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New approach for e-cigarette aerosol collection by an original automatic aerosol generator utilizing *melt-blown* non-woven fabric

Justyna Aszyk[1], *Paweł Kubica*[1,*], *Jacek Namieśnik*[1], *Agata Kot-Wasik*[1], *Andrzej Wasik*[1]

[1] Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology, 11/12 Narutowicza Street, 80-233 Gdańsk, Poland

[*]Corresponding Author:

Paweł Kubica

tel: +48 58 347 18 33

fax: +48 58 347 26 94

e-mail: pawkubic@pg.edu.pl

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Abstract

Currently, there is lack of standardized conditions for the collection and analysis of e-cigarette (EC) aerosol. Considering the urgent need for the development of these guidelines, a procedure for EC aerosol analysis was developed. A novel automatic e-cigarette aerosol generator was designed. For the first time, *melt-blown* non-woven fabric was applied for the effective uptake of compounds released from vaporized e-liquid. The extraction procedure was optimized in terms of type of extraction solvent, amount of sorbent and solvent volume. For optimization, a model e-liquid containing flavour additives belonging to various chemicals group with various chemical properties was investigated. The aerosol trapping efficiency was satisfactory and was equal to 92 ± 7%. Final determination was performed by GC-MS/MS. Quantitation was based on the mass change tracking approach (MCT), which assumes the monitoring of e-liquid mass changes before and after vaping. The combination of non-woven fabric and sampling approach (MCT) was proven to be effective in acquisition of reliable data. Thus, the concentrations in aerosol and emission factors were calculated for aerosols collected during the vaping of both model e-liquids and real samples. Validation was performed by evaluating key analytical parameters, such as linearity, accuracy, precision, limit of detection (LOD) and quantitation (LOQ). For all investigated compounds, recoveries from 70% to 118% together with precision and reproducibility below 12% were achieved. The applicability of the described approach was examined by analysing EC refill solutions commercially available on the Polish market.

Keywords

electronic cigarettes, gas chromatography–tandem mass spectrometry, smoking machine, e-cigarette aerosol collection, flavouring compounds, nicotine

1. INTRODUCTION

E-cigarettes (ECs) are becoming increasingly popular, and the current market is full of many different models and e-liquids for them. These devices are rather simple in construction and consist primarily of the battery and a tank with a heating element, and the whole device is controlled in many cases by complicated electronics [1–3], which enables users to experience unrestricted aerosol generation. Recently, scientific research has focused on analysing the chemical composition of e-liquids, which may contain many different compounds [4–10] in addition to the major ingredients, propylene glycol, vegetable glycerine, nicotine and water [5,11]. Currently, more research needs to be performed on aerosol composition and generation under many different conditions and from different EC models. To adsorb the aerosols generated during heating, simple equipment is used. For instance, the connection of a syringe to the mouth piece of the EC [12], gas washing bottles [13,14] or an EC connected to a TD (thermal desorption) tube with a syringe [15]. However, only a small number of research groups have utilized electronically controlled devices (TE-2 and TE-2E) for aerosol generation and sorption [16–18] or cigarette-smoking robots (SCIREQ, Canada) [19]. Most of the available smoking devices are designed for conventional cigarettes or are multipurpose.

The most frequently analysed substances present in the aerosol are aldehydes and carbonyl compounds [14,19–21] determined by GC-MS (gas chromatography – mass spectrometry) or by LC-MS (liquid chromatography – mass spectrometry). Other methods are based on regulations for conventional cigarettes (Health Canada, 1999. Official Method T-115. Determination of “tar”, nicotine and carbon monoxide in mainstream tobacco smoke) and were applied for determination of the main ingredients of the aerosol and for carbon monoxide, carbonyls, phenolics, other volatiles, metals, tobacco-specific nitrosoamines and polycyclic aromatic hydrocarbons [22]. However, the amounts of all of the determined compounds were below the limits of detection and/or quantitation in the aerosol samples

collected from 99 puffs. Other researchers successfully applied methods for generating aerosol to determine the same compounds in comparison with traditional smoke from cigarettes [23]. Nevertheless, the majority of research has focused on the determination of harmful and toxic substances and not on the effective isolation of the generated aerosol as a potential source of many different compounds.

Scientific research regarding the composition and formation of aerosol during the heating of e-liquid is an important task at present. At the moment, there are no standardized conditions for aerosol generation and collection. Therefore, there is a need for a simple procedure and quick aerosol generation/sorption from any available EC on the market. The task was to construct a machine that could be easily modified to have the capability to connect different models of ECs without interfering with the electronics of the tested products. Moreover, the designed collection tube can be filled with the desired solid sorbent and has the possibility to attach TD tubes. To avoid contamination of indoor air, activated carbon filters were attached. Every part responsible for aerosol collection can be easily replaced with minimal cost.

The main objective of the presented research was to optimize the conditions of aerosol generation from laboratory made e-liquids. The innovative machine has been designed as a basic tool to contain the aerosol formed during heating of the e-liquid in the EC under controlled conditions. The sorbent (*melt blown* non-woven) was chosen due to its remarkable ability to adsorb the aerosol and the easiness of eluting compounds/aerosol from its structure with popular organic solvents. According to [24,25] polypropylene *melt-blown* non-woven fabric is widely used in air filtration due to its low cost, availability, high specific surface area, compatibility with most of the organic solvents, high filtration efficiency, high chemical resistance and low pressure drop observed. Moreover, this filter media maintain its properties in acid and alkali conditions. A common EC model was used (eGo AIO) as a basis for aerosol

generation from laboratory made e-liquid. Aerosol trapping efficiency was calculated by comparing the mass lost from the e-liquid during vaping with the mass gained on the sorbent. known as MCT (mass change tracking) [20,26]. The combination of MCT along with presented aerosol collection procedure with *non-woven* fabric was simple to perform and provided reliable results. Furthermore, the presented research is the first approach to monitor the recoveries based on the exemplary flavouring compounds ratio of the e-liquid/aerosol. In addition to using the MCT approach, collected aerosols from model e-liquids and aerosols from real samples were analysed to determine the representative flavouring compounds by a previously published GC-MS/MS method [9].

2. MATERIALS AND METHODS

2.1. Design of an automatic generator of aerosol from ECs

For aerosol collection, a software-controlled innovative automatic generator of aerosol from ECs was designed in the Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology (Figure 1).

<insert Figure 1>

The scheme of the machine is illustrated in Figure 2.

<insert Figure 2>

The automatic EC aerosol generator consists of the EC (***10***), an electromagnet activator switch for the EC (***13***), a steel tube packed with replaceable *melt-blown* non-woven fabric (***8***), a TD tube (optionally) (*7*) and a polyethylene syringe (150 mL) as a suction pump (***1***). The syringe plunger is moved by an electric linear actuator (***2***) controlled by stepper motor. The number of steps taken by motor was strictly related to the puff volume. The EC, steel tube with non-woven fabric and TD tube are placed in the appropriate guides (***9***) and are connected in series with each other and mounted in connector sockets. The connector sockets

are equipped with o-rings made of Viton with appropriately selected diameters. Additionally, to avoid contamination of indoor air, an activated carbon filter (***12***) is attached. The tube packed with polypropylene *melt-blown* non-woven fabric and the TD tube are made of acid-resistant steel passivated with a SilcoNert-2000 layer.

The sorption tube is attached to the syringe via a three-way solenoid valve (***3***). The valve works in two states. In state A, the air flows from the EC through the non-woven fabric, then through the TD tube to the pump's cylinder, and in state B, the air flows out from the pump's cylinder through the electromagnetic two-way solenoid valve outside the apparatus. Similarly, the two-way solenoid valve (***4***) has two states: state A, in which the flow of air through the valve is closed, and state B, in which the flow of air is opened.

The machine functions as follows:

1) A leak test is performed to check the tightness of the pump and connections. The pressure sensor (***5***), which is located at the pump inlet, is used to measure the underpressure created in the pump cylinder during the suction step. To perform the test, the tube is plugged, and such a closed system allows checking the tightness of the pneumatic connections between individual components of the device and the tightness of the pump before conducting each puff set.

2) Indoor air is pressed by a diaphragm pump (***11***) and purified through an activated carbon filter (***12***).

3) After 20 s from the start-up of the pump, the following parts are turned on:

a) the power supply of the electromagnet activator (***13***), which turns on the EC device (***10***)

b) subsequently, after 1s, the power supply of syringe plunger actuator (***2***) moves the syringe plunger with the specified suction speed to move the generated aerosol in the stream of purified air to the collection tube filled with non-woven fabric. The underpressure created during this process is measured by a pressure sensor.

3) After introducing the specified air volume into the syringe, the piston of the actuator is stopped.

4) After the pressure in the syringe equilibrates with the atmospheric pressure (up to 1.5 second), the three- and the two-way solenoid valves are switched to position B, and the actuator moves the plunger to the zero position. The air from the syringe is removed from the machine through the activated carbon filter (***6***).

5) The three- and two-way solenoid valves are switched to position A.

6) The device is subsequently ready for the next work cycle. The number of puffs, the puff-to-puff interval, puff time and the puff volume are entered by the user into the controller programme.

In this study, polypropylene melt-blown non-woven fabric was applied. Fabrics produced using *melt-blown* technology have high packing densities. This allows the retention of dispersed liquid-phase particles of aerosol and facilitates high coalescing properties. Round discs of 26.3 ± 3 mm diameter (n=10 of randomly selected discs) were cut using a hole cutter from a *melt-blown* non-woven sheet (Figure 3). The discs were packed one-by-one in the stainless steel collection tube (internal diameter equal to 26.0 mm). The mass of each disc was equal to 286 ± 21 mg (*n*=10 of randomly selected discs). Therefore, the amount of sorbent was expressed in the number of discs instead of mass. The discs were utilized several times after the cleaning steps. The washing procedure for the melt-blown discs involved stirring the discs with different solvents in the following sequence: deionized water, MeOH for 10 min using an ultrasonic bath, and drying in a drying oven at 100°C for 20 min. Notably, each disc can be effectively used within 10 repeated cycles. After this time, discs adopted the heterogeneous structure caused by washing with MeOH and drying. Therefore, suggested limit of use per one discs is equal to 10 repeated puff sessions

<insert Figure 3>

2.2. Reagents and standards

All of the following standards were obtained from Sigma-Aldrich (St. Louis, USA): 2-acetylpyridine, 2-acetylpyrrole, 2-isopropyl-4-methylthiazole, 2,3,5-trimethyl-pyrazine, 2,3,5,6-tetramethylpyrazine, 4-methyl acetophenone, benzaldehyde, benzyl acetate, benzyl alcohol, ethyl vanillin, ethyl 3-(methylthio)propionate, ethyl maltol, eugenol, furaneol, furfural, isoamyl isovalerate, isopentyl acetate, leaf aldehyde, leaf alcohol (*cis*-3-hexen-1-ol), L-menthyl acetate, maltol, melonal, menthol, menthone, methyl cyclopentenolone, n-hexanol, nicotine, theaspirane, *trans*-2-hexenol, vanillin, β-damascone, γ-nonanolactone, γ-undecalactone, γ -decalactone. Naphthalene-d_8 was used as the internal standard (IS) and was purchased from Isotec/Sigma-Aldrich (St. Louis, USA). Vegetable glycerine (VG) and propylene glycol (PG) were purchased from Anwit (Warsaw, Poland), while acetonitrile (ACN) and methanol (MeOH) (MS grade) were obtained from Merck (Darmstadt, Germany). Ethyl acetate (MS grade) was obtained from Sigma-Aldrich (St. Louis, USA).

Melt-blown non-woven sheets were obtained from Eko Komes (Kolnik, Poland).

2.3. Standards, calibration solutions and validation formulations

Standard stock solutions of the flavours and the IS (naphthalene-d_8) were prepared separately in ACN (5 mg/mL). The working standard mixture of the analytes was prepared by diluting the standard stock solutions with ACN to obtain a solution with a concentration of 100 µg/mL of each substance.

Six calibration solutions (n=3) were prepared in aerosol-blank MeOH extracts spiked with target analytes within the studied concentration range (50–5000 ng/mL). Calibration curves were constructed using the peak area ratio (analytes vs IS) plotted against the corresponding concentration. The concentration of the IS in every solution was kept at 500

ng/mL. In certain cases, the analyte concentration was higher than calibration curve range, for which the samples were later diluted 50-fold to fall within the mentioned concentration ranges.

Blank aerosol extracts were prepared by collecting 10 puffs of vaporized e-liquid prepared from PG (65%), VG (30%), and H_2O (5%) produced with an eGo AIO EC. Blank aerosols were analysed with the same equipment and reagents used for the EC emission analysis.

For extraction optimization, a model e-liquid was prepared by dissolving standards of target analytes in analyte-free prepared e-liquid to obtain concentrations of each substance equal to approximately 1 mg/mL. For method validation, three e-liquids were prepared on the same basis at three concentration levels (0.02, 0.05, 0.4 mg/mL of analyte-free e-liquid) of target analytes. These samples underwent the same aerosol collection and extraction procedures as the real samples did. Validation samples were used for evaluation of the accuracy and precision of the developed procedure.

2.4. Composition of model e-liquid

The test model e-liquid was applied to investigate the effect of the extraction parameters to remove analytes from the *melt-blown* discs on the recoveries. The laboratory selected 33 representative flavour compounds belonging to 11 groups of compounds and nicotine to cover the range of physical and chemical properties of compounds that are intended to be determined in aerosol. For each class of compounds, two to four representative compounds were chosen. The studied analytes are representatives from various groups of flavour chemicals, namely, aldehydes (leaf aldehyde, furfural, benzaldehyde, melonal), ketones (4'-methyl acetophenone, methyl cyclopentenolone, β-damascone), alcohols (n-hexanol, *trans*-2-hexenol, *cis*-3-hexen-1-ol, benzyl alcohol), esters (isopentyl acetate, isoamyl isovalerate, benzyl acetate), furans and furanoids (theaspirane, furaneol), terpenes and

terpenoids (menthol, menthone, L-menthyl acetate), sulphur-containing compounds (ethyl 3-(methylthio)propionate, 2-isopropyl-4-methylthiazole), phenols (vanillin, ethyl vanillin, eugenol), nitrogen-containing compounds - pyrroles, pyrazines, pyridines (2-acetylpyridine, 2-acetylpyrrole, 2,3,5-trimethylpyrazine, 2,3,5,6-tetramethylpyrazine), pyranones (maltol, ethyl maltol), lactones (γ-nonanolactone, γ-undecalactone, γ-decalactone) and nicotine.

2.5. Test product selection

One EC product (eGo AIO) was used in the current work. The EC device consists of a mouthpiece; an atomizer consisting of a 2 mL-cartridge for EC refill solution storage, a coil made of steel wire and a wick with a resistance of 0.6 Ω; and a 1500 mAh USB-rechargeable battery. The EC battery needed to be fully charged before conducting each puff set. This approach was required to maintain the same conditions for the generation of aerosol. The cartridge was filled to the upper marked line of the tank (80% of its volume) every time to ensure sufficient supply of liquid to the heating element and to avoid occurrence of ”dry puff” conditions. For each model e-liquid and all real samples, a separate coil was used. To avoid cross contamination, all parts of the EC that made contact with the liquid and/or aerosol were cleaned with water and isopropanol after every collection set.

2.6. Real samples

Eight e-liquid samples were investigated to demonstrate the applicability of the developed procedure. E-liquids were bought on the local market from four companies. The concentrations of flavouring compounds in the samples were quantitated using a recently published procedure [9]. The selected e-liquids were labelled containing nicotine with concentration ranges of 6 to 18 mg/mL in tobacco, vanilla, menthol, cherry and apple flavours. Samples were analysed within two weeks of purchase. Each sample was stored at room temperature without sunlight, similar to the shop conditions.

2.7. Aerosol generation parameters

The puffing protocol consisted of 4-s-duration puffs (puff volume of 50 mL) and inter-puff periods of 15 s. Each puffing session included a total of 10 puffs. The average puff volume (n=50) was equal to 50.57 ± 0.09 mL, while actual flow rate (based on calculated puff volume) was equal to 12.64 ± 0.02 mL/s. The topography of e-smoking investigated in this study was within the ranges reported in previous studies [27,28]. The square wave puff profile expressed as created pressure overt time of puff is presented on the Figure S1.

The mass change tracking (MCT) approach, in which the consumed amount of EC solution was monitored regarding each variable, was used [26].Since the consumption rate of the e-liquid is controlled by a large number of variables, quantitation results based on the simple criterion of "pollutant mass per puff" basis cannot be easily reproduced. The MCT approach allows the study of the conversion of liquid to aerosol on the basis of the quantity of e-liquid consumed and estimation of the emission rate through direct quantitation of the analytes (transferred or converted). Thus, the mass change of the EC solution before and after vaping and the weight of the vaporized e-liquid adsorbed onto the *melt-blown* discs was monitored.

2.8. Extraction of analytes from *melt-blown* non-woven discs

After aerosol collection, 10 mL of MeOH was added into the tube containing the discs and left for 10 min to facilitate the extraction process. Subsequently, aerosol extracts were gravitationally collected into a 15 mL glass tube. The extraction solution residue was removed by blowing a stream of air. An aliquot of 990 µL of aerosol extract was transferred into an autosampler vial, and 10 µL of IS working solution was added. Assuming that in every puff set, approximately 100 mg of aerosol was collected and elution was performed with 10 mL of solvent, the aerosol samples were diluted nearly 100-fold before analysis.

2.9. Quality assurance/quality control

To assess possible background contamination by target compounds within the analytical equipment and to distinguish between potential background contaminants and actual EC emissions, blank samples were collected. Background blank measurements were performed by collecting 10 puffs of vaporized analyte-free prepared e-liquid and analysing the aerosol with the same equipment and reagents used for the EC emission analysis. Blank samples were collected after cleaning the EC parts followed by changing of the EC refill solutions and heating element. Meanwhile, to avoid possible contamination, all equipment (EC cartridge and stainless steel tube) was washed with isopropanol before conducting each puff set. No peaks from target analytes were observed in the blank samples (Figure S2), which proved that the cleaning procedures were properly set.

2.10. GC-MS/MS parameters

GC-MS/MS analysis was performed on a Shimadzu GC-2010 PLUS System coupled with a Shimadzu TQ8050 triple quadrupole mass spectrometer (Kyoto, Japan). Separation of the target compounds was achieved with a Phenomenex ZB-5 MSi (30 m x 0.25 mm i.d., 0.25 µm film thickness) capillary column. A split injection mode (1:10) of 2 µL was applied. The oven temperature programme was set as follows: 50°C for 4 min, 10°C/min to 130°C, then 25°C/min to 300°C and a hold for 3 min. The parameters were set as follows: temperature of the transfer line: 285°C; injector temperature: 250°C; and ion source temperature: 220°C. Helium (purity ≥ 99.999%) was applied as a carrier gas at an initial flow rate of 1 mL/min, and then the linear velocity was controlled at 36.6 cm/s by the system. Argon (purity ≥ 99.999%) was applied as the collision-induced dissociation (CID) gas. The specific MRM conditions were set to those used in a previous study [9]. Two MRM transitions (quantifier and qualifier) were monitored. Additionally, for verification of the presence of the target compounds in each sample, the quantifier/qualifier transitions ratios were monitored. Established MRM ratios in the investigated e-liquid samples were required to be within ±

20% of those recorded for analytes in the standard solutions. Data acquisition and quantitation were accomplished using GCMS Solution and Insight software (version 4.45, Shimadzu Corporation). The chromatogram obtained during analysis of the standards mixture in the aerosol extract is presented in Figure S2.

3. RESULTS

3.1. Optimization of the extraction procedure

A series of preliminary experiments was performed to achieve satisfactory recovery of the tested compounds from the *melt-blown* non-woven discs. The extraction process was optimized in terms of the following key parameters affecting the extraction process: the type of solvent, the number of *melt-blown* discs and the extraction solvent volume. The recoveries (%) were calculated as the ratio of the mass of each compound emitted from a single 10-puff session to the mass of the compound in the consumed e-liquid.

3.2. Effect of the extraction solvent

Three solvents (methanol, acetonitrile and ethyl acetate) differing in polarity index and one mixture of solvents (acetonitrile:methanol, 1:1, *v*/*v*) were employed for evaluation of the extraction efficiency of the analytes. Aerosol generation and collection steps were performed as indicated in section 2.7. The effect of solvent type on the extraction efficiency under the preliminary extraction conditions (solvent volume: 40 mL, extraction time: 10 min, number of *melt blown* discs: 8) was investigated. The results are shown in Figure 4. The recoveries of the tested compounds were in the ranges of 74% to 107% (CV=0.2–11%) for MeOH, 74% to 120% (CV=0.5–23%) for ACN, 56% to 114% (CV=1.3–30%) for ethyl acetate and 37% to 78% (CV=1.8–16%) for the mixture of ACN:MeOH (1:1,*v*/*v*). Among the solvents tested, MeOH was identified as the most effective extraction solvent. One of the reasons for this result may be the amphiphilic character of MeOH. This allows it to effectively extract tested compounds which vary in polarity. Although comparable values of recoveries were observed

for ACN, MeOH is considered as less toxic and "greener" than ACN [29]. In addition, the low values of CVs obtained with MeOH indicated the highest degree of precision and reliability of the experiments among the tested solvents.

<insert Figure 4>

3.3. Effect of the number of *melt-blown* discs

To select the number of *melt-blown* discs for effective adsorption of analytes from the aerosol, experiments were conducted with 4–8 *melt-blown* discs. The preliminary extraction conditions (extraction time: 10 min and 40 mL of MeOH) were used. In this experiment, an empty glass tube was additionally installed on the stainless tube packed with sorbent to visually monitor possible aerosol breakthrough across the non-woven fabric. Figure 5 summarizes the final results of the evaluation experiments in terms of recoveries of compounds. When five or more discs were used, recoveries distributed approximately 100% with CVs below 14% were obtained. Lower recoveries (<59%) and low repeatability (CVs values up to 50%) were yielded in the case when four discs were used. Moreover, visual aerosol breakthrough across the non-woven fabric also resulted in the decrease of the percent recovery of aerosol by nearly 10%. No further reduction either in aerosol or analytes recovery was observed with use of more than 5 discs. Thus, after reviewing all aspects described above, a number of discs equal to 5 was finally chosen.

3.4. Effect of the MeOH volume

Once the number of *melt-blown* discs was selected, the optimization process was focused on adjustment of the MeOH volume. The effect of the MeOH volume was studied in the range of 10 to 40 mL. In this experiment, the volume of 10 mL was the smallest volume of extraction solvent to completely immerse the *melt-blown* discs. Based on the obtained results (Figure 6), recoveries were in the range of 72% to 118% with CVs below 17%,

regardless of the solvent volume tested. When a lower volume than 10 mL of solvent was used, low repeatability was observed due to the ineffective desorption of analytes (data not shown). Application of 10 mL of MeOH resulted in high recoveries in the ranges 74-117%, together with low CVs values ≤ 12%. Moreover, elution with an additional 10 mL portion of MeOH did not result in any further elution of analytes. Hence, 10 mL of MeOH was used in future experiments.

<insert Figure 5>

<insert Figure 6>

3.5. Aerosol trapping efficiency

The use of an MCT approach should be considered a prerequisite for the establishment of simple and general guidelines needed for an EC sampling protocol. Tracking the mass of consumed e-liquid allowed precise determination of the percent recovery of aerosol. Before conducting each experiment, both the EC device and the collection tube filled with *melt-blown* discs was weighed before and after vaping. Fifteen randomly selected samples were used for calculation of the recovery of aerosol. The average weight of consumed e-liquid under the optimized conditions was 106 ± 12 mg. The average weight of vaporized e-liquid adsorbed onto the *melt-blown* discs was 99 ± 14 mg. Therefore, the percent recovery of aerosol on the *melt-blown* discs was equal to 92 ± 7% after a 10-puff session on the tested EC device. The incomplete recovery of aerosol may have been a result of condensation of aerosol on the surface of the cold mouthpiece and parts of the machine, thermal decomposition of PG and VG to CO_2 and steam or direct generation of steam from water present in the e-liquids. Part of aerosol may be deposited in the vapour phase and not collected on the non-woven fabric surface or evaporated before performance of gravimetric analysis, which corresponds to the previous research [30].

3.6. Method validation

The method outlined in the present study was validated according to the guidelines for analytical method validation [31–33]. The GC–MS/MS matrix effects were investigated as described in previous research [9,34]. Six calibration solutions (n=3) were prepared in MeOH and in MeOH aerosol blank extracts spiked with target analytes. For 75% of the tested compounds, negligible matrix effects (≤± 20%) were observed. Nonetheless, some compounds exhibited significant ion enhancement (74.7%, 47.2%. 51.3%, 151.5%, 81.8%, 36.3%, 53.6%, 32.2% for methyl cyclopentenolone, benzyl alcohol, 2-acetylopyrrole, maltol, ethyl maltol, nicotine, vanillin and ethyl vanillin, respectively), as observed and explained in

previous research [9]. In view of the above results, matrix-matched calibration curves were employed for quantitation and validation purposes.

The linearity of the calibration curves was assessed within a concentration range of 50 to 5000 ng/mL (final concentration in aerosol extracts**)** at six concentration levels (n=3). Calibration curves were linear with coefficients of determination (r) greater than 0.997 (**Table S1**).

The limit of detection (LOD) was calculated according to the following formula: $LOD=3.3*S_b/a$, where S_b is the standard deviation of the intercept of the calibration curve and a is the slope of the calibration curve [7–9]. The limit of quantitation (LOQ) was defined as *3*LOD*. Quantitation limits varied between 40 and 150 ng/mL in the aerosol extracts, which correspond to 0.04 ng of substance emitted/mg of consumed e-liquid and 15 ng of substance emitted/mg of consumed e-liquid, with assumption of a 100-fold dilution of the aerosol.

The accuracy was assessed by determination of the recovery in spiked samples at three concentration levels. The accuracy was in the range between 70% and 118%, regardless of the spiking level. The precision of the method was investigated by examining the repeatability and intermediate precision conditions. The inter-day precision of the developed method was verified by the analysis (n=9) of model e-liquid with a concentration of 0.05 mg/mL of each substance over three days. The precision of the method was expressed as the values of the coefficients of variation (CV). Both the intermediate precision and repeatability were satisfactory, showing CV values ≤ 11% and ≤12%, respectively. The accuracy and precision data are summarized in **Table S2**.

3.7. Analysis of real samples

The applicability of the developed method was evaluated by analysing eight e-liquid samples available on the Polish market. An example chromatogram obtained during analysis of aerosol from one of the vaporised e-liquids is shown in Figure S2. The presented analytical

protocol was adequate for fast determination of the emission rates of compounds from e-liquid to aerosol. The obtained results are shown in Table 1. The concentrations of compounds in the aerosol were expressed as the ratio of the mass of each compound emitted to the mass of e-liquid consumed and expressed in ng/mg. The ratio was calculated according to the following formula:

$$C_{aerosol}\left[\frac{ng}{mL}\right] = \frac{Detected\ compound\ concentration\left[\frac{ng}{mL}\right] * 10\ mL}{Consumed\ EC\ solution\ during\ 10\ puff\ [mg]} \quad (1)$$

Emission factors were calculated as the ratio of the mass of each compound emitted to the mass of the aerosolized compounds and given in %.

$$EF\ [\%] = \frac{Detected\ compound\ concentration\left[\frac{ng}{mL}\right] * 10\ mL}{consumed\ EC\ solution\ during\ 10\ puff\ [mg] * concentration\ in\ EC\left[\frac{mg}{g}\right] * 10^6} * 100\% \quad (2)$$

Concentrations varied from tens to a few thousands of nanograms of flavours per milligram of e-liquid vaporized. Based on the results, compounds were released at high rates ranging from 69% to 116%. Incomplete release of compounds into the aerosol may result from a too-low heating temperature of the e-liquid or a too-high temperature which leads to the formation of thermal degradation products. Nonetheless, it is suspected that the composition of the sampled aerosol strictly reflects the composition of aerosol inhaled by the EC end-user.

Overall, only small variations in the emission factors for the compounds were observed across the investigated e-liquids, suggesting that the main source of these differences was in the e-liquid compositions from different manufacturers. Emission factors of specific compounds were similar to the recoveries obtained during method validation, which proves the reproducibility of the proposed method.

<insert Table 1>

4. DISCUSSION

The parameters and instrumentation used in this study, as well as the parameters described in the literature, are presented in Table 2. The wide range of vaping parameters and instrumentation demonstrates the lack of standardization in methodologies for aerosol generation from ECs [4]. To the best of the authors' knowledge, the presented work is the first attempt at applying the GC–MS/MS technique for simultaneous determination of the flavouring compounds and nicotine in aerosol generated from ECs. Additionally, the proposed analytical protocol offers several advantages, including enhancement of the sensitivity and selectivity. Comparing the presented protocol with others described in the literature, the number of puffs required for determination of analytes is sharply reduced—only one 10-puff session is sufficient to quantify the target analytes. Importantly, for the developed method, the estimation of aerosol recovery within the analytical equipment and full validation was performed. This approach is an advantage in comparison to published studies, wherein no information on the aerosol generation process yield was reported. Providing the concentrations of compounds in aerosol without proper estimation of the recovery of aerosol and analytes may cause problems in repeatability and raise uncertainties about whether the method fulfils the acceptance criteria for analytical method validation. Yield estimation is important for assessing the performance of the method and for interpretation of the data obtained. In the authors' opinion, such an approach should be required for all analyses of aerosol generated from EC. The use of a *melt-blown* non-woven sorbent proved to be an excellent choice for the adsorption of aerosol and analytes. The presented sorbent can be taken into account as an important part in the construction of a smoking machine for effective aerosol collection.

<insert Table 2>

Another limitation of published studies is that most of them provide concentrations as the mass of compounds per number of puffs (Table 2). Expressing the content of compounds

in one aerosol puff causes considerable confusion because such simplification does not include the puff duration, the puff interval or the number of puffs taken during one session. Furthermore, comparison of the results across different studies is challenging due to the fact that there is no strict definition of the parameters describing a puff. The concentrations of analytes in the collected puffs may vary as the parameters for the generation of aerosol vary. It should be clearly emphasized that there is a need for strict control of liquid loss and weight gain on used sorbents. However, the correct approach to use MCT is more clearly stated in the recent researches (Table 2) to evaluate the content of target compounds in aerosol.

The presented approach allows decoupling of the results from the smoking topography (standardization of results). The protocol reported provides results in concentration units [ng/of consumed e-liquid], which permits comparison of the results between studies. Few limitations were observed during the research. The lengthy procedure was needed to clean the discs after each collection of aerosol and as mentioned before observed limited use of sorbent was up to 10 times. Nevertheless, the sheets of melt-blown fabric are incomparably cheaper (~4€/1 m^2) than other typical sorbents commonly used, hence discs can be treated as disposable.

4. CONCLUSIONS

To the best of our knowledge, this report describes the first attempt at quantitation of 33 flavouring compounds and nicotine by a GC–MS/MS method in aerosol generated from EC. An innovative EC aerosol generator has been built for effective (recovery of aerosol above 90%) and repeatable aerosol sampling. The *melt-blown* non-woven discs, together with extraction using a small MeOH volume, was found to be a productive adsorption and desorption system for various classes of flavour additives (represented by the selected analytes) present in aerosol particles. The suitability of the developed method was evaluated in terms of matrix effects, recovery, linearity, accuracy and precision with the use of a model

e-liquid. Satisfactory intermediate precision (RSD ≤ 11%) and recoveries ranging from 70 to 118% were obtained. The low LODs, satisfactory accuracy, repeatability and sensitivity make the proposed method adequate for characterization of aerosol compositions. Accurate quantitation of the masses of emitted compounds was possible with the use of matrix matched-calibration standards and an MCT approach using *non-woven* fabric as a sampling media. The emission factors of flavouring compounds and nicotine were estimated with the aid of this approach in the investigation of several commercial EC refill liquids. The emission factors obtained from analysis of real samples were consistent with those obtained from analysis of the model e-liquid, which proves the suitability of the method for surveillance of EC samples. High emission factors suggested that the quantified analytes are directly inhaled by the EC user.

Future work could investigate of the feasibility of this analytical protocol for determination of other compounds intended to be present in aerosol, such as tobacco-specific nitrosamines, aldehydes or metals.

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List of tables:

Table 1 Concentration of compounds in the aerosol of vaporised investigated e-liquids and emissions factors

E-liquid description		E-liquid composition		Aerosol composition		
Brand	***Taste***	**Compound**	**Concentration [mg/g ± SD (n=3)]**	**Concentration in aerosol (the mass of each compound emitted to the mass of e-liquid consumed) [ng/mg ± SD (n=3)]**	**Emission factor (mass of each compound emitted to the mass of the aerolised compound) [% ± SD (n=3)]**	**Consumed quantity (mg) e-liquid solution per puff [mg ± SD (n=3)]**
A	Strawberry	Nicotine	5.7 +/- 0.2	6406 +/- 457	108 +/- 1	13.2 +/- 0.8
		Isopentyl isovalerate	0.082 +/- 0.001	81 +/- 8	99 +/- 10	
		γ – decalactone	0.279 +/- 0.02	266 +/- 26	95 +/- 9	
B	Vanilla	Nicotine	16.5 +/- 0.3	17728 +/- 2579	108 +/- 16	11.8 +/- 0.4
		Vanillin	2.07 +/- 0.02	1473 +/- 83	71+/- 4	
		Ethyl vanillin	0.905 +/- 0.02	830 +/- 123	92 +/- 14	
		Ethyl maltol	0.171 +/- 0.01	134 +/- 7	78 +/- 4	
B	Menthol	Nicotine	16.3 +/- 0.3	15210 +/- 1987	93 +/- 12	10.8 +/- 1.6
		Menthol	7.3 +/- 0.1	77310 +/- 3644	99 +/- 11	
		L-menthyl acetate	1.387 +/-0.03	1417 +/- 169	102 +/- 12	
		Menthone	2.313 +/-0.03	2043 +/- 195	88 +/- 10	
		Ethyl maltol	0.297 +/- 0.01	203 +/- 51	68 +/- 17	
		Benzyl acetate	0.059 +/- 0.004	57 +/- 8	99 +/- 13	
C	Crisp mint	Nicotine	5.7 +/- 0.3	6242 +/- 41	109 +/- 1	10.5 +/- 1.4
		Menthol	11.2 +/- 0.2	12144 +/- 331	110 +/- 3	
		L-menthyl acetate	0.119 +/-0.008	103 +/- 19	87 +/- 12	
		Menthone	0.504 +/- 0.008	505 +/- 75	100 +/- 5	
D	Cherry	Nicotine	5.4 +/- 0.2	6466 +/- 287	107 +/- 5	9.1 +/- 0.7
		Benzaldehyde	0.272 +/- 0.009	224 +/- 11	82 +/- 4	
		cis-3-hexen-1-ol	0.455 +/- 0.009	384 +/- 59	84+/- 13	
		trans-2-hexen-1-ol	0.288 +/- 0.008	272 +/- 35	94 +/- 12	
		n-Hexanol	0.311 +/- 0.009	352 +/- 45	113 +/- 14	
		Vanillin	1.12 +/- 0.04	913+/- 29	82 +/- 3	
		Benzyl alcohol	0.032 +/- 0.0007	32+/- 4	98 +/- 12	
		Ethyl maltol	0.118+/- 0.02	88 +/- 10	74 +/- 8	
C	Apple	Nicotine	5.9 +/- 0.2	6237 +/- 448	112 +/- 8	12.3 +/- 0.7
		cis-3-hexen-1-ol	0.127 +/- 0.003	139 +/- 17	97 +/- 10	
		Menthol	0.559 +/- 0.02	633 +/- 18	101 +/- 4	
		Isopentyl acetate	0.045 +/- 0.007	35 +/- 7	69 +/- 13	
B	Black Tea	Nicotine	16.0 +/- 0.5	14568 +/- 894	91 +/- 6	12.7 +/- 0.7
		Benzaldehyde	0.919 +/- 0.03	771 +/- 18	84 +/- 2	
		cis-3-hexen-1-ol	0.011 +/- 0.004	12 +/- 1	108 +/- 13	
		Benzyl alcohol	0.01 +/- 0.001	8.9 +/- 0.8	98 +/- 9	
		n-hexanol	1.10 +/- 0.03	903 +/- 72	82 +/- 7	
B	Tobacco	Nicotine	17.9 +/- 0.9	21552 +/- 4294	104 +/- 15	11.6 +/- 0.2
		Ethyl maltol	0.41 +/- 0.03	317 +/- 36	78 +/- 9	
		Methyl cyclopentenolone	1.05 +/-0.02	985 +/- 132	82 +/- 7	
		β - damascone	0.046 +/- 0.002	53 +/- 7	116 +/- 15	

• **Table 2** Comparison of the selected analytical parameters and instrumentation used for aerosol generation and determination (*N.A. – no information available)*

Analyte	Aerosol collection method	Final determination	Emission	Smoking machine	Puff duration [s]	Puffs/ session	Total puffs	Series	Ref.
Flavourings and nicotine	*melt-blown* nonwoven layer	GC-MS/MS	Overall: 12 +/- 1 to 21552 +/- 4294 (ng/mg of vaporized e-liquid	Lab-built device	4	10	10	1	This study*
Nicotine	Fritted cylinder	HPLC-DAD	0÷43.2 µg/100 ml puff	Lab-built device	2	30	N.A.	N.A.	[35]
Carbonyls	Adsorbent cartridge: DNPH coated silica gel	HPLC-UV	Formaldehyde: 24÷1559 ng/puff Acetaldehyde: 13÷350 ng/puff Acrolein: 2.5 ng/puff	Borgwaldt RM-1 Plus smoking machine	3	10	10	N.A.	[36]
VOCs	Carbopack sorbent	ST/TD-GC-MS	p-xylene: 30.1 methyl ethyl ketone:398 acetic acid: 166 to i-butyric acid: 5,850 (mass in aerosol/ consumed solution (ng/mL) .	ST connected to tube packed with Carbopack X and the vacuum pump interfaced with the mass flow controller	1-3	1-2	2	N.A.	[37]*
TSNAs	Gas washing bottles with methanol	UPLC-MS/MS	NNN: ND to 28±16 ng/ puff NNK: ND to 189±88 ng/150 puffs	Palaczbot	1.8	15	150	10	[18]
Flavours	PFBHA in a ethyl alcohol and water solution	GC-FID	Diacetyl: < LOQ to 239 2,3-Pentanedione: up to 64 Acetoin: 529 (µg/e-cigarette)	Lab-built device	N.A	N.A	N.A	N.A	[10]
Alkaloids	Gas washing fritted cylinder with acetonitrile and water	HPLC-DAD	Anatabine: 0.02-0.82 µg/device	Lab-built device	2	30	N.A.	N.A.	[35]
Metals	Gas washing bottles with methanol	ICP-MS	Cd: ND to 0.22±0.16 Ni: 0.11±0.05 to 0.29±0.08 Pb: 0.03±0.03 to 0.57±0.28 (µg/150 puffs)	Palaczbot	1.8	15	150	10	[18]

Carbonyls	Adsorbent cartridges: DNPH derivatization	HPLC-UV	Formaldehyde: 1.84 ÷ 8.31 Acetaldehyde: 7.03 ÷ 13.1 Acetone: 0.85 ÷ 1.24 Butyraldehyde: 2.31 ÷ 2.61 o-tolualdehyde: 14.8 ÷ 16.4	Lab-built device consisting of mini-vacuum pump	2	5,10,15	5,10,15	1	[38]*
Carbonyls	Adsorbent cartridges: DNPH derivatization	HPLC-UV	Formaldehyde: 10.4 ± 3.10 µg/mL(27.6 ± 7.43 ng/puff), Acetaldehyde 1.9 ± 0.83 µg /mL (4.4 ± 1.98 ng/puff) Butyraldehyde: 4.4 ± 2.82 µg/mL(12.0 ± 7.43 ng/puff)	Lab-built device consisting of mini-vacuum pump	2	5,10,15	5,10,15	1	[20]
Carbonyls	Cambridge filter pad/Glass impringer with DNPH	UPLC-MS	Formaldehyde: 0.07 ÷ 14.1 Acetaldehyde: 0.03 ÷ 13.61 Acrolein: <LOQ to 4.11 Crotonaldehyde: <LOD to 0.04	linear 5-port smoking machine (KC Automation, Richmond, VA)	4	20	20	1	[14]
Alkaloids	Carbopack sorbent tube	TD-GC-MS	Nicotyrine: for 3.8 V: initial (N.D. to 3459), steady state (N.D. to 6287); 4.8 V, initial (1580-1953), steady state (5439-6969) (ng per mg of consumed e-liquid) -By increasing the voltage applied to a single-coil device from 3.3 to 4.8 V, the mass of e-liquid consumed doubled from 3.7 to 7.5 mg puff	Laboratory made smoking-machine	5	50 (each puffing cycle)	50	1	[39]*
Flavours	Carbopack sorbent tube	TD-GC-MS	Diacetyl: for 3.8 V: initial (7 to 167), steady state (N.D. to 438); 4.8 V, initial (27-293), steady state (267-433) (ng per mg of consumed e-liquid)	Laboratory made smoking-machine	5	50 (each puffing cycle)	50	1	[39]*
Metals	The pipette tip-based e-cigarette collection system	ICP-qqq-MS	Ni: 4.35×10^{-6} to 1.12×10^{-1} Cr: 7.97×10^{-7} to 2.95×10^{-2} Pb: 1.49×10^{-6} to 2.75×10^{-2} Mn: 1.39×10^{-6} to 1.42×10^{-3} (mg/m^3), converted from mass fractions (µg/kg)	Lab-built device consisting of peristaltic pump	4	30-50	30-50	1	[40]

List of figures:

Figure 1. Automatic generator of aerosol from electronic cigarettes designed and constructed in the Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology

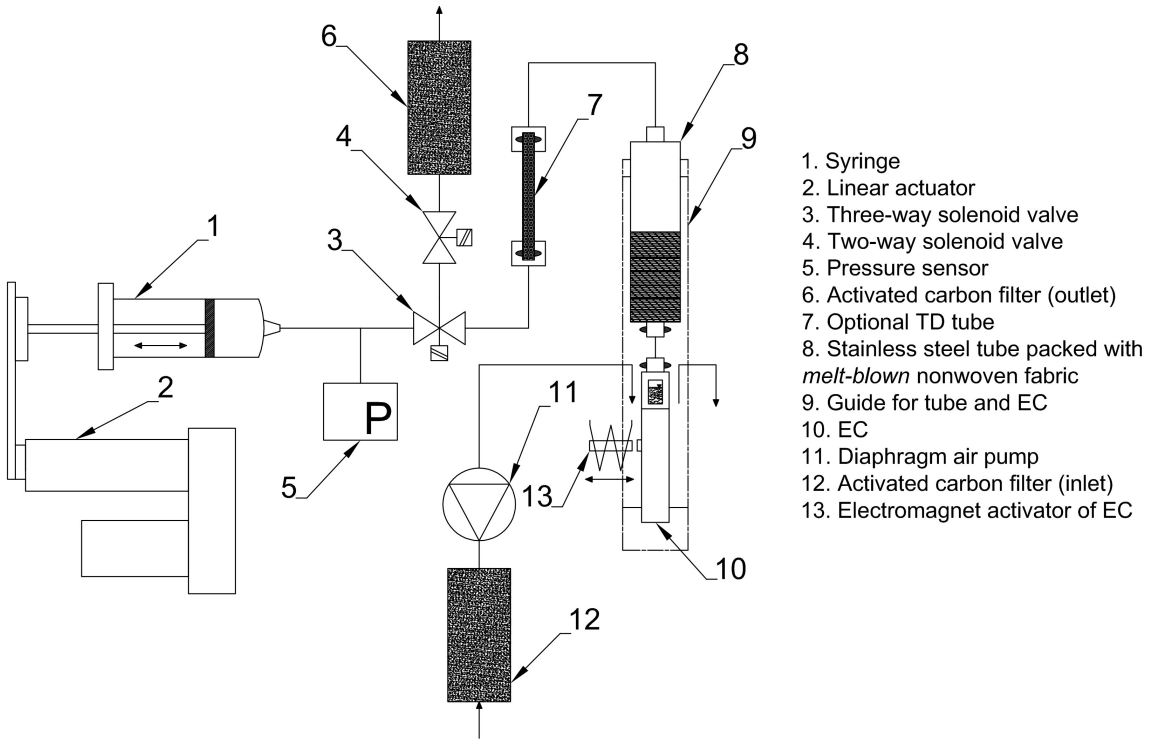

Figure 2. Scheme of the machine

Figure 3. *Melt-blown* discs

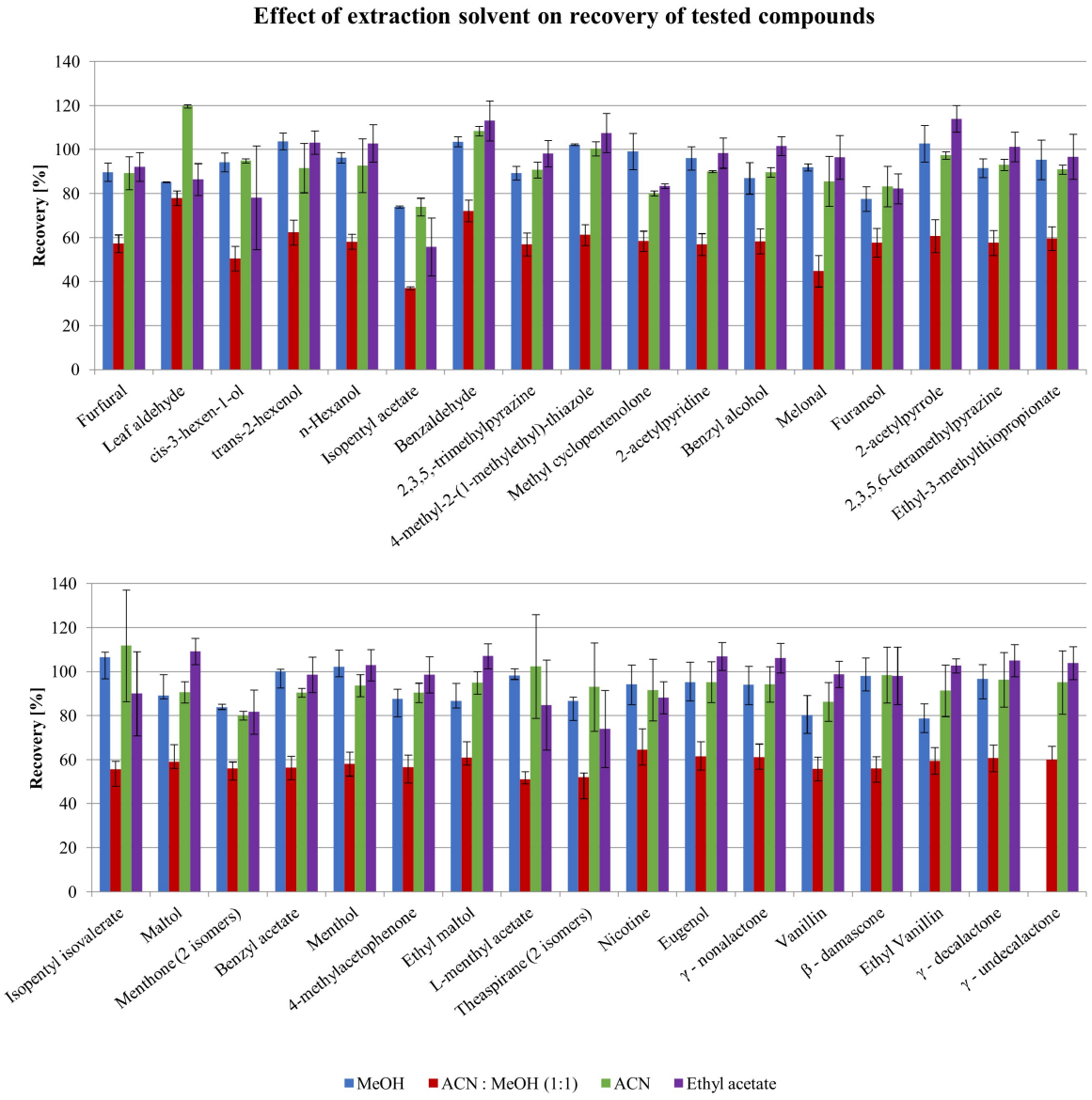

Figure 4. Selection of the extraction solvent based on the recovery of tested compounds from *melt-blown* discs

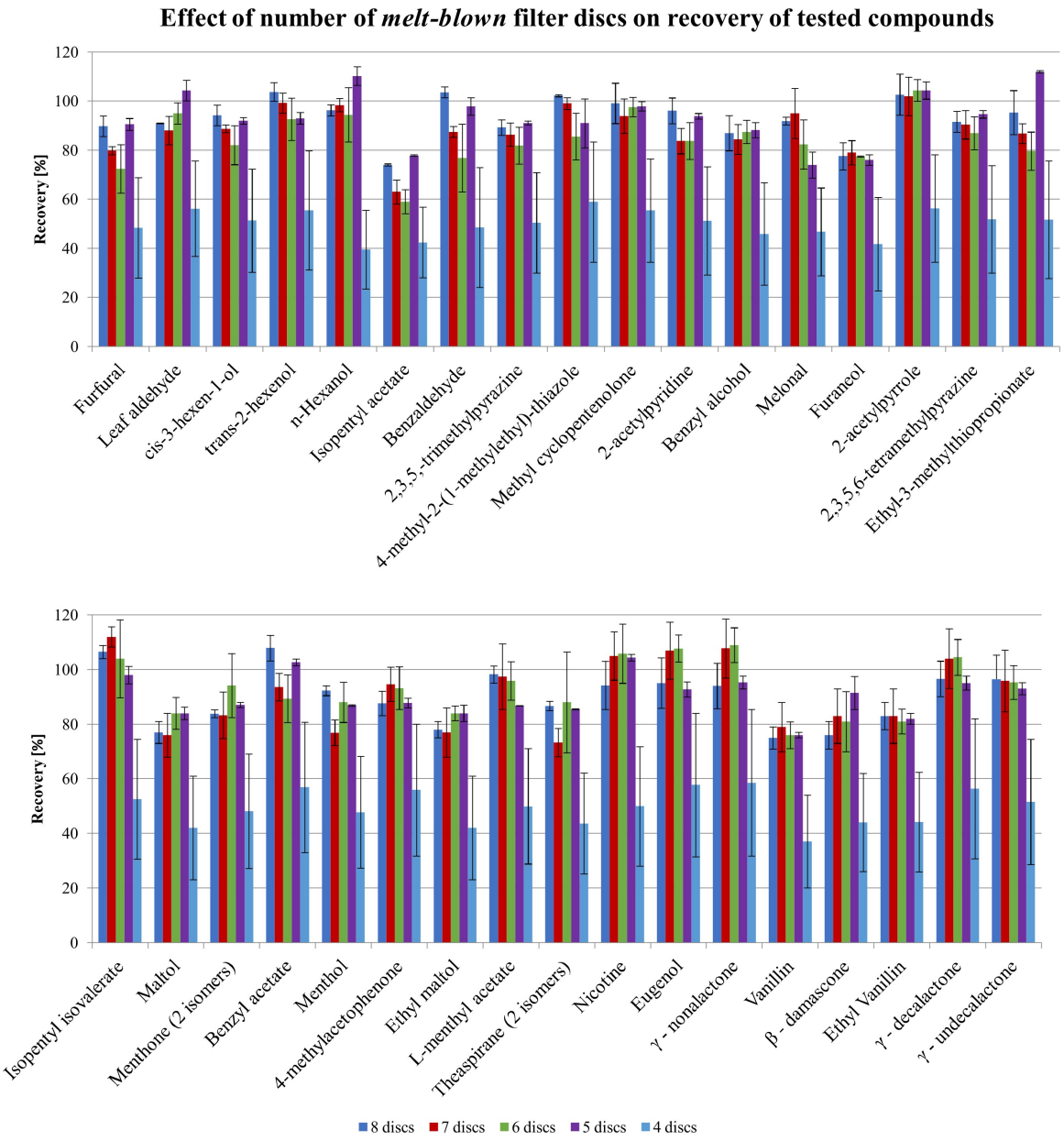

Figure 5. Selection of the number of *melt-blown* discs based on the recovery of tested compounds

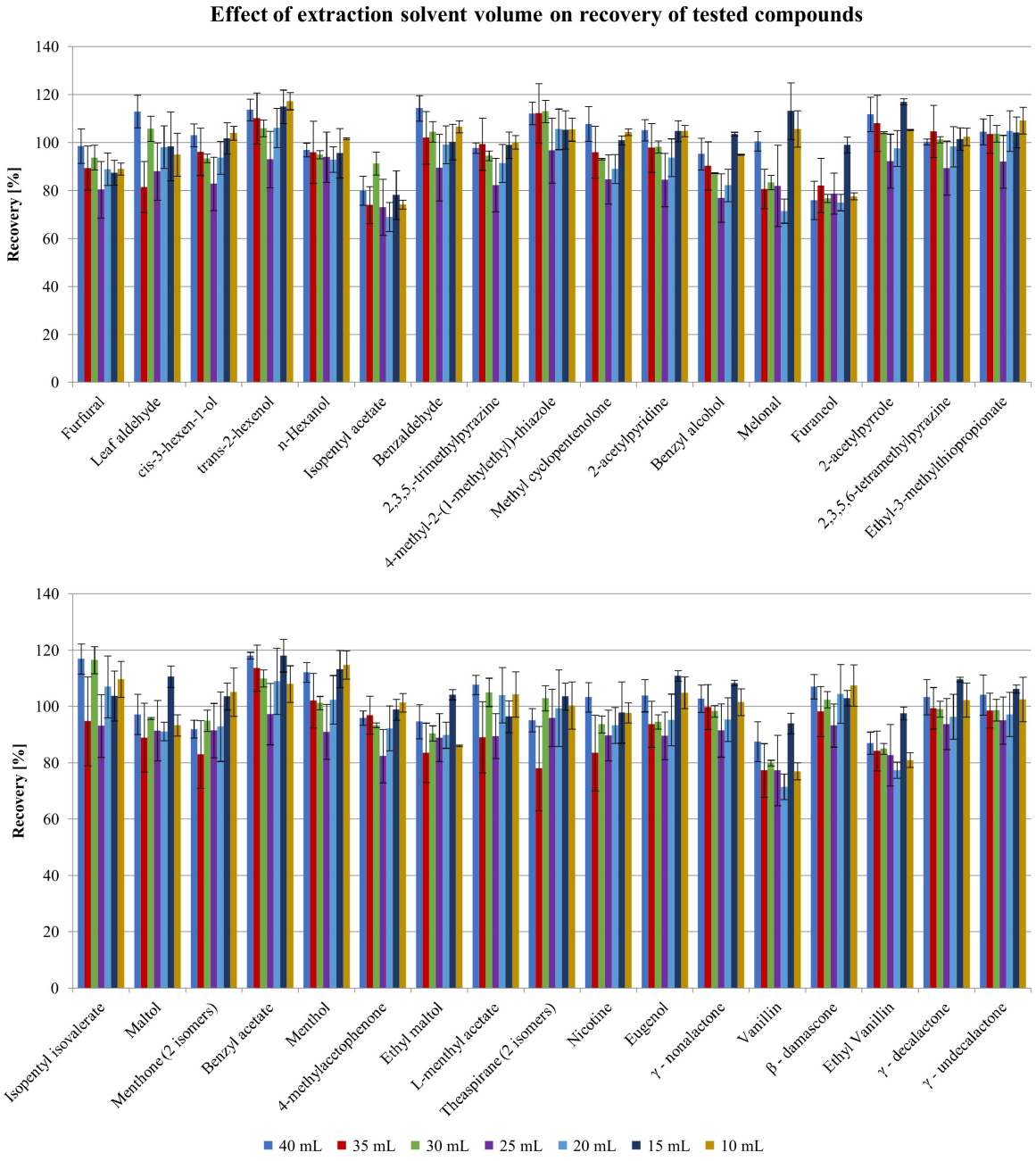

Figure 6. Selection of the MeOH volume for recovery of the tested compounds

List of supplementary material:

Figure S1. Square wave puff profile expressed as created pressure over time of puff.

Figure S2. Example of the chromatograms obtained for real samples (Strawberry - brand B) and for extract from the aerosol of the vaporised model e-liquid (0.05 mg/mL of each substance). The peak numbers correspond to the numbers given in Table S1.

Table S1. Calculated numerical values of parameters describing the matrix-matched calibration curve, LOD, LOQ and correlation coefficients of the developed method

Table S2. Repeatability and precision data for the developed method

Graphical abstract