



UNIVERSITI PUTRA MALAYSIA

***VAPING TOPOGRAPHY, ANALYSIS OF E-CIGARETTE VAPOURS AND
HEALTH RISK ASSESSMENT AMONG CURRENT MALE USERS IN
SELECTED POPULATION***

NAJIHAH BINTI ZAINOL ABIDIN

FPSK(p) 2022 16



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Thesis Submitted to the School of Graduate Studies, Universiti Putra
Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of
Philosophy

October 2021

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Chair : Emilia Zainal Abidin, PhD
Faculty : Medicine and Health Sciences

Rising use of electronic cigarettes (EC) and limited data on its local vaping topography raise concerns and a challenge for a comprehensive health risk assessment to be done. This study aimed to estimate the non-carcinogenic health risks due to exposure to aluminium, chromium, iron, and copper as well as carcinogenic health risks from the exposure to formaldehyde, acetaldehyde, nickel, cadmium, and lead that are present in the EC vapours produced by locally-manufactured e-liquids. This study which was conducted in the Klang Valley, Selangor from February 2017 to April 2019 were divided into four sub-studies: i) a community survey on vaping topography, ii) chemical analysis of EC vapours, iii) daily exposure prediction modelling, and iv) Health Risk Assessment (HRA) of EC use. Data on vaping topography were gathered through purposive distribution of survey questionnaires to 226 tobacco users, including EC users. For the chemical analysis of the EC vapours produced by the ten local e-liquid samples, High-Performance Liquid Chromatography-Ultraviolet (HPLC-UV) was used to determine the concentrations of selected aldehydes whereas heavy metals content was quantified using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS). Sub-study III predicted the range of the daily exposures potentially experienced by the EC users. The non-carcinogenic and carcinogenic health risks were estimated in sub-study IV based on the data obtained in sub-study I to III. Out of the 226 tobacco users involved, 38% (n=86) were EC users who mostly (58.1%) preferred the third generation EC and purchased the product from the nearby vape shops. Majority of them used nicotinic e-liquid of 6 mg/mL with preference of creamy and fruity flavours. They reported usage of 50 puffs/day with two e-liquid bottles used up every month. The mean concentrations of formaldehyde, acetaldehyde, aluminium, chromium, iron, nickel, copper, cadmium, and lead were 4.31 ppm, 3.34 ppm, 0.126 ppm, 0.0258 ppm, 0.646 ppm, 0.520 ppm, 0.118 ppm, 0.00453 ppm, and 0.0288 ppm respectively when operated in low wattage setting. In high wattage setting, the

concentrations were 7.04 ppm, 5.88 ppm, 0.205 ppm, 0.0323ppm, 1.51 ppm, 0.980 ppm, 0.0495 ppm, 0.00311 ppm, and 0.0256 ppm accordingly. The HRA estimated that the exposure to selected compounds in EC vapours may potentially result into 1 and 2 in every 10,000 EC user's population to develop cancer in their lifetime. In sum, this study proves that exposures to aldehydes and heavy metals in EC vapours have measurable carcinogenic and non-carcinogenic health effects on its users with some were not disclosed and misled by the vigorous promotions of this product. The growing trend of EC users' population among never-smokers and the rapid evolution of this product, continuous research focusing on local EC products and users is necessary to provide more scientifically-based evidences to authorities for comprehensive regulations on EC products to be formulated and implemented. Collaborative efforts from all stakeholders are vital to avert the initiation of tobacco use among never-smokers to facilitate the achievement of Malaysia as a tobacco-free nation by 2045.

Keywords: Electronic cigarette, aldehydes, heavy metals, e-liquid, health risk assessment, carcinogenic risk, Malaysia

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

**TOPOGRAFI PENGGUNAAN, ANALISIS WAP ROKOK ELEKTRONIK DAN
PENILAIAN RISIKO KESIHATAN DALAM KALANGAN PENGGUNA LELAKI
SEMASA DALAM POPULASI TERPILIH**

Oleh

NAJIHAH BINTI ZAINOL ABIDIN

Oktober 2021

Pengerusi : Emilia Zainal Abidin, PhD
Fakulti : Perubatan dan Sains Kesihatan

Peningkatan penggunaan rokok elektronik (EC) dan data terhad mengenai topografi *vaping* tempatan menimbulkan kebimbangan dan merupakan cabaran untuk penilaian risiko kesihatan yang komprehensif dilakukan. Kajian ini bertujuan untuk menganggarkan risiko kesihatan bukan karsinogenik akibat pendedahan kepada aluminium, kromium, besi, dan tembaga serta risiko kesihatan karsinogenik daripada pendedahan kepada formaldehid, asetaldehid, nikel, kadmium dan plumbum yang terdapat dalam wap EC dihasilkan oleh e-cecair buatan tempatan. Kajian yang dijalankan di Lembah Klang, Selangor dari Februari 2017 hingga April 2019 ini dibahagikan kepada empat sub-kajian: i) tinjauan komuniti mengenai topografi *vaping*, ii) analisis kimia wap EC, iii) pemodelan ramalan pendedahan harian, dan iv) Penilaian Risiko Kesihatan (HRA) penggunaan EC. Data mengenai topografi *vaping* dikumpul melalui pengedaran soal selidik tinjauan secara bersasar kepada 226 pengguna tembakau, termasuk pengguna EC. Untuk analisis kimia wap EC yang terhasil daripada sepuluh sampel cecair elektronik tempatan, High-Performance *Liquid Chromatography-Ultraviolet* (*HPLC-UV*) telah digunakan untuk menentukan kepekatan aldehid terpilih manakala kandungan logam berat dikira menggunakan *Inductively Coupled Plasma-Mass Spectrometry* (*ICP-MS*). Sub-kajian III meramalkan julat pendedahan harian yang berpotensi dialami oleh pengguna EC. Risiko kesihatan bukan karsinogenik dan karsinogenik dianggarkan dalam sub-kajian IV berdasarkan data yang diperoleh dalam sub-kajian I hingga III. Daripada 226 pengguna tembakau yang terlibat, 38% (n=86) adalah pengguna EC yang kebanyakannya (58.1%) memilih EC generasi ketiga dan membeli produk tersebut dari kedai vape berdekatan. Majoriti daripada mereka menggunakan cecair elektronik bernikotin 6 mg/mL dan menyukai perisa

berkrim dan buah-buahan. Mereka melaporkan penggunaan 50 sedutan/hari dengan dua botol cecair elektronik digunakan setiap bulan. Purata kepekatan formaldehid, asetaldehid, aluminium, kromium, besi, nikel, kuprum, kadmium, dan plumbum ialah masing-masing 4.31 ppm, 3.34 ppm, 0.126 ppm, 0.0258 ppm, 0.646 ppm, 0.520 ppm, 0.118 ppm, 0.00453 ppm dan 0.0288 ppm apabila dikendalikan dalam tetapan *watt* rendah. Dalam tetapan *watt* tinggi, kepekatan masing-masing adalah 7.04 ppm, 5.88 ppm, 0.205 ppm, 0.0323ppm, 1.51 ppm, 0.980 ppm, 0.0495 ppm, 0.00311 ppm, and 0.0256 ppm. HRA menganggarkan bahawa pendedahan kepada sebatian terpilih dalam wap EC berpotensi mengakibatkan 1 dan 2 dalam setiap 10,000 populasi pengguna EC untuk menghadapi kanser sepanjang hayat mereka. Kesimpulannya, kajian ini membuktikan bahawa pendedahan kepada aldehid dan logam berat dalam wap EC mempunyai kesan kesihatan karsinogenik dan bukan karsinogenik yang boleh diukur dalam kalangan penggunanya. Trend populasi pengguna EC yang semakin meningkat dalam kalangan mereka yang tidak pernah merokok dan kepantasan evolusi produk ini, penyelidikan berterusan yang memfokuskan pada produk dan pengguna EC tempatan adalah perlu untuk menyediakan lebih banyak bukti berdasarkan saintifik kepada pihak berkuasa agar peraturan komprehensif mengenai produk EC dapat dirumuskan dan dilaksanakan. Usaha kolaboratif daripada semua pihak berkepentingan adalah penting untuk mengelakkan permulaan penggunaan tembakau dalam kalangan bukan perokok; justeru memudahkan Malaysia untuk mencapai status negara bebas tembakau menjelang 2045.

Kata kunci: Rokok elektronik, aldehid, logam berat, cecair elektronik, penilaian risiko kesihatan, risiko karsinogenik, Malaysia

ACKNOWLEDGEMENTS

First and foremost, all the praises to the Most Compassionate, the Most Gracious and the Most Merciful, ALLAH who blessed me for the strengths and willpower given to me throughout this indeed a roller-coaster journey.

I would like to express my dearest appreciation to the loves of my life; my parents, Mr Zainol Abidin Lebai Hassan and Mrs Latifah Abdullah for their continuous supports, prayers and motivations for me throughout the entire research process and my life in general.

I would like to express my sincere gratitude to my supervisor Assoc. Prof. Dr Emilia Zainal Abidin for the continuous support of my PhD study and related research, for her patience, motivation, and immense knowledge. Her guidance has helped me in all the time of research and writing of this thesis. I could not have imagined having a better supervisor and mentor for my PhD study. I would also like to thank the rest of my supervisory committee: Dr Sharifah Norkhadijah Syed Ismail. Dr Karmegam Karuppiah and Assoc. Prof. Dr Amer Siddiq Amer Nordin, for their insightful comments and encouragement, but also for the hard question which incited me to widen my research from various perspectives.

My sincere thank also goes to Mr Hamezan Muhammad @ Ahmad and Mrs Noor Hezliza Muhamad Nodin, science officers from Faculty of Food Science and Technology, UPM and Mrs Nurul Ashikin Hazmi from Agro-Biotechnology Institute Malaysia (ABI), MARDI who are very friendly and helpful in helping me analysing my samples and gave access to their laboratories and research facilities. Not forgotten, Ms Siti Khatijah Ahmad Ramli and Mrs Norijah Kasim from the Department of Environmental and Occupational Health, UPM for their help and supports.

Special thanks to all my colleagues and labmates especially Aziemah Zulkifli, Syukriah Mohamad, Norsyazwani Mohammad and Huong Pei Zam for the stimulating discussions, sleepless nights, and for all the sweet and sour times we went through.

Last but not least, my deepest gratitude to the government agencies; the Ministry of Higher Education for MyBrain15 scholarship throughout my study period and the Ministry of Education for the Fundamental Research Grant Scheme (FRGS) for financially support my study. Thank you, everyone!

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

Emilia binti Zainal Abidin, PhD

Associate Professor

Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Sharifah Norkhadijah binti Syed Ismail, PhD

Senior Lecturer

Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Karmegam a/l Karuppiah, PhD

Associate Professor

Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Amer Siddiq bin Amer Nordin, PhD

Associate Professor

Department of Psychological Medicine
Faculty of Medicine
Universiti Malaya
(Member)

ZALILAH MOHD SHARIFF, PhD

Professor and Dean

School of Graduate Studies
Universiti Putra Malaysia

Date: 10 February 2022

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature:

Name of Chairman of
Supervisory Committee:

Assoc. Prof. Dr. Emilia Zainal Abidin

Signature:

Name of Member of
Supervisory Committee:

Dr. Sharifah Norkhadijah Syed Ismail

Signature:

Name of Member of
Supervisory Committee:

Assoc. Prof. Dr. Karmegam Karuppiah

Signature:

Name of Member of
Supervisory Committee:

Assoc. Prof. Dr. Amer Siddiq Amer Nordin

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LIST OF ABBREVIATIONS

ABI	Agro-Biotechnology Institute
ACE	Acetaldehyde
ACGIH	American Conference of Governmental Industrial Hygienists
ASH	Action On Smoking and Health
AT	Averaging Time
ATSDR	Agency For Toxic Substances and Disease Registry
BC	Before Century
BRFSS	Behavioural Risk Factor Surveillance Survey
CA	Measured Concentration
CC	Conventional Cigarette
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRM	Certified Reference Material
CTPR	Control of Tobacco Product
CU	Copper
CVD	Cardiovascular Diseases
DHHS	Department Of Health and Human Services
DNPH	Dinitrophenylhydrazine
DOSH	Department Of Occupational Safety and Health
EC	Electronic Cigarette/ Exposure Concentration
ED	Exposure Duration
EF	Exposure Frequency
EL	E-Liquid

ENDS	Electronic Nicotine Delivery Systems
EPA	Environmental Protection Agency
ET	Exposure Time
EU	European Union
FA	Formaldehyde
FCTC	Framework Convention on Tobacco Control
FDA	Food And Drug Administration
GATS	Global Adult Tobacco Survey
GTSS	Global Tobacco Surveillance System
HI	Hazard Index
HLS	Health And Lifestyles Survey
HPHC	Harmful And Potentially Harmful Constituents
HPLC-UV	High-Performance Liquid Chromatography-Ultraviolet
HQ	Hazard Quotient
HRA	Human Health Risk Assessment
IARC	International Agency for Research on Cancer
ICP-MS	Inductively Coupled Plasma-Mass Spectrometry
IPH	Institute Of Public Health
IQR	Interquartile Ratio
IRIS	Integrated Risk Information System
ITC	International Tobacco Control
IUR	Inhalation Unit Risk
LCR	Lifetime Cancer Risk
LCRT	Total Lifetime Cancer Risk
LED	Light-Emitting Diode
LT	Lifetime

MARDI	Malaysia Agriculture Research and Development Institute
MOH	Ministry Of Health
MOSTI	Ministry Of Science, Technology, And Innovation
MYR	Malaysia Ringgit
NATS	National Adult Tobacco Survey
NDSHS	National Drug Strategy Household Survey
NHS	National Health Service
NIBM	National Institute of Biotechnology Malaysia
NIOSH	National Institute of Occupational Safety and Health
NMAM	NIOSH Manual of Analytical Methods
NRT	Nicotine Replacement Therapy
NSPTC	National Strategic Plan for Tobacco Control
OR	Odds Ratio
OSHA	Occupational Safety Health Association
PEL	Permissible Exposure Limit
PG	Propylene Glycol
PHE	Public Health England
RAGS	Risk Assessment Guidance for Superfund
REL	Recommended Exposure Level
RSD	Relative Standard Deviation
SD	Standard Deviation
SME	Small and Medium Entrepreneurs
SOP	Standard Operating Procedures
SPSS	Statistical Package for Social Sciences
TLV	Threshold Limit Value

TUSCPS	Tobacco Use Supplement to The Current Population Survey
UFP	Ultrafine Particles
UK	United Kingdom
USD	United States Dollar
USECHH	Use and Standard of Exposure to Chemical Hazardous to Health
USEPA	United States Environmental Protection Agency
VG	Vegetable Glycerin
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

Smoking was introduced back in 6000 BC. It was first practised by the American Indians before being introduced to Europe by Christopher Columbus and other explorers (Drope et al., 2018). Today, the tobacco industry is one of the wealthiest industries globally. Six trillion cigarettes are produced every year and consumed by 1.3 billion smokers worldwide (Eriksen et al., 2015; Reitsma et al., 2021; WHO, 2020b). Smoking is widely recognised as the avoidable cause responsible for about 8 million deaths annually (WHO, 2020b). One in every five adults worldwide is a smoker, with males being five times more likely than females (Drope et al., 2018). In 2000, 33.3% of the world's population (both sexes and those aged 15 and older) were current users of some form of tobacco. However, the percentage decreased to 24.9% in 2015 (Bhatta & Glantz, 2020) (WHO, 2019). Despite the decreasing population of tobacco users, the number of annual deaths due to its usage is likely to keep growing as tobacco-related diseases often take time to manifest. Although the smoking prevalence shown to be declining, this may be due to the effect of world's population growth with apparently very little change in the numbers of smokers. The World Health Organization (WHO) predicted that by 2025, approximately one-fifth (20.9%) of the world's population, or 1300 million will become tobacco users (WHO, 2019).

In Malaysia, the prevalence of current smokers was 21.3% (95% CI: 19.86, 22.75) as reported in the National Health Morbidity Survey (NHMS) 2019. It showed a slight reduction of 1.5% from the 22.8% in NHMS 2015 (95% CI: 21.9, 23.8) (IPH, 2015b, 2020). Based on the NHMS finding, approximately 4.8 million Malaysians aged 15 years and above are current smokers. Among daily cigarette smokers, the mean number of cigarettes smoked daily was about 12.4 sticks/day. Nearly one-third of them smoked between 15 to 24 sticks of cigarette/day, equivalent to a pack and more of cigarettes/day. Furthermore, approximately 10000 deaths attributed to smoking are reported each year and smoking-related diseases have been identified as the major contributor to disability-adjusted life years and lost years of life among the Malaysian population, thus making it a primary cause of death since the 1980s (Lee & Tam, 2014; Lim et al., 2018; Reitsma et al., 2017). The greatest burden of ill health related to smoking globally includes respiratory and cardiovascular diseases (CVD); with CVD causing 1.69 million deaths, followed by chronic obstructive pulmonary disease (COPD) with 0.97 million deaths, and lung cancer with 0.85 million deaths (Goodchild et al., 2018; IPH, 2020; Reitsma et al., 2017).

As cigarette smoking continues to be a huge burden to health-related authorities worldwide, the introduction of electronic cigarettes (EC) into the market brings along another concern. In contrast to the conventional cigarettes (CC) that took many decades before becoming an addictive lifestyle among the public, the EC that was introduced in 2004 by a Chinese company, Ruyan, took only months to years prior to being accepted as a new smoking trend worldwide by both

smokers and non-smokers population around the world (Regan et al., 2013; Sanford & Goebel, 2014; U.S. DHHS, 2016). As a matter of fact, EC has been strongly marketed by the tobacco industry with among the known key players of the EC market are the Altria Group, Inc., Philip Morris International Inc., British American Tobacco, R.J. Reynolds Vapor Company, and Shenzhen Kangertech Technology Co., Ltd (Grand View Research, 2020).

The products were and still are aggressively promoted by these companies and their subsidiaries with claims that it is a safer form of smoking, helps in reducing nicotine addiction, and a promising smoking cessation tool. Although there were several published studies that showed promising results in EC being a smoking cessation tool (Berry et al., 2019; Glasser et al., 2021; Johnson et al., 2019), the concern is highlighted on the addiction of the behavioural ritual which really similar between smoking CC and using EC. For instance, the feeling of sticks (first generation of EC) between the index and middle fingers, the LED light of the EC that lightens up when inhale which resemble CC when being smoked and the EC vapours resembling CC smokes (Blackwell et al., 2020; King et al., 2018; Maloney & Cappella, 2015). These are among important cues that may constantly remind EC users of the similarity that it shares with CC.

1.1 Study background

1.1.1 E-cigarettes (EC)

Electronic cigarettes (EC) are battery-powered devices that heat a solution that typically contains nicotine to generate vapour for inhalation. It has been referred with many names by the manufacturers and users, including e-cigarettes, e-cigs, cig-a-likes, e-hookahs, mods, vape pens, vapes, tank systems, and electronic nicotine delivery systems (ENDS) (Lempert et al., 2016; Richtel, 2014; U.S. DHHS, 2016). Although EC ranges widely in its design, appearance, and complexity as shown in Figure 1.1, it generally contains similar components and operates in a similar manner (Brown & Cheng, 2014). The basic components of EC are a battery, a heating coil, an atomiser that transforms the e-liquid into aerosol, a cartridge that contains the e-liquid, and a mouthpiece (Bao et al., 2018b; Brown & Cheng, 2014; East et al., 2019; Grana et al., 2014).



Figure 1.1: Diversity of EC products (U.S. DHHS, 2016)

Unlike CC, the operation of EC does not involve any combustion process. Instead, it vaporised liquid into aerosol form to be inhaled by users. Figure 1.2 outlines a standard EC operation cycle that is shared by most EC brands and models (Brown & Cheng, 2014; Grana et al., 2014; Ingebrethsen et al., 2012). EC is activated by a single or multiple sensor response, with or without the use of an activation button. Once the sensor and/or a button is activated, it initiates power flow to the atomiser, heating the coil that surrounds a fibre or cotton wick. This wick is kept 'wet' with the e-liquid via capillary action. Due to the compositions of e-liquids and the high temperature of the coil, the e-liquids transform into vapours that the users referred to as "clouds" or "vape". When inhaled, the produced vapours travel through the central air passage to its users, giving them the satisfaction of either just the cloudy vapours or together with nicotine and other contents that were vapourised together.

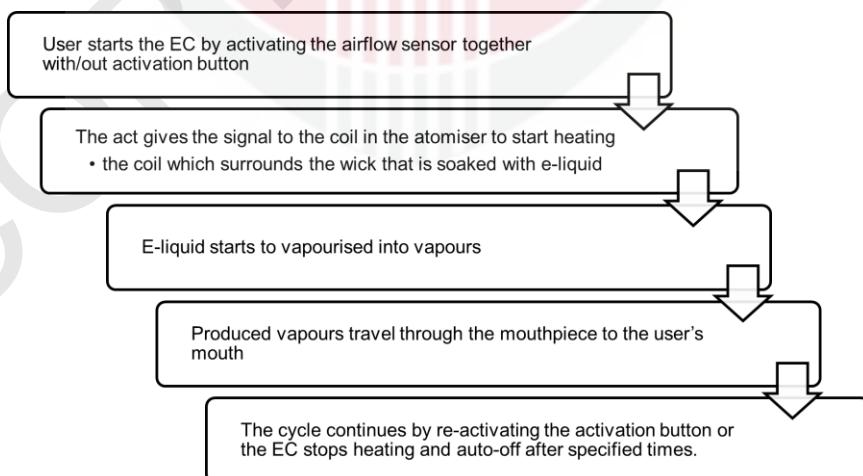


Figure 1.2: The standard operation cycle of an EC

1.1.2 The evolution of EC products

The EC has undergone rapid evolution in its design, quality, effectiveness in delivering nicotine to the users, as well as the materials used in its creation since the day it was invented. As described in Figure 1.3, there are three generations of EC; namely the 1st generation or cig-a-like, the 2nd generation known as clearomiser, and the 3rd generation that is usually referred to as mod. Identical to the shape, size, and colour, the 1st generation of EC closely mimics the CC completes with the LED that lights up when the device is being inhaled/activated by the user. The LED light resembles the burning tip of CC when being smoked; imitating as close as possible the experience when smokers smoking CC. As it was the first EC product to be introduced to the public, it was purposely designed to mirror the CC for a better acceptance, especially among the current smokers. In addition, the majority of the 1st generation EC were non-rechargeable and designed for single use which would be discarded once the nicotine-containing cartridge is emptied.

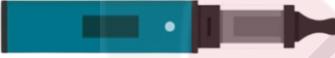
EC	Brief specifications
First generation	 • low price • size and shape similar to conventional cigarette • disposable and non-rechargeable • comes with cartridge/s • power settings not adjustable
Second generation	 • low to moderate price • refillable tank with limited volume of e-liquid • rechargeable battery • some permits adjustment of power settings
Third generation	 • moderate to high price • bigger refillable tank with more volume of e-liquid • higher battery power (rechargeable) • users free to customize almost everything (power settings, material of coil, compositions of e-liquid) • generate significantly more vapours than 1st and 2nd generations

Figure 1.3: Generations of EC (CDC, 2019)

The 2nd generation EC is more compact in size. It is equipped with a high-capacity lithium battery, thus rechargeable; allowing it to be used longer and can be refilled with e-liquid and nicotine according to the individual user's preferences. With the progression, the 3rd generation of EC, or more commonly known as 'mods', is much bulkier in size compared to the previous generations. With a higher battery capacity, this permits a longer operation time of the device within a single charging process. It also contains a larger refillable tank for e-liquid up to 5-7 mL of each refill. With the ability to better adjustment options of the power settings, this 3rd generation EC is able to produce better, thicker, and more condense vapours, giving a higher satisfaction to its user (Berg, 2016; Grana et al., 2014; Huang et al., 2014; Polosa, 2015). These adjustments were reported to help in enhancing the flavour of the e-liquid and the customisation of

the amount and thickness of vapour produced (Farsalinos et al., 2015b; Kośmider et al., 2014).

1.1.3 E-liquid

Following the introduction of the 2nd generation of EC in the market that allows the users to add e-liquid into the tank part of EC, a variety of e-liquid of different brands, flavours, and nicotine levels were introduced to the international and local markets (Figure 1.4). The e-liquid which basically contains a mixture of propylene glycol (PG), vegetable glycerin (VG), flavouring, with or without nicotine; is commonly sold in 30-50 mL glass or plastic bottles (CDC, 2019; IPH, 2016b; U.S. DHHS, 2016; Zulkifli et al., 2018b). This liquid is then aerosolized by the high temperature of the atomiser of the EC device. The PG and VG act as humectants to produce vapours that simulate the CC smoke. The ratio of these humectants in the e-liquid can be customised and changeable based on the user's preference to either have an intense flavour taste or to produce thicker and more clouds of vapours.



Figure 1.4: E-liquids with a variety of brands, flavours and nicotine levels available

In 2014, it was reported an average of 10.5 e-liquid brands were available in the market with 242 new flavours produced each month (Zare et al., 2018; Zhu et al., 2014). These numbers were estimated to reach up to 666 brands with 7764 unique flavours. At present, there are nearly 20,000 flavours of e-liquid available in the market that may have been produced either by the big established companies, small business entrepreneurs, or individually by experienced users (Havermans et al., 2019). Concerning the large variation in the flavour categories of e-liquids, Krüsemann and colleagues introduced a flavour wheel that systematically classifies all the flavours to be utilised by both manufacturers and researchers (Krüsemann et al., 2019). They summarised the flavours into 13 categories and 90 subcategories with the main 5 categories are fruity, tobacco, menthol, sweet, and creamy. These flavourful e-liquids or e-juice, the term applied by users, is one of the strong promoting factors for its usage among both

current and never-smokers (Ayers et al., 2017; Berg, 2016; Goh et al., 2017; Walker et al., 2020). The wide range of e-liquid flavours are specially formulated to attract specific gender or age groups. For instance, flavours such as tobacco and menthol are meant for current and former smokers to attract them without drastically changing the familiar taste of smoking CC. On the other hand, fruity and sweet flavours are aimed at novice users, women, and younger populations as these flavours are often perceived as less harmful. In terms of the local production, the flavours of e-liquids are customised to suit the palate of the local users with flavours such as *mango-lassi*, *sirap bandung*, *teh tarik*, and even *cendol durian* (Figure 1.5).



Figure 1.5: E-liquids with flavours to cater to the local palate of Malaysian EC users

The concentrations of nicotine content in e-liquids may range between 6 to 24 mg/mL (CDC, 2019; Dai et al., 2018; Goniewicz et al., 2013; Grana et al., 2014). As compared to CC, an average stick contains about 10-12 mg of nicotine; thus, a pack of 20 sticks CC carries between 200-240 mg of nicotine. However, it was said that smokers inhale about 1.1-1.8 mg of nicotine per stick (Benowitz et al., 2007; Hatsukami et al., 2010). Apart from never-smokers, EC users may start with a lower nicotine level before gradually raising the nicotine concentration until it meets their satisfaction. There were also substantial studies reporting that nicotine-free e-liquids actually contained nicotine (Chivers et al., 2019; Dunbar et al., 2018; Goniewicz et al., 2013; Hsu et al., 2018; Zulkifli et al., 2018b). Among e-liquids sold to and consumed by the Australian EC users, 50% of the 'nicotine-free' e-liquids that were analysed showed nicotine concentrations between 0.05% to 0.29%, whereas a recent study on e-liquids sold in the Malaysia market revealed almost 80% of the products stated zero-nicotine products do contain nicotine with an average of 1.092 mg/mL (Chivers et al., 2019; Zulkifli et al., 2020).

1.1.4 Population of EC users

With the worldwide sales reaching USD 6.5 billion (MYR 26.3 billion) in 2014 and USD 19.3 billion (MYR 70 billion) in 2019, the population of EC users is also rapidly increasing from 7 million in 2011 to 41 million in 2018, an increment of nearly 600% (Jones, 2019). Figure 1.6 shows the steady increase in the numbers of adults consuming vapour products. This number is expected to reach 55 million by 2021 with the United States (US), United Kingdom (UK), and France are the biggest markets. The EC users in these three countries spent more than USD 10 billion on smokeless tobacco and vaping products in 2018 (Euromonitor International, 2018).

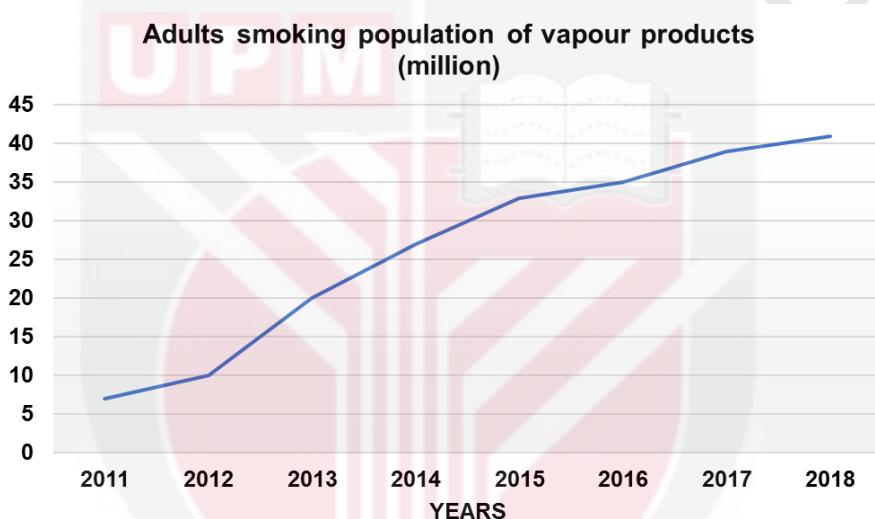


Figure 1.6: Trend of adult population using vapour products between 2011-2018 (million)

The 2014 National Health Interview Survey (NHIS) done among US adults revealed that out of 12.6% of respondents reported to ever tried EC, 3.7% of them were current EC users with 1.1% of them using EC daily (Delnevo et al., 2016; Schoenborn & Gindi, 2015). Another US-based population survey involving more than 60,000 adults, the National Adult Tobacco Survey (NATS), reported about 19.3% of them used EC daily, 29.3% used EC on some days, and 51.4% used EC rarely (Sharapova et al., 2018). Based on the two recent Eurobarometer surveys done in 2014 and 2017, the population analysis by Lavert and colleagues shows a boost of more than 20% of EC users among the 28 European Union (EU) countries (Laverty et al., 2018). Almost 2% of the total EU population, or 7.6 million people were regular EC users. On the other hand, the Action on Smoking and Health (ASH) estimated that over 3.2 million adults or 6.2% of the entire adult population in the UK reported having ever used EC

(ASH, 2019). Furthermore, the number has grown to 3.6 million in 2019 from 700,000 EC users as reported in 2014.

Besides current smokers, ex-smokers and never-smokers are also significant groups of EC users (Abdulrahman et al., 2020; Chen et al., 2016; Etter, 2010; Harrell et al., 2017). Based on a study involving 2,136 EC users in the US, even though a trial of EC was the highest among daily smokers, the odds of being a long-term established EC user were greater among ex-smokers ($OR=3.24$, 95% CI=1.13, 9.30, $p<0.05$) (Giovenco et al., 2014). In other words, the chance of former smokers becoming long-term EC users was higher compared to daily current smokers even though more of the latter group appeared to have tried out EC. This shows that even after the ex-smokers have successfully detached from nicotine addiction once they quit smoking, they have higher odds of staying using EC for a longer time as compared to current smokers. As for current smokers, they may opt to continue if they comfortable using EC or ditched the product and continue using CC which said to give higher satisfaction in nicotine delivery. Among the never-smokers, they were attracted into trying EC due to the variety of EC flavours and peer pressure (Jayakumar et al., 2020; Schneller et al., 2019; Straughan, 2019; Sullman et al., 2020; Zare et al., 2018). In other studies, about one-fourth of the 482,179 respondents in California reported that they had never smoked prior to using EC whereas, in Minnesota, 37% of the EC users were also initially non-smokers (Bostean et al., 2015; Boyle et al., 2019).

1.1.5 Exposure to EC vapours

The upgraded 1st generation of EC allows its users to recharge the device, thus permitting a longer usage. The 2nd and 3rd generation EC devices were equipped with a higher capacity battery. Following the introduction of the rechargeable EC, reports arose regarding the overheating of the device. Some even exploded and caused minor to major degrees of burns around the facial area and thighs (Harshman et al., 2018; Vaught et al., 2017). The location of burns can be linked to when the device is used or kept in the pocket when not in use (Dohnalek & Harley, 2019; Rossheim et al., 2019).

Putting aside the controversial aspects of EC such as safety issues from possible device explosions, overheating, leakage, or accidental ingestion of e-liquids, another worrying problem among the public health experts is the exposure towards the EC vapours among the users. Among the many chemicals detected in EC vapours, formaldehyde, acetaldehyde, and a few heavy metals are among the common compounds that affect health (Gillman et al., 2020; Goniewicz et al., 2014; Klager et al., 2017; Olmedo et al., 2018; Samburova et al., 2018). Some of the constituents are listed as Harmful and Potentially Harmful Constituents (PHPC) for tobacco products by the US Food and Drug Administration (FDA) (Brown & Cheng, 2014; FDA, 2020). Since formaldehyde is classified in the Group 1 of IARC carcinogen classifications, it is carcinogenic to humans. Acetaldehyde is listed in Group 2B as possibly carcinogenic to humans. Nevertheless, exposure to even a low concentration of these

compounds may be detrimental to health. These exposures are exacerbated depending on the pattern of EC usage by the users which typically more frequent and long-term.

Another topic widely discussed among researchers especially in public health field with regards to EC is the exposure to secondhand aerosol (SHA) (Czogala et al., 2014; Schober et al., 2014; Son et al., 2020; Tzortzi et al., 2020; Wang et al., 2017; Zhao et al., 2017). Recent studies have shown that the exposure to SHA among non-users of e-cigarettes is not negligible (Fowles et al., 2020; Melstrom et al., 2018; Scungio et al., 2018). There were about 16% of adults from the general population in 12 European countries reported to be exposed to SHA within the past 7 days and nearly 37% of smokers in six European countries reported to having ever-exposure to SHA (Protano et al., 2017; Tigova et al., 2019).

Unlike secondhand tobacco smoke (SHS), SHA do not produce side stream emissions as it originates solely from the aerosol exhaled by an EC user only (Protano et al., 2017). Although the evidence on the health impact of bystanders' exposure to SHA is still scarce, existing studies have agreed on some short-term effect of EC usage in confined spaces causing avoidable irritation symptoms such as dry throat, nose, eyes, and phlegm in bystanders (Amalia et al., 2021; Fernández et al., 2020; Tzortzi et al., 2020). Detection of hazardous compounds such as nicotine, particulate matter (PM1, PM2.5, PM10), volatile organic compounds, propylene glycol (PG), glycerol, metals, tobacco- specific nitrosamines (TSNAs), and flavourings in SHA may trigger other respiratory related illnesses especially among vulnerable population (Amalia et al., 2021; Bayly et al., 2019; Gentzke et al., 2019).

1.1.6 International stands on EC

In 2014, a survey on ENDS and novel tobacco products was sent to all WHO member states. Based on the findings, 22 countries classified ENDS as tobacco products, another 12 countries classified ENDS as therapeutic products, and 14 countries classified ENDS as consumer products. Following the survey, the WHO Framework Convention on Tobacco Control (FCTC) outlined a guideline for countries to regulate EC products through the six MPOWER (Monitor, Protect, Offer, Warn, Enforce, Raise) measures. Based on the WHO recommendation, countries should adopt legislation that can regulate ENDS effectively to protect people from potential harms of ENDS, apply bans on advertising and flavouring of products, and introduce policies such as plain packaging to reduce the attractiveness of the products in order to discourage the uptake of ENDS by young people and non-smokers.

1.2 Problem Statement

The use of EC is rising rapidly worldwide and Malaysia is not spared of the same problem. Compared to other countries involved in the population-based study by Gravely and colleagues, Malaysia reported the highest prevalence of current EC users (14%, n = 279), followed by the Republic of Korea (7%, n = 123) and Australia (7%, n = 104) (Gravely et al., 2014). Although the Global Adult Tobacco Survey (GATS) 2011-2013 revealed a lower prevalence of 0.8% (n = 34), the National Electronic Cigarette Survey (NECS 2016) reported the prevalence of ever-use and current EC users in Malaysia to be 11.9% and 3.2% respectively (Ab Rahman et al., 2019; Palipudi et al., 2016). In other words, the number translated to almost three million Malaysian adults for ever users of EC and more than 600,000 current EC users nationwide.

In the absence of local vaping topography data, the authorities, especially the government, are unable to take effective measures in assessing the gravity of the issues surrounding the use of EC in the local setting. Furthermore, comprehensive standards, regulations, or guidelines on EC cannot be formulated effectively without such data. Therefore, it is vital to capture vaping topography data such as users' preferences on the selection of EC devices and e-liquids, along with the frequencies and patterns of usage to facilitate the health and safety-related assessments.

As reported in an extensive number of studies, vapours produced by EC contain many potential health-threatening chemical compounds. Furthermore, it has been proven that the use of EC may result in varying detrimental health effects among its users. Besides nicotine (Etter, 2010; Goniewicz et al., 2013; Rahman et al., 2018), carbonyls such as aldehydes (Farsalinos et al., 2018; Gillman et al., 2016), heavy metals (Farsalinos et al., 2015a; Hess et al., 2017), ultrafine particles (UFP) (Melstrom et al., 2017; Ruprecht et al., 2014; Schripp et al., 2013), and diacetyl from the flavourings (Allen et al., 2016; Syamlal et al., 2018; Vas et al., 2019) are among the detected constituents in the EC vapours. However, there is a scarcity of data on the levels of these compounds in EC vapours produced by locally-manufactured e-liquids. Without these data, it is challenging to perform accurate health assessments among local EC users.

Although EC is currently covered under the Control of Tobacco Product (CTPR) 2004, other e-liquids without nicotine or claimed to be nicotine-free are not included (Kim et al., 2015; Zulkifli et al., 2018a, 2020). False, misleading, and excessive claims such as e-liquids being nicotine-free, contain food-grade flavourings, and produce only harmless water vapours are still being spread to actively promote the use of EC among the current users (Basáñez et al., 2019; Klein et al., 2016; Reinhold et al., 2017). These claims may also catch the interest of the never-smokers, especially women and adolescents. Even if they are just using the products occasionally, the effects to their health can be long-lasting.

Many health-related organisations, for instance, WHO, FDA, Centers for Disease Control and Prevention (CDC), and other national-level authorities share similar concerns on the releases of chemical compounds from EC, many of which have been consistently shown to cause unfavourable health effects (CDC, 2019, 2020; FDA, 2019; WHO, 2020a). With an abundance of EC products in the market easily available on various online platforms, coupled with false and misleading claims by the manufacturers, many people may continue to accept and use the products without realising the negative impact on their health, particularly those induced by carcinogenic and non-carcinogenic elements. Furthermore, there is a huge gap in assessing the actual gravity of the problem due to a lack of health risk assessment (HRA) on the locally manufactured EC products.

1.3 Study justification

There is a growing number of EC users worldwide, as stated in the problem statement earlier. Malaysia is experiencing a similar trend as the proportion of the adult and adolescent population who take up EC keeps on growing. Therefore, this study will help in giving some overview of the current proportion of EC users among the tobacco user population in Malaysia. This information will be valuable to the policy-makers and other relevant related bodies that work eagerly towards achieving the tobacco endgame. It may help them to gauge the actual severity of the problem related to EC usage in the local setting.

Without comprehensive data on the pattern of EC use, it is nearly impossible to produce reliable vaping topography data. Thus, this study aimed to provide such data involving the local EC population to assist in the HRA of EC usage. It may also be beneficial for researchers from other multidisciplinary fields who are exploring issues that may influence or be influenced by the introduction of EC to the local market, be it from the aspects of health, economy, or social of a society. In short, this data would fill in any gaps related to the trends and patterns of EC usage among the Malaysian population.

With the introduction of more attractive and sophisticated EC products into the market, it is possible for more unknown chemical compounds to be generated in EC vapours. Exposures to these chemical compounds which never mentioned to the current and potential EC users may probably cause unforeseen and unwanted negative health effects to them. Thus, this study aimed to provide the concentrations of the selected health-threatening constituents in the vapours produced by the locally-manufactured EC products. The findings can alert both the policymakers and the public on the danger associated with these products. In addition, it can aid in highlighting the urgency on the need for a comprehensive and exclusive regulation on ENDS products, especially EC.

1.4 Novelty of the study

The international and local researches related to EC have been focussing on the prevalence of EC users, reasons for its usage, the users and non-users' perception on EC as well as the physical safety of the device (Ab Rahman et al., 2019; Chan et al., 2019a; Dockrell et al., 2013; Elkalmi et al., 2016; Goh et al., 2017; Mohamed et al., 2018; Owusu et al., 2019; Perialathan et al., 2018; Romijnders et al., 2018; Wackowski et al., 2016). These parts of the research were done from time to time due to the fast growing of EC products as well as its users and to always grasp the current trend of this products' usage among world's population. Another concentrated area of EC related research is the chemical analysis of the e-liquids and it produced vapours. In fact, majority are more focused on e-liquids rather than EC vapours (Goniewicz et al., 2015; Herrington et al., 2015; Schober et al., 2014). This is due to the lack of information on the vaping pattern and protocol of its usage; causing study involving EC vapours were harder to be conducted. It is indeed that both are equally important. However, as the main source of EC exposure is through inhalation, information on the EC vapours may provide better input towards the understanding of the actual weightage of the health-related problems related to EC usage.

To date, very limited literature on EC reported on the concentrations of the chemical compounds in EC vapours produced by locally manufactured e-liquids. As reported by Puteh (2018), more than half (55.6%) of the local EC users preferred e-liquids that are locally manufactured. Therefore, reliable and scientific-proven research evidence on this matter is highly needed. It has been shown in studies that the compositions of the locally manufactured and imported e-liquids are different (Wong et al., 2016; Zain et al., 2019). Similar claims are made by EC users. They encounter different vaping experiences when using both types of products, and most of them prefer the local ones due to the extensive strong 'throat hit' of the imported products as well as too intense in term of its nicotine taste; causing unpleasant vaping experience (Puteh et al., 2018; Rahman et al., 2018). Apart from that, the local e-liquids are majority accustomed according to the local palate which more towards familiar taste among Malaysia smokers and EC users. Thus, this study focused on the top ten most popular locally manufactured e-liquids.

In terms of HRA of EC usage, not many studies have been done locally. Most of the locally published studies either reported the prevalence and pattern of EC usage or the chemical analysis of the e-liquids or its vapours (Ab Rahman et al., 2019; Ho et al., 2019; Lim et al., 2019; Ting et al., 2019). No comprehensive work was dedicated to integrate these two parts to obtain a reliable HRA of EC usage. To the best of our knowledge, this study is among the pioneer study that utilised the local vaping topography to produce an accurate HRA of EC vapours among the local population of EC users.

1.5 Conceptual framework

Figure 1.7 presents the conceptual framework of the study. Among the aerosolised tobacco delivery devices available in the market, this study focused on the EC, a type of product that simulates conventional cigarettes. EC delivers nicotine and other chemical compounds in the form of vapours to its users. Although EC is being used by both the adolescent and adult population, this study focused on the latter group because of their higher purchasing power. Besides, the uptake of EC was more significant among adult smokers as they claimed that EC was able to help them to quit smoking (Caponnetto et al., 2012; Franks et al., 2018; Hammond et al., 2019; Polosa et al., 2011; Wong et al., 2016).

Apart from the safety aspects of the EC device that involve the physical structures such as the battery, LED display and the sub-tank, exposures to the e-liquids and vapours of EC can also be detrimental. This study focused on the exposure to the vapours produced by locally manufactured e-liquids. Although there are imported e-liquid products in the local market, we narrowed down our focus to the e-liquids manufactured by local EC entrepreneurs since it they are more preferred by the local EC users. Furthermore, there is also a lack of data published on the chemical compounds in the EC vapours produced by locally manufactured e-liquids (IPH, 2015b; Rahman et al., 2018; Zulkifli et al., 2018a).

This study emphasised aldehydes and heavy metals contents that were the most commonly detected contents in EC vapours (Bekki et al., 2014; Goniewicz et al., 2014; Klager et al., 2017; Williams et al., 2013; Zhao et al., 2020). Among others, aldehydes (formaldehyde and acetaldehyde) and heavy metals (aluminium, chromium, iron, nickel, copper, cadmium, and lead) are the contents of interest in this study.

An increasing number of studies pointed out that the use of EC was not only limited to current smokers but also included former smokers, never-smokers, female users, and the younger population (Callahan-Lyon, 2014; Hammond et al., 2019; Schoenborn & Gindi, 2015). Therefore, the main objective of this study was to evaluate the health impact of EC usage among the local population. Equipped with the data on vaping topography among the local EC users, the carcinogenic and non-carcinogenic health risks were assessed to better understand the severity of the issues pertaining to EC use in the local population. In summary, this study aimed to evaluate the carcinogenic and non-carcinogenic health risks due to exposures to formaldehyde, acetaldehyde, aluminium, chromium, iron, nickel, copper, cadmium, and lead produced in the EC vapours among the its users who used locally-manufactured e-liquids.

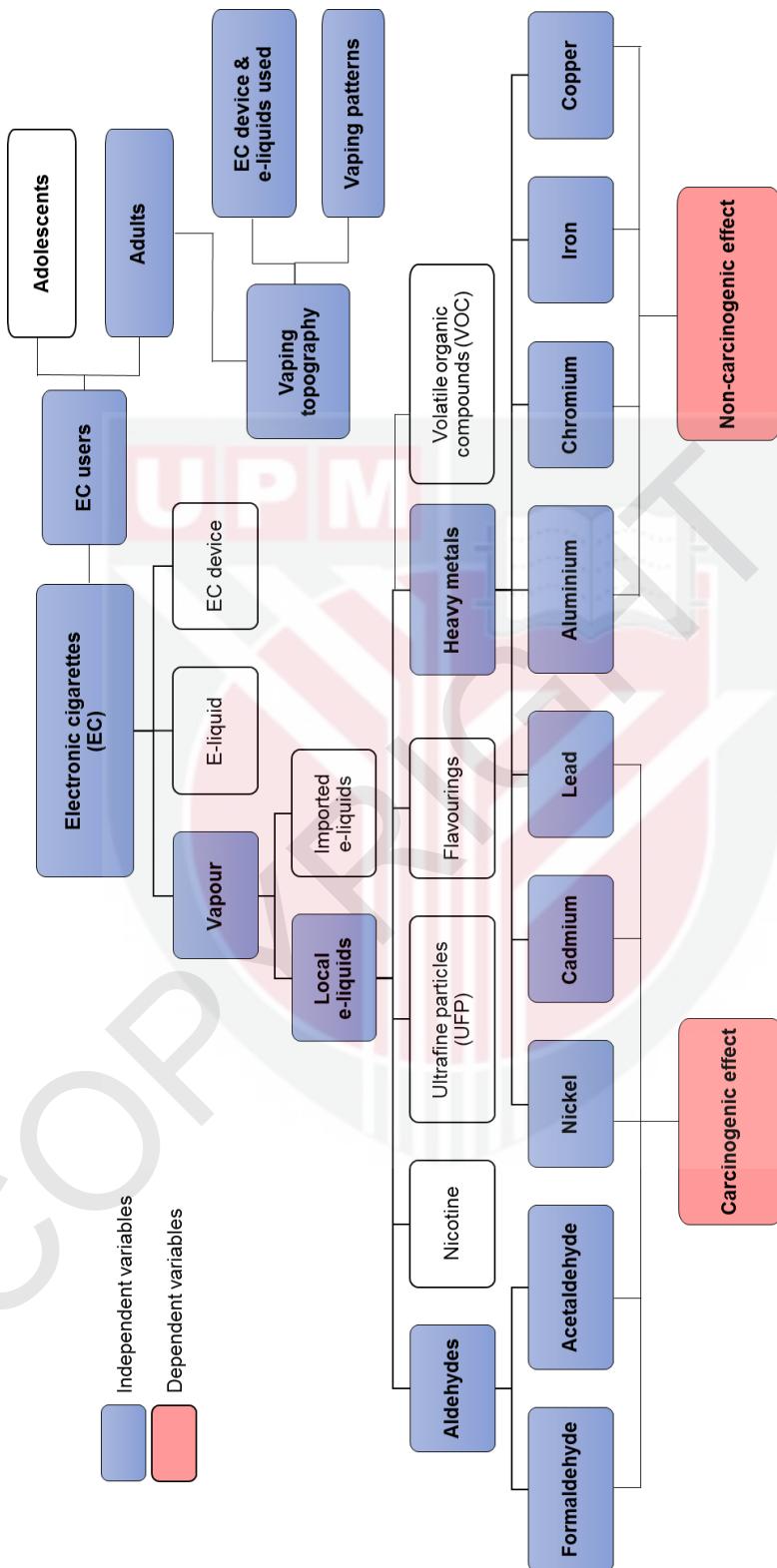


Figure 1.7: Conceptual framework of the study

1.6 Research Questions

In general, this study consisted of four sub-studies, namely i) sub-study I: a community survey on vaping topography among EC users in Klang Valley, ii) sub-study II: chemical analysis of selected chemical constituents in EC vapours produced using locally-manufactured e-liquids, iii) sub-study III: modelling of EC users' daily exposures to selected chemical constituents analysed in sub-study II, and iv) sub-study IV: HRA of exposure to EC vapours by its users. All of the sub-studies would be linked to answer the following research questions.

1.6.1 Sub-study I: Community Survey on Vaping Topography among EC Users in the Klang Valley

1. What is the proportion of EC users among tobacco users in the selected populations in Klang Valley, Selangor?
2. What is the vaping topography among EC users in the selected populations in Klang Valley, Selangor?

1.6.2 Sub-study II: Chemical Analysis of Selected Aldehydes and Heavy Metals in EC Vapours Produced by Locally Manufactured E-liquids

1. What are the concentrations of formaldehyde and acetaldehyde in EC vapours produced by the selected locally manufactured e-liquids?
2. What are the concentrations of aluminium, chromium, iron, nickel, copper, cadmium, and lead in EC vapours produced by the selected locally manufactured e-liquids?

1.6.3 Sub-study III: Prediction Modelling of EC User's Daily Exposure

1. What are the predicted concentrations of daily exposure to selected aldehydes and heavy metals in EC vapours produced by the selected locally manufactured e-liquids among EC users in Klang Valley, Selangor?

1.6.4 Sub-study IV: Health Risk Assessment

1. Does the exposure to EC vapours containing aluminium, chromium, iron, and copper produced by locally manufactured e-liquids pose any non-carcinogenic health risk to the EC users in Klang Valley, Selangor?

2. Does the exposure to EC vapours containing formaldehyde, acetaldehyde, nickel, copper, cadmium, and lead produced by locally manufactured e-liquids pose any carcinogenic health risk to the EC users in Klang Valley, Selangor?

1.7 Definition of variables

1.7.1 Conceptual definitions

1.7.1.1 Electronic cigarettes (EC)

EC is a battery-powered electronic nicotine delivery system (ENDS) device that does not burn or use tobacco leaves. Instead, EC vapourises a solution that typically contains nicotine to produce the vapours that the user subsequently inhales (WHO, 2015, 2020a). It is also known by many other names such as e-cigs, cig-a-likes, e-hookahs, mods, vape pens, vapes, and tank systems (Lempert et al., 2016; Richtel, 2014; U.S. DHHS, 2016).

1.7.1.2 EC users

An EC user, or typically known as a vaper, is anyone who uses an EC. They are further grouped into current and dual users.

1) Current users

Current users are those who had used EC once or more during the previous 30 days but currently do not smoke conventional cigarettes.

2) Dual users

Dual users are those who have smoked more than 100 cigarettes in their lifetime and currently smoke every day or some days and have used EC in the previous 30 days.

3) Never-smokers

Never-smokers are those who have never smoked CC in their lifetime and did not use EC for the previous 30 days.

1.7.1.3 EC vapours

EC vapour is the cloud-like aerosol produced when the EC device components undergo the heating process that vaporises the e-liquid (Alexander et al., 2016;

Dawkins et al., 2013). It typically contains nicotine and other chemical compounds that are inhaled and exhaled by the EC users. Comparatively, EC vapours may be referred in a similar manner to how 'smoke' is being referred to the combustion of CC conventional cigarette, except that EC does not undergo any combustion process.

1.7.1.4 E-liquids

E-liquids typically contain nicotine, as well as varying compositions of flavourings, propylene glycol, vegetable glycerine, additives, and other ingredients (FDA, 2020; Geiss et al., 2016). It is inserted into EC and heated up to produce the vapours that are subsequently inhaled by the users.

1.7.1.5 Health Risk Assessment (HRA)

A human HRA is a process to estimate the nature and probability of adverse health effects in humans who may be exposed to chemicals in contaminated environmental media, now or in the future (US EPA, 2016).

1) Hazard identification

Hazard identification is the first step of HRA. It involves the process of determining whether exposure to a stressor can cause an increase in the incidence of specific adverse health effects (US EPA, 2016).

2) Dose-response

Dose-response is the numerical relationship between exposure and effects in which it describes the likelihood and severity of adverse health effects caused by the amount and condition of specific exposure (US EPA, 2016).

3) Exposure assessment

Exposure assessment involves the process of measuring or estimating the magnitude, frequency, and duration of exposure to the substance of interest or estimating future exposures of it. It involves information as follows:

a. Exposure duration (ED)

The length of contact time between an agent/chemical/substance and a target (US EPA, 2019).

b. Exposure frequency (EF)

The number of exposure events in an exposure duration (US EPA, 2019).

- c. Averaging time (AT)
The average time of the exposure (in days).
 - d. Inhalation Unit Risk (IUR)
An estimate of the increased cancer risk from inhalation exposure to a concentration of 1 µg/m³ for a lifetime (US EPA, 2016). The IUR can be multiplied by an estimate of lifetime exposure (in µg/m³) to determine the lifetime cancer risk.
- 4) Risk characterisation
Risk characterisation is the final step of HRA where all the information obtained from each step are integrated and summarised to synthesise an overall conclusion about risk (US EPA, 2016).

1.7.2 Operational definitions

1.7.2.1 Electronic cigarettes (EC)

The EC used in this study, *iPV D₂*, (*iPV Vaping Technology Co. Limited, Shenzhen, China*) was reported as the most commonly used EC by users involved in this study. It is a 3rd generation EC that allows the users to refill the e-liquid in the sub-tank part of the EC.

1.7.2.2 EC users

- 1) Current users
Current EC users are those who responded to the question of “Are you currently using the electronic cigarette?” with either “Yes, occasionally (not daily),” or “Yes, I use it every day” in the distributed questionnaire.
- 2) Dual users
Dual users are those who responded either “Yes, occasionally (not daily),” or “Yes, I smoke every day” for both of the questions below:
 - a) “Do you currently smoke tobacco (conventional cigarette)?”
 - b) “Are you currently using the electronic cigarette?”
- 3) Never-smokers
Never-smokers are those who responded with:
 - a) “I never smoke a conventional cigarette” for the question “Do you currently smoke tobacco (conventional cigarette)?” and
 - b) “Yes, occasionally (not daily),” or “Yes, I use it for the question “Are you currently using the electronic cigarette?”

1.7.2.3 EC vapours

EC vapours are the cloud-like aerosol produced from the locally-manufactured e-liquids using an EC device called the *iPV D₂* through simulations in laboratory settings.

1.7.2.4 E-liquids

E-liquids used in this study were those locally-manufactured and purchased from available retail EC shops in Klang Valley, Selangor based on the preferences of local EC users. This study used the ten most commonly used e-liquids among local EC users as reported in the survey.

1.7.2.5 Health Risk Assessment (HRA)

1) Hazard identification

This step was done with an extensive literature search and systematic review on the exposure of selected chemical constituents contained in EC vapours, focusing on selected aldehydes i.e. formaldehyde and acetaldehyde as well as heavy metals i.e. aluminium, chromium, iron, nickel, copper, cadmium, and lead.

2) Dose-response

To assess the risk through inhalation, the reference dose concentration (RfC) values were obtained based on the toxicological profile of each chemical compound of interest from the Integrated Risk Information System (IRIS).

3) Exposure assessment

This step was carried out with the integration of information on vaping topography (ED and EF) derived from the questionnaires answered by the EC users. The data on the concentration of selected chemical constituents in the produced EC vapours (formaldehyde, acetaldehyde, aluminium, chromium, iron, nickel, copper, cadmium, and lead) obtained from laboratory analysis was applied in the subsequent steps of HRA.

a. Exposure duration (ED)

In assessing ED, the following question was asked to the respondents: “In total, during your life, for how long (month) did you use the EC?”

b. Exposure frequency (EF)

For EF, the following question was asked to the respondents: “Currently, how many days per week do you use the EC?”

- c. Averaging time (AT)
The average time of exposure (in days).
 - d. Inhalation Unit Risk (IUR)
The IUR values for chemical compounds of interest were obtained from the Integrated Risk Information System (IRIS, US EPA).
- 4) Risk characterisation
For non-cancer risk, hazard quotient (HQ) and hazard index (HI) were calculated using Equation 3.5 and Equation 3.6 before being interpreted according to Table 3.3. Lifetime Cancer Risk (LCR) was calculated using Equation 3.8 and Equation 3.9 for the total LCR (LCR_T) and interpreted according to Table 3.4.

1.8 Objectives

1.8.1 General objectives

This study aimed to determine the vaping topography and harmful substances in EC vapours produced by locally manufactured e-liquids and assess the associated health risk among selected adult EC users in Klang Valley, Selangor.

1.8.2 Specific objectives

1.8.2.1 Sub-study I: Community Survey on Vaping Topography among EC users in Klang Valley

- 1) To determine the proportions of EC users among tobacco users in Klang Valley, Selangor.
- 2) To determine the vaping topography of the EC usage among EC users in Klang Valley, Selangor.
- 3) To determine the types of EC device and e-liquids of interest among EC users in Klang Valley, Selangor.

1.8.2.2 Sub-study II: Chemical Analysis of Selected Aldehydes and Heavy Metals in EC Vapours Produced by Locally Manufactured E-liquids

- 1) To determine the concentrations of selected aldehydes; namely formaldehyde and acetaldehyde in EC vapours produced by locally-manufactured e-liquids.
- 2) To determine the concentrations of selected heavy metals; namely aluminium, chromium, iron, nickel, copper, cadmium, and lead in EC vapours produced by locally-manufactured e-liquids.

1.8.2.3 Sub-study III: Prediction Modelling of EC User's Daily Exposure

- 1) To estimate the daily exposures among EC users towards selected aldehydes and heavy metals in EC vapours produced by locally-manufactured e-liquids.

1.8.2.4 Sub-study IV: Health Risk Assessment

- 1) To estimate the carcinogenic and non-carcinogenic risks associated with the exposures to EC vapours among EC users in Klang Valley, Selangor.

1.9 Hypotheses

- 1) Exposure to formaldehyde, acetaldehyde, nickel, cadmium, and lead in the EC vapours produced by locally-manufactured e-liquids pose a carcinogenic health risk to the EC users in Klang Valley, Selangor.
- 2) Exposure to aluminium, chromium, iron, and copper in the EC vapours produced by locally-manufactured e-liquids pose a non-carcinogenic health risk to the EC users in Klang Valley, Selangor.

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