

Evaluation Of Laboratory Tests For E-Cigarettes In Indonesia Based On Who's Nine Toxicants

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Abstract:

Concern for the potential health risks, social and economic-impacts, and regulatory requirements of electronic cigarettes has grown with their expanding use globally. The study evaluated the nicotine content and nine toxicants the World Health Organization targeted in 60 e-cigarette samples in Indonesia. Three types of conventional cigarettes were also tested for comparison. The test results indicates that the nicotine levels in e-liquid are generally lower than those stated on the label. Carbon monoxide (CO) does not exist in vapor; while 1,3-butadiene, benzene, N-nitrosornicotin (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are below the limit of detection (LOD) in all samples analyzed. One freebase nicotine sample and five salt-based nicotine samples were positive for benzo[a]pyrene (BaP), with levels lower than the limit of quantification (LOQ). Only one sample contained detectable acrolein at 0.43 µg/puff. Formaldehyde was found in all the closed-system e-cigarettes and some freebase nicotine at levels below LOQ, while the remaining samples had an average formaldehyde content of just 0.7 µg/puff. Both samples registered acetaldehyde below LOQ except for that of one sample of salt-based nicotine and freebase nicotine with values of 1.55 µg/puff and 1.75 µg/puff, respectively. Overall, the levels of toxins in e-cigarettes were significantly lower than those of conventional cigarettes. These results indicate the necessity for consumer awareness regarding potential health risks of e-cigarette use. To ensure transparency in nicotine delivery and toxicant exposure, policymakers need to be urged to implement standardized testing methods and labelling practices.

Keywords: e-cigarettes, harmful constituents, laboratory tests, tobacco, toxicant

1. Introduction

Electronic cigarettes (e-cigarettes) have gained significant popularity worldwide as an alternative to conventional tobacco products. The increasing use of e-cigarettes, particularly among young adults, has raised concerns about their potential health risks and the adequacy of existing regulations (Farsalinos & Polosa, 2014). In Indonesia, the e-cigarette market has expanded rapidly, with various nicotine levels and flavors available to consumers. E-cigarette product is an emerging technology for alternative tobacco product without a combustion process. According to the regulation and the availability in the Indonesian market, e-cigarette products falls into two main categories: e-liquids, which use vaporized nicotine, and heated tobacco. The difference between those two lies in the mechanism of action e-cigarettes produce vapor from heating e-liquid, while the other heats the tobacco so that it retains the flavor and nicotine elements of conventional cigarettes but with lower emissions (Miller et al., 2022). However, there is limited scientific data regarding the toxicant composition of e-cigarettes in the country, making it

crucial to evaluate their chemical constituents and associated potential risks.

E-cigarettes liquid comes in an assortment of nicotine levels and flavor combinations. Other than nicotine and flavoring, the ingredients mostly include propylene glycol (PG) and vegetable glycerin (VG). They also come in both disposable and rechargeable variants. Consequently, both the liquid and devices available in the market may have different flavor configurations, nicotine level, coil resistances, and power settings to suit consumer preferences.

Despite e-cigarettes being widely debatable, the number of users is growing. The possible risks and benefits of e-cigarettes must be investigated by proper testing (Murphy et al., 2017; Wang et al., 2019), so that the available data can be related to cigarette toxicology (Fagerström & Bridgman, 2014; Hajek et al., 2014). Tests on e-liquids, e-cigarette devices, and the resultant aerosols can be performed in a toxicological way (Belushkin et al., 2018; CORESTA, n.d, 2015; ISO, 2018). However, except for a few sets of experimental conditions in different countries for these three types, there are few tests, and they are also not the same. Some of the harmful potentials in e-

cigarette are mainly aerosols full of the carbonyl compounds from the e-liquid heating process, which includes such substances as acetaldehyde, acetone, acrolein, butyraldehyde, crotonaldehyde, formaldehyde, methyl ethyl ketone, and propionaldehyde (etc.) (Geiss et al., 2016; Sleiman et al., 2016; Uchiyama et al., 2016). E-cigarettes that work with the help of a heated coil with a material made from metal with electrical resistance have some effects (Beauval et al., 2016; Cheng, 2014; Farsalinos et al., 2015a; Hess et al., 2017; Lerner et al., 2015; Mishra et al., 2017; Williams et al., 2017). The e-liquid was also found contaminating due to impurity. Nitrosamine is a chemical element typically found in cigarette smoke, and it has different forms, including 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone [NNK], N-Nitrosoanabasine [NAB], N-Nitrosoanatabine [NAT], and N-Nitrosornicotine [NNN] (Farsalinos et al., 2015a; Flora et al., 2016; Kosmider et al., 2014, 2016; Tayyarah & Long, 2014; Wagner et al., 2018). Regardless of this, research has shown that the level of dangerous and potentially dangerous components (HPHC) in e-cigarettes is much lower than the figures in ordinary cigarette aerosols (Dautzenberg & Garelik, 2017; Farsalinos et al., 2015b; Hutzler et al., 2014; Margham et al., 2016).

To date, there are growing evidence to suggest the reduced risk nature of e-cigarettes over standard cigarettes (Polosa et al., 2013; Farsalinos & Polosa, 2014; Hajek et al., 2017; Stephens, 2018). This fact is evident in many studies, but remains a subject for discussion (Soneji et al., 2018). Despite being considered a safer alternative to conventional cigarettes, e-cigarettes still pose health concerns due to the presence of harmful chemicals. The World Health Organization (WHO) has identified nine toxicants that should be minimized in tobacco products, yet their presence in e-cigarettes remains largely unexplored (Eldridge et al., 2017; WHO, 2014). Previous studies have suggested that e-cigarette aerosols contain toxic substances, such as formaldehyde and benzo[a]pyrene, which are linked to respiratory and cardiovascular diseases (Kosmider et al., 2016; Wagner et al., 2018). These findings highlight the need for comprehensive laboratory testing to assess the safety of e-cigarettes, which has never been done in Indonesia.

The lack of standardized testing and regulation in Indonesia raises concerns about the chemical or toxic content and quality of e-cigarettes available in the market. While some studies suggest that e-cigarettes contain fewer harmful chemicals compared to conventional cigarettes, the actual levels of toxicants in Indonesian e-cigarette products remain unclear, still under estimation (Abelia et al., 2023). Moreover,

discrepancies between labelled and actual nicotine content may mislead consumers, posing additional health risks. Therefore, a thorough evaluation of e-cigarette products is essential to provide accurate information for policymakers, health professionals, and consumers. This study aims to evaluate the chemical composition of e-cigarettes in Indonesia by analyzing nicotine content and the nine WHO-targeted toxicants only on e-cigarette with e-liquid, meanwhile heated tobacco will be discussed in separate paper.

The findings of this study will benefit multiple stakeholders, including regulators and policymakers, who can use the results to develop evidence-based regulations for e-cigarettes, and health professionals, who will gain insights into potential health risks to support public health recommendations. Consumers will also benefit by obtaining accurate information on e-cigarettes' vapor chemical content, allowing them to make informed choices, while the tobacco and vaping industry can leverage the findings to reduce products' potential health risks of e-cigarette and regulatory compliance. This paper is structured as follows: Section 1 describes the introduction, Section 2 describes the review of literature, Section 3 describes the research methodology, including sample selection and testing procedures, Section 4 presents the results of toxicant and nicotine content analysis, Section 5 discusses the implications of these findings, focusing on health risks and regulatory considerations and Section 6 concludes with key takeaways and recommendations for stakeholders.

2. Literature Review

2.1 Overview of Toxicants in E-Cigarettes

E-cigarettes have gained popularity as an alternative to conventional cigarettes, but concerns persist regarding their chemical composition and potential health risks. Research has identified various toxicants present in e-cigarette aerosols, including carbonyl compounds, volatile organic compounds, and tobacco-specific nitrosamines (Farsalinos & Gillman, 2018; Kosmider et al., 2016). While previous studies suggest that e-cigarettes generally contain fewer harmful substances than conventional cigarettes, variations in product composition, device type, and user behavior influence toxicant levels (Goniewicz et al., 2018).

Despite ongoing debates, the growing number of e-cigarette users underscores the importance of assessing their potential risks through proper testing (Murphy et al., 2017; Wang et al., 2019). Evaluations of e-liquids, e-cigarette devices, and resultant aerosols have revealed that toxicant levels can vary

significantly due to differences in product formulations and heating mechanisms (Belushkin et al., 2018; CORESTA, 2015). Carbonyl compounds such as acetaldehyde, acrolein, and formaldehyde are known to form during the heating process of e-liquids, with their concentrations dependent on factors like coil temperature and e-liquid ingredients (Geiss et al., 2016; Sleiman et al., 2016).

Furthermore, studies have shown that e-cigarette aerosols may contain trace amounts of tobacco-specific nitrosamines, including NNN and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), which are known carcinogens present in traditional cigarette smoke (Farsalinos & Polosa, 2014; Kosmider et al., 2016). The presence of heavy metals such as nickel, cadmium, and lead has also been reported in some e-cigarette samples, likely originating from the heating coil material (Beauval et al., 2016). Although overall toxicant levels in e-cigarettes tend to be lower than those in combustible cigarettes, inconsistencies in product quality and manufacturing highlight the need for standardized testing.

2.2 General Categories of Toxicants in E-Cigarettes

The WHO has identified key toxicants that should be minimized in tobacco products, including e-cigarettes (Eldridge et al., 2017; WHO, 2014). These toxicants fall into three major categories:

1. Carbonyl Compounds (e.g., formaldehyde, acetaldehyde, acrolein) – Generated during the heating process of e-liquid, these compounds are linked to respiratory irritation and carcinogenicity (Jensen et al., 2017; Salamanca et al., 2018).
2. Volatile Organic Compounds (e.g., benzene, 1,3-butadiene) – Highly reactive compounds found in tobacco smoke and some e-cigarette aerosols, with known associations to leukemia and respiratory diseases (Rahimpoor et al., 2023).
3. Tobacco-Specific Nitrosamines (NNN, NNK) – Carcinogenic compounds present in both conventional and e-cigarettes, although at lower levels in the latter (Farsalinos, Voudris, et al., 2015b).

2.3 Findings from Previous Studies

Several studies have examined the toxicant levels in e-cigarette aerosols compared to conventional cigarette smoke. Kosmider et al. (2014) found that formaldehyde and acetaldehyde were present in e-cigarette vapor, though at significantly lower

concentrations than in traditional tobacco smoke. Similarly, a study by Margham et al. (2016) reported that e-cigarette emissions contained significantly reduced levels of carcinogens and carbonyls compared to combustible cigarettes. However, concerns remain regarding variability in e-liquid ingredients, heating temperature, and user puffing behavior, which may influence toxicant generation (Geiss et al., 2016; Sleiman et al., 2016).

The availability of testing results from testing in other countries that already exist do not reduce the importance of the need for similar testing in Indonesia, as the raw materials, composition and processes can be different. According to Wu et al. (2005), the ingredient formula can differ between countries. This indicates that the content can be regulated differently by manufacturers, especially for e-cigarettes whose ingredients are mixed into e-liquid. This different content (in one brand) is also analyzed in relation to regulations and the level of strictness of its implementation. Previous studies on formaldehyde concentrations in e-cigarette vapor circulating in Indonesia have been published by Lestari et al. (2018) who recommended further research on the chemical contents of e-cigarettes. Thus, it is important to conduct localised testing.

2.4 Research Gap and Novelty

Although existing literature provides valuable insights into e-cigarette toxicants, most studies focus on Western markets, leaving a gap in research specific to Indonesia. Additionally, variations in product regulations and formulations across different countries necessitate localized studies. This study addresses this gap by conducting a comprehensive chemical analysis of e-cigarette samples in Indonesia, comparing them with conventional cigarettes, and providing data to support policy making.

3. Methods

3.1 E-Liquid Samples and Selection Criteria

This study tested a total of 63 cigarette samples, comprising 60 e-cigarette samples and three conventional cigarette samples for comparison, namely machine-made white cigarettes (SPM), hand-rolled kretek cigarettes (SKT), and an 1R6F reference cigarette. A detailed sample list is given in Table 1. The e-cigarette samples were divided into two major categories: closed system (6 samples) and open system (54 samples), with the open system further categorized into 45 freebase nicotine and 9 salt nicotine variants. Each e-liquid sample had a sample capacity of 30 ml, and conventional cigarette sample

had 100 sticks to evaluate 10 parameters. This satisfies the testing requirements for preserved backups and two testing repetitions. Table 2 shows in full the average and standard deviation of the content values of the test parameters for each type of cigarette.

The sample selection was conducted using a stratified random sampling approach to ensure representativeness of the Indonesian e-liquid market. Samples were obtained from various e-cigarette retail stores in the Greater Jakarta area, considering factors such as brand diversity, nicotine levels, and popular flavor variants. The nicotine concentrations in the selected samples ranged from 3 mg/ml to 50 mg/ml (according to label), reflecting the broad range of products available in the market. This selection approach ensures that the study findings can be generalized to a larger population of e-cigarette users in Indonesia.

3.2. Testing Laboratory

The laboratory testing was conducted at the Scientific Service Laboratory of Filtrona Manufacturing Indonesia (FMI) located in Surabaya, an independent and internationally recognized facility accredited under ISO/IEC 17025 by Indonesia National Accreditation Committee (LP-1443-IDN). This laboratory has extensive experience in tobacco and e-cigarette product testing, having performed similar analyses for regulatory bodies such as the Department of Health and Social Care (DHSC) UK, ANVISA Brazil, and the City of Honolulu, Hawaii, USA. In addition, Filtrona is an active member of CORESTA and has a worldwide reputation.

3.3. Device

The dedicated vaporizers were used for testing the closed system type. Meanwhile, for testing the open-system e-liquid, the vaporizer utilized adjustable power and air flow pod device (Figure 1a), which comes with two cartridge options with 0.4 Ω and 0.8 Ω coils (Figure 1b). For power settings, 30 watts and 15 watts were used for nicotine concentrations of less than 24 mg/ml and more than 24 mg/ml respectively. To prevent excessive pressure decreases that could cause the puffing process to fail, the device's airflow was adjusted to match the suction of the puffing machine. The puffing process did not work when the vaporizer's air flow setting was completely open during piloting. Four cartridges were used for each brand in order to prevent scale buildup on the coil, which may have an impact on the test results. Smoke and vapor samples were then collected using Cerulean SM450 NGP puffing machine. The selected samples have several types of vaporizer device shapes, so that

the connection between the pod container and the vaporizer device used an additional connector (Figure 2).

3.4. Testing Provisions and Data Analysis

To determine the ideal steam sampling (puffing) procedure parameters, a pilot test was conducted prior to the main test. The warming-up procedure was subsequently found to be 10 puffs, and the puff count was 30 times, based on this piloting process. The testing requirements do not restrict puff count or warming up. The goal of warming up is to provide stability to the actual puffing process and allow the amount of puff count to be modified to suit the requirements of the substance analysis to be performed. While nicotine levels in e-cigarettes were examined in liquid and vapor form, other parameter test results were acquired from smoke or vapor only. For extraction, the method used impinger (for carbonyl groups) and non-impinger (see Figure 3a and 3b).

The laboratory puffing method uses an internal procedure based on the ISO 20768 standard, with a square wave puff profile, a puff volume of 55 mL with a tolerance of 0.3 mL, a puff duration of 3 seconds, and a puff frequency of 30 seconds. Additionally, weight per puff is used to compare the analysis method with the results of the smoke and vapor tests. For data analysis, descriptive and inferential statistical methods were applied. The Mann-Whitney U test was used to compare differences in nicotine and toxicant levels between closed-system and open-system e-cigarettes. Additionally, mean and standard deviation values were calculated for each toxicant parameter across different sample groups.

4. Results

4.1. Comparison between Conventional Cigarettes and E-cigarettes

Descriptively, overall toxicant contents of e-cigarette samples were significantly lower than conventional cigarettes. The average values reach 190 times lower for ben[a]pyrene, 10 times lower for formaldehyde, 168 times lower for acetaldehyde, 115 times lower for acrolein, 75 times lower for 1,3-butadiene, 6500 times lower for benzene, 52 times lower for NNN and 28 times lower for NNK.

A biplot display of each type of cigarette was based on the ten selected WHO test variables. After factor analysis of the 10 variables, which resulted in their reduction to two main components in Figure 4, this biplot display was produced. While the second main component could only represent 13,95% of the diversity of the data, the first main component could

account for up to 86,05% of the diversity. Therefore, the total diversity of the data can be explained by these two major components up to 100% of the time.

The biplot display makes the differences between electronic and traditional cigarettes more evident. The difference between conventional and e-cigarettes can be found in the quantity of formaldehyde, acetaldehyde, acrolein, 1,3-butadiene, benzene, benzo[a]pyrene, N-nitrosamine NNN, and NNK aerosol compared to the contain in conventional cigarettes. An average of 109.6 µg/puff is the highest concentration seen in conventional cigarettes, particularly in acetaldehyde aerosol, meanwhile it is only an average of 0.37 µg/puff for e-cigarette. Furthermore, an average of 0.58 µg/puff is the highest concentration seen in formaldehyde in e-cigarette, meanwhile it is found 7.17 µg/puff in the conventional cigarette.

The statistical value of the Z test = -1.76 with p-value of 0.078, which is greater than 0.05, is derived from the Mann-Whitney test results in Table 3 and indicates that, at the 95% confidence level, there is no significant difference between the average nicotine aerosol content in conventional and e-cigarettes.

4.2. Comparison between Open System and Closed System E-Cigarettes

The fact that e-cigarettes are taste-specific is one of their features. The flavors of e-cigarettes are numerous. A graph of the taste distribution of the 60 e-cigarettes sampled for this investigation is presented in Figure 5. The most prevalent taste is strawberry, which is followed by grape, watermelon, and distinctive flavors. The other 29 come in 29 distinct flavors.

Information regarding the nicotine level of e-cigarettes can also be found on the label or package. The data for nicotine based on the e-liquid test results from two different types of e-cigarettes and the packaging are displayed in Table 4. It is evident that, for both closed and open e-cigarette types, the average nicotine content value of the e-liquid obtained from the test results is less than the figure stated on the label of the e-cigarette.

Using the Mann-Whitney test at a significance threshold of 5%, the amount of nicotine e-liquid content difference between the two types of e-cigarettes was determined. The analysis's findings are displayed in Table 5's SPSS output. The Mann-Whitney test obtained the Z-value of -3.697 and p-value of 0.000 for nicotine e-liquid variable in Table 5, which is less than 0.05, therefore, it can be said that at a 95% confidence interval there exists a significant difference between the two types of e-cigarettes with different nicotine content. The nicotine content in

closed e-cigarettes was 2.22% greater than it was in open e-cigarettes on average. Moreover, Table 5 displays the results of the Mann-Whitney test for the nicotine and formaldehyde aerosol variables. In these two cases, we obtained p-value is smaller than 0.05. Consequently, the type of e-cigarettes with these two variations also differed significantly in the concentration of nicotine. In contrast, the tested seven variables (acetaldehyde aerosol, acrolein aerosol, 1,3-butadiene aerosol, benzene aerosol, benzo[a]pyrene aerosol, N nitrosamines NNN aerosol, and NNK aerosol) for both type of e-cigarette have nearly the same content value, really fall below the Limit of Detection (LOD) or Limit of Quantification (LOQ).

4.3. Comparison between Freebase Nicotine and Salt Nicotine E-Cigarettes

Freebase nicotine and salt nicotine (saltnic) are two types of e-liquid for open system e-cigarettes. There were 45 cigarettes samples of freebase nicotine (71% of the total sample). A Mann-Whitney test was run on the average value of these ten parameters to see a more thorough comparison between salt nicotine and freebase nicotine cigarettes with respect to the ten chosen WHO test parameters. Table 6 displays the outcomes by examining the signature and shows that five variables nicotine in e-liquid, nicotine in aerosol, benzo[a]pyrene aerosol, formaldehyde aerosol, and acrolein aerosol have p-value less than 0.05. Therefore, the average content values for these five variables show substantial differences between salt nicotine and freebase nicotine cigarettes at the 95% confidence level. In comparison to freebase nicotine cigarettes, salt nicotine cigarettes often contain a larger amount of the five factors in concern, according to the data from Table 2. In the meantime, the content values of both freebase nicotine and salt nicotine cigarettes for the remaining five variables (acetaldehyde aerosol, 1,3-butadiene aerosol, benzene aerosol, N nitrosamines NNN aerosol, and NNK aerosol) are nearly identical, and most of the lab test results fall below the limit of quantification (LOQ) or limit of detection (LOD).

5. Discussion

This study provides important insights into the chemical composition of e-cigarettes in Indonesia, specifically concerning nicotine content and the presence of WHO-designated toxicants. The findings confirm that while e-cigarette aerosols contain significantly lower toxicant levels than conventional cigarettes, variations between product types indicate that device characteristics, e-liquid formulation, and heating mechanisms can influence toxicant emissions. These findings are consistent with previous studies,

such as those by (Goniewicz et al., 2013) and Kosmider et al. (2014) which emphasize that e-cigarette emissions are not entirely risk-free, despite being marketed as a safer alternative.

A key concern identified in this study is the presence of formaldehyde, acetaldehyde, and benzo[a]pyrene, albeit at levels lower than those in conventional cigarettes. Previous research by Jensen et al. (2017) and Salamanca et al. (2018) has shown that these compounds, particularly aldehydes, are formed during the heating of e-liquid components and have been linked to respiratory irritation and carcinogenicity. The detection of acetaldehyde in certain samples at levels comparable to some conventional cigarettes raises concerns about cumulative exposure effects, especially for long-term users. Margham et al. (2016) also found that while e-cigarette emissions contain reduced toxicants compared to conventional cigarette, the presence of carbonyl compounds remains a significant issue. These results suggest that while e-cigarettes reduce exposure to certain toxicants, they still present potential health risks that warrant further investigation.

Another critical finding is the discrepancy between labelled and actual nicotine content in e-liquid samples. This aligns with research by Geiss et al. (2016) and Sleiman et al. (2016), which reported inconsistencies in nicotine labelling across different brands. Such discrepancies could mislead consumers, particularly those attempting to control their nicotine intake. Williams et al. (2017) further highlighted similar concerns, demonstrating that heavy metal contaminants in e-cigarette aerosols originate from heating elements and that could contribute to inhalation toxicity.

Referring to the content value of the 10 selected test parameters in Table 2, it shows that there is no significant difference between the closed system and open-system e-cigarette. These differences may be attributed to the controlled formulation of closed-system pods, whereas open-system devices allow greater e-liquid formulation and manufacturers, leading to higher heating temperatures. This finding reinforces the importance of standardized device regulations to ensure consistent and safe product use. The implications of these findings extend beyond individual consumer health to broader public health and regulatory considerations. Despite reduced toxicant levels, the presence of harmful compounds in e-cigarette aerosols suggests that these products should not be considered completely safe. Regulatory authorities in Indonesia should consider implementing stricter testing protocols, mandatory labelling accuracy checks, and quality control measures to ensure product integrity to minimize consumer exposure to potentially harmful substances. Studies

such as those by Murphy et al. (2017) emphasize that effective regulation is essential for mitigating potential health risks associated with e-cigarette use.

Additionally, this study underscores the need for further research on long-term exposure to e-cigarette emissions. While laboratory testing provides valuable baseline data, cell-based and in vivo toxicity studies are necessary to fully understand the biological impact of prolonged e-cigarette use. Wagner et al. (2018) highlight that controlled clinical trials are crucial in determining the long-term effects of e-cigarette exposure. Future research should focus on expanding the sample size, incorporating a wider range of e-cigarette brands and formulations, and investigating potential health outcomes through further studies.

6. Conclusion

This study evaluated the chemical composition of e-cigarette aerosols in Indonesia, focusing on nicotine content and nine WHO-designated toxicants. The findings confirm that e-cigarettes generally contain lower levels of harmful substances compared to conventional cigarettes. However, variations in toxicant levels across different products indicate that e-cigarette's toxicant in vapor is influenced by factors such as device type and e-liquid formulation. Key findings of this study include:

- In general, the toxicity level of e-cigarettes is lower than that of conventional cigarettes. This is analysed due to differences in production and product quality, so enhanced regulations and standardized testings are needed.
- Carbon monoxide, 1,3-butadiene, benzene, NNN, and NNK were not detected in any e-cigarette samples, confirming the reduced presence of major toxicants compared to conventional cigarettes.
- Benzo[a]pyrene was detected in one freebase nicotine sample and 50% of the salt nicotine samples, but at levels below the LOQ.
- Acrolein was present in one salt nicotine sample, while formaldehyde and acetaldehyde were detected at low levels in various samples, highlighting the need for further quality control.
- Nicotine content in e-liquids was generally lower than the levels stated on product labels, indicating inconsistencies in labelling accuracy.

Policy and Practical Implications

Given these findings, policymakers should consider implementing further regulations to improve product labelling accuracy, to ensure consumer health and safety. Regulatory measures could include standardized testing protocols and mandatory nicotine content verification. Furthermore, public awareness campaigns should educate consumers about the potential risks associated with e-cigarette use, particularly concerning exposure to aldehydes and other substance.

Limitations of the Study

Despite its contributions, this study has certain limitations. The sample size, while representative of the Indonesian market, does not capture the full range of available e-cigarette brands and formulations. Additionally, the study focused on chemical analysis without assessment of the biological effects of exposure to e-cigarette aerosols. Variability in user behaviours, such as puffing patterns and device setting, may also influence toxicant emissions but was not addressed in this research.

Recommendations for Future Research

The method used in this study is not complete yet; many substances in e-cigarette samples still cannot be measured or detected. In international standards, there are still many parameters that cannot be tested because the support of testing tools and methods has not been validated. In addition to the testing of chemical substances in the liquid and vapor, cell-based clinical trials are needed for confirmation. This is a topic that needs to be pursued in future studies. Further studies should explore long-term health impacts through clinical trials and epidemiological research. Future research should also examine the presence of additional hazardous substances not covered in this study. Expanding independent and accredited testing facilities in Indonesia improve the accuracy and reliability of e-cigarette evaluations, thereby providing a stronger basis for evidence-based and risk-based regulation.

References

1. Abelia, X. A., Lesmana, R., Goenawan, H., Abdulah, R., & Barliana, M. I. (2023). Comparison impact of cigarettes and e-cigs as lung cancer risk inductor: a narrative review. *European Review for Medical and Pharmacological Sciences*, 27(13), 6301–6318. https://doi.org/10.26355/eurrev_202307_32990
2. Beauval, N., Howsam, M., Antherieu, S., Allorge, D., Soyez, M., Garçon, G., Goossens, J. F., Lo-Guidice, J. M., & Garat, A. (2016). Trace elements in e-liquids - Development and validation of an ICP-MS method for the analysis of electronic cigarette refills. *Regulatory Toxicology and Pharmacology*, 79, 144–148. <https://doi.org/10.1016/j.yrtph.2016.03.024>
3. Belushkin, M., Esposito, M., Jaccard, G., Jeannet, C., Korneliou, A., & Tabin Djoko, D. (2018). Role of testing standards in smoke-free product assessments. *Regulatory Toxicology and Pharmacology*, 98(July), 1–8. <https://doi.org/10.1016/j.yrtph.2018.06.021>
4. Cheng, T. (2014). Chemical evaluation of electronic cigarettes. *Tobacco Control*, 23(SUPPL. 2). <https://doi.org/10.1136/tobaccocontrol-2013-051482>
5. CORESTA. (n.d.). Determination of glycerin, propylene glycol, water, and nicotine in the aerosol of e-cigarettes by gas chromatography analysis. 2017.
6. CORESTA. (2015). Routine Analytical Machine for E-Cigarette Aerosol Generation and Collection - Definitions and Standard Conditions.
7. Dautzenberg, B., & Garelik, D. (2017). Patients with lung cancer: Are electronic cigarettes harmful or useful? *Lung Cancer*, 105, 42–48. <https://doi.org/10.1016/j.lungcan.2016.05.011>
8. Eldridge, A. C., McAdam, K. G., Betson, T. R., Gama, M. V., & Proctor, C. J. (2017). Impact assessment of WHO TobReg proposals for mandated lowering of selected mainstream cigarette smoke toxicants. *Regulatory Toxicology and Pharmacology*, 86, 332–348. <https://doi.org/10.1016/j.yrtph.2017.02.022>
9. Farsalinos, K. E., & Gillman, G. (2018). Carbonyl emissions in e-cigarette aerosol: A systematic review and methodological considerations. *Frontiers in Physiology*, 8(JAN), 1–14. <https://doi.org/10.3389/fphys.2017.01119>
10. Farsalinos, K. E., Gillman, G., Poulas, K., & Voudris, V. (2015). Tobacco-Specific Nitrosamines in Electronic Cigarettes: Comparison between liquid and aerosol levels. *International Journal of Environmental Research and Public Health*, 12(8), 9046–9053. <https://doi.org/10.3390/ijerph120809046>
11. Farsalinos, K. E., & Polosa, R. (2014). Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: A systematic review. *Therapeutic Advances in Drug Safety*, 5(2), 67–86. <https://doi.org/10.1177/2042098614524430>
12. Farsalinos, K. E., Voudris, V., & Poulas, K. (2015a). Are Metals Emitted from Electronic Cigarettes a Reason for Health Concern? A

- Risk-Assessment Analysis of Currently Available Literature. *International Journal of Environmental Research and Public Health*, 12(5), 5215–5232. <https://doi.org/10.3390/ijerph120505215>
13. Farsalinos, K. E., Voudris, V., & Poulas, K. (2015b). E-cigarettes generate high levels of aldehydes only in “dry puff” conditions. *Addiction*, 110(8), 1352–1356. <https://doi.org/10.1111/add.12942>
14. Flora, J. W., Meruva, N., Huang, C. B., Wilkinson, C. T., Ballentine, R., Smith, D. C., Werley, M. S., & McKinney, W. J. (2016). Characterization of potential impurities and degradation products in electronic cigarette formulations and aerosols. *Regulatory Toxicology and Pharmacology*, 74(June 2015), 1–11. <https://doi.org/10.1016/j.yrtph.2015.11.009>
15. Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health*, 219(3), 268–277. <https://doi.org/10.1016/j.ijheh.2016.01.004>
16. Goniewicz, M. L., Kuma, T., Gawron, M., Knysak, J., & Kosmider, L. (2013). Nicotine levels in electronic cigarettes. *Nicotine and Tobacco Research*, 15(1), 158–166. <https://doi.org/10.1093/ntr/nts103>
17. Goniewicz, M. L., Smith, D. M., Edwards, K. C., Blount, B. C., Caldwell, K. L., Feng, J., Wang, L., Christensen, C., Ambrose, B., Borek, N., Van Bommel, D., Konkel, K., Erives, G., Stanton, C. A., Lambert, E., Kimmel, H. L., Hatsukami, D., Hecht, S. S., Niaura, R. S., ... Hyland, A. J. (2018). Comparison of Nicotine and Toxicant Exposure in Users of Electronic Cigarettes and Combustible Cigarettes. *JAMA Network Open*, 1(8), 1–16. <https://doi.org/10.1001/jamanetworkopen.2018.5937>
18. Hajek, P., Etter, J. F., Benowitz, N., Eissenberg, T., & McRobbie, H. (2014). Electronic cigarettes: Review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction*, 109(11), 1801–1810. <https://doi.org/10.1111/add.12659>
19. Hajek, P., Przulj, D., Phillips, A., Anderson, R., & McRobbie, H. (2017). Nicotine delivery to users from cigarettes and from different types of e-cigarettes. *Psychopharmacology*, 234(5), 773–779. <https://doi.org/10.1007/s00213-016-4512-6>
20. Hess, C. A., Olmedo, P., Navas-Acien, A., Goessler, W., Cohen, J. E., & Rule, A. M. (2017). E-cigarettes as a source of toxic and potentially carcinogenic metals. *Environmental Research*, 152(September 2016), 221–225. <https://doi.org/10.1016/j.envres.2016.09.026>
21. Hutzler, C., Paschke, M., Kruschinski, S., Henkler, F., Hahn, J., & Luch, A. (2014). Chemical hazards present in liquids and vapors of electronic cigarettes. *Archives of Toxicology*, 88(7), 1295–1308. <https://doi.org/10.1007/s00204-014-1294-7>
22. ISO. (2018). Vapour products - Routine analytical vaping machine - Definitions and standard conditions.
23. Jensen, R. P., Strongin, R. M., & Peyton, D. H. (2017). Solvent Chemistry in the Electronic Cigarette Reaction Vessel. *Scientific Reports*, 7(November 2016), 1–11. <https://doi.org/10.1038/srep42549>
24. Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., & Goniewicz, M. L. (2014). Carbonyl compounds in electronic cigarette vapors: Effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research*, 16(10), 1319–1326. <https://doi.org/10.1093/ntr/ntu078>
25. Kosmider, L., Sobczak, A., Prokopowicz, A., Kurek, J., Zaciera, M., Knysak, J., Smith, D., & Goniewicz, M. L. (2016). Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, Benzaldehyde. *Thorax*, 71(4), 376–377. <https://doi.org/10.1136/thoraxjnl-2015-207895>
26. Lerner, Chad A; Sundar, Isaac K; Watson, Richard M; Elder, Alison; Jones, Ryan; Done, Douglas; Kurtzman, Rachel; Ossip, Deborah J; Robinson, Risa; McIntosh, Scott; Rahman, I. (2015). Environmental Health Hazards of E-cigarettes and their Components. *Environ Pollut*, 198, 100–107. <https://doi.org/10.1016/j.envpol.2014.12.033>
27. Lestari, K. S., Humairo, M. V., & Agustina, U. (2018). Formaldehyde Vapor Concentration in Electronic Cigarettes and Health Complaints of Electronic Cigarettes Smokers in Indonesia. *Journal of Environmental and Public Health*, 2018. <https://doi.org/10.1155/2018/9013430>
28. Margham, J., McAdam, K., Forster, M., Liu, C., Wright, C., Mariner, D., & Proctor, C. (2016). Chemical Composition of Aerosol from an E-Cigarette: A Quantitative Comparison with Cigarette Smoke. *Chemical Research in Toxicology*, 29(10), 1662–1678. <https://doi.org/10.1021/acs.chemrestox.6b0018>

- 8
29. Miller, C. R., Sutanto, E., Smith, D. M., Hitchman, S. C., Gravely, S., Yong, H. H., Borland, R., O'Connor, R. J., Cummings, K. M., Fong, G. T., Hyland, A., Quah, A. C. K., & Goniewicz, M. L. (2022). Characterizing Heated Tobacco Product Use among Adult Cigarette Smokers and Nicotine Vaping Product Users in the 2018 ITC Four Country Smoking & Vaping Survey. *Nicotine and Tobacco Research*, 24(4), 493–502. <https://doi.org/10.1093/ntr/ntab217>
 30. Mishra, V. K., Kim, K. H., Samaddar, P., Kumar, S., Aggarwal, M. L., & Chacko, K. M. (2017). Review on metallic components released due to the use of electronic cigarettes. *Environmental Engineering Research*, 22(2), 131–140. <https://doi.org/10.4491/eer.2017.056>
 31. Murphy, J., Gaca, M., Lowe, F., Minet, E., Breheny, D., Prasad, K., Camacho, O., Fearon, I. M., Liu, C., Wright, C., McAdam, K., & Proctor, C. (2017). Assessing modified risk tobacco and nicotine products: Description of the scientific framework and assessment of a closed modular electronic cigarette. *Regulatory Toxicology and Pharmacology*, 90, 342–357. <https://doi.org/10.1016/j.yrtph.2017.09.008>
 32. Polosa, R., Rodu, B., Caponnetto, P., Maglia, M., & Raciti, C. (2013). A fresh look at tobacco harm reduction: The case for the electronic cigarette. *Harm Reduction Journal*, 10(1), 1–11. <https://doi.org/10.1186/1477-7517-10-19>
 33. Rahimpoor, R., Jalilian, H., Mohammadi, H., & Rahmani, A. (2023). Biological exposure indices of occupational exposure to benzene: A systematic review. *Heliyon*, 9(11), e21576. <https://doi.org/10.1016/j.heliyon.2023.e21576>
 34. Salamanca, J. C., Meehan-Atrash, J., Vreeke, S., Escobedo, J. O., Peyton, D. H., & Strongin, R. M. (2018). E-cigarettes can emit formaldehyde at high levels under conditions that have been reported to be non-averse to users /639/638/11/872 /639/638/899 /128 /140 /140/131 /82/16 article. *Scientific Reports*, 8(1), 6–11. <https://doi.org/10.1038/s41598-018-25907-6>
 35. Sleiman, M., Logue, J. M., Montesinos, V. N., Russell, M. L., Litter, M. I., Gundel, L. A., & Destaillats, H. (2016). Emissions from electronic cigarettes: Key parameters affecting the release of harmful chemicals. *Environmental Science and Technology*, 50(17), 9644–9651. <https://doi.org/10.1021/acs.est.6b01741>
 36. Soneji, S. S., Sung, H. Y., Primack, B. A., Pierce, J. P., & Sargent, J. D. (2018). Quantifying population-level health benefits and harms of e-cigarette use in the United States. *PLoS ONE*, 13(3), 1–19. <https://doi.org/10.1371/journal.pone.0193328>
 37. Stephens, W. E. (2018). Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. *Tobacco Control*, 27(1), 10–17. <https://doi.org/10.1136/tobaccocontrol-2017-053808>
 38. Tayyarah, R., & Long, G. A. (2014). Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air. *Regulatory Toxicology and Pharmacology*, 70(3), 704–710. <https://doi.org/10.1016/j.yrtph.2014.10.010>
 39. Uchiyama, S., Senoo, Y., Hayashida, H., Inaba, Y., Nakagome, H., & Kunugita, N. (2016). Determination of chemical compounds generated from second generation e-cigarettes using a sorbent cartridge followed by a two-step elution method. *Analytical Sciences*, 32(5), 549–555. <https://doi.org/10.2116/analsci.32.549>
 40. Wagner, K. A., Flora, J. W., Melvin, M. S., Avery, K. C., Ballentine, R. M., Brown, A. P., & McKinney, W. J. (2018). An evaluation of electronic cigarette formulations and aerosols for harmful and potentially harmful constituents (HPHCs) typically derived from combustion. *Regulatory Toxicology and Pharmacology*, 95(December 2017), 153–160. <https://doi.org/10.1016/j.yrtph.2018.03.012>
 41. Wang, G., Liu, W., & Song, W. (2019). Toxicity assessment of electronic cigarettes. *Inhalation Toxicology*, 0(0), 1–15. <https://doi.org/10.1080/08958378.2019.1671558>
 42. WHO. (2014). FCTC/COP/6/14 - Work in progress in relation to Articles 9 and 10 of the WHO Framework Convention on Tobacco Control: FOURTH SESSION (Issue July). http://apps.who.int/gb/fctc/PDF/cop4/FCTC_COP4_ID2-en.pdf
 43. Williams, M., Bozhilov, K., Ghai, S., & Talbot, P. (2017). Elements including metals in the atomizer and aerosol of disposable electronic cigarettes and electronic hookahs. *PLoS ONE*, 12(4), 1–24. <https://doi.org/10.1371/journal.pone.0175430>
 44. Wu, W., Zhang, L., Jain, R. B., Ashley, D. L., & Watson, C. H. (2005). Determination of carcinogenic tobacco-specific nitrosamines in mainstream smoke from U.S.-brand and non-U.S.-brand cigarettes from 14 countries. *Nicotine and Tobacco Research*, 7(3), 443–451. <https://doi.org/10.1080/14622200500125898>

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Table 1. Sample List

Code	Category	Vol. per pack (stick or ml)	Nicotine as label (mg)
K1	Conventional SKT	12	2.3
K2	Conventional SPM	20	1
K3	Conventional SPM 1R6F reference cigarette		
PILOTING	Closed system EC	1.6	30
CL1	Closed system-EC	4.8	34
CL2	Closed system-EC	1.9	34
CL3	Closed system-EC	2.9	30
CL4	Closed system-EC	1.9	50
CL5	Closed system-EC	1.6	30
CL6	Closed system-EC	4.2	20
OP1	Open system-EC	60	3
OP2	Open system-EC	60	3
OP3	Open system-EC	60	6
OP4	Open system-EC	60	3
OP5	Open system-EC	60	3
OP6	Open system-EC	60	6
OP7	Open system-EC	60	3
OP8	Open system-EC	30	12
OP9	Open system-EC	60	6
OP10	Open system-EC	60	3
OP11	Open system-EC	25	30
OP12	Open system-EC	60	6
OP13	Open system-EC	30	30
OP14	Open system-EC	30	30
OP15	Open system-EC	30	30
OP16	Open system-EC	30	30
OP17	Open system-EC	60	9
OP18	Open system-EC	60	3
OP19	Open system-EC	60	3
OP20	Open system-EC	60	3
OP21	Open system-EC	60	6
OP22	Open system-EC	30	9
OP23	Open system-EC	30	40
OP24	Open system-EC	60	6
OP25	Open system-EC	60	6
OP26	Open system-EC	30	25
OP27	Open system-EC	60	6
OP28	Open system-EC	60	3
OP29	Open system-EC	60	3
OP30	Open system-EC	60	6
OP31	Open system-EC	30	48
OP32	Open system-EC	60	3
OP33	Open system-EC	60	3
OP34	Open system-EC	60	3

Code	Category	Vol. per pack (stick or ml)	Nicotine as label (mg)
OP35	Open system-EC	60	6
OP36	Open system-EC	30	12
OP37	Open system-EC	30	24
OP38	Open system-EC	60	3
OP39	Open system-EC	60	6
OP40	Open system-EC	30	15
OP41	Open system-EC	30	15
OP42	Open system-EC	60	9
OP43	Open system-EC	60	9
OP44	Open system-EC	60	9
OP45	Open system-EC	60	6
OP46	Open system-EC	60	3
OP47	Open system-EC	60	7
OP48	Open system-EC	60	6
OP49	Open system-EC	60	6
OP50	Open system-EC	60	3
OP51	Open system-EC	30	15
OP52	Open system-EC	30	10
OP53	Open system-EC	30	10
OP54	Open system-EC	30	10

Table 2. Average content value of 10 selected test parameters for each type of cigarette

Substances	Conventional Cigarette		Closed System		Open system freebase		Open system salt nic	
	Mean	Std.Dev	Mean	Std.Dev	Mean	Std.Dev	Mean	Std.Dev
Nicotine e-liquid (%)	0.00	0.00	2.84	1.02	0.36	0.17	1.99	1.09
Nicotine_Aerosol (mg/puff)	0.18	0.05	0.19	0.07	0.06	0.04	0.30	0.18
Benzo[a]pyrene_Aerosol (ng/puff)	2.13	0.43	0.01	0.00	0.01	0.00	0.02	0.01
Formaldehyde_Aerosol (µg/puff)	7.17	2.58	0.43	0.03	0.54	0.15	0.76	0.36
Acetaldehyde_Aerosol (µg/puff)	109.64	46.39	0.33	0.04	0.34	0.23	0.46	0.43
Acrolein_Aerosol (µg/puff)	12.46	4.80	0.08	0.00	0.08	0.00	0.12	0.12
1,3-butadiene_Aerosol (µg/puff)	8.93	3.24	0.10	0.00	0.10	0.00	0.10	0.00
Benzene_Aerosol (µg/puff)	7.60	2.58	0.00	0.00	0.00	0.00	0.00	0.00
NNN_Aerosol (ng/puff)	11.64	11.18	0.10	0.00	0.10	0.00	0.10	0.00
NNK_Aerosol (ng/puff)	10.31	8.16	0.20	0.00	0.20	0.00	0.20	0.00

Table 3. Comparison of average value of nicotine content in conventional and e-cigarettes
Nicotine_Aerosol (mg/puff)

Type	N	Mean	Std. Deviation
Conventional Cigarette	3	0.1767	0.05132
Electronic cigarettes	59	0.1119	0.11704

Total	62	0.1150	0.11536
Test Statistics			
Mann-Whitney U	35.000		
Wilcoxon W	1805.000		
Z	-1.760		
Asymp. Sig. (2-tailed)	0.078		

Table 4. Statistics of nicotine content on labels and nicotine e-liquid test results

Type		Labal Claim Nicotine (%)	Nicotine_e-liquid (%)
Closed system	N	6	6
	Minimum	2.0	1.59
	Maximum	5.0	4.71
	Mean	3.300	2.8433
	Std. Deviation	0.9778	1.01929
Open system	N	54	54
	Minimum	0.3	0.13
	Maximum	4.8	4.27
	Mean	1.061	0.6281
	Std. Deviation	1.0550	0.76153

Table 5. Comparison of the average values of nicotine e-liquid, nicotine aerosol, and formaldehyde aerosol content in closed and open e-cigarettes

Type		Nicotine_e-liquid (%)	Nicotine_Aerosol (mg/puff)	Formaldehyde_Aerosol (µg/puff)
Closed system - EC	Mean	2.8433	0.1920	0.4250
	Std. Deviation	1.01929	0.07190	0.03017
Open system - EC	Mean	0.6281	0.1044	0.5789
	Std. Deviation	0.76153	0.11806	0.21016
Test Statistics				
Mann-Whitney U		12.000	41.500	30.500
Wilcoxon W		1497.000	1526.500	51.500
Z		-3.697	-2.554	-3.243
Asymp. Sig. (2-tailed)		0.000	0.011	0.001

Table 6. Mann-Whitney test for comparison of the average content values of 10 selected test parameters in Freebase Nicotine and Salt Nicotine cigarettes

Substances	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig. (2-tailed)
Nicotine_e-liquid (%)	0.000	1035.000	-4.702	0.000
Nicotine_Aerosol (mg/puff)	2.500	1037.500	-4.662	0.000
Benzo[a]pyrene_Aerosol (ng/puff)	93.000	1128.000	-4.660	0.000
Formaldehyde_Aerosol (µg/puff)	56.000	1091.000	-3.404	0.001
Acetaldehyde_Aerosol (µg/puff)	201.500	246.500	-.023	0.981
Acrolein_Aerosol (µg/puff)	180.000	1215.000	-2.236	0.025
1,3-butadiene_Aerosol (µg/puff)	202.500	247.500	0.000	1.000
Benzene_Aerosol (µg/puff)	202.500	247.500	0.000	1.000
N nitrosaminas NNN_Aerosol (ng/puff)	202.500	247.500	0.000	1.000
NNK_Aerosol (ng/puff)	202.500	247.500	0.000	1.000



Figure 1a. Adjustable power and air flow pod device (for testing e-liquid for open system)



Figure 1b. Corresponding adjustable power and air flow pod device, e-liquid cartridge (2 ml) with 0.8 Ω (top) and 0.4 Ω (bottom) coils



Figure 2. Connector to vaporizer device

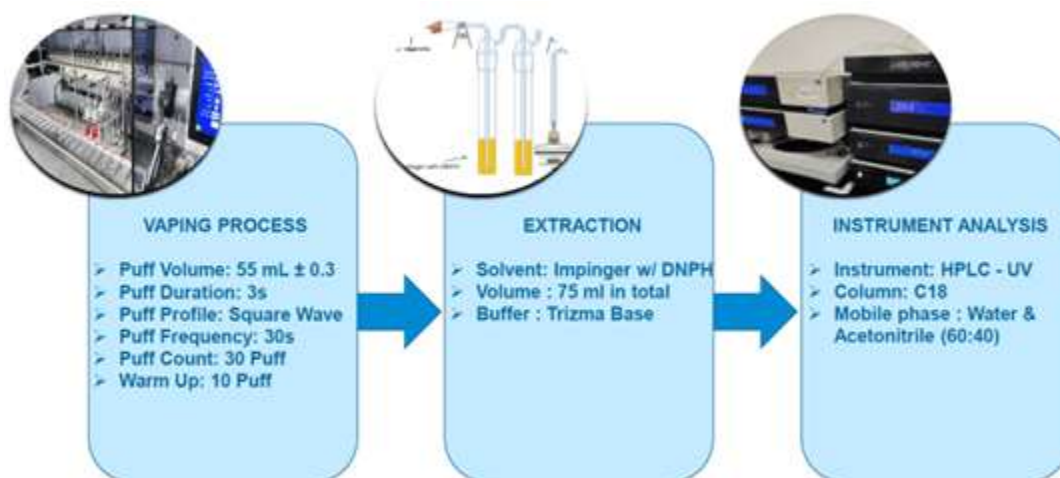


Figure 3a. Test process stages with impinger for carbonyl groups



Figure 3b. Test process stages for other substances

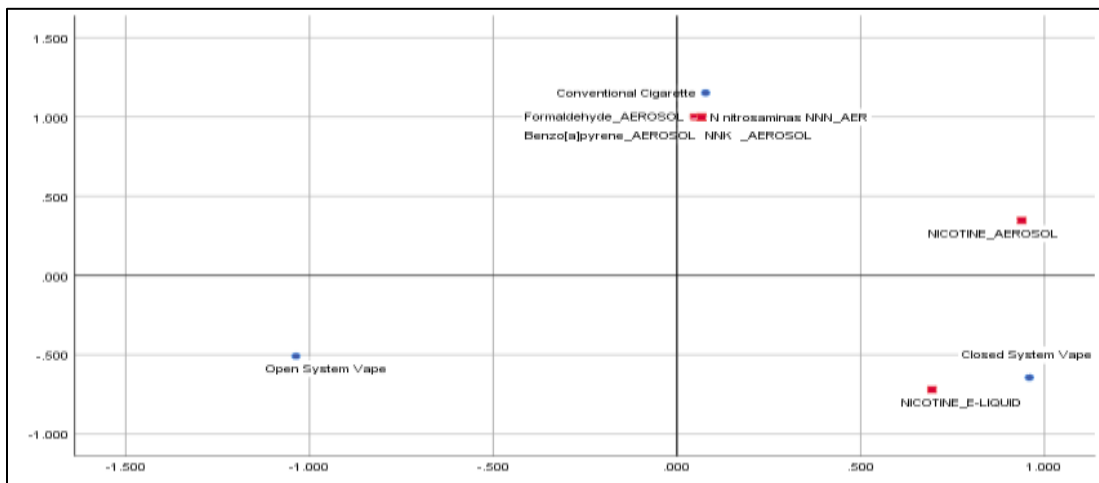


Figure 4. Biplot of each type of cigarette with the selected test parameters

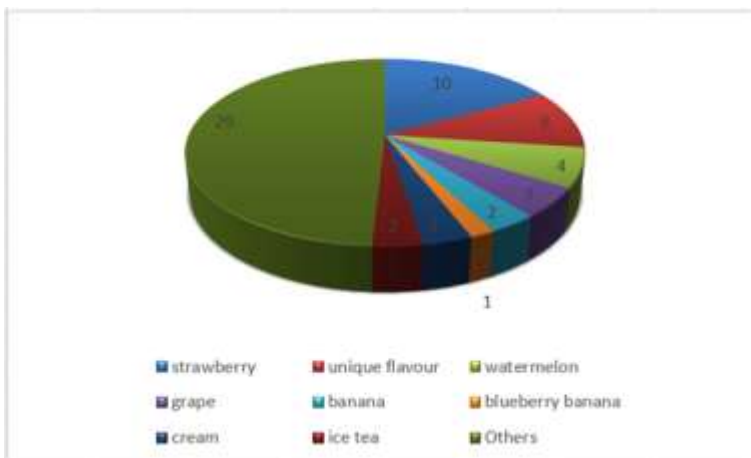


Figure 5. Graph of distribution of e-cigarette flavors