Application Note

Determination of nicotine, propylene glycol, and glycerol in e-liquids according to ISO/CD 20714 using an Agilent Intuvo 9000 GC

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Abstract

Accurate quantification of propylene glycol, glycerol, and nicotine in liquids used in electronic nicotine delivery devices (e-cigarettes) could be achieved by GC-FID analysis using the Agilent Intuvo 9000 GC system. A standard method, based on the draft ISO/CD 20714 standard, and a high-throughput method were tested. Excellent linearity, repeatability, and sensitivity were obtained for both methods using a DB-BAC1 Ultra Inert column designed for volatile polar analytes. Using the fast GC-FID method, run-to-run time was under five minutes.

Introduction

Electronic cigarettes have become increasingly popular. Different electronic devices, consisting of a battery-powered heating element and a liquid container, are commercially available. These devices typically produce an aerosol vapor from a solution of fragrance compounds, with or without nicotine, in a high boiling solvent, such as a mixture of propylene glycol and glycerol (e-liquid).

For quality control of these e-liquids, quantitative analysis of propylene glycol, glycerol, and nicotine content is required. According to EU regulation 269, the nicotine content is regulated to levels between 3 and 20 mg/mL in e-liquid[1]. Liquids containing more than 20 mg nicotine per mL are considered tobacco products, and are regulated by the Tobacco Product Directive[2]. For the qualitative and quantitative determination of minor constituents, such as fragrance additives, GC/MS solutions are available[3].

Recently, a method based on GC-FID analysis was proposed as reference standard ISO/CD 20714 for the determination of nicotine, propylene glycol, and glycerol in liquids used in electronic nicotine delivery devices[4]. Since the test solutes are relatively polar, proper column choice is essential for quantitative analysis. On standard apolar columns, peak shapes for underivatized glycols and glycerol might be unsatisfactory, disabling accurate quantification. In the method draft of ISO/CD 20714, a DB-ALC1 (30 m × 0.32 mm, 1.8 µm) column is proposed as a separation column. Excellent peak shapes can be obtained for glycerol and nicotine on this column, which was designed for the analysis of polar volatiles, including blood alcohol determination. Recently, the Ultra Inert DB-BAC1 UI column was introduced for the analysis of these volatile polar analytes. The Ultra Inert DB-BAC1 UI column was used in this study.

Method performance also depends on the inertness and quality of the full sample pathway, from inlet to detector. Therefore, tests were performed to evaluate the applicability of the Agilent Intuvo 9000 GC system with a dedicated DB-BAC1 UI column for the quantitative analysis of propylene glycol, glycerol, and nicotine in e-liquids. First, the draft ISO method was used. Linearity, sensitivity, and repeatability were tested and compared to results obtained on an Agilent 7890 GC.

A high-throughput GC method was developed and validated, taking advantage of the fast heating and cooling capabilities of the Intuvo 9000 GC.

Experimental

Sample preparation

Propylene glyceol, glycerol, nicotine, 1,4-butanediol (IS 1), and quinaldine (IS 2) were purchased as pure standards from Sigma-Aldrich (Beerse, Belgium). Iso-propanol (solvent) was from BioSolve (Valkenswaard, The Netherlands).

Calibration solutions were prepared according to ISO/CD 20714. Five calibration levels plus one blank, were prepared, as summarized in Table 1.

GC Parameters

GC-FID analyses were performed on an Agilent 7890B GC and on an Agilent Intuvo 9000 Series gas chromatograph, respectively. Both systems were equipped with a split/splitless inlet, a flame ionization detector, and an Agilent 7693 Automated Liquid Sampler (ALS) with 10 µL syringe.

On both GCs, a 30 m × 0.32 mm, 1.8 µm DB-BAC1 UI column was installed (p/n 123-9334UI or 123-9334UI-INT for the 7890B GC and Intuvo 9000 GC, respectively).

Table 1. Calibration solutions prepared in iso-propanol for the quantitative analysis of propylene glycol, glycerol, and nicotine in e-liquids.

	Concentration (mg/mL)					
	Blank	L1	L2	L3	L4	L5
Propylene glycol	0.00	0.12	0.60	2.42	6.05	12.09
Glycerol	0.00	0.12	0.41	1.64	4.10	8.20
Nicotine	0.00	0.022	0.075	0.300	0.749	1.499
IS 1 (1,3-butandediol)	1.00	1.00	1.00	1.00	1.00	1.00
IS 2 (quinaldine)	0.20	0.20	0.20	0.20	0.20	0.20

For the standard GC analyses, method parameters were based on the parameters described in ISO/CD 20714. Table 2 summarizes these parameters. A high-throughput method with a three-fold speed increase was programmed on the Intuvo 9000 GC. Table 3 gives the high-throughput parameters.

Results and discussion

Figure 1 shows the GC-FID analysis of calibration sample L1 (lowest concentration) on the Intuvo 9000 GC. Good separation was obtained in approximately 10 minutes, with propylene glycol eluting at 3.34 minutes, IS 1 (1,4-butanediol) at 4.31 minutes, glycerol at 5.00 minutes, IS 2 (quinaldine) at 6.87 minutes, and nicotine at 7.24 minutes. The retention times of these peaks were within 0.2 minutes from the retention times measured using the same method on a 7890B GC. This is remarkable, considering that two columns (classical format versus Intuvo format) were used, and all peak shapes were excellent. Even at the lowest level, glycerol and nicotine can easily be detected.

Table 2. Standard GC-FID parameters for the quantitative analysis of propylene glycol, glycerol, and nicotine in e-liquids.

Parameter	Value
Inlet	Split (1/50) - 250 °C, split liner UI (p/n 5190-2295)
Injection volume	1 µL
Constant column flow	1.5 mL/min hydrogen
Column temperature program	100 °C (1 minute) 15 °C/min to 130 °C 40 °C/min to 220 °C (5 minutes)
Intuvo Guard Chip temperature	Oven track mode
Intuvo bus temperature	220 °C
Intuvo detector tail	275 °C
Detector	Flame ionization at 275 °C, 40 mL/min hydrogen, 400 mL/min air

Table 3. High-throughput GC-FID parameters for the quantitative analysis of propylene glycol, glycerol, and nicotine in e-liquids.

Parameter	Value
Inlet	Split (1/50) - 250 °C, split liner UI (p/n 5190-2295)
Injection volume	1 µL
Constant column flow	6 mL/min hydrogen
Column temperature program	100 °C (0.33 minutes) 45 °C/min to 130 °C 120 °C/min to 220 °C (1.75 minutes)
Intuvo Guard Chip temperature	Oven track mode
Intuvo bus temperature	220 °C
Intuvo detector tail	275 °C
Detector	Flame ionization at 275 °C, 40 mL/min hydrogen, 400 mL/min air

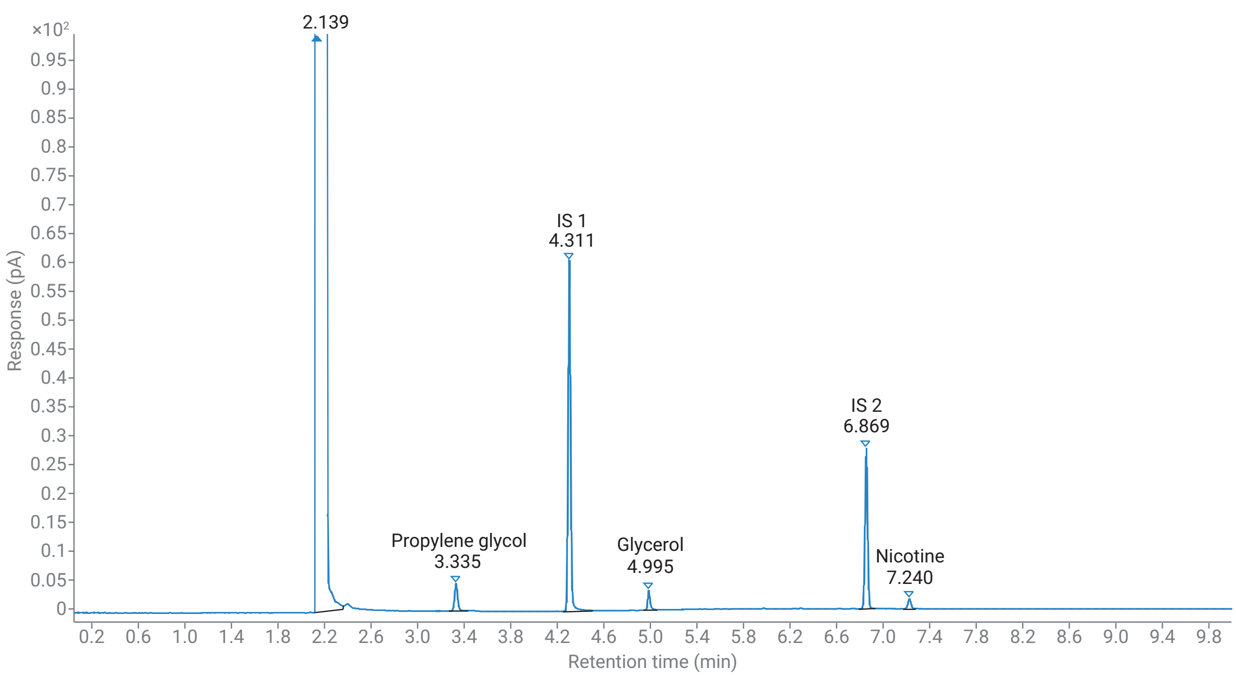

Figure 1. GC-FID analysis of calibration mixture L1 on an Agilent Intuvo 9000 GC.

Next, calibration curves were calculated for concentration levels 0.1 to 10 mg/mL for propylene glycol and glycerol, and from 0.02 to 1.5 mg/mL for nicotine. Figures 2–4 give the calibration curves obtained on the Intuvo 9000 GC. All calibration curves show a linearity better than 0.999 R^2.

The same calibration samples were analyzed on a 7890B GC, and similar calibration curves were obtained. Table 4 compares the slopes, intercepts, and R^2 values for the three target solutes on both GCs. These data show that both systems perform equally well. The similarity of curve slopes is remarkable, indicating that response factors and sensitivities are the same on both systems.

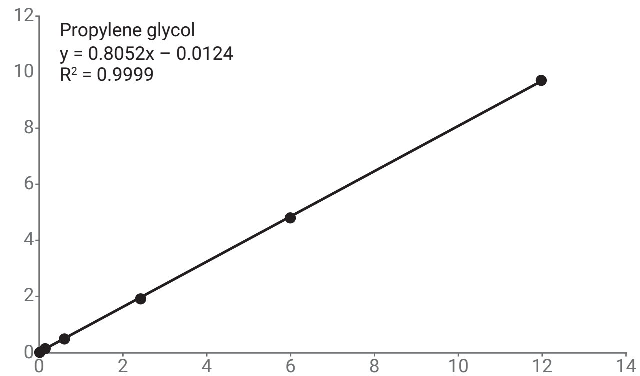

Figure 2. Calibration curve for propylene glycol using 1,4-butanediol as internal standard.

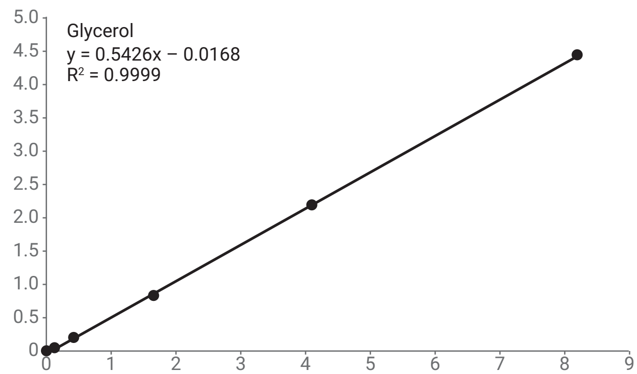

Figure 3. Calibration curve for glycerol using 1,4-butanediol as internal standard.

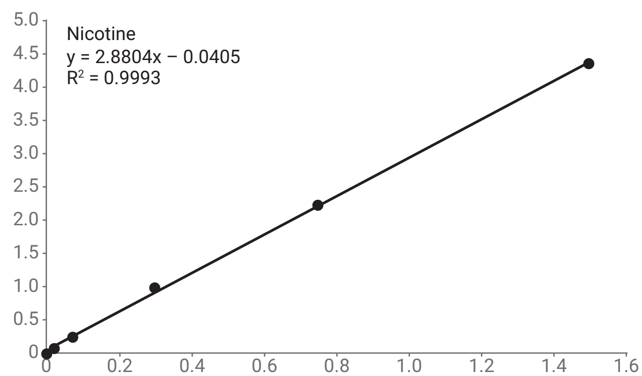

Figure 4. Calibration curve for nicotine using quinaldine as internal standard.

Table 4. Calibration curve data (slope, Y-axis, intercept, and R^2) for target solutes analyzed on an Agilent 7890B GC and an Agilent Intuvo 9000 GC.

	Agilent 7890B GC			Agilent Intuvo 9000 GC		
Calibration	Slope	Intercept	R^2	Slope	Intercept	R^2
Propylene glycol	0,8052	-0.0125	1,0000	0,8052	-0.0124	0,9999
Glycerol	0,5400	-0.0184	0,9999	0,5426	-0.0168	0,9999
Nicotine	2,8833	0.0461	0,9991	2,8804	0.0405	0,9993

Next, two e-liquid samples were analyzed in six-fold. Figures 5 and 6 show representative chromatograms. Both samples primarily consist of propylene glycol (3.3 minutes) and glycerol (5.0 minutes), and also contain nicotine (7.24 minutes). The other smaller peaks correspond to fragrance compounds.

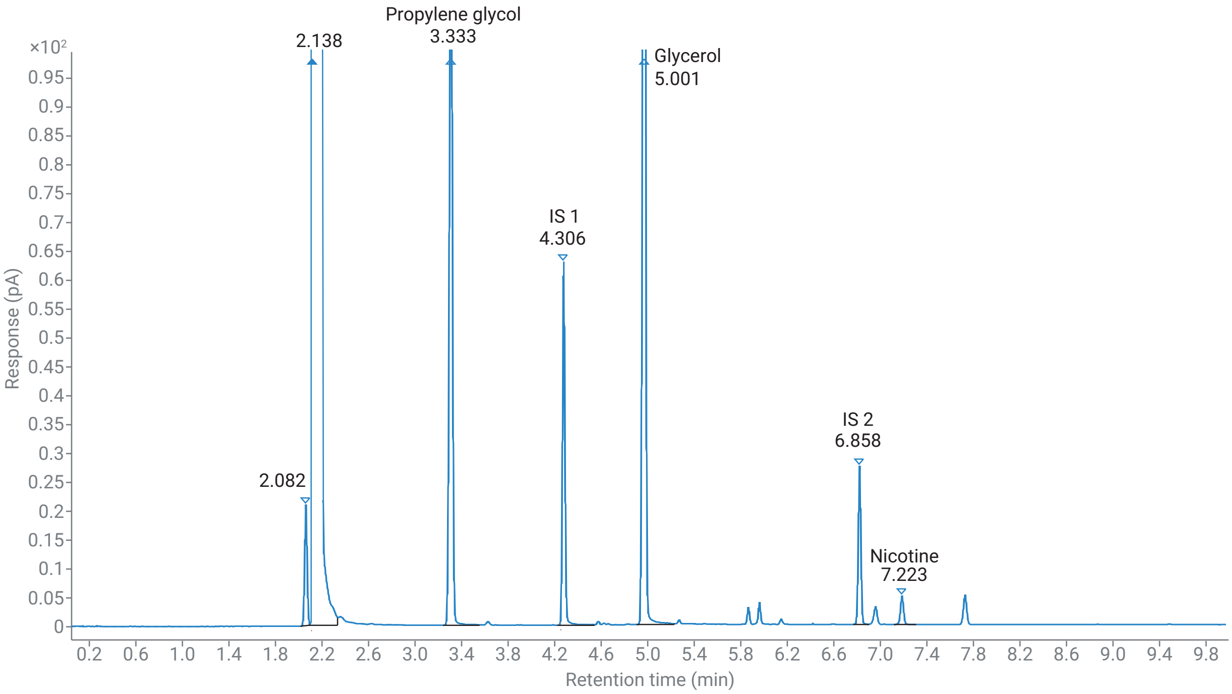

Figure 5. GC-FID analysis of e-liquid sample 1 on an Agilent Intuvo 9000 GC using standard GC conditions.

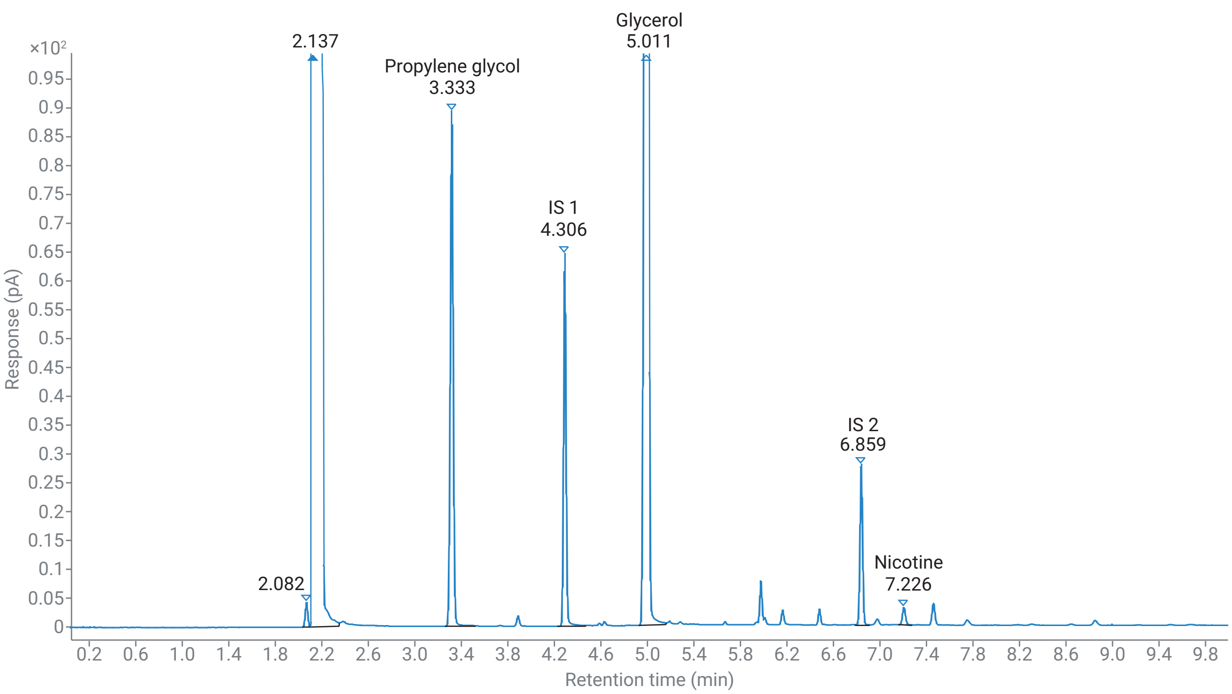

Figure 6. GC-FID analysis of e-liquid sample 2 on an Agilent Intuvo 9000 GC using standard GC conditions.

The concentrations of the target compounds in both samples were determined using the calibration curves. Table 5 compares the data collected on both GCs. Sample 1 contains approximately 7.8 mg/g nicotine, while sample 2 contains 3.6 mg/g nicotine; both are well below the 20 mg/g limit. Excellent repeatability was obtained, with RSDs below 1 % for propylene glycol and glycerol, and below 2 % for nicotine.

Calibration solutions and samples were also analyzed on the Intuvo 9000 GC using a fast temperature program and higher flow rate (6 mL/min). Figure 7 shows the chromatogram for the lowest calibration level. Figures 8–10 show calibration curves for propylene glycol, glycerol, and nicotine. Equally good linearity and relative response factors, as reflected by the slopes of the curves, were obtained. Analysis time was reduced to 3.5 minutes, with run-to-run time below 5 minutes.

Table 5. Quantitative data obtained on an Agilent 7890B GC and an Agilent Intuvo 9000 GC for the determination of propylene glycol, glycerol, and nicotine in two e-liquid samples.

	Agilent 7890B GC			Agilent Intuvo 9000 GC		
Sample 1	**Mean (mg/g)**	**s**	**RSD (%)**	**Mean (mg/g)**	**s**	**RSD (%)**
Propylene glycol	318	1	0,4	320	2	0,5
Glycerol	664	4	0,6	667	2	0,3
Nicotine	8,01	0,07	0,88	7,78	0,05	0,68
Sample 2	**Mean (mg/g)**	**s**	**RSD (%)**	**Mean (mg/g)**	**s**	**RSD (%)**
Propylene glycol	140	0	0,2	142	1	0,4
Glycerol	838	4	0,5	847	4	0,5
Nicotine	3,60	0,03	0,96	3,58	0,06	1,77

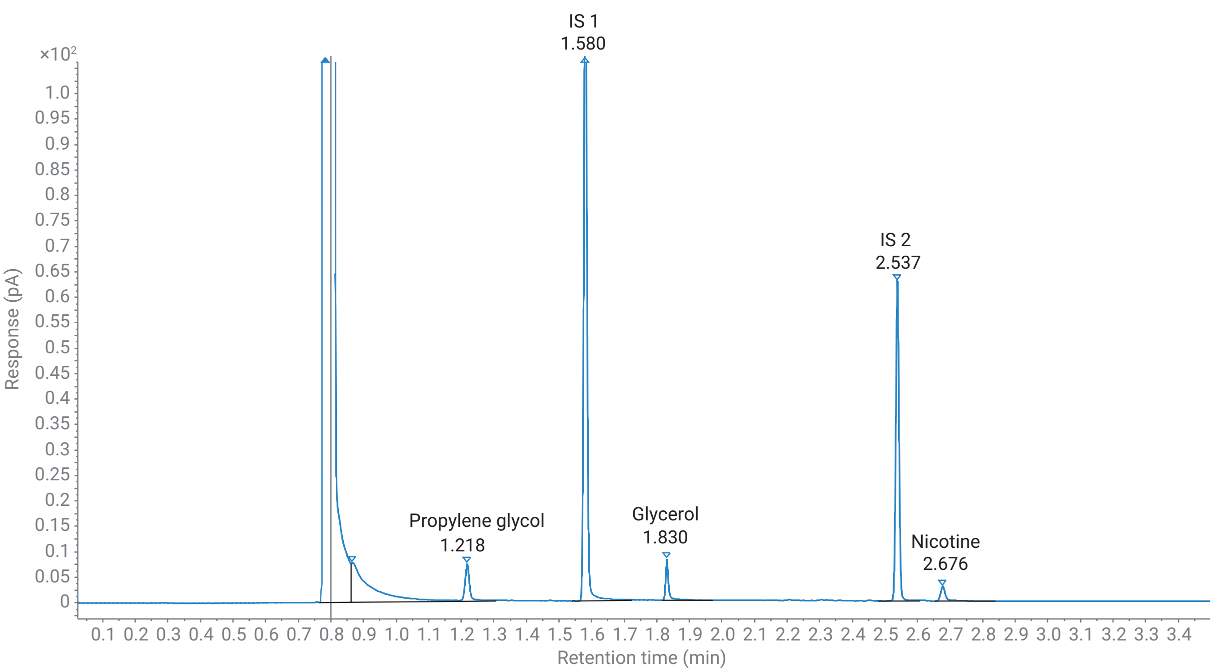

Figure 7. Fast GC-FID analysis of calibration mixture L1 on an Agilent Intuvo 9000 GC.

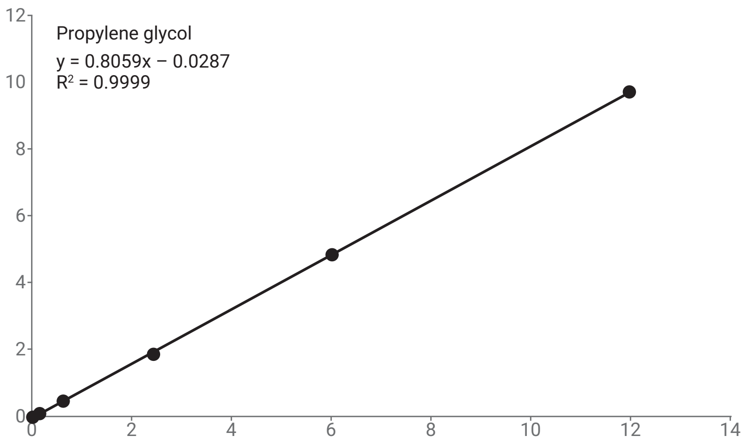

Figure 8. Calibration curve for propylene glycol using 1,4-butanediol as internal standard, fast GC method.

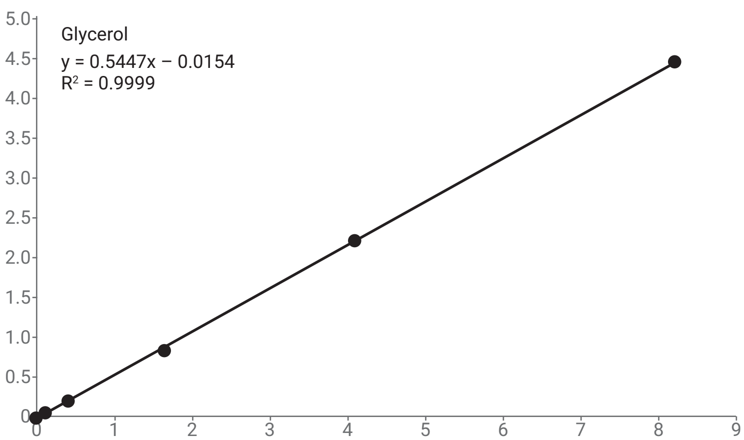

Figure 9. Calibration curve for glycerol using 1,4-butanediol as internal standard, fast GC method.

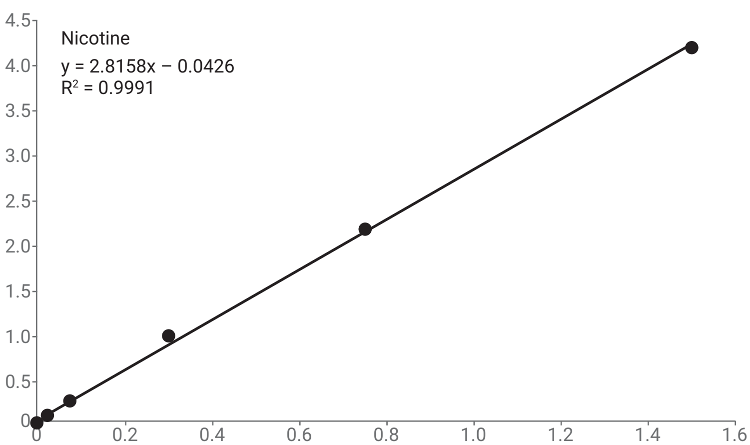

Figure 10. Calibration curve for nicotine using quinaldine as internal standard, fast GC method.

Figures 11 and 12 present the chromatograms obtained using the fast GC-FID method for samples 1 and 2. The resolution is almost identical to the standard method, and is sufficient for the accurate determination of the target compounds. Peak height and sensitivity are approximately a factor 2 higher, due to faster eluting peaks.

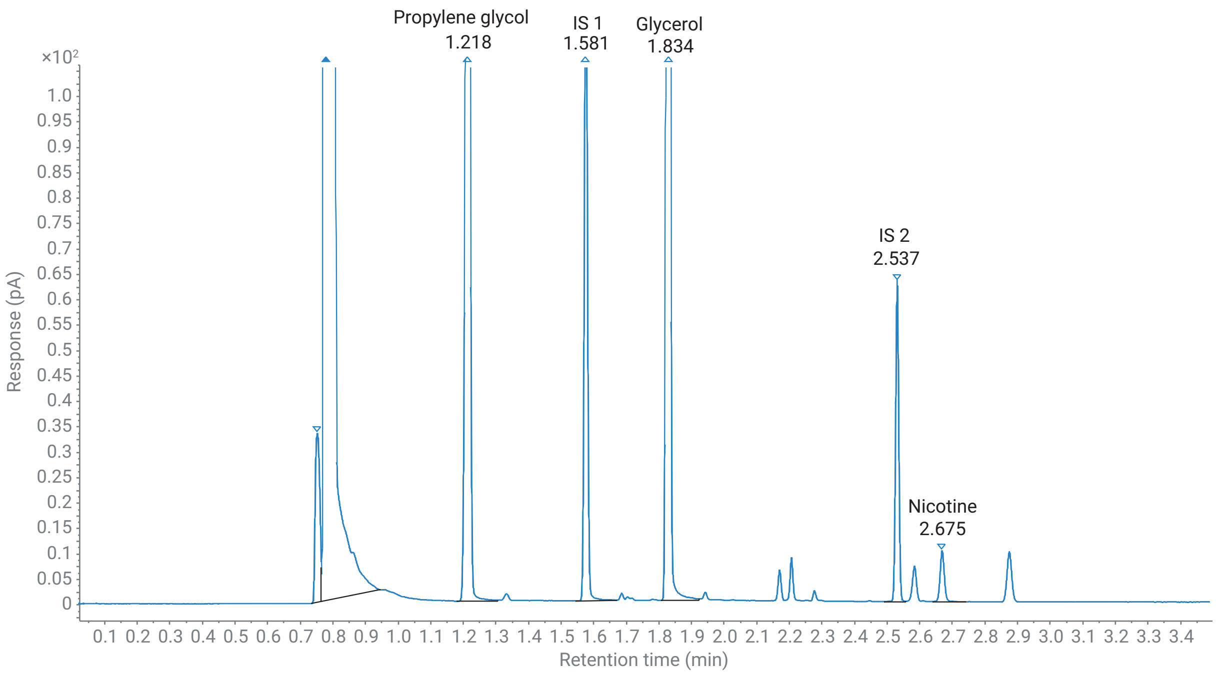

Figure 11. Fast GC-FID analysis of e-liquid sample 1 on an Agilent Intuvo 9000 GC.

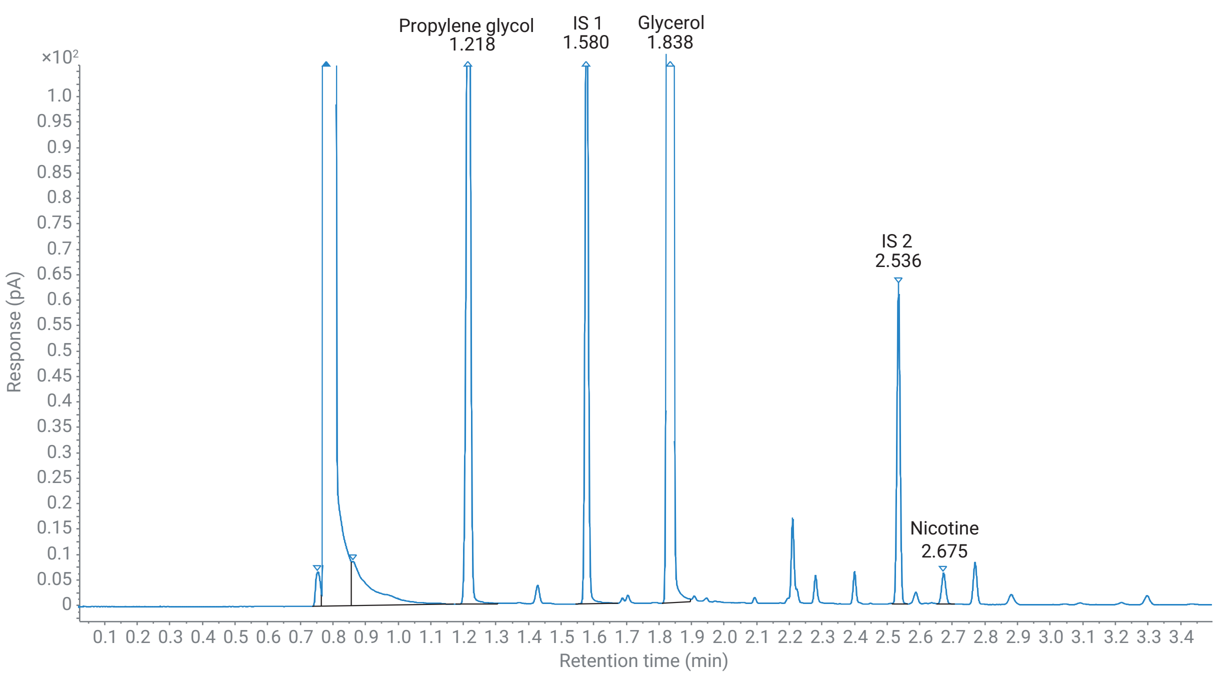

Figure 12. Fast GC-FID analysis of e-liquid sample 2 on an Agilent Intuvo 9000 GC.

The repeatability was tested by analyzing both samples in six-fold. Table 6 gives the results. RSDs were all below 1 %, indicating excellent repeatability and robustness. The calculated concentrations for propylene glycol, glycerol, and nicotine match well, with the values determined using the standard method.

Conclusions

Quantitative determination of propylene glycol, glycerol, and nicotine in e-liquids can be performed according to ISO/CD 20714 on an Agilent Intuvo 9000 GC-FID system. Excellent linearity, sensitivity, and repeatability were obtained using a dedicated Agilent Ultra Inert DB-BAC 1 column. Neither the Guard Chip nor the Intuvo flowpath had a negative impact on peak shape or method performance. The quantitative results obtained on the Intuvo 9000 GC were equivalent to those results obtained on an Agilent 7890B GC.

The fast heating and cooling of the Intuvo 9000 GC also enables a three-fold speed increase of the standard method. Using the high-throughput method, equal quantitative results, linearity, and repeatability were obtained compared to the standard method. The sensitivity was improved, and run-to-run time was reduced to less than five minutes.

Table 6. Repeatability test of fast GC-FID analysis of e-liquid samples (n = 6).

Sample 1	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Mean	s	RSD (%)
Propylene glycol	319	319	319	319	319	319	319	0	0,1
Glycerol	663	662	664	663	663	663	663	1	0,1
Nicotine	7,82	7,82	7,80	7,76	7,79	7,78	7,79	0,02	0,28
Sample 2	**Run 1**	**Run 2**	**Run 3**	**Run 4**	**Run 5**	**Run 6**	**Mean**	**s**	**RSD (%)**
Propylene glycol	140	139	139	139	139	140	140	0	0,2
Glycerol	841	839	839	837	841	840	839	2	0,2
Nicotine	3,54	3,53	3,56	3,57	3,55	3,53	3,55	0,02	0,44

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