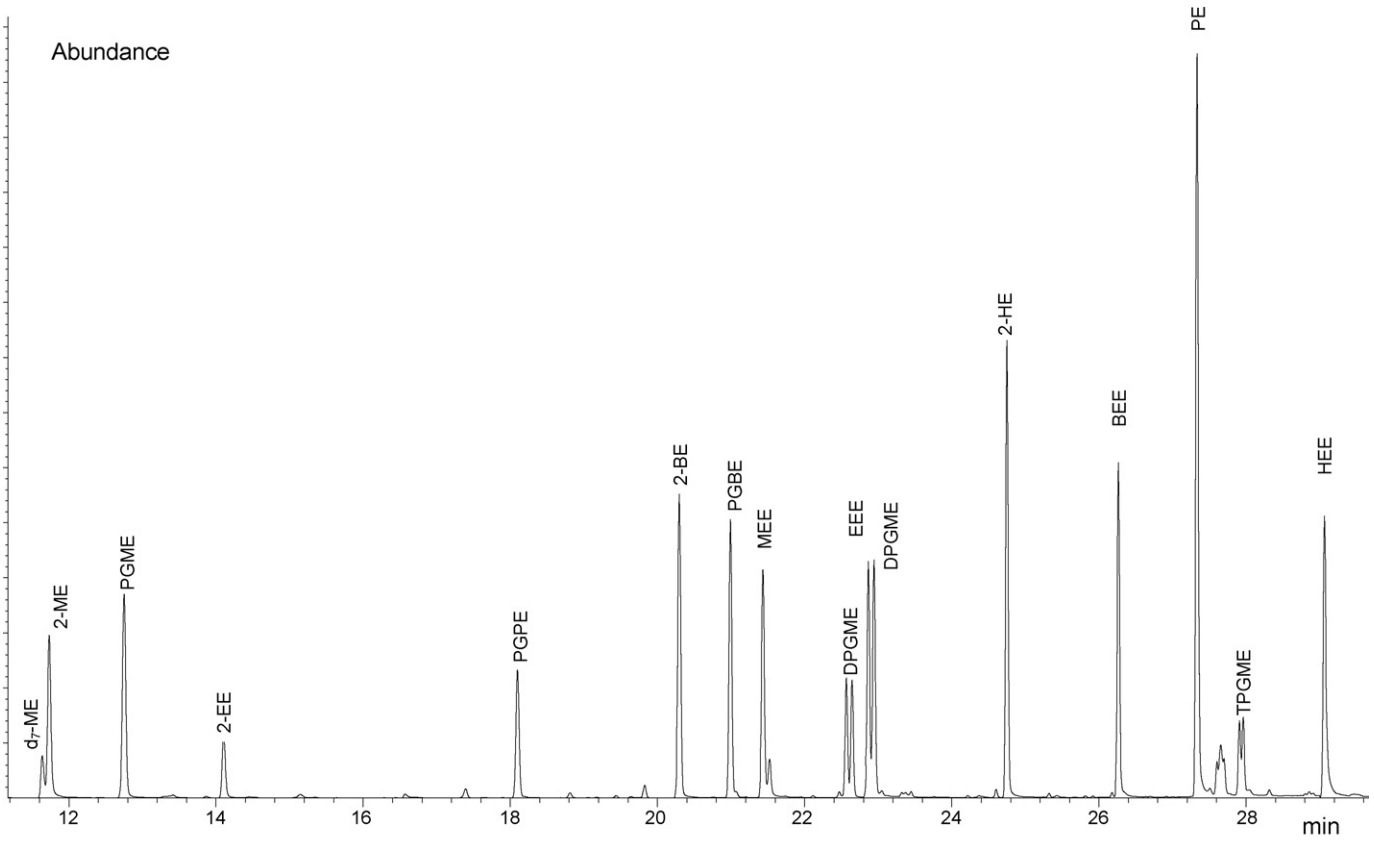

Fig. 1. Total ion chromatogram showing the separation of all 14 glycol ethers on a DB-624 column (1 μL injection, 40 ppm).

2.3. Samples and preparation

Commercial products with liquid and aerosol matrices were analysed for the presence of glycol ethers and used for method validation. Preparation techniques differ between liquid and aerosol samples.

For liquid products, three samples of 1 mL each were withdrawn from the sample container. Each sample was transferred to 1.5 mL volume septum capped glass chromatographic vial, weighted, and then spiked with ^{13}C labelled 2-butoxyethanol to the concentration of 0.1% (w/w). The samples were thoroughly mixed and kept closed to stabilize for about 1 h, after which time small subsamples were withdrawn and diluted with methanol by a factor of 1000 (10 μL to 10 mL).

For aerosol samples, small (100–400 mg) aliquots were injected from the can using a custom made nozzle needle adapter, through a septum to a sealed 40 mL volume glass vial filled with approximately 5 mL of methanol. The exact amount of methanol as well as that of added aerosol was checked gravimetrically to ±0.1 mg. After calculating the weight ratio of the aerosol sample to the methanol, the sample was spiked with ^{13}C-labelled 2-butoxyethanol, to a concentration which after bringing the sample to its final 1/1000 dilution resulted in a surrogate concentration of exactly 1 ppm (same final concentration as in diluted liquid samples). For example: where the sample of 100 mg of aerosol is added to 3900 mg of methanol resulting in the primary 1:40 dilution, 100 μg of ^{13}C-BE needs to be added to that solution, so after the additional 25× dilution the surrogate final concentration equals 1 ppm, while the total sample dilution 25 × 40 = 1000.

After being diluted with methanol both types of samples were spiked with the recovery standard (D_7-ME) to the concentration of 1 ppm, and mixed thoroughly. Approximately 0.4 mL of each sample was than transferred to the Whatman Mini-UniPrep Syringless Filter, (PTFE, 0.2 μm pore size) and analysed. The unique design of the Whatman Mini-UniPrep filter enables its use as an autosampler vial removing the need for further sample transfer.

2.4. Method validation

The method was validated following the ACS and IUPAC guidelines [9–11]. Blank samples were used to assess background contamination and sample carryover. Calibration standards were used to assess selectivity, sensitivity and calibration linearity of the method. Precision and recovery of the method was tested using liquid and aerosol products samples with blank matrices spiked with glycol ethers. In addition various commercial products (household cleaners, solvents and paints) were analysed for the content of glycol ethers.

3. Results and discussion

3.1. Separation

Results demonstrate that chromatographic separation of all 14 glycol ethers can be achieved on a 60-m DB-624 capillary column. Fig. 1 shows a typical chromatogram for a 1 μL sample containing 40 ng/μL of each of the glycol ethers in methanol. At concentrations above 10× instrument detection limit all peaks are typically well resolved, however, at concentrations close to the detection limit potential problems may arise for EEE if it coelutes with DPGME isomer. In such situations, examining the ratios between ion fragments m/z 59 and 45 reveals peaks identities (the ion m/z 45 is the main fragment of EEE, while the ion m/z 59 is the main fragment of DPGME main isomer), but precision of the EEE measurements may be affected.

Table 2
Glycol ethers method detection limits (MDL). SD standard deviation, MDL method detection limit for samples before dilution, *t* Student's *t*-distribution coefficient (1-sided test, 95% confidence level, $n = 8$), IDL instrument detection limit, *F* sample dilution factor = 1000.

Compound	SD (ng/μL)			MDL = $t \times SD \times F$ (ng/μL)			MDL = IDL × *F* (ng/μL)
	Methanol	Water base	Oil base	Methanol	Water base	Oil base	
2-ME	0.002	0.005	0.009	5	9	17	10
PGME	0.002	0.002	0.003	4	4	6	10
2-EE	0.004	0.008	0.007	8	15	13	10
PGPE	0.005	0.007	0.008	9	13	16	20
2-BE	0.013	0.016	0.016	25	30	30	90
PGBE	0.010	0.013	0.015	19	25	28	40
MEE	0.165	0.203	0.140	313	385	265	1000
DPGME	0.090	0.116	0.104	171	220	197	250
EEE	0.310	0.246	0.339	587	466	642	1000
2-HE	0.122	0.158	0.147	231	299	279	450
BEE	0.120	0.145	0.131	227	275	248	500
PE	0.009	0.009	0.012	17	17	23	30
TPGME	0.085	0.223	0.089	161	423	169	500
HEE	0.195	0.200	0.189	370	379	358	500

Note that under the condition of the method the 2-ME and D_7-ME peaks are separated on the DB-624 column, but 2-BE and the $^{13}C_2$-BE peaks are not. The latter must be separated by MS using different monitoring ions (Table 1). Isotope dilution technique must be applied to correct for the fraction of ion *m*/*z* 45 from $^{13}C_2$-BE standard when calculating the 2-BE concentration.

3.2. Blanks and sample carryover

Methanol, the solvent used in the study was tested for the presence of glycol ethers and was found to be free from analytical interferences. No glycol ether was detected in any of the solvent samples. Solvent blanks were run at the beginning and at the end of each batch of 8–10 samples to ensure that the solvent and the system are free of contaminations. Additional solvent blanks were run after every sample with a glycol ether concentration >40 ng/μL to make sure that there is no sample carryover. Method blanks consisting of solvent spiked with recovery standard and surrogate were also run daily. Sample carryover was found negligible under typical circumstances. Only when a high concentration sample (>100 ng/μL) was processed, small carryover in the range of 0.2 ng/μL was observed for some of glycol ethers in the first blank, typically dropping below the instrument detection limit in the second. To avoid potential problems with carryover when analysing product samples of unknown concentration, we recommend injecting a solvent blank in between each of analysed samples.

3.3. Detection limits

The instrument detection limit (IDL) defined as the lowest concentration of analyte which can be positively identified by the instrument under the condition of the method, was established for each of the glycol ethers from multiple injections of calibration solutions of gradually increasing concentration. The criterion that the peak response for each of characteristic (target) ions must be at least three times the standard deviation of the background noise level for that ion and that the ion ratios between target, and qualifying ions remain within 20% of their expected values (NIST mass spectra database) was applied. The IDL varied from 0.01 ng/μL (2-ME, 2-EE, PGME), through 0.02 ng/μL (PGPE, 2-PE), 0.05 ng/μL (PGBE), 0.10 ng/μL (2-BE), 0.25 ng/μl (DPGME), 0.50 ng/μL (2-HE, BEE, TPGME, HEE) to 1.0 ng/μL (MEE, EEE).

When the sample handling is minimal the method detection limit (MDL) can often be estimated directly from the IDL and the sample dilution (MDL = IDL × *F*, where *F* = dilution factor). This approach yields MDL values for undiluted product samples from 10 ng/μL (2-ME, 2-EE, PGME) to 1 μg/μL for MEE and EEE (Table 2).

An alternative and often preferred method of calculating the MDL is based on the standard deviation of the results from the series of samples independently carried through all preparation steps. In this approach MDL is calculated according to the formula:

$$MDL = t_{(n-1)} \times SD$$

where *t* = Student's distribution coefficient (1-tailed test) at the required confidence level, *n* = number of measurements, SD = standard deviation of the concentration measurements near the detection limit (<10 × IDL). We used this approach to verify direct MDL estimates and to examine possible matrix effects at the detection limit. Water compatible *Fabric Stain Remover* and oil based *Wood Finish* were selected to represent products with water and oil compatible matrices; methanol was used as a sample matrix for which no effects were expected (solvent matrix). We spiked eight 10 mL samples of each with the same amount of native glycol ether standards and $^{13}C_2$-BE surrogate. After mixing, we subsampled 2 μL of each sample and diluted it to 2 mL in methanol, spiked with 2 μL of d_7-ME recovery standard and analysed. In the diluted samples the concentration of native glycol ethers was 9.9 × IDL; the surrogate and recovery (internal) standard concentrations were 2.5 and 1 ng/μL respectively. The use of the surrogate allowed us to correct for small changes in the sample volume used for dilution and any losses that may have occurred during the process, while the recovery standard allows correction for instrument drift and volume changes during the injection. Standard deviations of the glycol ethers concentrations (Table 2) fall in a similar range for all 3 categories of samples; however the methanol samples typically show less variability than the product samples. Method detection limits calculated from the standard deviations using the *t* value at 95% confidence level were slightly lower than those calculated from the IDL and varied from 4 to 642 μg/mL. Note that the sample dilution factor was included in MDL calculations (Table 2) to relate the results to glycol ethers concentration in the initial product rather than to the diluted samples injected to the system. The dilution factor can be modified by the operator to change the applicable concentration range if necessary; however, with lower dilution the matrix effect can be more pronounced.

The limit of quantification (LoQ) typically estimated as either 10 × SD or 5 × MDL can be calculated using values from Table 2 assuming both values apply to the same sample dilution.

3.4. Linearity of calibration

The linearity of calibration for each analyte was examined within the concentration range of 0.1–200 ng/μL using 14 calibration levels (0.1, 0.25, 0.5, 1, 2, 4, 6, 8, 10, 40, 80, 120, 160, 200 ng/μL).

Table 3
Linearity of calibration within the range 0.1–200 ppm.

Compound	Low concentration range		Medium concentration range		Upper concentration range	
	ng/μL	R^2	ng/μL	R^2	ng/μL	R^2
2-ME	0.1–10	1.000	0.1–120	0.996	80–200	0.999
PGME	0.1–10	0.999	0.1–120	0.994	80–200	0.997
2-EE	0.1–10	1.000	0.1–120	0.999	0.1–200	0.999
PGPE	0.1–10	0.998	0.1–120	0.998	0.1–200	0.995
2-BE	0.2–10	1.000	0.2–120	0.993	80–200	0.995
$^{13}C_2$-BE	0.2–10	1.000	0.2–120	0.993	10–200	0.994
PGBE	0.2–10	0.997	0.2–120	0.993	80–200	0.993
MEE	2–10	0.998	4–120	0.993	80–200	0.995
EEE	2–10	1.000	4–120	0.994	80–200	0.994
DPGME	0.5–10	0.998	0.5–120	0.993	80–200	0.995
2-HE	0.2–10	0.998	0.2–80	0.995	80–200	0.992
BEE	0.2–10	0.996	0.2–40	0.995	Quadratic fit > 40	
PE	0.1–10	1.000	0.2–40	0.990	Quadratic fit > 40	
TPGME	0.5–10	0.999	0.5–120	0.999	0.5–200	0.999
HEE	1–10	0.999	1–40	0.999	Quadratic fit > 40	

R: coefficient of determination for linear regression.

Some non-linear effects were observed at the low calibration levels when the standard concentration approached the analytes detection limit. A linear fit can be applied for 2-EE, PGPE and TPGME over the entire calibration range. For the rest of glycol ethers a linear fit extends to concentrations between 40 and 100 ng/μL and is best in the range 0.1–10 ng/μL (Table 3). At high concentrations (>40–100 ng/μL) a second linear regression fit can be applied if necessary, with the exception of BEE, 2-PE and HEE for which non-linear effects are too strong. For these compounds a quadratic polynomial fit need to be used within the range of 10–200 ng/μL range. Alternatively a sample can be diluted to bring its concentration back to a linear range.

3.5. Precision

To evaluate the method precision a series of independent samples of methanol, *Fabric Stain Remover*, *Oil Wood Finish* and *Upholstery and Carpet Cleaner* spiked with native glycol ethers (and ^{13}C-2BE surrogate) were analysed. Methanol samples represent the "ideal case scenario" where no matrix interference is expected, *Fabric Stain Remover*, *Wood Finish* and *Upholstery and Carpet Cleaner* were chosen as products of water compatible, oil compatible and aerosol based respectively. Products were screened for the presence of glycol ethers; none were detected. Liquid product samples were spiked to a concentration of 0.1% (w/w) for most of glycol ethers, except for glycol ethers with high MDL values for which the concentration was increased to fulfill the requirement of concentration being at least 10 × MDL (Table 4). A series of 7 independent samples were used to evaluate precision. A concentration of 0.1% (w/w) represents the lowest Canadian regulatory limit for 2-BE concentration in commercial products [8].

Aerosol product samples which are more difficult to handle than liquid ones were screened with more scrutiny. Tests were performed by using a series of 8 independent samples spiked to concentrations of 0.01% and 10% of aerosol content (Table 5) (weight/weight) representing 1/10 of the lower regulatory limit and twice the upper regulatory limit for 2-BE content in aerosol type products. Precision was calculated according to the formula:

$$P = \mathrm{RSD} \times t_{(n-1)} \times 100\%$$

where RSD—relative standard deviation for concentration measurements, *t*—Student's test coefficient for 2-tailed distribution at 95% confidence interval, *n*—number of measurements.

Precision varied from 3% to 5% for methanol samples, 4–8% for *Fabric Stain Remover* and 7–12% for *Oil Wood Finish*. Methanol values represent the best precision which both instrument and method can deliver. Depending on the product being analysed and the amount of interference its matrix creates, these values could increase. This is confirmed by measurements. Precision for products with water and oil compatible matrices were slightly worse than these obtained with the use of pure solvent (Table 4). Aerosol samples were most difficult to handle due to product foaming tendency during sample injection to septum sealed vials. As a result precision for these sets of samples varied from 9% to 16% in the low

Table 4
Uncertainty and precision of glycol ethers measurements calculated at 95% confidence level from spiked samples of methanol and products with water compatible (*Fabric Stain Remover*) and oil compatible matrices (*Oil Wood Finish*).

Compound	Concentration % (w/w)	Methanol		Fabric Stain Remover		Oil Wood Finish	
		Uncertainty	Precision	Uncertainty	Precision	Uncertainty	Precision
2-ME	0.1	1.8%	4.8%	1.7%	4.5%	3.5%	9.4%
PGME	0.1	1.8%	4.7%	2.6%	6.7%	2.8%	7.5%
2-EE	0.1	1.9%	4.9%	1.6%	4.8%	3.3%	8.8%
PGPE	0.1	2.0%	5.2%	1.8%	4.7%	3.6%	9.4%
2-BE	0.1	1.7%	4.5%	1.6%	4.3%	4.0%	10.5%
PGBE	0.1	1.6%	4.3%	1.9%	5.0%	3.1%	8.1%
MEE	1.0	1.4%	3.6%	2.7%	7.1%	4.1%	10.7%
DPGME	1.0	1.3%	4.1%	2.9%	7.7%	4.3%	11.5%
EEE	1.5	1.5%	3.5%	2.8%	7.5%	4.2%	11.2%
2-HE	0.5	1.6%	4.2%	2.2%	5.8%	3.2%	8.5%
BEE	0.5	1.2%	3.1%	1.3%	3.5%	3.0%	7.9%
PE	0.1	1.4%	3.7%	2.1%	5.4%	2.7%	7.2%
TPGME	1.0	1.1%	3.0%	2.0%	5.3%	4.3%	11.3%
HEE	0.5	1.6%	4.2%	1.8%	4.9%	3.0%	7.8%

Table 5
Uncertainty and precision of glycol ethers measurements calculated at 95% confidence level from spiked samples of aerosol based *Upholstery and Carpet Cleaner*. Spikes are relative to the aerosol content in the samples.

Compound	Aerosol Carpet Cleaner					
	% aerosol (w/w)	Uncertainty	Precision	% aerosol (w/w)	Uncertainty	Precision
2-ME	0.01	5.3%	15.0%	10	1.6%	4.5%
PGME	0.01	5.1%	14.3%	10	0.6%	1.7%
2-EE	0.01	5.0%	14.1%	10	1.2%	3.3%
PGPE	0.01	4.6%	12.9%	10	0.9%	2.6%
2-BE	0.01	3.3%	9.4%	10	1.0%	2.9%
PGBE	0.01	4.1%	11.7%	10	0.9%	2.4%
MEE	0.01	4.7%	13.2%	10	5.1%	14.4%
DPGME	0.01	4.4%	12.3%	10	1.1%	3.1%
EEE	0.01	4.7%	13.3%	10	4.2%	12.0%
2-HE	0.01	5.4%	15.2%	10	0.9%	2.6%
BEE	0.01	4.6%	13.1%	10	1.0%	2.9%
PE	0.01	4.5%	12.8%	10	0.8%	2.3%
TPGME	0.01	5.6%	15.8%	10	1.0%	2.8%
HEE	0.01	4.2%	11.8%	10	1.3%	3.6%

concentration range and 2–12% in the high concentration range (Table 5).

3.6. Recovery

Recovery of the glycol ethers was assessed for liquid and aerosol products samples with blank matrices (free from glycol ethers). *Fabric Stain Remover* and *Oil Wood Finish* (products with water and oil compatible matrices) samples were spiked with glycol ether standards to the concentration of 0.1–1.5% (same as for precision estimates) and carried through the steps of the liquid sample preparation procedure. Controlled amounts of the aerosol *Upholstery and Carpet Cleaner* were injected from the product container into a known amount of methanol sealed in septum caped vials and spiked with glycol ethers to 0.01% of aerosol content by weight (10% of lower regulatory limit for 2-BE concentration in aerosol type products). Small amounts (100 μL) of each sample were withdrawn through the septum port using a chromatographic syringe and carried through the aerosol sample preparation procedure. Recoveries of glycol ethers were calculated for each of the samples individually and then averaged. The original samples in the septum vials were next re-spiked with native glycol ethers to 10% of aerosol content by weight (2 × upper regulatory limit for 2-BE) and carried through the rest of sample preparation procedure. Sets of 7 independent samples were used for recovery calculations from liquid products and 8 from aerosol product. Recoveries were calculated according to the formula:

$$\text{Recovery} = \left(\frac{\text{MC}}{\text{SC}}\right) \times 100\%$$

where MC = mean concentration value from replicate measurements, SC = spiked concentration.

Values obtained vary from 87% to 119% for water compatible matrix and from 92% to 116% for oil compatible samples. The majority of the results fall within ±7% of the spiked amount. Recoveries of glycol ethers from aerosol matrix varied between 89% and 112% for low level spike and between 94% and 107% for the high level spike. Recoveries for 2-BE were 98% and 100%, respectively (Table 6).

3.7. Uncertainty

Systematic and random errors in the measurements such as sample volume, amount of surrogate spike, gravimetric analysis as well as purity of reagents, all contribute to the uncertainty of the results. While models of different complexity are available to calculate the uncertainty from the analytical results, it is common in the laboratory practice to estimate uncertainty (u) from the standard deviation of independent measurements using the formula:

$$u = \sqrt{\frac{\text{SD}^2}{n}}$$

where u = standard uncertainty, SD is the standard deviation and n = number of (independent) samples.

Expanded uncertainty U which describes uncertainty of measurements at certain confidence level is next calculated from standard uncertainty as:

$$U = u \times t$$

Table 6
Recoveries of glycol ethers from selected liquid and aerosol products.

Glycol ether	Stain Remover		Wood Finish		Aerosol Carpet Cleaner			
	Spike	Recovery	Spike	Recovery	Spike	Recovery	Spike	Recovery
2-ME	0.1%	97%	0.1%	116%	0.01%	96%	10%	103%
PGME	0.1%	94%	0.1%	107%	0.01%	93%	10%	106%
2-EE	0.1%	102%	0.1%	98%	0.01%	100%	10%	107%
PGPE	0.1%	95%	0.1%	113%	0.01%	99%	10%	106%
2-BE	0.1%	92%	0.1%	109%	0.01%	98%	10%	100%
PGBE	0.1%	93%	0.1%	109%	0.01%	98%	10%	102%
MEE	1.0%	104%	1.0%	92%	0.01%	106%	10%	94%
DPGME	1.0%	111%	1.0%	99%	0.01%	89%	10%	106%
EEE	1.5%	103%	1.5%	101%	0.01%	112%	10%	97%
2-HE	0.5%	101%	0.5%	107%	0.01%	95%	10%	105%
BEE	0.5%	119%	0.5%	111%	0.01%	104%	10%	104%
PE	0.1%	87%	0.1%	111%	0.01%	104%	10%	100%
TPGME	1.0%	109%	1.0%	96%	0.01%	103%	10%	98%
HEE	0.5%	102%	0.5%	97%	0.01%	101%	10%	105%

Table 7
Concentration of glycol ethers from product analysis (SD = standard deviation, U = expanded uncertainty of the concentration measurements at 95% confidence level).

Product	Glycol Ether	Concentration	SD	U
Liquid products				
Glass and Hard Surface Cleaner	2-HE	0.85%	0.02%	0.04%
General Purpose Kitchen Cleaner	PGBE	2.26%	0.11%	0.20%
Acrylic Dry Paint Solvent	2-BE	0.32%	0.04%	0.07%
Acrylic White Paint	2-BE	8.79%	0.35%	0.64%
Polyacrylic Protective Finish	PGBE	5.2%	0.05%	0.09%
	EEE	0.1%	0.01%	0.02%
	DPGME	1.7%	0.007%	0.01%
	BEE	0.2%	0.005%	0.01%
Aerosol products				
Disinfectant and Bathroom Cleaner	BEE	6.8%	0.24%	0.44%
Invisible Glass Cleaner	2-BE – full can	4.8%	0.05%	0.05%
	2-BE – half can	4.7%	0.06%	0.06%

where u = standard uncertainty, t = Studnets's t-distribution coefficient for 2-sided test ($n-1$ degree of freedom) at the particular confidence level.

Expanded uncertainties of the concentration measurements of glycol ethers in methanol, water and oil based matrices calculated at 95% confidence level are presented in Tables 4 and 5, while the expanded uncertainties of products analysis are included in Table 7. Expanded uncertainties approximately equal 2 × SD when smaller number (3–4) of measurements were taken and approximately equal SD where number of measurements ≥7.

3.8. Product analysis

The method was tested on samples of commercial products obtained from local suppliers which could contain glycol ethers. Eight liquid products (*Glass and Hard Surface Cleaner*, *Fabric Stain Remover*, *Carpet Stain Remover*, *General Purpose Kitchen Cleaner*, *Acrylic Dry Paint Solvent*, *Acrylic White Paint*, *Oil Wood Finish*, and *Polyacrylic Protective Finish*) and four aerosol products (*Disinfectant and Bathroom Cleaner*, *Invisible Glass Cleaner*, *Upholstery and Carpet Cleaner* and *Insect Repellent*) were analysed for the content of glycol ethers. Triplicate products samples were withdrawn from each single container for the purpose of method testing. Additional tests were performed using a full and a partially empty aerosol container to examine the consistency of sample composition. The results show that 5 out of 8 liquid products tested contain various glycol ethers at levels of 0.1–9% (Table 7). Two of the four tested aerosol products were found to be free of glycol ethers, while the *Disinfectant and Bathroom Cleaner* and the *Invisible Glass Cleaner* contained BEE and 2-BE respectively (Table 7).

Invisible Glass Cleaner containing 2-BE was further tested to assess the reproducibility of the sampling and consistency of sample composition. Seven aerosol samples were withdrawn from the full can into 5 mL of methanol, spiked with the surrogate and processed according to the sampling procedure. The can was then emptied to half of its content (by weight) and seven additional aerosol samples were analysed. The results show no statistical difference between the 2 sets of data demonstrating good reproducibility of the aerosol sampling technique (Table 7).

4. Summary and conclusion

The results demonstrate that simple isotope dilution GC–MS technique can be used for the analysis of the glycol ethers in a variety of commercial products, with a precision adequate for legislative purposes. Relatively large product dilution combined with sample filtration through 0.2 μm pore size PTFE filters (Whatman Mini-UniPrep Syringless Filter) eliminates the need for extensive sample cleanup; diluted and filtered samples can be directly injected in GC–MS system with minimal risk of contamination. With a suggested dilution factor of 1000×, the linearity of the calibration is upheld for glycol ethers in the concentration range from 0.01% to about 4–10%. Products containing larger amounts of glycol ethers may need to be further diluted in order to fall into linear range. The precision of the measurement at concentrations close to the MDL vary from 2% to 12% for all analytes. Oil compatible matrices seems to cause more interference that water compatible ones, thus slightly worse precision can be expected when analysing oil compatible products. The recovery of glycol ethers from products of different matrices was good and remained in the range 87–119%. Tests performed with different household products demonstrate that glycol ethers are common additives to water based cleaners and paints. Six glycol ethers analysed with the method were found in 7 out of 12 products tested and with concentrations ranging from 0.1% to 8.8%. None of the oil based products tested contained any of the glycol ethers and all of the water soluble paint products contained at least one of the glycol ethers analysed.

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