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A simple method for the parallel quantification of nicotine and major solvent components in electronic cigarette liquids and vaped aerosols

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ABSTRACT

An analytical method was developed for the parallel quantitation of nicotine (Nic) and two key solvents (propylene glycol (PG) and vegetable glycerin (VG)) in e-cigarette (EC) liquids before vaping and from aerosols after vaping. For analysis of the EC refill solutions, the samples were diluted by a factor of about 100 in methanol. The aerosol samples generated by a modified international puffing protocol were initially collected on Cambridge filter pads and extracted with methanol. Both types of samples were analyzed by a gas chromatography-flame ionization detector (GC-FID) together with the mass change tracking (MCT) procedure introduced in our earlier study. The recovery of all three target components (Nic/PG/VG) in both EC liquid and aerosol samples was assessed after spiking Nic at four different concentrations (2, 5, 10, and 20 mg g^{-1}) in the e-solutions (prepared in the laboratory at three different PG:VG mass ratios of 10:0, 5:5, and 0:10). The method recoveries of Nic, PG, and VG in the e-liquid samples were 96.0 ± 1.0, 96.0 ± 1.2, and 101.4 ± 6.9%, respectively, while those in the aerosol samples were slightly lower at 94.7 ± 5.6, 85.5 ± 3.0, and 91.4 ± 15.7%, respectively. The amounts of VG and Nic in the e-liquid had a significant influence on the emission factors of PG, VG, and Nic. The detection limit values (ng) were 0.36 (Nic), 0.72 (PG), and 8.15 (VG) for the liquid samples and 0.51 (Nic), 0.96 (PG), and 3.99 (VG) for the aerosol samples. Overall, this method was reliable enough to determine each target in both liquid and aerosol samples.

1. Introduction

The electronic cigarette (EC) is an electronic nicotine delivery system. It was initially designed in China to help smokers quit smoking tobacco-based cigarettes. However, it has become increasingly popular among smokers worldwide [1,2]. A third-generation e-cigarette has become the most popular among regular EC users based on an online survey [3–5]. Regardless of type, an EC is composed of three main parts: (1) a battery with integrated electronics for power adjustments, (2) an atomizer (or clearomizer: most popular used), and (3) a wide variety of EC refill solutions. The industry standard battery is commonly set at 3.7 V, but some users adjust the EC vaping power in the range of 3.0 to 7.0 V to control (or maximize) the vapor generation rate [6,7]. The clearomizer houses the heating element (or battery connector), a replaceable coil (a wicking material with user specified resistance and geometry configurations), and an e-solution reservoir (cartridge), which are all contained within one unit. The amount of e-solution remaining in the cartridge is generally identifiable through the transparent clearomizer [8]. By supplying battery power to the clearomizer heating element, ECs deliver aerosolized Nic and other chemicals such as flavors or water in user inhaled puffs into the lungs [9]. Newer EC devices allow the user to choose the resistance on the atomizer/cartomizer (by substituting a coil with different resistance) as well as adjusting the heater power to vary the heating element temperature, resulting in user desired aerosol delivery [3].

The EC refill solution is commonly a mixture of propylene glycol (PG) or vegetable glycerin (VG), water, and aromas (or flavors). This mixture can be vaped with or without the addition of Nic [2]. PG and VG are generally recognized to be safe for humans and have been approved by the FDA [10]. PG is a colorless liquid primarily used in food processing, while VG is an organic liquid (made from plant oils) mostly used in cosmetic products and foodstuffs. Higher concentrations of PG can provide a strong throat hit and longer storage time due to its powerful moisturizing properties. In contrast, a higher content of VG can lead to the generation of more aerosol [11,12]. The manufacturer labels claim that the Nic concentration in commercial refill e-liquids varies from 0 to 36 mg mL^{-1}. Recent European Union regulations have limited the maximum Nic in commercial e-liquids to 20 mg mL^{-1} [3, 5]. However, in some jurisdictions, higher Nic solutions (e.g., ≥100 mg mL^{-1}) are permissible to prepare custom liquids for user satisfaction.

A number of studies have reported that toxic substances (e.g., formaldehyde, acetaldehyde, and toluene) were detected in EC vapor when an excessive heater power was used to induce PG and VG pyrolysis

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[13]. Hence, it is important to more clearly understand the chemical components in both EC refill solutions and EC generated vapors/aerosols. Many studies have focused on the Nic and impurity levels in EC liquids, and some analytical methods have been proposed [14–16]. Most of the studies used standard official methods [17,18] specified for Nic quantification in conventional cigarettes. However, for the application of those approaches, the pre-treatment is relatively complex and requires specialized analytical instruments.

In this study, a simple method was developed for parellel quantitation of PG, VG, and Nic in EC from both solution and vaped aerosol samples (Cambridge filter pad sampling) by employing a gas chromatograph-flame ionization detector (GC-FID) system. For the basic information of the target compounds, refer to Table 1S. The aersosol samples were generated in an in-house custom puffing regime based on standard methods used for conventional cigarettes [17,18]. The standard analytical method for PG and VG quantification was followed (NIOSH). A custom-designed EC auto-sampler was used for the generation of aerosol samples from EC. In addition, the mass change tracking (MCT) approach developed for the accurate quantification of consumption rate of EC solution during puffing was also employed [19–21]. The results of this study will help broaden the use of a facile, but highly accurate, approach to quantify nicotine and major components of e-solution in both liquid (before) and aerosol phase (after smoking).

2. Materials and methods

2.1. Preparation of e-liquid working standard (L-WS)

For the preparation of the L-WS, an internal standard solution (INSD) was initially prepared by adding 1 mL of reagent grade quinoline (Sigma-Aldrich, USA; purity: ≥98.0%) into a 2 L volumetric flask. Then, methanol (Sigma-Aldrich, USA; purity: ≥99.0%) was added to this 2 L flask. The primary standard (PS) was prepared by mixing reagent grade chemicals (RGC) of PG (1400.1 mg), VG (1400.5 mg), and Nic (39.6 mg) (RGC, Sigma-Aldrich, USA, purity ≥99.0%) with the INSD to give 20 mL of the PS. The PG/VG to Nic mass ratio was fixed as 35:1, which is similar to commercial EC refill solutions (Table 2S A and B). Ideally, the ISTD concentration should match the median L-WS analyte concentration range. Quinoline was chosen as an internal standard for all three targets. However, in this study, the quinoline concentration (536 ng μL^{-1}) was similar to the PG and VG concentrations in the first and second L-WSs, which is about 10 times larger than the Nic concentration (49.5 ng μL^{-1}) in the third L-WS.

The final L-WSs were prepared at five different concentrations by diluting the PS with the ISTD (concentration of PG and VG: 350 (1st) to 7000 ng μL^{-1}(5th) and Nic (9.90 to 198 ng μL^{-1})) in a stepwise manner for a 5-point calibration (Table 2S **C**). The internal calibration was performed by injecting 1 μL of the final L-WSs into a GC-FID (Shimadzu 2010 plus, Japan) equipped with an auto-injector and sampler (AOC-20i + s, Shimadzu, Japan) (AI-GC-FID), as described below.

The internal calibration results were analyzed as follows

$$\frac{A}{A_{IS}} = a \times \frac{C}{C_{IS}} + b \quad (1)$$

where A and A_{IS} are the peak areas of the target compound and the ISDS, respectively, C and C_{IS} are the concentrations of the target compound (ng μL^{-1}) and ISTD (536 ng μL^{-1}), and 'a' and 'b' are relative response factor (RRF) and the intercept.

2.2. Instrumental set-up

All GC analysis was carried out using a Shimadzu GC-FID equipped with an auto-injector and sampler (AI-GC-FID) (Figure 1S). Table 3S shows the operational details for the AI-GC-FID system. The 10 μL syringe equipped on the auto-injector (Shimadzu, Australia) was rinsed (with methanol) three times before and after the injection to reduce cross contamination and interference effects. The analytes were separated on an Agilent CP-WAX capillary column (30 m length, 1 mm inner diameter, and 0.53 μm film thickness). It is recommended to use a shorter length (30 m or less) and larger inner diameter (0.5 mm or more) column and a higher column flow (5 mL min^{-1} in this study) to reduce column contamination by VG due to its comparatively higher concentration and boiling point [22,23]. The GC oven temperature program was initialized at 160 °C and immediately ramped at 10 °C/min to 220 °C, with a final hold time of 2 min (total analysis time: 8 min). The injector and detector temperatures were both 250 °C. The injector was purged at 1 mL min^{-1}.

2.3. Standard calibration method (SD-CM) and spiked calibration method (SP-CM)

In general, the concentration of target compounds in an unknown sample is determined from a calibration using standards of known concentrations. Normally, we used the above mentioned calibration method (Equation 1) with the aid of an internal standard for GC analysis. An internal standard method was reported to give better repeatability and reproducibility as well as a lower relative standard deviation (RSD: approximate ≤2%) relative to an external standard method. However, the selection of a suitable compound for an internal standard that has a similar response to the actual target analyte is not necessarily simple [24,25]. In this study, quinoline was chosen as an internal standard by referring to the standard method for the determination of Nic using GC [17,18]. Nicotine (97%) and quinoline (100%) have similar FID responses, while PG (46%) and VG (32%) have relatively lower FID responses than quinoline (100%) according to the effective carbon number concept (ECN) [26]. However, relatively little is known about analytical biases when some target compounds are present in bulky quantities (i.e., PG/VG relative to nicotine) in the Cambridge filter pad method.

As a simple means to improve the analytical accuracy, a spiking calibration method (SP-CM) was used and compared to the standard calibration method (SD-CM) in Section 2.1. In this study, the generated aerosol sample was captured on a Cambridge filter pad (CFP, 44 mm, BORGWALDT, Germany). After the collection of vapors, the CFP samples were immersed in INSD and ultrasonicated (MUJIGAE, Korea). Hence, modified standard samples were prepared by simulating the experimental procedure described in detail in the next section.

Initially, five different quantities of PS (50, 100, 250, 500, and 1000 μL) were loaded on five separate fresh CFPs and left to stand for 2 min. Later, each CFP was placed in a separate brown 20 mL vial to be extracted with 10 mL of INSD through a 30 min ultrasonic treatment (Table 2S D). Then, 2 mL of each treated standard sample was transferred and filtered into a 2 mL vial (Agilent, USA). The filtering was necessary to remove CFP debris (filter medium: 13 mm diameter, 0.45 μm pore size, Whatman, USA). Finally, a 1 μL sample from each of the five SP-CM standards was collected and analyzed by AI-GC-FID for calibration.

2.4. EC auto-sampler

An EC auto-sampler designed by Chemtekins (Korea) was used for the EC aerosol generation (Figure 2S). The EC auto-sampler consists of five main parts: a pneumatic control valve, a flow controller, an EC holder, a 6-port valve, and a console. A compressed air cylinder was used to power the pneumatic control valve that automatically presses the EC button. The user defined puff duration and puff interval are adjustable from 1 to 10 s. The user defined air flow rate (accurate to ±5%) over the EC was set using an external mass flow controller (MFC) pump (VC740, Bio Lab Tech., Korea). The EC holder was principally designed for third-generation ECs. A 6-port valve was connected to the end to