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# Chemical Constituents in E-Cigarette Liquids and Aerosols

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## Abstract

Electronic cigarettes (e-cigarettes, EC) form an aerosol from the heating element and liquid-containing cartridge. The heating element aerosolizes the refill solutions (e-liquids) when the power source of e-cigarette is pressed. E-liquids consist of combinations of propylene glycol, glycerine, nicotine and flavouring ingredients. Puffing activates the battery-operated heating element in the atomizer and will produce smoke that is similar to conventional cigarette (CC). This study evaluated the chemical composition of e-liquid and aerosol samples available in Malaysia. We analyzed the volatile organic compounds in e-liquids and the aerosols samples from EC using gas chromatography mass spectrometer. Seventy-two EC e-liquids were analyzed through different flavours from more than 60 brands. Samples consisted of 32 nicotine-free (0 mg) and 40 nicotine-containing refill solutions (3 - 12 mg). Overall, 116 compounds were identified from EC e-liquids. On the other hand, 275 compounds were identified from their resultant aerosol samples. There were 42 compounds found in both e-liquids and aerosols. Seven compounds were only found in e-liquids and 38 compounds were only found in aerosols. Propylene glycol was found in all of the e-liquid and aerosol samples. Glycerin was found in 99% of the e-liquid and 100% of aerosol samples. At least 60% of the EC e-liquids and the resultant aerosol contain piperidine, butanoic acid ethyl ester and nicotine. It was also found that at least 9 out of 35 nicotine free labeled e-liquids contain nicotine. Some of these compounds were known to be detrimental to health and were detected in aerosol although they were not present in e-liquids. While some of the compounds are flavouring ingredients, it is necessary to evaluate its long-term effects on EC users.

**Keywords**

E-Cigarette, Volatile Organic Compounds, Aerosols, E-Liquids, Constituents

## 1. Introduction

Electronic cigarettes (e-cigarettes, EC) form an aerosol from the heating element and liquid-containing cartridge [1]. The heating element aerosolizes the refill solutions (e-liquids) when the power source of EC is pressed. The heating element is made up of metal and can be powered by the battery. E-liquids consist of a mixture of propylene glycol, glycerine, nicotine and flavouring ingredients. Puffing triggers the heating element in the atomizer and will produce smoke that is similar to conventional cigarette (CC). These similarities with CC combined with the same way of smoking have contributed to the rise in the usage of EC all-around the globe [2]. The spread of EC raises huge concern among public health practitioners and great enthusiasm in others, who endorse reducing harm and consider EC as a potential substitute to CC. Starting June 2019, health-care practitioners in USA have recorded 1888 cases of acute lung injury linked to EC usage. The accumulation of cases of EC product use associated lung injury (EVALI) has attracted worldwide attention to the safety of the usage of EC [3]. The common factor among all cases is the use of EC during the 3 months preceding the onset of respiratory disease symptoms. Tetrahydrocannabinol (THC) was found in most of the samples tested by Food Drug Administration (FDA) to date and the majority of patients have admitted consumption of THC-containing products [4].

The analytical results of the products as well as the patients' consumption history suggested that products purchased on the street or informally (family, dealer) were most often involved. Following the trend, selling and usage of EC become widespread in Malaysia market [5]. The prevalence of EC users among Malaysian adults is 3.2% with an estimated number of 602,122 [6]. Another local population survey found that 27% (n = 277) respondents agree with the idea that CC is more harmful than EC. On the other hand, 47% respondents believe that EC deliver less nicotine than CC [7]. EC could act as an introduction to tobacco addiction for a new generation of users. It will also help the renormalization of tobacco-containing products. Discussion with regards to EC is characterized by strong feelings, beliefs and economic considerations which lead to difficulty in getting reliable and credible information [8]. Despite its increasing usage, little is known about the e-liquids chemical constituents. Several recent studies have identified harmful pollutants in aerosol generated by EC [9]. This includes fine and ultrafine particles, reactive oxygen species and toxic compounds associated with flavouring ingredients [10]. It was found that propylene glycol, glycerine, nicotine and various flavouring ingredients are the significant compounds detected in e-liquids [11] [12] [13]. Other researchers have also identified aldehydes (acetaldehyde and acrolein) which can be linked with the irritation of respiratory tract [14] [15]. While the aerosols affect the users of EC, it may also impact non users through second hand exposure [16]. The characterization of aerosol is necessary because the aerosolization process was said to be responsible for the formation of aerosol-only compounds. A simple sampling device that can evaluate e-liquids and aerosols for potential differences was developed [17].

At the time of publication, a standard on the manufacturing of e-liquids is not available in Malaysia [5]. Due to this, the quality of e-liquids available in the market is uncertain. This study evaluated the chemical composition of e-liquid and aerosol samples available in Malaysia.

## 2. Methods

### 2.1. Study Design and Setting

We conducted an experimental study that started in January to December 2016. The e-liquids were purchased in June 2016 within all ten (10) districts area in Klang Valley, Selangor, Malaysia. All samples were analyzed within three months of purchase.

### 2.2. E-Liquid Sampling

#### 2.2.1. E-Liquid Sample Collection

The study team purchased the e-liquid samples directly from different local shops and night markets. The e-liquids were bought based on the nicotine content varying from 0 to 12 mg/mL. The selection of the e-liquids was based on popular and best-seller brands as claimed by the local dealers.

#### 2.2.2. E-Liquid Sample Preparation

The e-liquid samples were prepared by weighing 10 mg of the sample from the e-liquids bottle and added with 1.0 ml of isopropyl alcohol into a 2 mL vial. The volatile organic compounds (VOCs) that were present in the e-liquid were dissolved entirely and ready to be analyzed.

### 2.3. Aerosol Sampling

#### 2.3.1. Sampling Technique

At the time of publication, there was no established smoking machine that was designed for the EC sampling. Aerosol sampling for VOC was based on NIOSH Manual of Analytical Methods No. 2549, Volatile organic compounds (screening) (with modification) [18]. The technique involved using thermal desorption (TD) tubes. This TD tube was a multi-bed sorbent tube containing graphitized carbons and carbon molecular sieve sorbents that trapped VOCs in aerosol samples before analysis [5].

#### 2.3.2. EC Device

At the time of publication, there was no established smoking machine that was designed for the EC sampling (**Table 1**). Aerosol sampling for VOC was based

**Table 1.** Characteristics of the EC atomizer and solution tank used for aerosol sampling.

| Device part | Atomizer | Solution tank |
|---|---|---|
| Name | Elfin Mod | Subtank$^{TM}$ Mini |
| Manufacturer | Shenzen S-Body Electronics Technology Co., Ltd., Shenzhen, China | Shenzen Kanger Technology Co., Ltd., Shenzhen, China |
| Features | 1 - 40 W; Resistance 0.16 - 2.0 Ω; Built-in 18,500 battery | Atomizer head 1.2 Ω; RBA Plus Base 0.5 Ω/30W coil; Japanese organic cotton |
| Material | Zinc alloy; Stainless steel | Stainless steel; Strengthen pyrex glass |
| Size | 65 × 32 × 22 mm | 22 mm diameter × 48 mm length |
| Capacity | 1400 mAh battery | 4.5 mL |

on NIOSH Manual of Analytical Methods No. 2549, Volatile organic compounds (screening) (with modification) [18]. The technique involved using thermal desorption (TD) tubes. This TD tube was a multi-bed sorbent tube containing graphitized carbons and carbon molecular sieve sorbents that trapped VOCs in aerosol samples before analysis [5].

#### 2.3.3. Sampling Apparatus

A 50 mL Hamilton syringe, 1000 series GASTIGHT, (Cat.no 20707) was bought from Sigma-Aldrich Corporation (Missouri, USA). Stainless steel prepacked thermal desorption sorbent tube type Carbotrap 349 was used (Perkin Elmer Inc.). The tubes approximate analyte volatility in the range between n-C3 to n-C16 and the typical analytes for NIOSH Method 2549 [18]. Two sizes of latex rubber tubing black from SKC Inc. were used, which are type 1/4-inch ID × 3/8-inch OD (Cat. No 226-03-004) and type 3/16-inch ID × 5/16-inch OD (Cat. No 226-03-003) [5].

#### 2.3.4. Sample Collection

A simple sampling device was adapted from Herrington and Myers [17] approach using a gas tight syringe connected to a sorbent tube and then to the EC device. In this study, the 50 mL gas tight syringe was connected to one end of the TD tube using a 3/16-inch ID latex tubing. The other end of the sorbent tube was connected to the EC device using the 1/4-inch ID latex tubing (**Figure 1**). After the e-liquid was filled into the solution tank, the EC device was activated (LED light up) to heat the e-liquid until aerosol was produced. The EC was observed to light each time the aerosol was drawn through the sorbent tube. The syringe was used to draw 10 mL of the aerosol generated from the EC device. VOCs that were present in the aerosol was drawn through and trapped by the TD tube. The tubes were then capped securely and ready to be analyzed [5].

### 2.4. VOC Analysis

#### 2.4.1. Chemicals

All analytical standards and solvents used were of an analytical grade. Isopropyl alcohol was obtained from Sigma-Aldrich (Missouri, USA).


**Figure 1.** Apparatus set-up for aerosol sampling consists of 50 mL Hamilton air-tight syringe, latex tubings, TD tube and e-cigarette devices [5].

### 2.4.2. Analytical Methods

VOCs in e-liquid and aerosol were analyzed using Clarus® SQ 8 gas chromatography-mass spectrometer detector (GC-MS, Perkin Elmer Inc.). Chromatographic separation was achieved by Elite-VMS (e-liquid sample) and Elite-VRX column (aerosol sample) (30 m, 0.25 mm ID, 1.4 μm). The analytical GC parameters were described in **Table 2**. Individual peaks were identified by library search against the NIST 11 mass spectral database. The Total Ion Chromatogram (TIC) mode was applied to acquire the maximum number of compounds. For the TIC, a mass range of 15 - 400 m/z was selected. Identification of VOCs was based on mass spectra interpretation and Turbo Mass Software version 6.1.0. The VOCs were classified into different classes such as alcohol, ketone, aldehyde and other classes according to PubChem Database (National Center for Biotechnology Information).

## 2.5. Statistical Analysis

The results for e-liquids and aerosols for each compound were compared by SPSS17.0. Two paired sample t-test was employed as the statistical methods. $\alpha = 0.1$ was set as the risk level in all statistical analysis, and $p < 0.1$ was considered to be statistically significant.

## 2.6. Ethical Considerations

This study protocol was approved by the Ministry of Health Research and Ethics Committee, Ministry of Health Malaysia with exemption as no ethical issues involved.

# 3. Results

Seventy-two EC e-liquids were analyzed through different flavours from more than 60 brands. Samples consisted of 32 nicotine-free (0 mg) and 40 nicotine-containing refill solutions (3 - 12 mg). The amount of nicotine, propylene glycol and glycerin were declared in 75% of the samples. Overall, 116 compounds were identified from EC e-liquids. On the other hand, 275 compounds

Table 2. Analytical system and parameters used for identification of VOCs in refill solutions and aerosol using gas chromatography-mass spectrometry (GC-MS).

| Analytical equipment | |
|---|---|
| VOC in e-liquids | Clarus® SQ 8 Gas Chromatograph/Mass Spectrometer (Perkin Elmer Inc.) |
| VOC in aerosol | Clarus® SQ 8 Gas Chromatograph/Mass Spectrometer (Perkin Elmer Inc.) |
| Column (liquid sample) | Elite-VMS (30 m, 0.25 mm ID, 1.4 μm) (Perkin Elmer Inc.) |
| Column (aerosol sample) | Elite-VRX (30 m, 0.25 mm ID, 1.4 μm) (Perkin Elmer Inc.) |
| Injection mode | Split 10:1 |
| Injection temperature<br>Injection volume | 250˚C<br>1.0 μL |
| Carrier gas | Helium (purity 99.999%), constant flow |
| Flow rate | 2.0 mL/min |
| Oven | 35˚C was held for 1 minute then ramped at rate of 11˚C/minute to 190˚C, and then ramped at rate 15˚C/minute of which was further held for 3 minutes |
| Source temperature | 220˚C |
| Interface temperature<br>Run time | 250˚C<br>20 min |
| Acquisition mode<br>Scan range | Full scan mode<br>m/z 15 - 400, library search against the NIST 11 mass spectral database |
| Data processing | Turbo Mass Software version 6.1.0 |

were identified from their resultant aerosol samples. Only compounds that were detected in more than five samples were shown (Tables 3-5).

There were 42 compounds found in both e-liquids and aerosols. Seven compounds were only found in e-liquids and 38 compounds were only found in aerosols. 108 compounds could not be identified. Propylene glycol was found in all of the e-liquid and aerosol samples. Glycerin was found in 99% of the e-liquid and 100% of aerosol samples. At least 60% of the EC e-liquids and the resultant aerosol contain piperidine, butanoic acid ethyl ester and nicotine. It was also found that at least 9 out of 35 nicotine-free labeled e-liquids contain nicotine. Various compounds such as ethyl maltol, vanillin, 1-butanol 3-methyl-acetate, ethyl acetate were found in more than 30% of the e-liquid and aerosol samples.

There was a significant difference between the amount of e-liquid (n = 24) and aerosol (n = 37) samples that contain ethyl acetate. Butanoic acid 2-methyl-ethyl ester, 1,2,3-propanetriol, 1-acetate, 2(3H)-furanone, 5-hexyldihydro-, 2(3H)-furanone, 5-heptyldihydro-, maltol, triacetine, menthol, 1,2-propanediol, 2-acetate, isobutyl acetate and ethyl vanillin were found in more than 10% of the samples. A significant difference was also observed for e-liquid and aerosol samples that contain compounds such as butanoic acid 3-hydroxy-methyl ester, propanoic acid ethyl ester, 1,4-dioxane-2 6-dimethanol, 1,2-propanediol 1-acetate and 1,2-propanediol 2-acetate. The compounds were detected in e-liquid (4% - 13%) and aerosol (3% - 15%) samples. Compounds such as 2-Propanol, 1,

Table 3. VOC found in e-liquids.

| No | Compounds | e-liquid (n = 72) | Aerosol (n = 72) | P Value |
|---|---|---|---|---|
| 1 | 2-Propanol, 1, 1-oxybis- | 14 | 0 | <0.0001 |
| 2 | Butanoic acid, 3-methylbutyl ester | 12 | 0 | 0.0003 |
| 3 | D-Limonene | 10 | 0 | 0.001 |
| 4 | 2-Cyclopenten-1-one, 2-hydroxy-3-methyl- | 7 | 0 | ns |
| 5 | Hexanoic acid, ethyl ester | 6 | 0 | ns |
| 6 | Linalool | 6 | 0 | ns |
| 7 | Acetic acid, hexyl ester | 5 | 0 | ns |

$\alpha = 0.1$ was set as the risk level in all statistical analysis, and $p < 0.1$ was considered to be statistically significant.

Table 4. VOC found in aerosol samples from EC.

| No | Compounds | e-liquid (n = 72) | Aerosol (n = 72) | P Value |
|---|---|---|---|---|
| 1 | Acrolein [2-Propenal] | 0 | 57 | <0.0001 |
| 2 | Acetic acid | 0 | 45 | <0.0001 |
| 3 | Nicotyrine | 0 | 41 | <0.0001 |
| 4 | 2-Propen-1-ol | 0 | 39 | <0.0001 |
| 5 | α-Nicotine[Pyridine, 2-(1-methyl-2 pyrrolidinyl)- | 0 | 35 | <0.0001 |
| 6 | 1-Propen-2-ol, acetate | 0 | 35 | <0.0001 |
| 7 | 1,3-Dioxan-5-ol | 0 | 33 | <0.0001 |
| 8 | Ethanol | 0 | 30 | <0.0001 |
| 9 | 1,3-Dioxane, 2-methyl- | 0 | 27 | <0.0001 |
| 10 | Glycidol | 0 | 23 | <0.0001 |
| 11 | Acetic formic anhydride | 0 | 19 | <0.0001 |
| 12 | 1,2-Propanediol, 3-chloro | 0 | 16 | <0.0001 |
| 13 | Acetaldehyde, chloro- | 0 | 14 | <0.0001 |
| 14 | Acetone | 0 | 13 | 0.0002 |
| 15 | Butanoic acid, 2,3-dihydroxypropyl ester | 0 | 12 | 0.0003 |
| 16 | 1,2-Propanediol, diformate | 0 | 10 | 0.001 |
| 17 | 1,3-Propanediol, diacetate | 0 | 10 | 0.001 |
| 18 | Acetaldehyde | 0 | 10 | 0.001 |
| 19 | 1H-Pyrazole, 4-chloro- | 0 | 9 | 0.003 |
| 20 | Isopropyl alcohol | 0 | 9 | 0.003 |
| 21 | *β*-D-Glucopyranose, 1,6-anhydro- | 0 | 9 | 0.003 |
| 22 | Oxalacetic acid | 0 | 8 | 0.006 |
| 23 | Isopropyl acetate | 0 | 7 | 0.01 |
| 24 | 2,3-Butanedione | 0 | 7 | 0.01 |

**Continued**

| | | | | |
|---|---|---|---|---|
| 25 | 1,3-Dioxane | 0 | 7 | 0.01 |
| 26 | 1,2-Propanediol, 3-methoxy- | 0 | 7 | 0.01 |
| 27 | Methyl glyoxal | 0 | 7 | 0.01 |
| 28 | 1,2,3,4-Butanetriol | 0 | 7 | 0.01 |
| 29 | *β*-Citronellol | 0 | 7 | 0.01 |
| 30 | 2-Hexanone | 0 | 6 | 0.03 |
| 31 | Glycidol [1-Propanol, 2,3-epoxy-] | 0 | 6 | 0.03 |
| 32 | 1,3-Dioxolane, 4-methanol | 0 | 6 | 0.03 |
| 33 | 1-Propen-1-ol, acetate | 0 | 6 | 0.03 |
| 34 | Prophyl 2-methylvalerate | 0 | 6 | 0.03 |
| 35 | Benzene | 0 | 5 | 0.06 |
| 36 | Butyl acetate | 0 | 5 | 0.06 |
| 37 | Furan, 2-methyl- | 0 | 5 | 0.06 |
| 38 | Hexanoic acid, propyl ester | 0 | 5 | 0.06 |

$\alpha = 0.1$ was set as the risk level in all statistical analysis, and $p < 0.1$ was considered to be statistically significant.

**Table 5.** Percentage and compound classification.

| No | Compounds | Percentage (%) | | Classification |
|---|---|---|---|---|
| | | e-liquid (n = 72) | Aerosol (n = 72) | |
| 1 | Propylene glycol | 100.00 | 100.00 | Alcohol |
| 2 | Glycerin | 98.61 | 100.00 | Alcohol |
| 3 | Piperidine | 70.83 | 68.06 | Amine |
| 4 | Nicotine | 62.50 | 68.06 | Pyridine |
| 5 | Ethyl maltol | 44.44 | 55.56 | Ketone |
| 6 | Vanillin | 41.67 | 36.11 | Aldehyde |
| 7 | 1-Butanol, 3-methyl-, acetate | 38.89 | 41.67 | Ester |
| 8 | Ethyl Acetate | 33.33 | 51.39 | Ester |
| 9 | 3-Hexen-1-ol | 27.78 | 15.28 | Alcohol |
| 10 | Butanoic acid, 2-methyl-, ethyl ester | 26.39 | 31.94 | Ester |
| 11 | 1,2,3-Propanetriol, 1-Acetate | 26.39 | 25.00 | Ester |
| 12 | 2(3H)-Furanone, 5-hexyldihydro- | 20.83 | 41.67 | Ketone |
| 13 | 2(3H)-Furanone, 5-heptyldihydro- | 16.67 | 27.78 | Ketone |
| 14 | Maltol | 16.67 | 15.28 | Ketone |
| 15 | Triacetine | 16.67 | 12.50 | Ester |
| 16 | Menthol | 15.28 | 13.89 | Alcohol |
| 17 | Acetic acid, butyl ester | 13.89 | 6.94 | Ester |
| 18 | 1,2,3-Propanetriol, 1,2-Diacetate | 13.89 | 5.56 | Ester |

**Continued**

| | | | | |
|---|---|---|---|---|
| 19 | 1,2-Propanediol, 2-Acetate | 12.50 | 33.33 | Ester |
| 20 | Isobutyl acetate | 12.50 | 11.11 | Ester |
| 21 | 2-Propenoic acid, 3-phenyl-, methyl ester | 12.50 | 5.56 | Ester |
| 22 | Ethyl vanillin | 11.11 | 15.28 | Aldehyde |
| 23 | Diphenyl ether | 11.11 | 9.72 | Ether |
| 24 | 1,2-Propanediol, 1-Acetate | 11.11 | 2.78 | Ester |
| 25 | Butanoic acid, 3-methyl-, ethyl ester | 9.72 | 13.89 | Ester |
| 26 | Butanoic acid | 9.72 | 12.50 | Carboxylic Acid |
| 27 | Cyclohexanepropanoic acid, 2-propenyl ester | 9.72 | 6.94 | Ester |
| 28 | Butanoic acid, 3-methyl-,3-methylbuthyl ester | 9.72 | 5.56 | Ester |
| 29 | 6-Octen-1-ol, 3,7-dimethyl- | 9.72 | 1.39 | Terpenoid |
| 30 | Hexanoic acid, 2-propenyl ester | 9.72 | 2.78 | Ester |
| 31 | Acetoin | 8.33 | 1.39 | Ketone |
| 32 | 2(3H)-Furanone, 5-butyldihydro- | 6.94 | 16.67 | Ketone |
| 33 | Methyl Anthranilate | 6.94 | 6.94 | Ester |
| 34 | 1,4-Dioxane-2, 6-dimethanol | 5.56 | 30.56 | Alcohol |
| 35 | Propanoic acid, ethyl ester | 5.56 | 19.44 | Ester |
| 36 | 5-Thiazoleethanol, 4-methyl- | 5.56 | 12.50 | Azole |
| 37 | Propanoic acid | 5.56 | 11.11 | Carboxylic Acid |
| 38 | Butanoic acid, 3-hydroxy-, methyl ester | 4.17 | 15.28 | Ester |
| 39 | 1-Propanol, 2-methyl- | 4.17 | 11.11 | Alcohol |
| 40 | Triethyl citrate | 4.17 | 6.94 | Ester |
| 41 | 1,2,3-Propanediol, 1-Acetate | 2.78 | 8.33 | Ester |
| 42 | 1,2,4-Butanetriol, 2-acetate | 2.78 | 6.94 | Ester |
| 43 | 2-Propanol, 1, 1-oxybis- | 19.44 | 0 | Alcohol |
| 44 | Butanoic acid, 3-methylbutyl ester | 16.67 | 0 | Ester |
| 45 | D-Limonene | 13.89 | 0 | Terpenoid |
| 46 | 2-Cyclopenten-1-one, 2-hydroxy-3-methyl- | 9.72 | 0 | Ketone |
| 47 | Hexanoic acid, ethyl ester | 8.33 | 0 | Ester |
| 48 | Linalool | 8.33 | 0 | Terpenoid |
| 49 | Acetic acid, hexyl ester | 6.94 | 0 | Ester |
| 50 | Acrolein [2-Propenal] | 0 | 79.17 | Aldehyde |
| 51 | Acetic acid | 0 | 62.50 | Carboxylic Acid |
| 52 | Nicotyrine | 0 | 56.94 | Pyridine |
| 53 | 2-Propen-1-ol | 0 | 54.17 | Alcohol |
| 54 | α-Nicotine[Pyridine,2-(1-methyl-2 pyrrolidinyl)- | 0 | 48.61 | Pyridine |
| 55 | 1-Propen-2-ol, acetate | 0 | 48.61 | Ester |

**Continued**

| | | | | |
|---|---|---|---|---|
| 56 | 1,3-Dioxan-5-ol | 0 | 45.83 | Alcohol |
| 57 | Ethanol | 0 | 41.67 | Alcohol |
| 58 | 1,3-Dioxane, 2-methyl- | 0 | 37.50 | Aldehyde |
| 59 | Glycidol | 0 | 31.94 | Ether |
| 60 | Acetic formic anhydride | 0 | 26.39 | Carboxylic anhydride |
| 61 | 1,2-Propanediol, 3-chloro | 0 | 22.22 | Alcohol |
| 62 | Acetaldehyde, chloro- | 0 | 19.44 | Aldehyde |
| 63 | Acetone | 0 | 18.06 | Ketone |
| 64 | Butanoic acid, 2,3-dihydroxypropyl ester | 0 | 16.67 | Ester |
| 65 | 1,2-Propanediol, diformate | 0 | 13.89 | Ester |
| 66 | 1,3-Propanediol, diacetate | 0 | 13.89 | Ester |
| 67 | Acetaldehyde | 0 | 13.89 | Aldehyde |
| 68 | 1H-Pyrazole, 4-chloro- | 0 | 12.50 | Azole |
| 69 | Isopropyl alcohol | 0 | 12.50 | Alcohol |
| 70 | *β*-D-Glucopyranose, 1,6-anhydro- | 0 | 12.50 | Anhydrohexose |
| 71 | Oxalacetic acid | 0 | 11.11 | Carboxylic Acid |
| 72 | Isopropyl acetate | 0 | 9.72 | Ester |
| 73 | 2,3-Butanedione | 0 | 9.72 | Ketone |
| 74 | 1,3-Dioxane | 0 | 9.72 | Ether |
| 75 | 1,2-Propanediol, 3-methoxy- | 0 | 9.72 | Ether |
| 76 | Methyl glyoxal | 0 | 9.72 | Aldehyde |
| 77 | 1,2,3,4-Butanetriol | 0 | 9.72 | Alcohol |
| 78 | *β*-Citronellol | 0 | 9.72 | Amine |
| 79 | 2-Hexanone | 0 | 8.33 | Ketone |
| 80 | Glycidol [1-Propanol, 2,3-epoxy-] | 0 | 8.33 | Ether |
| 81 | 1,3-Dioxolane, 4-methanol | 0 | 8.33 | Alcohol |
| 82 | 1-Propen-1-ol, acetate | 0 | 8.33 | Ester |
| 83 | Prophyl 2-methylvalerate | 0 | 8.33 | Ester |
| 84 | Benzene | 0 | 6.94 | Hydrocarbon |
| 85 | Butyl acetate | 0 | 6.94 | Ester |
| 86 | Furan, 2-methyl- | 0 | 6.94 | Furan |
| 87 | Hexanoic acid, propyl ester | 0 | 6.94 | Ester |

1-oxybis-Butanoic acid, 3-methylbutyl ester and D-Limonene were only detected in e-liquid samples.

The differences between e-liquid and aerosol samples for these three compounds were found to be statistically significant. 2-Cyclopenten-1-one, 2-hydroxy-3-methyl-, Hexanoic acid ethyl ester, Linalool, Acetic acid hexyl ester was the other compounds detected in e-liquid samples. Acrolein was detected in 79% of the aerosol samples. Acetic acid, nicotyrine, 2-propen-1-ol were found in more than half of the aerosol samples (54% - 63%). $\alpha$-nicotine [pyridine, 2-(1-methyl-2 pyrrolidinyl)-, 1-propen-2-ol, acetate, 1,3-dioxan-5-ol, ethanol, 1,3-dioxane, 2-methyl- and glycidol were found in 30% to 48% of aerosol samples. Several compounds such as oxalacetic acid, isopropyl alcohol, acetaldehyde, 1,2-propanediol diformate and acetone were present in 11% to 18% of the aerosol samples. Benzene, glycidol [1-propanol 2,3-epoxy], methyl gloxal and isopropyl acetate were few of the compounds detected in 7% to 10% of the aerosol samples. Propylene oxide, xylene and styrene were detected in only 1% of aerosol samples (result not shown).

## 4. Discussion

We identified the compounds in e-liquids and aerosols. Some compounds are present in both e-liquids and aerosols. However, we also found certain compounds that are present in either one of them. Certain compounds detected in were required as main ingredients for the production of e-liquids; propylene glycol and glycerine. Propylene glycol mainly functions as a humectant and is necessary for the production of EC e-liquids. Combination of propylene glycol and glycerin produce aerosols that simulate CC smoke [19]. Heating voltage higher than 3V will oxidize the humectants during the aerosol generation process [20]. The oxidation process forms aldehydes found in conventional cigarette smoke [21]. Estimated levels of exposure to propylene glycol and glycerin are a cause of concern [22]. Volunteers subjected to propylene glycol mist for 1 min reported a slight airway obstruction and increased self-rated shortness of breath [23].

Long term exposure to propylene glycol has been linked to the deterioration of multiple allergic symptoms in children [24]. Propylene glycol is a minor respiratory irritant which can cause sore throat or cough [25]. One puff on EC can produce 430 - 630 mg of propylene glycol per $m^3$ which is enough to irritate the lungs [26]. Ethylene glycol has been used to replace glycerol or propylene glycol in several brands of e-liquids although this was not observed in this study [27]. Ethylene glycol has been linked with various toxicological risks [28]. Glycerin is non-toxic but can form toxic acrolein and glycidol when subjected to heat at higher temperatures [29]. A fellow research group postulated a pathway and by-products formed during thermal degradation of propylene glycol and glycerine [9]. When e-liquids are heated to create aerosol, propylene glycol and glycerine are oxidized and can form potentially hazardous by-products.

Acrolein and acetaldehyde were formed when the coil heats up glycerin in e-liquids. Acrolein is a carbonyl compound that has the potential to be toxic. Inhalation of acrolein can cause severe pulmonary diseases [30]. Acetaldehyde is a probable human carcinogen and listed as carcinogenic [31]. They were formed due to the aerosolization process or from any of the components of the EC device itself. The different voltage used for the EC can lead to higher presence of toxic chemicals [32]. The presence of these two carbonyls in the aerosol was consistent with previous observations although formaldehyde was not found in current study [33]. This is in line with the pyrolysis process of propylene glycol. Pyrolysis of propylene glycol is the process that helps in the formation of acetaldehyde and acrolein [17]. Nicotine in e-liquids is extracted from tobacco. It also extracted various impurities such as anabasine, cotinine, beta-nicotyrine and myosmine [34].

Majority of e-liquid manufacturers do not specify health warnings and comprehensive ingredient lists or levels [35]. EC can deliver nicotine in their vapour, with the amount of nicotine differs based on the e-liquid, power of EC and smoking topography [36]. Several studies have reported that e-liquids tested do not contain the same amount of nicotine claimed on the bottle by the manufacturer [37]. Some studies found that e-liquids contain tobacco specific nitrosamines (TSNAs) although this was not observed in this study [36]. TSNAs are derived from tobacco leaves. TSNAs are very potent carcinogens due to their ability to produce DNA adducts, inhibit tumour suppressor genes and activate oncogenes [38]. EC do not contain tobacco so they should not contain TSNAs, which shows that their formation is due to nicotine contaminants [39]. Abramovitz hypothesizes that presence of nicotine degradation products such as beta-nicotyrine is due to accumulation in e-liquids over time but only with exposure to air [40]. Majority of regular users of EC report that they use it with nicotine [41]. Nicotine is highly addictive and those who wish to quit do so because they don't like being dependent on it [42]. Changing to EC does not break the nicotine dependency. Nicotine is considered harmless by some health practitioners while others do not agree [43].

Nicotine stimulates the release of essential neurotransmitters and hormones in central nervous system [44]. In addition, nicotine stimulates the release of catecholamines in the peripheral system. This causes vasoconstriction, increase in heart rate and myocardial contractility [45]. Animal studies suggest that nicotine accelerates atherosclerosis and can fasten growth of cancer cells and the proliferation of endothelial cells [46]. E-liquid flavours are used to recreate the taste of cigarettes or to create a new sensation by giving the aerosol a pleasant taste (fruity, coffee, chocolate or cinnamon flavours) [36]. Compounds such as piperidine, butanoic acid ethyl ester, ethyl maltol, vanillin, 1-butanol 3-methyl-acetate, ethyl acetate come from flavourings added to the e-liquids [47]. The compounds give the e-liquids its distinct flavour.

The compounds are classified as "generally recognized as safe" (GRAS) due to its usage in food production. However, GRAS certification by the Flavor Extracts Manufacturers Association (FEMA) is limited only to ingestion, not inhalation [48]. Butanoic acid ethyl ester is classified as an ester that is used as a flavouring ingredient. It is found in fruits such as apples and gives the e-liquids the fruity flavour. Ethyl maltol is a ketone that is a common flavouring ingredient in confectioneries. It has a sweet smell that is described as caramelized sugar and cooked fruit. Vanillin is classified as an aldehyde and a flavouring ingredient that gives the vanilla smell. 1-butanol 3-methyl-acetate is also an ester that is added to e-liquids for odour that is similar to banana and pear. There is a possibility that similar compounds are present in certain types of the flavourings.

Discussion of all flavourings used in e-liquids is impractical given the high diversity of products with unique flavours. Diacetyl (buttery flavour) and acetyl propionyl (caramel or buttery flavour) in 74% of e-liquids tested [39]. Both compounds were also found in this study (results not shown). Inhalation of diacetyl has been linked to development of bronchiolitis obliterans which is an obstructive respiratory disease [49]. According to Farsalinos, 47.3% of samples contain diacetyl that is above what is deemed safe for inhalation by NIOSH [39]. Other flavouring ingredients such as vanillin caused alterations in cellular physiology and compromised the ability of airway epithelial cells to maintain homeostasis [50]. The formation of other compounds such as $\alpha$-Nicotine [Pyridine, 2-(1-methyl-2 pyrrolidinyl)-1-Propen-2-ol, acetate 1,3-Dioxan-5-ol, Ethanol, 1,3-Dioxane, 2-methyl-, methyl gloxal and glycidol can be attributed to pyrolysis of flavours and other ingredients added to e-liquids. Methyl gloxal was detected in nine out of 13 aerosol samples and is classified as a mutagen [51]. A research group has postulated that propylene oxide, methyl gloxal, acetaldehyde and formaldehyde were formed during the thermal degradation of propylene glycol [9]. In addition, leaching from other materials used to manufacture the EC could be a potential origin of the compounds [52]. EC often use lithium batteries to power the heating mechanisms, which are susceptible to leak, fires or explosions [53]. Heating mechanisms of ECs are capable of emitting metallic particles such as tin, chromium, lead, tin and cadmium [54]. FDA considers these metals harmful or potentially harmful to human health [53]. EC heating filaments usually is made of nickel and chromium and coated with tin or silver [21] [55]. Tin is a friable metal and can be present in EC aerosol in large amount. It is cytotoxic to human lung fibrolasts and can cause inflammation [55].

Williams also found that nickel levels to be 2 - 100 times the amount found in cigarette smoke and can also lead to lung inflammation. The effect of metals from EC is beyond the scope of this article. Health professionals who promoted 'harm reduction' consider that ECs have no adverse long-term health effects. The EC/tobacco industry endorses these views. The usage of EC is spreading to never-smokers and ex-smokers. Many smokers are using both CC and EC or switch instead of quitting and widespread usage of EC will renormalize smoking. Even though EC considered to help in promoting smoking cessation, a recent National Academies of Sciences, Engineering, and Medicine (NASEM) study suggested possible public health harm of EC use [56]. NASEM concluded that although EC usage will increase cessation rate among adults in the short run, the public health benefit is significantly less as even more young EC users switch to use combustible tobacco products in the long run.

The following limitations are acknowledged when interpreting the study results. The study consisted of samples within one state in Malaysia and relied on the information from the sellers which the samples were purchased. There was a lack of standardization in methodologies for aerosol generation used for EC analysis. The aerosol sampling method used in this study was manually handled. This might have resulted in loss of samples, inconsistencies and inaccuracy. Due to large number of compounds analyzed, it is also impossible to obtain all the reference standards required for quantification purposes. Hence, this study is only able to report on the presence of the compound (qualitative) instead of the actual amount of the compound (quantitative). Future work would benefit from standardizing laboratory protocols, development of minimally informative detection limits that are needed for risk assessment and quality control experiments. Detailed recommendations on standardization of such protocols are outside of scope of this article.

## 5. Conclusion

E-liquids contain compounds in addition to vendor listed such as propylene glycol, glycerine and nicotine. Some of these compounds were known to be detrimental to health and were detected in aerosol although they were not present in e-liquids. While some of the compounds are flavouring ingredients, it is necessary to evaluate its long-term effects on EC users. Findings of this study can be used by stakeholders such as Ministry of Health Malaysia to develop a standard guideline to regulate the sale and consumption of e-liquids and EC device. Further studies could determine the exact level of the compounds present in e-liquids and aerosols to accurately evaluate its risk assessment to the public and decide whether EC is a public health problem or a useful smoking cessation tool.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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