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Thesis for the Degree of Master of Engineering

Characteristics of indoor air pollutant generated from heat-not-burn products

by

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Division of Earth Environmental System Science
(Major of Environmental Engineering)
The Graduate School

Pukyong National University

February 19, 2021

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(궐련형 전자담배에서 배출되는 실내 공기오염물질의 특성)

Advisor: Prof. Youn-Suk Son

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궐련형 전자담배에서 배출되는 실내공기오염물질의 특성

권민구

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요 약

본 연구는 궐련형 전자담배 (Heat-not-burn tobacco, HnB) 제품을 이용하여 실내공기질에 미치는 영향을 평가하기 위해 수행되었다. 이를 위해 HnB 제품에서 직접 배출되는 니코틴, PG, VG의 농도를 분석하고 기존 담배의 농도와 비교하였다. 또한, 실험 대상자가 챔버에서 HnB를 사용했을 때 실내공기상에서 검출되는 VOCs, 알데하이드, 미세입자 및 나노입자의 수치를 평가하여 실내공기질에 미치는 영향을 평가했다. 그 결과, HnB 제품 (0.83 – 1.16 mg/cigarette)에 의해 전달되는 니코틴 수치는 기존 연초 담배 (2.4 – 3.5 mg/cigarette)에 비해 낮다. 반면, HnB 제품 (3.14 – 5.9 mg/cigarette)에서 배출되는 VG 수치는 기존 연초 담배 (0.62 – 3.03 mg/cigarette)에서 배출되는 VG 수치보다 많았다. 추가적으로 HnB 제품에서 발생하는 양은 기존의 담배 제품에 비해 적지만 다양한 종류의 VOCs, 알데하이드, 미세입자 및 나노입자가 생성되어 실내 공기질에 영향을 미치는 것으로 확인되었다.

Ⅰ. Introduction

1.1 Background

Tobacco has historically been used in many cultures around the world (Baran et al., 2020). It had mystical uses in South America and was introduced to Europe by Christopher Columbus (Borio, 2001). Tobacco finally made it to Korea through the 16th century Japanese invasion. According to the story of the Sperwer yacht wreck, tobacco was used throughout the time of the Joseon Dynasty, and many farmers cultivated tobacco as the crop. Since the 1800s, tobacco products produced in the western hemisphere have been introduced and formed the basis of today's modern tobacco industry (Noh et al., 2020). Tobacco is presently treated as a carcinogen due to substances such as nicotine, polycyclic aromatic hydrocarbons (PAHs), tobacco-specific nitrosamines (TSNAs), volatile organic compounds (VOCs), and heavy metals (Torres et al., 2018). In fact, about 8,000 compounds are found in cigarette smoke (Rodgman and Perfetti, 2013). Health agencies and researchers have identified 100 potentially harmful substances in cigarettes as the cause of smoking-related diseases such as lung cancer, heart disease, and emphysema (Health Canada (HC), 2000; World Health Organization (WHO), 2008; U.S. Food and Drug Administration (FDA), 2012). For this reason, the WHO recommends smoking cessation worldwide, and in response, international tobacco companies such as Philip Morris International (PMI) and British American Tobacco (BAT), have started to develop and sell heat-not-burn tobacco (HnB) products to replace conventional cigarettes (Jankowski et al., 2019).

HnB products are a type of electronic cigarette in which tobacco vapor is produced without combustion (Liu et al., 2019). Usually, these products consist of three components: holders, chargers, and a tobacco sticks. The tobacco sticks are heated to a temperature below combustion, and a vapor similar to a conventional cigarette is generated. IQOS, an HnB products from PMI, could not function continuously for the experiment, as it requires recharging between uses (Smith et al., 2016). Alternatively, Lil (Korean Tobacco & Ginseng - KT&G) and Glo (BAT) can be used continuously, like conventional cigarettes, until their batteries are depleted. While a conventional cigarette is combusted at 900 ℃, HnB products are heated by blades embedded in the holder to 350 ℃. Because HnB products systems heat the tobacco stick to this lower temperature (Smith et al., 2016), they use less energy than a conventional cigarette, and yet can still emit aerosols to adult smokers (Schaller et al., 2016).

In 1988, R. J. Reynolds (RJR) launched the first HnB products, Premier, on the market (Kaunelienė et al., 2019). After this, Eclipse (RJR) and Accord (PMI) were developed. The Eclipse, developed in 2015, heats carbon tips that are wrapped in fiberglass, and was later relaunched under the name Revo. However, Revo failed to meet the needs of consumers and was taken off of the market largely due to its unpleasant taste. In recent years, HnB products such as IQOS, Glo, Lil, and Ploom (Japan Tobacco) have become available globally, and the number of users is increasing due in part to TV marketing (Tabuchi et al., 2016; Nyman et al., 2018; Liu et al., 2019; Kim et al., 2018) and the HnB market is expected to continue its rapid increase into the future (Caputi et al., 2017; Kim et al., 2018). Tobacco companies have reported that HnB products are less harmful than conventional cigarettes, but most of these reports were published by the research agency under PMI (Food and Drug Administration (FDA); TPSAC meeting materials and information, 2018). In addition, there is a lack of research on the effect of HnB products on indoor air quality, and its ultimate effects are still unknown. Furthermore, there are many smokers who use both HnB products and conventional cigarettes, as well as non-smokers who strictly use HnB products (Tabuchi et al., 2016; Liu et al., 2019).

1.2 Purpose

With the advent of HnB products, users have increased rapidly. Primary reasons for the surge in HnB products use are the manufacturer advertisements that claim HnB products smell less and deliver similar amounts of nicotine. Therefore, this study aimed to analyze whether HnB products actually release equivalent amounts of nicotine and fewer harmful substances than conventional cigarettes. For this analysis, we targeted three compounds: nicotine, propylene glycol (PG), and vegetable glycerin (VG). PG and VG are often used in liquid-type electronic cigarettes, as they help with moisture condensation and a simulated 'throat hit'. PG and VG are also used in conventional cigarettes to similarly help with moisture condensation. The reason for targeting these three compounds was that they are thought to have a direct impact on smokers. PG and VG are widely considered nontoxic, so they are used in cosmetics, foods, etc.; however, some studies have shown that PG and VG can produce harmful substances when pyrolyzed, such as aldehydes, that can affect the human body (Ooi et al., 2019). Nicotine is the addictive component of tobacco, so it too was selected as a target compound.

The use of conventional cigarettes indoors was banned in Korea because of its smell and generation of harmful secondhand smoke; however, it is still unclear how HnB products affect indoor air quality. The study here further aimed to evaluate whether HnB products can affect indoor air quality, assuming that HnB products are also releasing harmful substances. Four compounds were targeted for analysis: VOCs, aldehydes, particulate matter (PM), and nanoparticles. The reason for targeting these compounds is their documented effect on indoor air quality. When people inhale VOCs, it can affect the respiratory system and cause cancer (Kampa and Castanas, 2008). Formaldehyde and acetaldehyde are known carcinogens in humans according to the International Agency for Research on Cancer (IARC) (Klager et al., 2017). PM and nanoparticles that are generated indoors have similar toxicity to outdoor PM. These particulates can penetrate into human alveoli, causing lung damage, and lead to respiratory diseases, such as lung cancer and pneumonia (Scungio et al., 2018). If these materials exist in the indoor space, they can potentially affect people more rapidly than when used outdoors, so they too were selected as target compounds.

Therefore, the purposes of this study were as follow:

1) When using HnB products, we evaluated which substances can affect smokers through their concentration of emissions. To this end, we compared them with conventional cigarettes.

2) When using HnB products indoors, we evaluated how they affect indoor air quality. To this end, we compared them with the combustion of conventional cigarettes indoors.

Ⅱ. Literature review

2.1 Cigarette smoke constituents

2.1.1. Propylene glycol

Propylene glycol (PG; Fig. 2.1) is a colorless and odorless liquid with hygroscopic and viscous properties. It primarily mixes with water, acetone, ethanol and so on (Pubchem, 2004). PG is often used in the cosmetic, grocery and pharmaceutical industries (Jacob et al., 2018). The FDA has defined PG as an additive that is generally considered safe for use in foods and medicine (Pubchem, 2004). In conventional cigarettes and HnB products, PG is used to maintain the moisture content of the tobacco filler (Hoffmann and Hoffmann, 2001; Klus et al., 2012). Moreover, when PG is heated, a vapor resembling cigarette smoke is produced, which is an irritant (About Electronic Cigarettes). Additionally, if the amount of PG was high, the excellent suction force was offered (Papaefstathiou et al., 2019). Previous studies on rats exposed to PG for 28 days resulted in a small amount of bleeding around the eyes and nose, and there was a trace of stimulation in the eye and nasal cavity as well (Werley et al., 2011; Phillips et al., 2017).

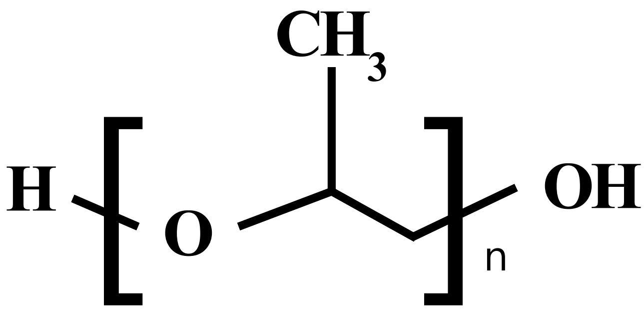


Fig. 2.1 Structural formula of propylene glycol (PG)

2.1.2. Vegetable Glycerin

Vegetable glycerin (VG; Fig. 2.2) is another colorless, viscous liquid with several names, such as glycerin and glycol (ChemSrc, 2020). VG is chemically very similar to PG, and is also used as a pharmaceutical and food additive. VG is used for e-cigarettes in a role similar to PG. VG can produce more vapor per unit, so if this is the manufacturer's goal, they include more VG than PG (About Electronic Cigarettes). If the ratio of VG is greater than PG, a more mild throat and mouth feel are produced (Papaefstathiou et al., 2019). In previous studies, PG and VG were analyzed together. Even when the exposure period to VG was long, it did not show biotoxicity; but if pyrolysis occurred, it could produce aldehydes such as formaldehyde (Philips et al., 2017; Ooi et al., 2019).

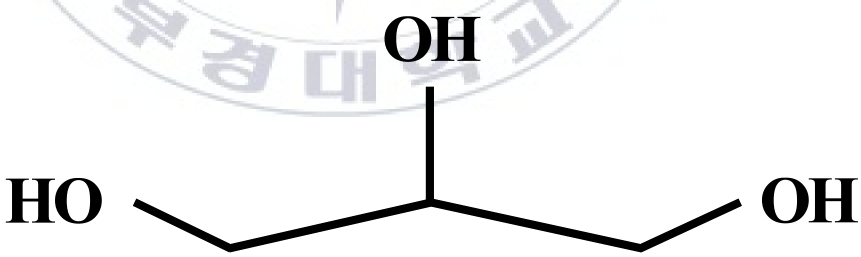


Fig. 2.2 Structural formula of propylene glycol (VG)

2.1.3. Nicotine

Nicotine (Fig. 2.3) is a naturally produced substance in tobacco, and has a strong toxicity and irritative capacity. It is addictive and threatens public health by increasing its reliance on tobacco (D'souza et al., 2011). In the past, nicotine has been used as an anti-herbivorous chemical and insecticide (Rodgman and Perfetti, 2013). On average, a conventional cigarette contains 2 mg of nicotine (Mayer 2014). Nicotine causes lung cancer and plays a role in promoting metastasis of cancer cells (Merecz-Sadowska et al., 2020). Moreover, nicotine has the effect of increasing cancer cell's tolerance to anti-cancer drugs (Kothari et al., 2014).

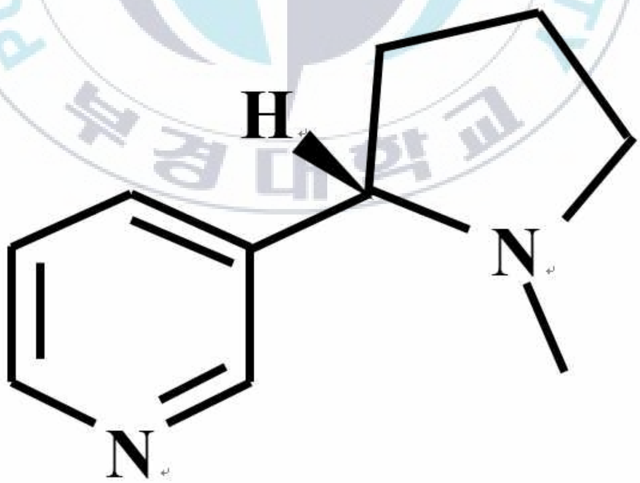


Fig. 2.3 Structural formula of nicotine

2.2 Secondhand smoke constituents

2.2.1. Volatile Organic Compounds

Volatile organic compounds (VOCs) are liquid or gaseous organic compounds that are easily evaporated into the atmosphere due to the ir low boiling points. Almost all commonly used hydrocarbons are V OCs, such as liquid fuels, paraffins, olefins and aromatic compounds (Ministry of Environment Metropolitan Air Quality Administration, ht tps://www.me.go.kr/mamo/web/index.do?menuId=10006). VOCs produc e ozone by photochemical reaction with NO_x in the atmosphere and can also cause photochemical smog (National Research Council, 1991; Roger Atkinson, 2000). VOC species, such as toluene and xylene, are also found in livestock fertilizers and are classified as odorous subst ances (Liang and Liao, 2004; Liang and Liao, 2007). When smoked, c onventional cigarettes emit various type of VOCs, and exposure indo ors can cause dizziness, dry cough, and symptoms of discomfort in t he eyes and bronchus (Yu et al., 2009).

2.2.2. Aldehydes

Aldehydes refer to organic compounds with a C(=O)H binder at the end. The binder is usually marked as R-CHO, where R refers to various combiners (Moss et al., 1995). Aldehydes are artificially or naturally generated in the air, and also through the incomplete combustion and photooxidation of hydrocarbons (Oston and Fellin, 1988; Carlier et al., 1986). Aldehydes are even produced in the human body. For example, cyclophosphamide is used as a chemotherapy agent and can be produced during acrolein metabolism (Gurtoo et al., 1981). Aldehydes are emitted through smoking, and although the type of emissions vary greatly, most of them are highly reactive and toxic to humans. Aldehydes are reported to show cytotoxicity, mutation, and genetic effects (Laskar and Younus et al., 2019).

2.2.3. Particulate matter

Particulate matter (PM) refers to all solid and liquid particles floating in the air. PM are mixed with a wide variety of materials, such as dust, pollen, soot etc. They are classified by diameter: particles with diameter < 10 μm are called fine particles (PM_{10}), and those with diameter < 2.5 μm are called ultrafine particles ($PM_{2.5}$). These particles occur in various places, such as roads and industrial sites (WHO, 2003). Previous studies have shown that PM exposure is a major cause of cardiovascular disease (Tertre et al., 2002; Wellenius et al., 2005; Klot et al., 2005; Chang et al., 2005; Zeka et al., 2005; Dominici et al., 2006; Ballester et al., 2006). In particular, the risk of myocardial infarction increased with PM_{10} exposure (Burnett et al., 1999; Morris, 2001; Maheswaran et al., 2005; Zanobetti and Schwartz, 2006; Lanki et al., 2006; Miller et al., 2007).

2.3 Heat-not-burn tobacco products

2.3.1. IQOS

IQOS is an HnB products developed by PMI, short for 'I-Quit-Ordinary-Smoking' (Auer et al., 2017). IQOS is composed of a holder that heats a tobacco stick without combustion, and a main body that charges the holder. The official website of IQOS Korea explains that the harmful or potentially harmful substances are remarkably decreased because it heats without combustion of the tobacco (https://kr.iqos.com/ko/products/iqos/what-is).

2.3.2. Lil

Lil is an HnB products developed by Korea Tobacco Ginseng Corporation (KT&G), whose name was derived from 'a little is a lot'. Lil uses a charging method for the cigarette holder by directly inserting a charger. As of 2020, Lil is sold on the market in three types: an HnB products type that uses tobacco sticks, a liquid type that uses e-liquid in a cartridge, and a hybrid type that puts the tobacco stick on the outside (https://its-lil.com/contents/brand).

2.3.3. Glo

Glo is an HnB products developed by British American Tobacco

(BAT), and similar to Lil, it uses a form of charging directly into the tobacco holder. Glo uses tobacco sticks in the holder like other HnB products; however, since the Glo tobacco stick is longer and structurally weaker than other tobacco sticks, it is often broken when used.

Ⅲ. Method and materials

The experiments here were conducted in two ways: First, the materials directly emitted when HnB products were vaporized were detected. At this time, a smoking machine was used to simulate a person's smoking more accurately and stably. In addition, a chamber simulated indoor environment was designed and manufactured to evaluate the effect of HnB products on indoor air quality. In order to evaluate its impact on the indoor environment, PM, nanoparticles, aldehydes and VOCs were analyzed. To measure which substances exist in indoor air when vaporizing HnB products indoors, an experiment was conducted with volunteer smokers vaporizing HnB products and conventional cigarettes inside of the chamber.

3.1 Materials

3.1.1. Chemicals

The reagents used in this study were methanol, nicotine, PG, VG, and acetonitrile. Methanol, nicotine, PG, VG were purchased from Sigma-Aldrich. The purchased methanol was HPLC grade (≥ PL 9%), and nicotine was (-)-nicotine of GC grade. Acetonitrile was HPLC grade (≥99.9%), and purchased from Honeywell. Methanol was used as a solvent for extracting nicotine; while PG, VG and acetonitrile were used as solvents for extracting aldehydes. In addition, methanol was also used to dilute standard solutions. The PG used was general grade (ACS), and the VG was USP grade.

3.1.2. Sampling tobaccos

The e-cigarettes used for experimentation were all HnB products. In addition, conventional cigarettes produced by the same company were used to compare and analyze the emission characteristics according to direct and indirect use of HnB products. All products were purchased in offline stores, and the batteries of HnB products were kept fully charged. Conventional cigarettes used as a comparison group with HnB products were selected as the highest sales volume among the products of the selected company such as HnB products. Conventional cigarettes had tar and nicotine concentrations labeled on the outside of the cigarette pack (Table 3.1), but HnB products are classified as pipe cigarettes, and thus not required to display this information.

Table 3.1 Meteorological Administration ground station location

Tobacco company	Conventional cigarette (Tar/Nicotine)	Heat-not-burn tobacco (Tobacco sticks)
KT&G	This Plus (5.5 mg/0.55 mg)	Lil (Fit change)
Philip Morris International	Parliament Aqua 5 (5.0 mg/0.4 mg)	IQOS (HEETS Amber)
British American Tobacco	Dunhill (6.0 mg/0.6 mg)	Glo (Neo Bright tobacco)

3.2 Experimental methods

3.2.1. Firsthand smoke

This experiment was performed to analyze the components of the vapor emitted during use of HnB products. In order to compare the emitted substances, we also analyzed the smoke components that are emitted when conventional cigarettes are combusted. The experiment was performed using a smoking machine according to the Health Canada machine smoking regime (HCI, puff volume – 55 mL, puff interval – 30 sec, puff duration – 2 sec, puff number – 14 times). According to previous studies using HCI, the number of puffs actually varies between 10 - 14 times (Bekki et al., 2017; Liu et al., 2019; Forster et al., 2018; Schaller et al., 2016; Jaccard et al., 2017). In this study, after 12 puffs, just one more puff was performed that sampled remaining residue. The mainstream smoke of conventional cigarettes and HnB products was collected in 44 mm Cambridge Borgwaldt glass fiber filter pads (CFP, Borgwaldt, Germany). The sampling was performed 18 times in total, three times per sample. The pump flow rate of the smoking machine was set to 1.65 $L \cdot min^{-1}$, so a volume of 55 mL could be collected every time. The experimental setup can be seen in Figure 3.1.

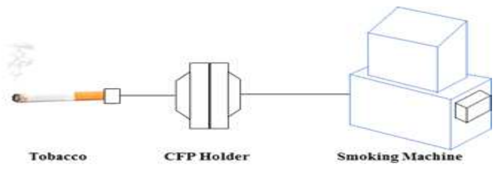


Fig. 3.1 Design of firsthand smoke experiment

3.2.2. Secondhand smoke

The purpose of this experiment was to investigate the effects of vaporized HnBs on indoor air quality when compared to conventional cigarettes smoked indoors. In order to evaluate the indoor environment, a 4.4 m x 2.7 m x 6.8 m simulated office environment was set up as an exposure chamber (Fig. 3.2). When performing the experiment, furniture was put in place to replicate an actual office environment. Additionally, the walls were painted, and the floor was finished. The indoor air quality was gauged by concentration of PM, nanoparticles, VOCs, and aldehydes. The concentrations of PM and nanoparticles were confirmed by SMPS and Aerocet 531S in real time; and VOCs and aldehydes were collected by installing an adsorption tube and DNPH cartridge at the front end of the sampling pump. The measuring devices were placed 1 m aboveground to reduce ground interaction as much as possible. To consider pollutants generated from within the exposure chamber, a blank test was performed before and after the experiment.

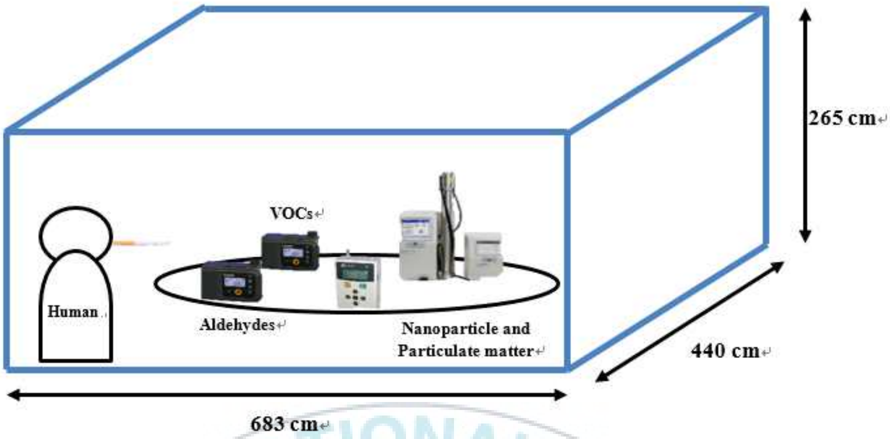


Fig. 3.2 Simulated office chamber system for secondhand smoke experiment

3.2.3. Sampling

Samples of the firsthand smoke experiment were collected in CFPs as described in Section 3.2.1. One filter was used per sample, and the filters were placed into a 10 mL amber vial after sampling.

Samples of the secondhand smoke experiment were measured and collected through various instruments, as described in Section 3.2.2. Measuring instruments were a VOC sampling pump (MP-Σ30KN II Mini Pump, Sibata, Japan), an aldehyde sampling pump (MP-Σ100KN II Mini Pump, Sibata, Japan), a scanning mobility particle sizer (SMPS Model 3938, TSI, USA), and an Aerocet 531S (Met One Instrument, USA). The sampling process consisted of one hour of ventilation sessions, and one hour of smoking sessions, which were repeated three times. The ventilation session was carried out using an air conditioner and air purifier with the windows opens to ensure that the indoor concentration was maintained at the background level prior to sampling. Following the ventilation session, all windows were closed, and the air purifier and air conditioner were shut down. When the smoking session began, a volunteer smoker entered the chamber, smoked for 5 min in the direction of the devices, and then immediately came out from the chamber. The measuring devices collected the indoor air continuously for the remainder of the hour. The subjects were selected and the smokers voluntarily participated in the experiment. At this time, there was no financial support for the participants. Additionally, this experiment was performed with the approval of the Institutional Review Board (IRB) because it involved the use of human subjects.

3.2.3.1. Nicotine, PG, VG

Nicotine, PG and VG were extracted and analyzed by collecting vapor and smoke from HnB products and conventional cigarettes, respectively. Sampling of the three compounds was done at the same time, and the extraction methods used were also identical. The three compounds were sampled with a Health Canada machine smoking regime (HCI, puff volume - 55 mL, puff interval - 30s, puff duration - 2 second, puff number - 13 times (After 12 puffs, one puff was performed that sampled remaining residue)), and collected in a CFP. After sampling, the filter was placed into a 10 mL amber vial and filled with 10 mL of methanol. The ultrasonic sonicator was then activated for 30 min for extraction. Following the extraction process, the solution was filtered with a 0.45 μm membrane filter (0.45 μm PVDF filter media, Whatman, U.K.) to remove impurities, and stored in 2 mL amber vial until the time of the analysis.

3.2.3.2. VOCs

To effectively extract VOCs, self-made adsorption tubes were used. VOCs were collected using each adsorption tube filled with 110 mg Tenax TA (60/80 mesh, Supelco, USA) in an empty pyrex tube at the front end of the VOC sampling pump. A pump that only collects VOCs was used. The flow rate of the pump was maintained at 0.15 L·min^{-1}, and the samples were stored and refrigerated before analysis to minimize the loss of the sample.

3.2.3.3. Aldehydes

Aldehydes were collected with an Lp DNPH S10 cartridge (60/100 mesh Supelco, USA). A 2, 4-dinitrophenylhydrazine (DNPH) cartridg e had a 4 cm polyethylene tube-type, with polyethylene filters at bot h ends and a high purity, refined DNPH in the middle. Ozone can al so reduce DNPH derivatives or react with DNPH to form impurities in aldehydes analysis (Uchiyama and Ostubo, 2008), so an ozone scr ubber (ReZorian Ozone scrubber, Supleco, USA) was attached to the front end of the cartridge to minimize the effects of ozone. Light ca n also trigger ozone's quick reaction with aldehydes, so light was bl ocked as much as possible during sampling (KSCI, 2007). The sampl e was collected at a flow rate of 1 L·min^{-1}, using an aldehydes sam pling pump. The sample was refrigerated before analysis to minimize loss.

3.2.4. IRB

The secondhand smoke experiment was performed with the help of smokers, not machines. Therefore, we requested the approval of the Institutional Review Board (IRB) of Pukyong National University. The IRB is a committee officially organized to protect the rights and welfare of subjects in medical and behavioral studies targeting humans. Without IRB approval, human and behavioral experiments cannot be performed. The secondhand smoke experiment was conducted after the IRB's formal approval, and the participants were protected by the committee. The participants were recruited voluntarily, and the request to suspend the experiment was always available. This experiment did not require human derived materials such as blood or urine of any participants, and their personal information is protected by law.

3.3 Experimental equipment

3.3.1. Smoking machine

Smoking machines are equipment that mimic a human smoking. Because it is difficult to collect the smoke generated when people smoke a cigarette, aerosols are collected mainly by using a smoking machine in a laboratory setting. The types of machines are diverse, and the equipment is designed based on protocols such as the International Organization for Standardization 3308 (ISO 3308), Health Canada machine smoking regime (HCI), and CORESTA E-cigarette methods. The smoking machine used in this experiment (Modified TE-2 system, Teague Enterprises, CA, USA) was renovated ready-made products. The machine can smoke four cigarettes at the same time, and it is possible to adjust the suction time. The equipment was fitted with a solenoid valve, which allowed it to inhale cigarette smoke at regular time intervals. A pump was attached behind the solenoid valve, allowing smoke at a constant flow rate of 1.65 $L \cdot min^{-1}$.

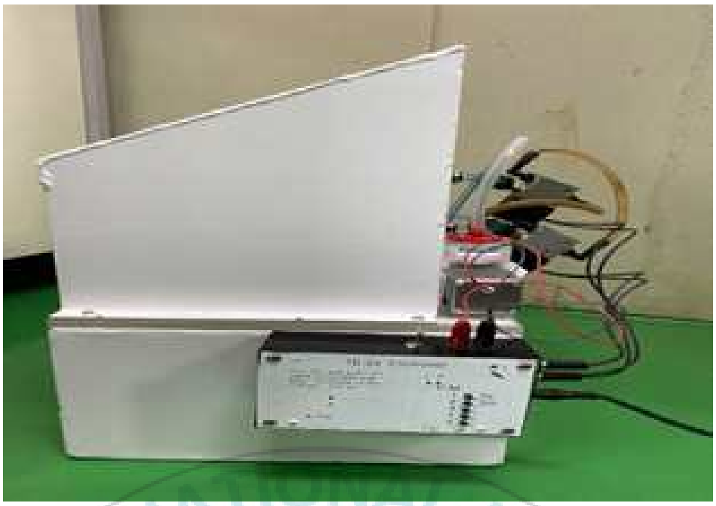


Fig. 3.3 TE-2 smoking machine

3.3.2. SMPS

SMPS is a device that measures particle and nanoparticle concentrations from diameters ranging 2.5 – 1000 nm. Generally, SMPS consists of three or four devices. The equipment used in this study were an electrostatic classifier (3082, TSI, USA), 1 nm-differential mobility analyzer (DMA; DMA 3081, TSI, USA), and a condensation particle counter (CPC, TSI, USA). Particles enter the inlet of the electrostatic classifier at the customized flow rate, and then enter the DMA through the connected tube. At this time, if (−) kV is hung on the electric rod inside of the DMA, only the particles with a (+) charge can pass through in accordance with the electrical mobility of particles within the DMA internal electric field. The particles that pass through the DMA go to the CPC but are too small to be measured. So, the size of the particles is grown using butanol (C_4H_9OH), and the measurement can proceed. The particles that are grown in size pass through the condenser and are detected by the optical detector to calculate the concentration. The measurement process is thus completed, and data can be extracted through a dedicated software (AIM Instrument, USA).

3.4 Analysis

3.4.1. Nicotine, PG, VG

Nicotine, PG, and VG was quantitatively and qualitatively analyzed using a Hp 6890 gas chromatography – flame ionization detector (GC – FID, Agilent, USA) for the solution extracted from the CFP. The analysis conditions are shown in Table 3.2.

Table 3.2 Analytical condition of the gas chromatography – flame ionization detector

Parameter	Condition
Column	SUPELCO-WAX (Length : 30 m, Diameter : 0.32 mm, Film thickness : 0.25 μm)
Carrier	Nitrogen, 1.0 mL/min Purge flow, 5.0 mL/min Column flow, 106 mL/min Total flow)
Inlet	Oven Temp : 160℃, Injector temp : 250℃ (temp changed at a rate of 10℃ per min up to 220℃ (maintained 4 min))
FID	Detector Temp : 320℃ Detector gas : Hydrogen, Nitrogen, Air

3.4.2. VOCs

VOCs were detached from solid adsorption tubes using a thermal desorber (TD, Model Unity 2, Markes International, UK), and then quantitatively and qualitatively analyzed using a gas chromatography - mass spectrometer detector (MS, Model 5975, Agilent, USA). Standard gases were used, including BTEX, for analyzing various kinds of VOCs and ozone precursor/PAMS mix (57 components, 100 ppb each component in nitrogen, Cat. No. 41975-U, Supelco, USA). The VOC species selected for the evaluation of indoor air quality are shown in Table 3.3.

Table 3.3 Target VOCs

Full name	Concentration (ppb)	MWp (g/mol)	Formula	CAS No.
Benzene	110	78.11	C_6H_6	71-43-2
Toluene	110	92.14	C_7H_8	108-88-3
Ethylbenzene	100	106.17	C_8H_{10}	100-41-4
mp-Xylene	100	106.17	C_8H_{10}	106-42-3
o-Xylene	98	106.17	C_8H_{10}	95-47-6
Styrene	93	106.15	C_8H_8	100-42-5

3.4.3. Aldehydes

Aldehydes samples in the DNPH cartridge were extracted by acetonitrile, and quantitatively and qualitatively analyzed using high performance liquid chromatography (HPLC). The front end of the DNPH cartridge was fixed on the test tube or the volumetric flask entrance, and a fixed 10 mL luer type injector on a stand allowed for the DNPH cartridge to be inserted. Then, the volume of the acetonitrile solution was passed through slowly until the yellow part (DNPH derivative) disappeared inside of the cartridge. At this time, the extracted solution had a volume of 5 mL. After the extraction, samples were put into an amber vial of the appropriate size and refrigerated until the analysis. The aldehydes analysis condition through HPLC is shown in Table 5, and the target aldehydes analyzed are indicated in Table 3.4.

Table 3.4 Target aldehydes

Full name	MWp (g/mol)	Formula	CAS No.
Formaldehyde	30.03	HCHO	50-00-0
Acetaldehyde	44.05	C_2H_4O	75-07-0
Acrolein	56.06	C_3H_4O	107-02-8
Acetone	58.08	C_3H_6O	67-64-1
Propionaldehyde	58.08	C_3H_6O	123-38-6
Crotonaldehyde	70.09	C_4H_6O	4170-30-3
Butyraldehyde	72.12	C_4H_8O	123-72-8
Benzaldehyde	106.12	C_7H_6O	100-52-7
Valeraldehyde	86.13	$C_5H_{10}O$	110-62-3
isovaleraldehyde	86.13	$C_5H_{10}O$	590-86-3
o-Tolualdehyde	120.14	C_8H_8O	107-87-0
m-Tolualdehyde	120.14	C_8H_8O	107-87-0
p-Tolualdehyde	120.14	C_8H_8O	107-87-0
Hexaldehyde	100.18	$C_6H_{12}O$	66-25-1

Table 3.5 Analytical condition of HPLC

Parameter	Condition
Injector	20 μL sample loop
Column	ODS (C18) 4.6 mm * 250 mm (Column Temp. - Room temperature)
Carrier	Carrier A : Acetonitrile 100 (V %) Carrier B : Water/Acetonitrile/tetrahydrofuran 50/45/5 (V %) (Flow : 1.0 mL/min)
Detector	UV detector (Detection wavelength : 360 nm)

3.4.4. Particulate matter and nanoparticles

The PM and nanoparticle aerosols generated when using HnB products and conventional cigarette smoking were measured continuously during the experiment. PM was measured with Aerocet 531S at diameters of 0.3 μm, 0.5 μm, 1.0 μm, 5.0 μm and 10 μm. In addition, SMPS was used to confirm the nano-sized aerosol distribution characteristics. SMPS was sampled at a constant flow rate (Sheath flow : 3 $L \cdot min^{-1}$, Aerosol flow : 0.5 $L \cdot min^{-1}$) and a diameter of 0 - 560 nm particles was measured. After measurement was complete, data were extracted with the dedicated software (Comet 2, USA) and analyzed using Microsoft Excel (Office 2019, USA). The samples collected one hour before and one hour after the experiment were applied to the analysis as the blank sample. When measuring the blank samples, the windows were closed, and the air conditioner and air purifier were shut down, as in the case of secondhand smoke sampling. The averages of the two blank values measured during the analysis were used. The average blank sample values subtracted from the conventional cigarette smoking and HnB products values were designated as the fine particle concentration emitted from conventional cigarette smoking and HnB products vaporization, respectively.

3.5 QA/QC

Quality control was performed to evaluate the accuracy of the harmful substances emitted and detected through firsthand and secondhand smoke experiments. The device analysis accuracy was expressed by the method detection limit (MDL) and relative standard deviation (RSD). RSD and MDL were calculated using Equations 1 (RSD calculation formula) and 2 (MDL calculation formula), respectively.

In this study, the lowest concentration sample (PG – 0.028 μg, VG – 0.07 μg, nicotine – 0.04 μg) of standard solution was analyzed seven times for RSD and MDL of firsthand smoke emissions. The RSD of PG, VG, and nicotine were 7.89%, 6.75%, and 6.09%, respectively. The MDL of PG, VG, and nicotine was 7.7 ng, 13.9 ng, and 10.6 ng, respectively. In the secondhand smoke experiment, RSD and MDL were also calculated for VOCs and aldehydes detected in the indoor air. RSD and MDL were calculated using the same method as with the emissions from the firsthand smoke experiments. VOCs were analyzed for six compounds: benzene, toluene, ethyl benzene, mp-xylene, o-xylene, and styrene. Their RSD values were 1.32%, 1.15%, 2.09%, 2.28%, 1.74%, and 2.65%; and their MDL values were: 0.17 ng, 0.11 ng, 0.08 ng, 0.10 ng, 0.10 ng, and 0.11 ng, respectively. Fourteen aldehyde compounds were analyzed: formaldehyde, acetaldehyde, acrolein, acetone, propionaldehyde, crotonaldehyde, butyraldehyde, benzaldehyde, valeraldehyde, isovaleraldehyde, o-tolualdehyde, m-tolualdehyde, p-tolualdehyde, and hexaldehyde. Their respective RSD values were: 8.81%, 2.63%, 3.22%, 8.59%, 7.02%, 7.45%, 2.99%, 6.42%, 2.01%, 8.57%, 5.99%, 7.91%, and 4.29%; and their MDL values were: 0.011 ng, 0.015 ng, 0.017 ng, 0.020 ng, 0.019 ng, 0.024 ng, 0.033 ng, 0.028 ng, 0.029 ng, 0.042 ng, 0.020 ng, and 0.034 ng.

$$RSD = \frac{Stadard\,Deviation\,of\ Target\ Compounds}{Average\,of\ Target\ Compounds\,Area} \times 100 \quad \cdots\cdots (1)$$

$$MDL = 3.14 \times Standard\,deviation \quad \cdots\cdots (2)$$

Ⅳ. Results and discussion

4.1 Firsthand smoke

4.1.1. Nicotine

The concentration of nicotine emitted from HnB products was analyzed. The nicotine concentration of conventional cigarettes, which was used as a comparative group, was also analyzed. The reason for comparing the two cigarette types was to find if HnB products produce a similar amount of nicotine as advertised by tobacco companies. The cigarette brands used in the experiment were introduced in Table 3.1 of 3.1.2. Figure 4.1 shows the nicotine concentration in smoke and vapor generated by conventional cigarettes and HnB products. Three samples per treatment were collected, and the sampling was repeated three times. When smoking a conventional cigarette, nicotine was emitted at an average concentration of 2.4 – 3.5 mg·cigarette^{-1}, and when vaporized, HnB nicotine was emitted at an average concentration of 0.83 – 1.16 mg·cigarette^{-1} in IQOS, Lil, and Glo. In previous studies, 3R4F, IQOS and Glo were primarily used as reference cigarettes. Nicotine was emitted at an average concentration of 1.0 – 2.6 mg·cigarette^{-1} in 3R4F, IQOS emitted nicotine ranging from 1.0 – 1.7 mg·cigarette^{-1}, and Glo emitted nicotine concentrations averaging 0.41 mg·cigarette^{-1} (Mallock et al., 2018; Godec et al., 2019; Kopa and Pawliczak, 2019; Gasparyan et al., 2018; Bekki et al., 2017; Schaller et al., 2016; Jaccard et al., 2017). Comparing the results found here with previous studies, HnBs provided relatively smaller amounts of nicotine than conventional cigarettes. Therefore, smokers must use more HnBs to receive the same dose of nicotine as a conventional cigarette.

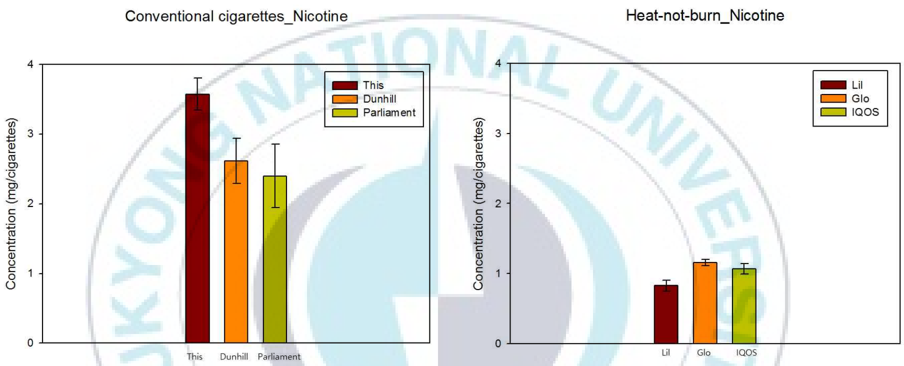


Fig. 4.1 Nicotine emitted by conventional cigarette smoke and heat-not-burn tobacco vapor

4.1.2. PG, VG

Propylene glycol (PG) and vegetable glycerin (VG) are colorless and odorless compounds that are responsible for delivering vapor to smokers when HnB is vaporized. PG and VG are used in e-liquid of electronic cigarettes to simulate the ‘throat hit’ of conventional cigarettes. The more PG present in the e-liquid, the more smokers feel aroma; and the more VG in the e-liquid, the greater the soft smoker feel. For the same reason, PG and VG are also added to HnB products. HnB products primarily use VG rather than PG, which increases flavor.

Among conventional cigarettes, PG was emitted from This and Parliament. PG was emitted at an average concentration 0.10 – 0.61 mg·cigarette^{-1} in conventional cigarettes. Unlike conventional cigarettes, HnB products emitted PG in all types. PG was emitted at an average concentration of 0.23 – 0.32 mg·cigarette^{-1} in HnB products. PG was mainly used for liquid type e-cigarettes. So in HnB studies do not select them as target material. For this reason, previous studies on PG were rarely existed. When think about this situation, this study is expected to provide guideline for PG emission in future studies because it has measured PG concentration.

Among conventional cigarettes, VG was primarily emitted from This Plus, Dunhill and Parliament. VG was emitted at an average concentration of 0.62 – 3.03 mg·cigarette^{-1} in conventional cigarettes. HnB products emitted VG in all types of HnB as like conventional cigarettes. Nevertheless, HnB products emitted VG at an average concentration of 3.14 – 5.90 mg·cigarette^{-1}, which was about 1 – 9 times higher than observed in conventional cigarettes. In previous studies, reference cigarettes 3R4F, IQOS and Glo were used to compare VG emissions and found that HnB products, IQOS and Glo emitted VG at a concentration of 3 – 4.6 mg·cigarette^{-1}, 3R4F at concentrations of 2.3 – 2.4 mg·cigarette^{-1} (Mallock et al., 2018; Godec et al., 2019; Kopa and Pawliczak, 2019; Gasparyan et al., 2018; Bekki et al., 2017; Schaller et al., 2016; Jaccard et al., 2017). VG is not toxic by itself, but when used in cigarettes, it can act as a toxic substance by producing aldehydes through pyrolysis (Ooi et al., 2019). Therefore, further research is needed to see how pyrolyzed VG affects human health.

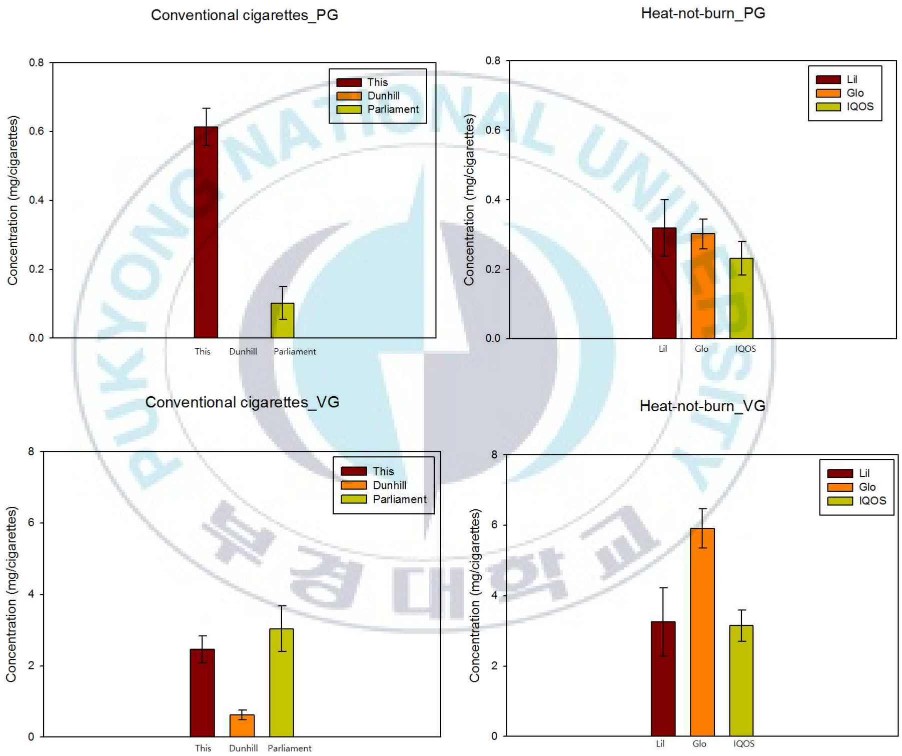


Fig. 4.2 PG and VG emitted by conventional cigarette smoke and heat-not-burn tobacco vapor

4.2 Secondhand smoke

4.2.1. VOCs

VOCs selected as the target compounds affecting indoor air quality in this study are shown in Table 3.3 of 3.4.2. When conventional cigarette smoke and HnB vapor are released indoors, the average concentration of VOCs present indoors can be seen in Table 4.1. When IQOS and Glo were used indoors, styrene was detected at 0.03 – 0.05 ppb concentration in indoor air, while when This plus, Dunhill, and Parliament were smoked indoors, styrene were detected at a concentration of 0.38 – 0.42 ppb, a difference of about 1.4 – 7.6 times. Among HnB products, toluene was detected only when Glo was used indoors at a concentration of 0.35 ppb. In comparison, toluene was detected for all conventional types of cigarettes indoors. Among conventional cigarettes, the smallest amount of toluene was detected in the indoor air for Parliament. Benzene was detected in Glo and IQOS HnB products, and all conventional cigarette types. Benzene in Glo was detected at 0.075850 ppb and 0.000442 ppb in IQOS, so one could potentially conclude that it was only detected at significant levels in the indoor air when Glo was used. In comparison, conventional cigarette benzene levels were detected in the range of 0.46 – 0.75 ppb, showing an increase between 3 – 5 times from HnB levels. Ethylbenzene was the only VOCs detected indoors across all type of cigarettes analyzed. HnB ethylbenzene was detected in the range of 0.03 – 0.08 ppb, and conventional cigarettes were detected in the range of 0.29 – 0.52 ppb, an increase of about 2 – 12 times. O-xylene was detected with Glo, IQOS, This plus, Dunhill, and Parliament. When using Glo and IQOS, it was detected at a concentration of 0.012 – 0.052 ppb, and when using This plus, Dunhill and Parliament, it was detected at 0.13 – 0.21 ppb concentration, 2 – 20 times greater. Mp-xylene was present in indoor air for Glo and all brands of conventional cigarettes. When using Glo, mp-xylene was detected at a concentration of 0.11 ppb, and a range of 0.64 – 0.79 ppb when using This plus, Dunhill, or Parliament, showing an increase of 5 – 7 times. Cancelada et al. (2019) used a 200 L chamber to analyze which compounds existed in indoor air when using HnB products. The prominent VOCs found was benzene at a concentration of 0.08 – 0.12 μg·stick^{-1}, greater than the values observed in the experiment here. The difference in concentrations between the two experiments is likely due to chamber size. Mitova et al. (2016) created a 72.3 m^3 environmental control room and simulated three scenarios representing 'office', 'residential', and 'hospital' environments. Three people entered the 'office' and 'residential' environment simulation, and five people entered the 'hospital' environment simulation. The commonly found VOCs were benzene and toluene, where office benzene concentrations were 0.21 – 0.31 μg·m^{-3}, and toluene concentrations were 1.11 – 7.72 μg·m^{-3}, residential benzene and toluene concentrations were 0.43 – 0.67 μg·m^{-3} and 1.86 – 3.29 μg·m^{-3}, respectively, and hospital benzene and toluene concentrations were 0.18 – 0.29 μg·m^{-3} and 0.78 – 1.4 μg·m^{-3}, respectively. The VOCs concentration of this previous study showed higher levels than in the present study. The likely reason for the observed difference between the two studies is the number of people in the experimental group participating in the experiment.

Figure 4.3 shows the average concentration of VOCs present in indoor air when Volunteers 1, 2, and 3 were smoking conventional cigarettes or HnB products based on Table 4.1. Each dot represents the average concentration per sample with Volunteer 1, 2, or 3. Figure 4.3 shows that when conventional cigarettes and HnB products were used indoors, the concentration difference of VOCs present in indoor air were readily apparent. Indoor air VOCs concentration ranged from 0.012 – 0.112 ppb for HnB products, and 0.13 – 4.52 ppb for conventional cigarettes, a difference of 1.2 – 370 times. Both Figure 4.3 and Table 4.1 show that smoking conventional cigarettes had a greater influence on indoor air quality by generating more VOCs; however, since the target materials were detected in HnB products as well, it is difficult to ignore the effect of indoor HnBs vaporization on indoor air quality.

Figure 4.4 shows the comparison of VOCs in indoor air according to the experimental group. Figure 4.4 is based on the target substances, and Figure 4.5 is based on conventional cigarettes and HnB products. According to previous studies, the detection level of smokers may vary according to their smoking habits, so a comparison was performed between the experimental groups (Alonso et al., 2010; Capone et al., 2017) compared VOCs from the breath of 10 nonsmokers and 16 smokers. VOCs were detected across a variety of ranges, suggesting that differences may be attributable to smoking habits. According to Figure 4.4, as in previous studies, the concentration of VOCs detected when using conventional cigarettes was higher than that of HnB products, and the concentration of VOCs detected varied by cigarette type. In Volunteer 1, the concentration of VOCs detected when using conventional cigarettes This plus and Parliament was lower than all VOCs species detected in Volunteers 2 and 3. This was expected, however, as the smoking habits of Volunteer 1 were different. Figure 4.5 shows that the concentration of toluene was the highest among all VOCs, except for Volunteers 1 and 3 using Parliament. Toluene was detected at a concentration of 1.06 – 6.28 ppb, regardless of conventional cigarette type, and about 1.06 ppb when using Glo. Figures 4.4 and 4.5 show that mp-xylene was detected at the next highest concentration for all VOCs after toluene, and was emitted regardless of the type of conventional cigarette, but it was not detected in Volunteer 3. Concentrations of mp-xylene ranged from 0.204 – 1.732 ppb for conventional cigarettes, and 0.012 – 0.323 ppb for Glo. The differences between mp-xylene and toluene were only detected in the cases of Glo use by Volunteers 1 and 3. After toluene and mp-xylene, benzene was the next most prevalent substance present in indoor air for all HnB products and conventional cigarettes examined. Benzene was detected in indoor air when Volunteers 1, 2, and 3 used conventional cigarettes This plus, Dunhill, and Parliament, and benzene was similarly detected in HnB products Glo, and when Volunteer 3 used IQOS. Benzene was detected in the range of 0.001 – 0.113 ppb in HnB products, and 0.36 – 0.68 ppb in conventional cigarettes. Figures 4.4 and 4.5 display the difference in the concentration of VOCs in each person, which can also vary according to smoking habit. The concentration of VOCs detected when HnB tobacco was used indoors was so small that it is difficult to conclude it has a significant effect on indoor air quality like conventional cigarettes. However, when HnB products are used indoors, they can still detrimentally affect indoor air quality because of the other VOCs present.

Figures 4.6, 4.7, and 4.8 show the concentration difference of VOCs detected by type of cigarettes when Volunteers 1, 2, and 3 used HnB products and conventional cigarettes indoors. These figures show that when the same person smoked the same conventional cigarette or the same HnB, the detected substances and concentrations often varied. The graphs show that when Lil was used, VOCs were rarely emitted regardless of the experimental group. When Volunteer 2 vaporized HnB, ethylbenzene was detected at 0.35 ppb in indoor air. Regardless of the experimental group, the most diverse VOCs species were detected when using Glo. VOCs of all species were detected when using Glo, particularly for Volunteer 3. The VOCs concentrations ranged from 0.01 – 2.11 ppb. In particular, toluene was detected at 2.11 ppb, and styrene was detected at 0.01 – 0.19 ppb. VOCs were detected only when IQOS was used by Volunteers 1 and 3. When Volunteer 1 vaporized HnB products, styrene was detected at 0.05 ppb. When Volunteer 3 vaporized HnB products, benzene, ethylbenzene, o-Xylene, and styrene were detected at concentrations of 0.003 – 0.23 ppb, 0.17 – 0.48 ppb, 0.07 – 0.17 ppb, and 0.01 – 0.25 ppb, respectively. The concentration of VOCs detected in conventional cigarettes showed a significant difference from that of HnB products. While HnB products detected only some VOCs, all species were detected in conventional cigarettes (although only some VOCs were detected in Volunteer 3, as in the case of using HnB products). The concentration of VOCs detected when conventional cigarettes were used indoors was 0.31 – 9.24 ppb, about 3 – 920 times greater than the VOCs emitted from HnB products. VOCs were detected in indoor air when Volunteers 1 and 2 used any of the conventional cigarettes. When Volunteer 1 used conventional cigarettes indoors, VOCs were detected in the range of 0.03 – 8.89 ppb, and Volunteer 2 VOCs levels ranged from 0.17 – 7.50 ppb. Unlike Volunteers 1 and 2, Volunteer 3 detected only levels of benzene, toluene, ethylbenzene and styrene when using conventional cigarettes, but no xylenes were detected at any of using the HnB products. Volunteer 3 showed a VOCs concentration ranging from 0.003 – 9.240 ppb, similar to other experimental groups. Among VOCs detected in conventional cigarettes, toluene was detected at the highest concentration, and showed a difference of 1.1 – 9 times even between cigarettes of the same types. This was similar to HnB products, which varied by 1.3 – 20 times within the same types. The likely reason for the difference in the results is individual smoking habits, even though the number of puffs between the experimental groups was the same. Previous studies have also shown that when conventional cigarettes and HnB products were smoked or vaporized indoors, the detection concentration of VOCs could vary depending on the number of puffs (Blair et al., 2015).

In addition, an ANOVA test was performed through Microsoft Excel to determine the significance between the data. The difference in the amount of discharge according to the type of cigarette was tested using Table 4.1 (significance level, $P < 0.05$). The test results showed that the amount of VOCs varied by the type of cigarette. It was also found that VOCs were detected in indoor air when HnB products were used indoors, albeit at lesser levels than conventional cigarettes. Furthermore, even when HnB products were vaporized indoors, it was found that VOCs were produced, and also that it would require smokers to use HnB products more frequently to receive similar doses of nicotine obtained with conventional cigarettes. Therefore, this situation should be considered when evaluating the impact on indoor air quality.

Table 4.1 Mean concentration of VOCs after vaporizing heat-not-burn tobacco and smoking conventional cigarettes

Sample(ppb)	Benzene	Toluene	Ethyl benzene	mp-Xylene	o-Xylene	Styrene
Glo	0.07585	0.351751	0.028663	0.111713	0.051772	0.039617
Lil	-	-	0.059031	-	-	-
IQOS	0.000442	-	0.079791	-	0.012156	0.05178
This Plus	0.745576	4.520819	0.307736	0.639802	0.172561	0.424057
Dunhii	0.570636	4.394437	0.52128	0.794024	0.205016	0.383762
Parliament	0.465543	2.528168	0.286654	0.645431	0.125406	0.382898

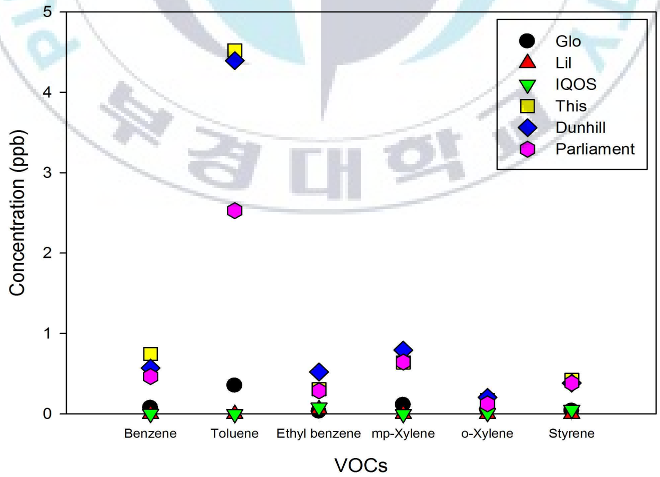


Fig. 4.3 Average concentration of detected VOCs

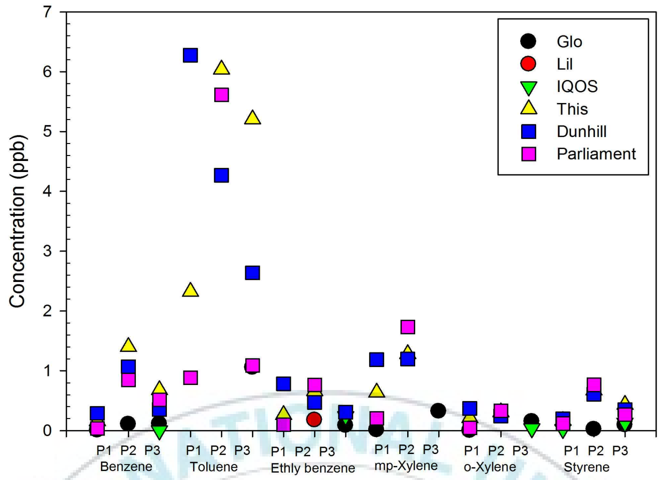


Fig. 4.4 Indoor VOCs concentration when volunteer 1, 2 and 3 smoked conventional cigarettes and vapored heat-not-burn tobacco, by VOCs species

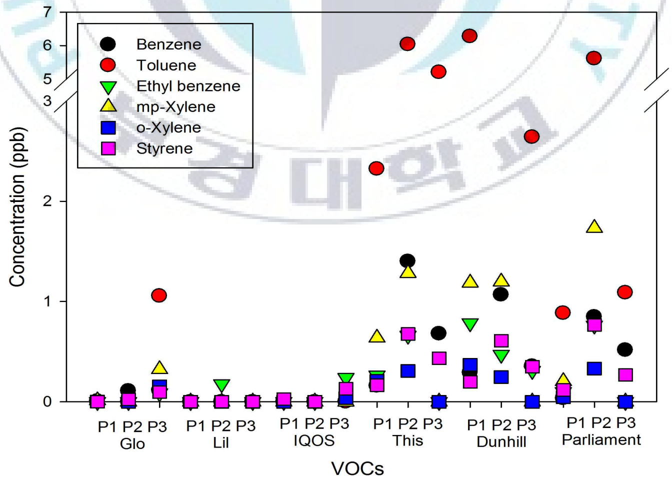


Fig. 4.5 Indoor VOCs concentration when volunteer 1, 2 and 3 smoked conventional cigarettes and vapored heat-not-burn tobacco, by cigarette type

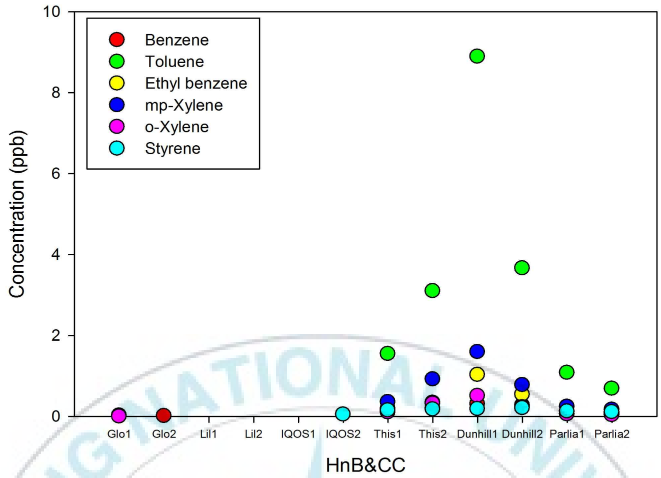


Fig. 4.6 Indoor VOCs concentration when volunteer 1 smoked conventional cigarettes or vapored heat-not-burn tobacco

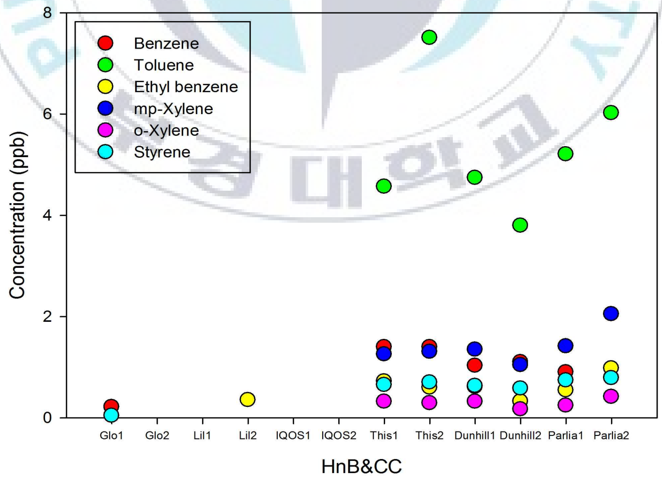


Fig. 4.7 Indoor VOCs concentration when volunteer 2 smoked conventional cigarettes or vapored heat-not-burn tobacco

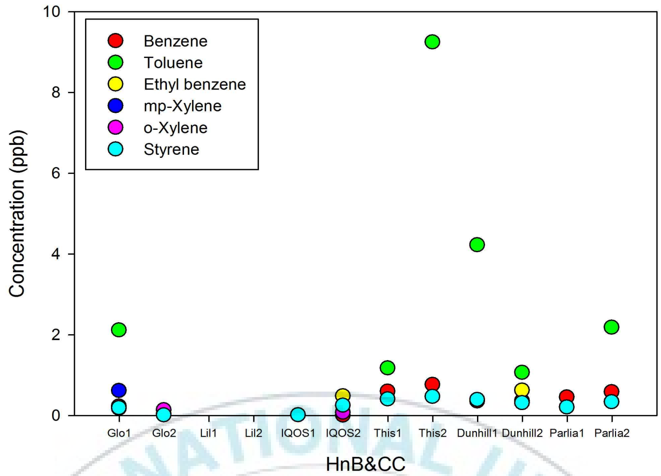


Fig. 4.8 Indoor VOCs concentration when volunteer 3 smoked conventional cigarettes or vapored heat-not-burn tobacco

4.2.2. Aldehydes

The target aldehydes species affecting indoor air quality are listed in Table 3.4 of section 3.4.3. Table 4.2 displays the aldehydes species that commonly exist in indoor air samples when conventional cigarettes are smoked or HnB products are vaporized among 14 target aldehydes species. The results focused on the aldehydes species most commonly detected. Compared to VOCs, the concentrations of aldehydes were very low, averaging < 0.1 ppb.

Figure 4.9 displays the mean aldehydes concentration in indoor air sampled when the experimental group smoked conventional cigarettes and vaporized HnB products indoors. Aldehydes groups were more prevalent when conventional cigarettes were smoked compared to HnB products. Among the five aldehydes, conventional cigarettes and HnB products emitted three types of substances: formaldehyde, acetaldehyde and acetone. Cancelada et al. (2019) also detected aldehydes species along with VOCs. Their experiments were performed in a 200 L chamber and they analyzed acetaldehyde, acetone, formaldehyde and hexaldehyde, as done in the present study. The concentration of aldehydes emitted from THS 2.2 (IQOS) secondhand smoke concentrations were: acetaldehyde, 24.2 $\mu g \cdot stick^{-1}$; acetone, 3.8 $\mu g \cdot stick^{-1}$; formaldehyde, 0.4 $\mu g \cdot stick^{-1}$; and hexaldehyde, 0.1 $\mu g \cdot stick^{-1}$. Compared with the present study, there was a difference of 600 – 48,000 times likely due to the difference between chamber size and the experimental method used.

Figure 4.10 presents a comparison of the cigarettes used by the experimental groups. Overall, it can be seen that the largest amount of aldehydes was detected in indoor air when Parliament cigarettes were smoked. Compared to HnB products, there was a difference of about 1.8 – 4.6 times, which is similar to other substances. Also, when using conventional cigarettes indoors, there was a threefold difference when compared to the detected aldehydes concentration. This is thought to be due to the difference in smoking habits, as in the case of VOCs. With Volunteer 3, the concentration of aldehydes in indoor air was highest between the experimental groups when conventional cigarettes were smoked and HnB products were vaporized indoors. Volunteers 1 and 2 generated more aldehydes in indoor air when smoking conventional cigarettes than HnB products. Formaldehyde was detected in the range of 0.0021 – 0.0080 ppb when Volunteers 1 and 3 used Glo, Lil, and IQOS. When the Volunteers used conventional cigarettes, formaldehyde levels ranged from 0.0012 – 0.0173 ppb. Acetaldehyde was detected in the range of 0.0006 – 0.0024 ppb when Volunteers 2 and 3 used HnB products, and 0.0033 – 0.0233 ppb when any of the Volunteers used conventional cigarettes. Hexaldehyde was detected when Volunteer 3 used Glo, Volunteer 2 used This plus, Dunhill, and Parliament, and Volunteer 3 used Dunhill and Parliament. When Volunteer 3 used Glo indoors, hexaldehyde was detected at 0.00012 ppb, and when Volunteer 2 smoked This plus, hexaldehyde was detected at 0.000183 ppb. When Volunteers 2 and 3 smoked Dunhill and Parliament, hexaldehyde was detected at 0.0002 – 0.0003 ppb, and 0.000038 – 0.000039 ppb in indoor air, respectively. Acetone was always detected in indoor samples, regardless of the cigarette type. In Volunteer 1, no aldehydes was detected when vaporizing HnB products; however, it was detected when smoking conventional cigarettes. When Volunteer 1 used conventional cigarettes indoors, acetone was detected, which showed a higher than other experimental groups. Volunteer 1 yielded 0.0513 ppb acetone when smoking This plus, 0.0604 ppb when smoking Dunhill, and 0.0292 ppb when smoking Parliament. In Volunteer 2, acetone was found at 0.00089 ppb when using Glo, 0.00106 ppb when using Lil, 0.0041 ppb when smoking This plus, 0.0017 ppb when smoking Dunhill, and 0.0046 ppb when smoking Parliament. Volunteer 3 was the only one in the experimental group that detected acetone in indoor air, regardless of cigarette type. When Volunteer 3 vaporized Glo, Lil, and IQOS, acetone was detected at concentrations of 0.0028 ppb, 0.0029 ppb and 0.0024 ppb, respectively. Acetone was also detected when Volunteer 3 smoked conventional cigarettes indoors, 0.0076 ppb when smoking This plus, and 0.0013 ppb when smoking Dunhill, both notably lower than HnBs concentrations. Only smoking Parliament yielded a concentration of 0.01380 ppb, higher than the HnB products observed. Propionaldehyde was not detected in Volunteer 1 when HnB products and conventional cigarettes were used indoors. In Volunteer 2, propionaldehyde was detected only when conventional cigarettes were smoked; and in Volunteer 3, it was detected both when IQOS was vaporized and conventional cigarettes were smoked. Propionaldehyde was detected at concentrations of 0.00193 ppb when Volunteer 2 smoked This plus indoors, 0.00124 ppb for Dunhill, and 0.00261 ppb for Parliament. Propionaldehyde was detected at a concentration of 0.000083 ppb when IQOS was vaporized by Volunteer 3, and 0.00129 ppb, 0.00279 ppb and 0.00198 ppb when smoking conventional cigarettes This plus, Dunhill, and Parliament, respectively.

Figure 4.11 focuses on the conventional cigarettes and HnB products of the experimental groups using data from Figure 4.10. The most frequently detected aldehydes species were different between conventional cigarettes and HnB products. In HnB products, formaldehyde and acetone were the most abundant, while acetone, acetaldehyde and then formaldehyde were the most common constituents in conventional cigarettes.

Figures 4.12, 4.13, and 4.14 show the concentration of aldehydes in indoor air detected when the experimental groups used HnB products and smoked conventional cigarettes. These graphs show that the amount of aldehydes detected from the same person using the same conventional cigarette or HnB type varied. Figure 4.17 presents the aldehydes detected in vaporizing HnB products and smoking conventional cigarettes during the experimental period for Volunteer 1. Formaldehyde was detected in all cigarettes except for Glo. In addition, acetaldehyde and acetone were detected when smoking conventional cigarettes, and a difference was observed within the same cigarette brand. The first time Volunteer 1 smoked This plus, acetone concentrations were 0.0269 ppb, but the second time it was 0.0758 ppb, 2.8 times greater. In addition, it was found that acetone was detected at a concentration of 0.0866 ppb when Dunhill was first smoked by Volunteer 1, and 0.0343 ppb when smoked the second time, 2.5 times different. Volunteer 3 produced large amounts of aldehydes in the order of acetone, acetaldehyde and formaldehyde.

Like VOCs, aldehydes significance were also tested with an ANOVA in Microsoft Excel using data from Table 4.2. Table 4.2 was used to compare the amount of aldehydes according to the cigarette type, as with VOCs, regardless of the experimental group ($P < 0.05$). As a result, it was found that the aldehydes concentrations significantly varied with cigarette type.

Table 4.2 Detected aldehydes compounds by cigarette smoking and heat-not-burn tobacco product vaporization

Sample (ppb)	Formaldehyde	Acetaldehyde	Acetone	Propionaldehyde	Hexaldehyde
Glo	0.002243	0.000868	0.001236	-	0.000396
Lil	0.003458	0.000506	0.001325	-	-
IQOS	0.001642	0.00114	0.000791	0.0000275	-
This Plus	0.005083	0.010491	0.021012	0.001074	0.0000557
Dunhill	0.006201	0.011821	0.02115	0.001342	0.000176
Parliament	0.00793	0.013219	0.015873	0.001529	0.0000259

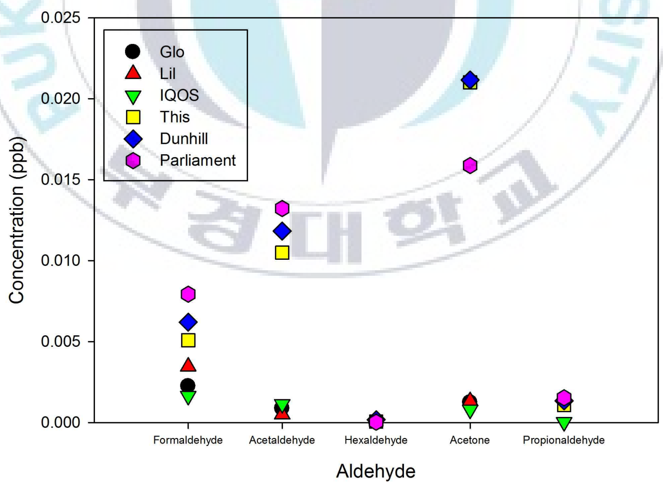


Fig. 4.9 Average concentration of detected Aldehydes

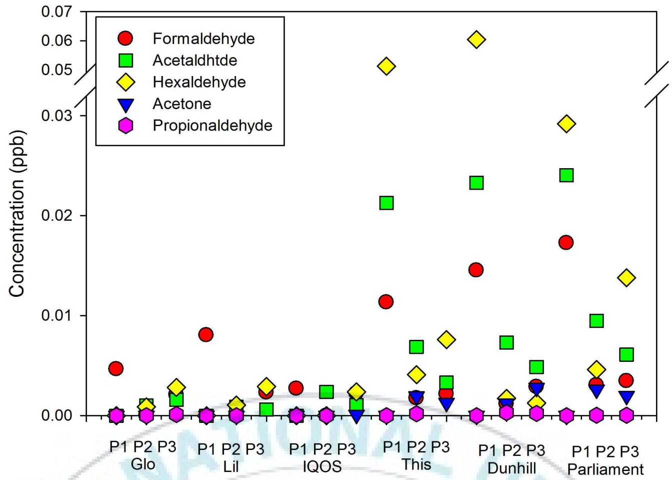


Fig. 4.10 Indoor aldeyde concentration when volunteers 1, 2 and 3 smoked conventional cigarettes and vapored heat-not-burn tobacco, by aldehydes species

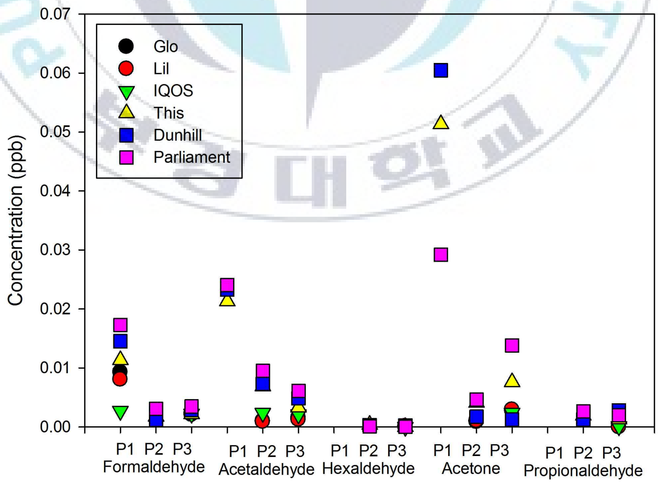


Fig. 4.11 Indoor aldehydes concentration when volunteer 1, 2 and 3 smoked conventional cigarettes and vapored heat-not-burn tobacco, by cigarette type

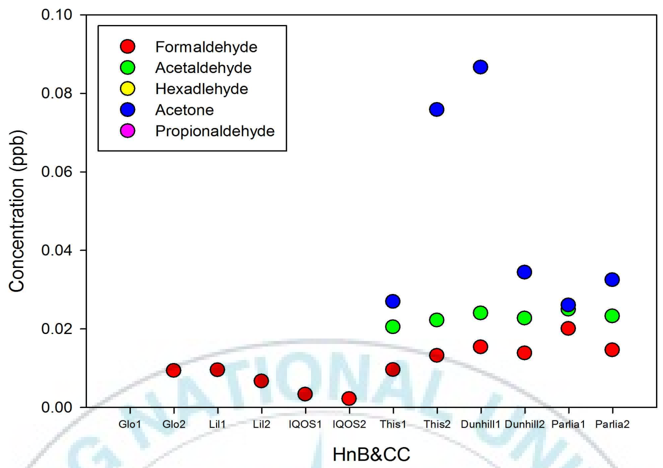


Fig. 4.12 Indoor aldehydes concentration when volunteer 1 smoked conventional cigarettes or vapored heat-not-burn tobacco

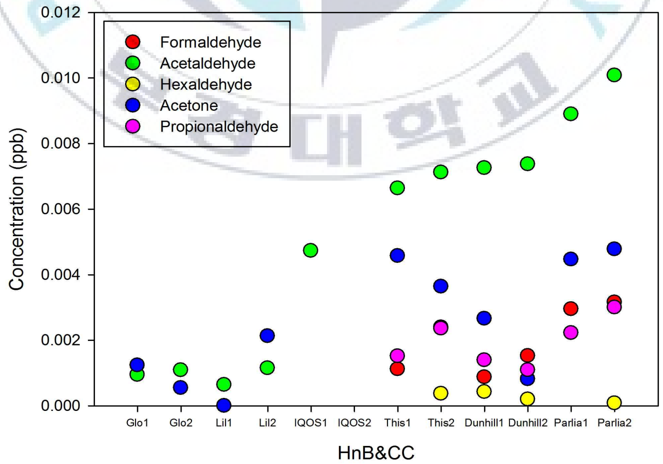


Fig. 4.13 Indoor aldehydes concentration when volunteer 2 smoked conventional cigarettes or vapored heat-not-burn tobacco

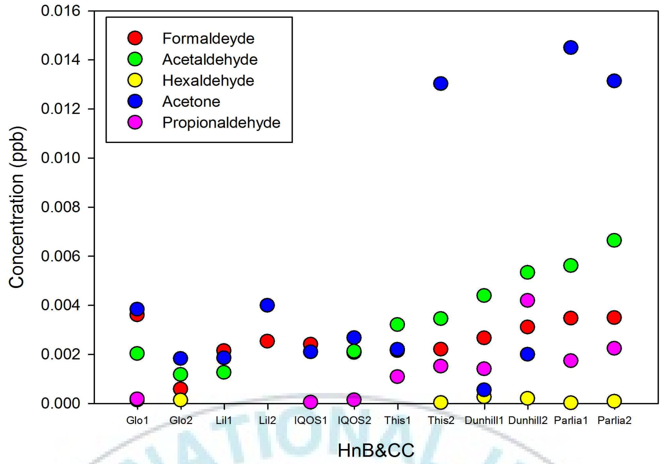


Fig. 4.14 Indoor aldehydes concentration when volunteer 3 smoked conventional cigarettes or vapored heat-not-burn tobacco

4.2.3. Particulate matter and nanoparticles

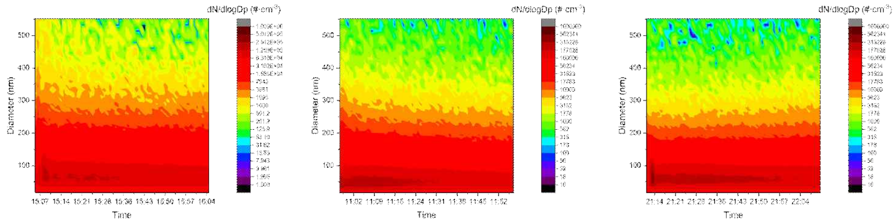
Particulate matter (PM) and nanoparticles were measured in an office size chamber of 4.4 m x 2.7 m x 6.8 m, as shown in section 3.2.2, and their effect on indoor air quality was evaluated. A primary goal was to see if PM and nanoparticles from the outside have similar adverse health effects when they occur indoors. There would be differences in the amount produced, as expected, but it was presumed that any quantity particulates present would be significant since it is occurring indoors. The PM and nanoparticles were measured using the equipment introduced in section 3.5.4. Nanoparticles were measured mainly by SMPS, and the PM were measured by Aerocet 531S.

The results of the simultaneous measurement of PM and nanoparticles in indoor air by SMPS and Aerocet 531S were obtained and are displayed in Figures 4.15 - 17. Data measured by Areocet 531S was presented only with representative results. With these figure, the redder the color, the more particles were present. Overall, HnB products were found to have more particles < 300 nm in the indoor air after vaporization, regardless of the experimental group. This finding was similar when measured with Aerocet 531S where it was found that particles ≤ 0.3 μm were present in the indoor air. In addition, the results of SMPS, which primarily examined nanoparticles, showed that HnB products produced an abundance of particles < 300 nm, but the majority of particles were

< 100 nm. After HnB products use, it was found that particles ≥ 5 µm were rarely present in indoor air.

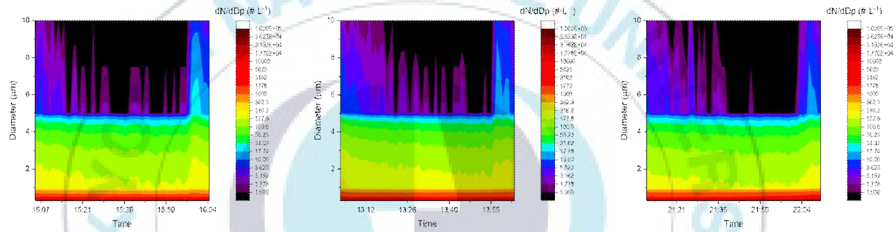
Figures 4.20 – 22 display SMPS and Aerocet 531S results for PM and nanoparticles after smoking conventional cigarettes indoors. At this time, only representative results were presented for data measured by Aerocet 531S. When the indoor air was measured, it was confirmed that nanoparticles existed. However, when HnB products were vaporized, only particles < 300 nm were found in the indoor air, whereas conventional cigarettes emitted PM ≤ 500 nm. Also, when vaporizing HnB products, the majority of particles present in indoor air were < 100 nm, but when smoking conventional cigarettes, peak abundance of particles was in the range of 300 – 500 nm. In case of conventional cigarettes, the tendency of particles detected in indoor space showed similar tendency among experimental group. Further verification of Aerocet 531S data showed that more particles ≥ 5 µm were observed than when observing HnB products.

The results of the experiment showed that the generation of PM and nanoparticles were observed when both HnB products and conventional cigarettes were smoked indoors. Particularly important, since nanoparticles are very small compared to average PM, they penetrate deeper into the lung tissue of smokers, and can cause diseases including pneumonia or lung cancer (Scungio et al., 2018).



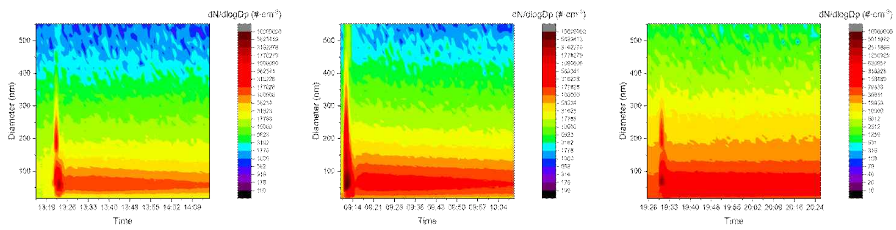
(a) Lil (b) Glo (c) IQOS

Fig. 4.15 Measurement of nanoparicles in indoor air by SMPS when volunteer 1 vapored heat-not-burn tobacco



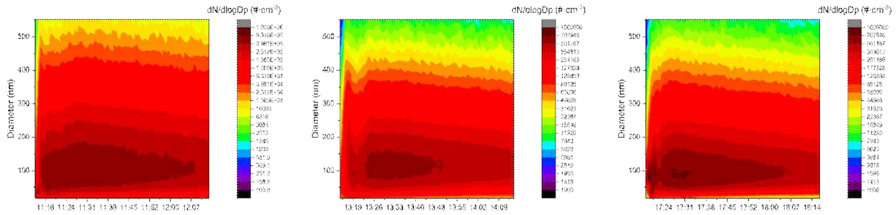
(a) Lil (b) Glo (c) IQOS

Fig. 4.16 Measurement of PM in indoor air by Aerocet 531S when volunteer 1 vapored heat-not-burn tobacco



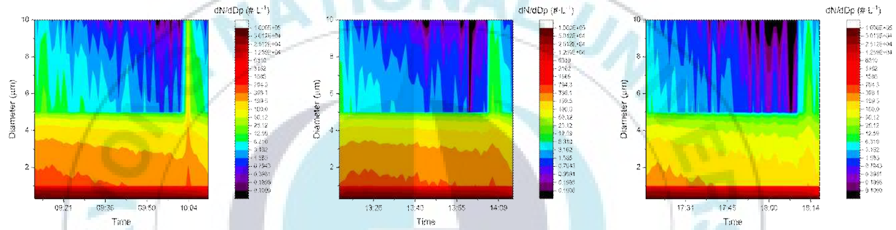
(a) Lil (b) Glo (c) IQOS

Fig. 4.17 Measurement of nanoparicles in indoor air by SMPS when volunteer 2 vapored heat-not-burn tobacco



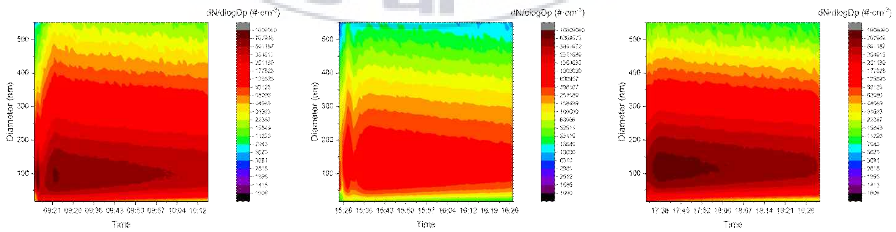
(a) This Plus (b) Dunhill (c) Parliament

Fig. 4.18 Measurement of nanoparicles in indoor air by SMPS when volunteer 1 smoked conventional cigarettes



(a) This Plus (b) Dunhill (c) Parliament

Fig. 4.19 Measurement of PM in indoor air by Aerocet 531S when volunteer 1 smoked conventional cigarettes



(a) This Plus (b) Dunhill (c) Parliament

Fig. 4.20 Measurement of nanoparicles in indoor air by SMPS when volunteer 2 smoked conventional cigarettes

V. Conclusion

This study analyzed the substances emitted from HnB products to evaluate the effect of these compounds on indoor air quality when used in indoor environment. To this end, two major experiments were performed: The first was an analysis of the substances in the vapor generated by HnB use. The substances in the smoke generated from conventional cigarettes were also analyzed for comparison. Second, the substances present in indoor air following HnB products vaporization were analyzed. Similar to the first experiment, conventional cigarettes were smoked in the same chamber for comparison. The first experiment showed, contrary to the tobacco company's claims that HnB products delivered a similar amount of nicotine to conventional cigarettes, HnB products emitted only 30 – 40% of this value. Therefore, HnB smokers who used conventional cigarettes before would need to use more HnB products to receive the same dose of nicotine. The second experiment concluded that when HnB products were vaporized indoors, VOCs and aldehydes were emitted, just as with conventional cigarettes, potentially affecting indoor air quality. Three experimental groups were selected to assess the values found according to smoking habits. The results were similar to those expected, but as the number of experimental groups was small, they could require further clarification in the future.

The results of this study can be summarized as follows:

1. The concentration of nicotine in the mainstream smoke during conventional cigarette smoking was 3.57 mg·cigarette^{-1}, 2.61 mg·cigarette^{-1}, and 2.39 mg·cigarette^{-1} for This plus, Dunhill, and Parliament, respectively; and 0.82 mg·cigarette^{-1}, 1.15 mg·cigarette^{-1}, and 1.07 mg·cigarette^{-1} in HnB products vapors of Lil, Glo, IQOS. Thus, unlike the tobacco company's claims that nicotine levels of HnB products are similar to conventional cigarettes, only 30 – 40% of the levels were obtained. Therefore, smokers who have switched to HnB products from conventional cigarettes will need to use more product to receive the same dose of nicotine.

2. The concentrations of VG in the mainstream smoke were 2.46 mg·cigarette^{-1}, 0.62 mg·cigarette^{-1}, and 3.03 mg·cigarette^{-1} in conventional cigarettes This plus, Dunhill, and Parliament, respectively; and the concentrations in HnB vapor were 3.25 mg·cigarette^{-1}, 5.90 mg·cigarette^{-1}, and 3.14 mg·cigarette^{-1} for Lil, Glo, and IQOS. Thus, more VG was emitted from HnB products than conventional cigarettes. VG is used in HnB products to mimic the 'throat hit' existing in conventional cigarettes. Although VGs are not directly toxic themselves, they can produce aldehydes when heated and pyrolyzed, which can be detrimental to human health (Ooi et al., 2019). Therefore, further research is needed to see how VG affects the human body.

3. The concentrations of PG in the mainstream smoke were 0.61

mg·cigarette^{-1}, 0.11 mg·cigarette^{-1} in conventional cigarettes This plus, Parliament, respectively; and the concentrations in HnB vapor were 0.32 mg·cigarette^{-1}, 0.30 mg·cigarette^{-1}, and 0.23 mg·cigarette^{-1} for Lil, Glo, and IQOS. Thus, more PG was emitted from HnB products than conventional cigarettes as like VG. However, PG is not mainly covered in the previous HnB research.

4. When conventional cigarettes were smoked and HnB products vaporized in a simulated office environment, the concentration of VOCs in indoor air was detected as 0.17 – 0.45 ppb for conventional cigarettes, and 0.01 – 0.35 ppb in HnB products, a difference of 2 – 450 times. The results of the experiment show that VOCs are emitted from HnB products. In addition, since HnB products require more use to receive the same nicotine dose as conventional cigarettes, this too should be considered when evaluating their impact on indoor air quality.

5. When conventional cigarettes were smoked and HnB products vaporized in a simulated office environment, the concentration of aldehydes in indoor air was detected as 0.0003 – 0.02 ppb for conventional cigarettes, and 0.0003 – 0.004 ppb for HnB products, a difference between the two cigarette types of about 1 – 66 times. The results of this experiment suggest that although aldehydes were emitted from HnB products, as with VOCs, it was in trace amounts.

6. In a simulated office environment, PM and nanoparticles present in the indoor space were detected when both HnB products were

vaporized and conventional cigarettes were smoked. The number of nanoparticles produced by conventional cigarettes was larger, and the size range of particles observed was wider than with HnB products. In comparison, HnB products mainly generated nanoparticles in the range of 100 – 300 nm and produced a large number of nanoparticles < 100 nm.

The purpose of this study was divided into two parts: 1) An analysis of substances emitted when smokers vaporized HnB products, and 2) An evaluation of the effects of HnB products on indoor air quality when used inside.

There have been many studies analyzing the types of emissions generated through firsthand or secondhand smoke, but there are few studies that have performed both at the same time as was done here in the present study. In addition, the research here is expected to help future studies by analyzing the effect of HnB products, which are rarely found in Korea, on indoor air quality; however, there are acknowledged limitations of this study. In the secondhand smoke experiment, the results varied according to the smoking habits of the smoker. Although the experimental group was designed to capture this variability, it is difficult to draw many accurate conclusions as the sample size was small. It was also unclear which smoking habits would change the results. Therefore, future studies should increase the number of experimental groups and compare which smoking habits affect the emission of harmful substances.

References

A. Rodgman, T A. Perfetti (2013), The chemical components of tobacco and tobacco smoke, CRC Press

A. Merecz-Sadowska, P. Sitarek, H. Zielinska-Blizniewska, K. Malinowska, K. Zajdel, L. Zakonnik, R. Zajdel, (2020). A summary of In vitro and in vivio studies evaluating the impact of e-cigarette exposure on living organisms and the environment, Int. J. Mol. Sci. 21(2), 652 https://doi.org/10.3390/ijms21020652

A N. Kothari, Z. Mi, M. Zapf, P C. Kuo, (2014). Novel clinical therapeutics targeting the epithelial to mesenchymal transition, Clinical and Translational Medicine. 3: 35 https://doi.org/10.1186/s40169-014-0035-0

A A. Laskar, H. Younus (2019), Aldehyde toxicity and metabolism: the role of aldehyde dehydrogenases in detoxification, drug resistance and carcinogenesis, Drug Metabolism Reviews, 51:1, 42-64, https://doi.org/10.1080/03602532.2018.155587

A L. Nyman, S R. Weaver, L. Popova, T F. Pechacek, J. Huang, D L. Ashley, M P. Eriksen, (2018). Awareness and use of heated tobacco products among US adults, 2016-2017, Tobacco Control, 27, s55-s61 https://dx.doi.org/10.1136/tobaccocontrol-2018-054323

A L. Tertre, S. Medina, E. Samoli, B. Forsberg, P. Michelozzi, A. Boumghar, J M. Vonk, A. Bellini, R. Atkinson, J G. Ayres, J. Sunyer, J. Schwartz, K. Katsouyanni, (2002). Short-term effects of particulate air pollution on cardiovascular diseases in eight European cities, Epidemiology and Community Health, 56, 773-779, https;//dx.doi.org/10.1136/jech.56.10.773

A. Zeka, A. Zanobetti, J. Schwartz, (2005). Short term effects of particulate matter on cause specific mortality: effects of lags and modific ation by city characteristics, Occupational and Environmental Medicine, 62:718-725, https://dx.doi.org/10.1136/oem.2004.017012

A. Zanobetti, J. Schwartz, (2006), Air pollution and emergency admissions in Boston, MA, Epidemiology and Community Health, 60:890-895, https://dx.doi.org/10.1136/jech.2005.039834

B F. Yu, Z B. Hu, M. Liu, H L. Yang, Q X. Kong, Y H. Liu, (2009). Review of research on air-conditioning systems and indoor air quailty control for human health, International Journal of Refrigeration, 32, 3-20 https://doi.org/10.1016/j.jrefrog.2008.05.004

B G. Ooi, D Dutta, K Kazipeta, N S. Chong, (2019). Influence of the e-cigarette emission profile by the ratio of glycerol to propylene glycol in e-liquid composition, ACS Omega. 4, 8, 13338-13348 https://doi.org/10.1021/acsomega.9b01504

B. Phillips, B. Titz, U. Kogel, D. Sharma, P. Leroy, Y. Xiang, G. Vuillaume, S. Lebrun, D. Sciuscio, J. Ho, C. Nury, E. Guedj, A. Elamin, M. Esposito, S. Krishnan, W K. Schlage, E. Velijkovic, N V. Ivanov, F. Martin, M C. Peitsch, J. Hoeng, P. Vansheeuwijck, (2017). Toxicity of the main electronic cigarette components, propylene glycol glycerin, and nicotine, in Sprague-Dawley rats in a 90-day OECD inhalation study complemented by molecular endpoints, Food and Chemical Toxicology, 109, 315-332, https://doi.org/10.1016/j.fct.2017.09.001

B. Mayer, (2014). How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century, Archives of Toxiclogy, 88, 5-7, https://doi.org/10.1007/s00204-013-1127-0

CC. Chang, SS. Tsai, SC. Ho, CY, Yang, (2005). Air pollution and hospital admissions for cardiovascular disease in Taipei, Taiwan, Environmental Research, 98, 114-119, https://doi.org/10.1016/j.envres.2004.07.005

ChemSrc, https://www.chemsrc.com/en/cas/56-81-5_401679.html

D. Hoffmann, I Hoffmann, (2001). The changing cigarette: Chemical studies and bioassay; in risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine, NIH Publication.

Electronic cigarette overview: About electronic cigarettes, https://www.casaa.org/electronic-cigarettes

E. Papaefstathiou, M. Stylianou, A. Agapiou, (2019). Main and side stream effects of electronic cigarettes, Jouranl of Environmental Management. 238, 10-17 https://doi.org/10.1016/j.jenvman.2019.01.030

Food and Drug Administration, TPSAC meeting materials and information, https://www.fda.gov/advisory-committes/tobacco-products-scientific-advisory-committe/2018-tpsac-materials-and-inforamtion

F. Dominici, R D. Peng, M L. Bell, L. Pham, A. McDermott, S L. Zeger, J M. Samet, (2006). Fine particulate air pollution and hospital admission for cardivascular and respiratory disease, JAMA, 295(10):1127-1134, https://doi.org/10.1001/jama.295.10.1127

F. Ballester, P. Rodríguez, C. Iñíquez, M. Saez, A. Daponte, I. Galán, M. Taracido, F. Arribas, J. Bellido, F B. Cirarda, A. Cañada, J J. Guillén, F. Guillén-Grima, E. López, S. Pérez-Hoyos, A. Lertxundi, S. Toro, (2006). Air pollution and cardiovascular admissions association in Spain: results within the EMECAS project. Epidemiology and Community Health, 60(4):328-336, https;//dx.doi.org/10.1136/jech.2005.037978

G A. Wellenius, J. Schwartz, M A. Mittleman, (2005), Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries, Stroke, 36:2549-2553, https://doi.org/10.1161/01.STR.0000189687.78760.47

G. Borio (2001), The tobacco timeline, Tobacco BBS. 212-982-4645

G. Jaccard, D T. Djoko, O. Moennikes, C. Jeannet, A. Kondylis, M. Belushkin, (2017). Compartive assessment of HPHC yields in the Tobacco Heating System THS2.2 and commercial cigarettes, Regulator y Toxicology and Pharmacology, 90, 1-8 https://doi,org/10.1016/j.yrtph.2017.08.006

G P. Moss, P A S. Smith, D. Tavernier, (1995). Glossary of class names of organic compounds and reactivity intermediates based on structure (IUPAC Recommendations 1995), Pure and Applied Chemistry, 67, 1307-1375 https://doi.org/10.1351/pac199567081307

H L. Gurtoo, J H. Hipkens, S D. Sharam, (1981), Role of gultathione in the metabolism-dependent toxicity and chemotherapy of cyclophosphamide, Cancer Research, 41, 3584-3591

Health Canada, Tobacco reporting regulations, https://www.hc-sc.gc.ca/hc-ps/pubs/tobac-tabac/rc/index-eng.php

H. Klus, G. Scherer, L Müller, Influence of Additives on cigarette related health risks, (2012). Beiträge zur Tabakforschung International/Contributions to Tobacco Research. https://doi.org/10.2478/cttr-2013-0921

H M. Liang, C M. Liao, (2004). Dynamic transport of livestock generated VOC-odor in a ventilated air space with mixing heterogeneity, Atmospheric Environment, 38, 345-355 https;//doi.org/10.1016/j.atmosenv.2003.10.023

H M. Liang, C M. Liao, (2007). Modeling VOC-odor exposure risk in livestock buildings, Chemosphere, 68, 781-789 https://doi.org/10.1016/j.chemosphere.2006.12.096

H. Gasparyan, D. Mariner, C. Wright, J. Nicol, J. Murphy, C. Liu, C. Proctor, (2018). Accurate measurement of main aerosol constituents from heated tobacco prdocuts (HTPs): Implications for a fundamentally different aerosol, Regulatory Toxicology and Pharmacology, 99, 131-141 https://doi.org/10.16/j.yrtph.2018.09.016

J. Noh, Y. Lee, S. Lee, (2020). A study of tobacco and smoking cessation based on old tobacco-related news in modern Korean history, Journal of the Korean Society for Research on Nicotine and Tobacco, 11(1):11-15, https://orcid.org/0000-0001-7648-3617

JP. Schaller, J P M. Pijnenburg, A. Ajithkumar, A R. Tricker, (2016). Evaluation of the Tobacco Heating System 2.2. Part 3: Influence of the tobacco blend on the formation of harmful and potentially harmful constituents of the Tobacco Heating System 2.2 aerosol, Regulatory Toxicology and Pharmacology, 81, S48-S58 https://doi.org/10.1016/j.yrtph.2016.10.016

J. Kim, H. Yu, S. Lee, Y. Paek, (2018). Awareness, experience and prevalence of heated tobacco product, IQOS, among young Korean adults, Tobacco Control, 27, s74-s77, https://dx.doi.org/10.1136/tobaccocontrol-2018-054390

K A. Miller, M S. David, S. Siscovick, L. Sheppard, K. Shepherd, J H. Sullivan, G L. Anderson, J D. Kaufman, (2007). Long-term exposure to air pollution and incidence of cardiovacular events in women, The New England Journal of Medicine, 356:447-458, https://doi.org/10.1056/NEJMoa054409

K. Bekki, Y. Inaba, S. Uchiyama, N. Kunugita, (2017). Comparison of chemicals in mainstream smoke in heat-not-burn tobacco and combustion cigarettes, Joural of UOEH, 80, 201-207, https://doi.org/10.7888/juoeh.39.201

KSCI, (2007). Aldehydes in ambient air-high performance liquid chromatography

L. Cancelada, M. Sleiman, X. Tang, M L. Russell, V N. Montesinos, M I. Litter, L A. Gundel, H. Destaillats, (2019). Heated tobacco products: Volatile emissions and their predicted impact on indoor air quality, Environmental Science and Technology, 53, 13, 7866-7876, https://doi.org/10.1021/acs.est.9b02544

M I. Mitova, P B. Campelos, C G. Goujon-Ginglinger, S. Maeder, N. Mottier, E G R. Rouget, M. Tharin, A R. Tricker, (2016). Comparison of the Tobacco Heating System 2.2 and a cigarette on indoor air quality, Regulatory Toxicology and Pharmacology, 80, 91-101, https;//doi.org/10.1016/j.yrtph.2016.06.005

M. Alonso, M. Castellanos, J M. Sanchez, (2010). Evaluation of potential breath biomarkers for active smoking: assessment of smoking habits, Analytical and Bioanalytical Chemistry, 396, 2987-2995, https://doi.org/10.1007/s00216-010-3524-z

M. Jankowski, G M. Brozek, J. Lawson, S. Skocynski, P. Majek, J E. Zejda, (2019). New ideas, old problems? Heated tobacco products – a systematic review, International Journal of Occupational Medicine and Environmental Health. 32(5), 595-634 https://doi.org/10.13075/ijomeh.1896.01433

M R. Smith, B. Clark, F. Lüdicke, JP. Schaller, P. Vanscheeuwijck, J. Hoeng, M C. Peitsch, (2016). Evaluation of Tobacco Heating System 2.2. Part 1: Description of the system and the scientific assessment program, Regulatory Toxicology and Pahrmacology, 81, S17-S26 https://doi.org/10.1016/j.yrtph.2017.07.006

M. Kampa, E. Castanas, (2008). Human health effects of air pollution, Environmental Pollution, 151, 362-367, https://doi.org/10.1016/j.envpol.2007.06.012

M. Scungio, L. Stabile, G. Buonanno, (2018). Measurements of electronic cigarette-generated particles for the evaluation of lung cancer risk of active and passive users, Journal of Aerosol Science. 115, 1-11 https://doi.org/10.1016/j.jaerosci.2017.10.006

M S. Werley, P. McDonald, P. Lilly, D. Kirkpatrick, J. Wallery, P. Byron, J. Venitz, (2011). Non-clinical safety and pharmacokinetic evaluations of propylene glycol aerosol in Spraque-Dawley rats and Beagle dog, Toxicology. 287, 76-90 https://doi.org/10.1016/j.tox.2011.05.015

M S. D'Souza, A. Markou, (2011). Neuronal mechanisms underlying development of nicotine dependence: Implications for novel smoking-cessation treatments, Addict Sci Clin Pract, 6(1): 4-16,

Ministry of Environment Metropolitan Air Quality Administration, https://www.me.go.kr/mamo/web/imdex.do?menuld=10006

M. Forster, J. McAughey, K. Prasad, E. Mavropoulou, C. Proctor, (2018). Assessment of tobacco heating products THP1.0. Part 4: Characterisation of indoor air quality and odour, Regulatory Toxicology and Pahrmacology, 93, 34-51, https//doi.org/10.1016/j.yrtph.2017.09.017

National Research Council (1991).

N. Mallock, L. Böss, R. Burk, M. Danziger, T. Welsch, H. Hahn, HL. Trieu, J. Hahn, E. Piper, F. Henkler-Stephani, C. Hutzler, A. Luch, (2018). Levles of selected analytes in the emissions of "heat-not-burn" tobacco products that are relevant to assess human health risks, Archives of Toxicology. 92, 2145-2149 https://doi.org/10.1007/s00204-018-2215-y

Pubchem, Propylene glycol, (2004). https://pubchem.ncbi.nlm.nih.gov/compound/1030

P N. Kopa, R Pwaliczak, (2019). IQOS-a heat-not-burn (HnB) tobacco product- chemical composition and possible impact on oxidative stress and inflammatory response. A systematic review, Toxicology Mechanisms and Methods. 2, 81-87 https://doi.org/10.1080/15376516.2019.1669245

P. Carlier, H. Hannachi, G. Mouvier, (1986). The chemistry of carbonyl compounds in the atmosphere-A review, Atmospheric Environment, 20, 2079-2099, https://doi.org/10.1016/0004-6981(86)90304-5

R. Auer, N. Concha-Lozano, I. Jacot-Sadowski, J. Cornuz, A. Berthet, (2017). Heat-not-burn tobacco cigarettes smoke by any other name, JAMA Internal Medicine, 177(7):1050-1052, https://doi.org/10.1001/jamainternmed.2017.1419

R. Atkinson, (2000). Atomospheric chemistry of VOCs and NOx, Atmospheric Environment, 34, 2063-2101 https://doi.org/10.1016/S1352-2310(99)00460-4

R. Otson, P. Fellin, (1998). A review of techniques for measurement of airborne aldehydes, Science of The Total Environment, 77, 95-131

https://doi.org/10.1016/0048-9697(88)90049-6
R T. Burnett, M. Smith-dorion, D. Stieb, S. Cakmak, J R. Brook, (1999). Effects of particulate and gaseous air pollution on cardiorepiratory hospitalizations, Archives of Environmental Health: An International Journal, 54:2, 130-139, https://doi.org/10.1080/00039899909602248
R D. Morris, (2001). Airborne particulate and hospital admissions for cardiovascular disease: a quantitative review of the evidance, Environmeantal Health Perspectives, 109, 495-500, https://doi.org/10.1289/ehp.01109s4495
R. Maheswaran, R P. Haining, P. Brindley, J. Law, T. Pearson, P R. Fryers, S. Wise, M J. Campbell, (2005). Outdoor air pollution and stroke in Sheffield, United Kingdom: A small-area level geographical study, Stroke, 36, 239-243, https://doi.org/10.1161/01.STR.0000151363.71221.12
S. Uchiyama, Y. Otsubo, (2008). Simultaneous determination of ozone and carbonyls using trans-1.2-Bis(4-pyridyl)ethylene as an ozone scrubber for 2,4-dinitrophenylhydrazine-impregnated silica cartridge, Analytical Chemistry, 80, 9, 3285-3290, https://doi,org/10.1021/ac702475s
S. Capone, M. Tufariello, A. Forleo, V. Longo, L. Giampetruzzi, A V. Radogna, F. Casino, P. Siciliano, (2017). Chromatographic analysis of VOC patterns in exhaled breath from smokers and nonsmokers, Biomedical Chromatography, 32:e4132, https://doi.org/10.1002/bmc.4132
S L. Blair, S A. Epstein, S A. Nizkorodov, N. Staimer, (2015). A real-time fast-flow tube study of VOC and particulate emissions from electronic, potentially reduced-harm, conventional, and reference cigarettes, Aerosol Science and Technology, 49:9, 816-827, https;//doi.org/10.1080/02786826.2015.1076156
S. Torres, C Merino, B. Paton, X. Corrig, N. Ramirez, (2018). Biomarkers of exposure to secondhand smoke and thirdhand tobacco smoke:

Recent advances and future perspectives, Int. J. Environ Res. Pub lic Health 15. 2693 https://doi.org/10.3390/ijerph15122693

S E. Jacob, A. Scheman, M A. McGowan, Propylene Glycol, Dermatitis. 1, p3-5 (2018). https://doi.org/10.1097/DER.0000000000000315

S. Klager, J. Vallarino, P. MacNaughton, D C. Christiani, Q. Lu, J G. A llen, (2017). Flavoring chemicals and aldehydes in e-cigarette emis sions, Environ. Sci. Technol. 51, 10806-10813 https://doi.org/10.102 1/acs.est.7b02205

S V. Klot, A. Peters, P. Aalto, T. Bellander, N. Berglind, D. D'Ippoliti, R. Elosua, A. Hörmann, M. Kulmala, T. Lanki, H. Löwel, J. Pekka nen, S. Picciotto, J. Sunyer, F. Forastiere, (2005). Ambient air pollu tion is associated with increased risk of hospital cardiac readmissio ns of myocardial infraction survivors in firv European cities, Circul ation, 112:3073-3079, https://doi.org/10.1161/CIRCULATIONAHA.10 5.548743

T. Lanki, J. Pekkanen, P. Aalto, R. Elosua, N. Berglind, D. D'Ippoliti, M. Kulmala, F. Nyberg, A. Peters, S. Picciotto, V. Salomaa, J. Sun yer, P. Tiittanen, S V. Klot, F. Forastiere, (2006). Associations of t raffic related air pollutants with hospitalisation for first acute myoc ardial infraction: the HEAPSS study, Occupational and Environmen tal Medicine, 63(12):844-851, https://dx.doi.org/10.1136/oem.2005.0239 11

T. Tabuchi, K. Kiyohara, T. Hoshino, K. Bekki, Y. Inaba, N. Kunugita, (2015). Awarness and use of electronic cigarettes and heat-not-bur n tobacco products in Japan, Society for the Study of Addiction. 1 11, 706-713 https;//doi.org/10.1111/add.13231

T L. Caputi, E. Leas, M. Dredze, J E. Cohen, J W. Ayers, (2017). The y're heating up: Internet search query trends reveal significant publ ic interest in heat-not-burn tobacco products, PloS one. 12(10), e01 85735 https://doi.org/10.1371/journal.pone.0185735

T L. Godec, I. Crooks, K. Scott, C. Meredith, (2019). In vitro mutagenic ity of gas-vapour phase extracts from flavoured and unflavoured heated tobacco products, Toxicology Reports, 6, 1155-1163 https://doi.org/10.1016/j.toxrep.2019.10.007

U.S. Food and Drung Administration, Harmful and potentially harmful constituents in tobacco products, https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/harmful-and-potentially-harmful-constituents-tobacco-products-and-tobacco-smoke-established-list

V. Kaunelienė, M. Meišutovič-Akhtarieva, T. Prasaukas, D. Čiužas, E. Krugly, K. Keraitytė, D. Martuzevičius, (2019). Impact of using a tobacco heating system (THS) on indoor air quality in a nightclub, Aerosol and Air Quality Research, 19, 1961-1968 https://doi.org/10.4209/aaqr.2019.04.0211

W. Baran, D. Madej-Knysak, A. Sobczak, E. Admek, (2020). The influence of waste from electronic cigarettes, conventional cigarettes and heat-not-burn tobacco products on microorganisms, Journal of Hazardous Materials. 385, 121591 https://doi.org/10.1016/j.jhazmat.2019.121591

World Health Organization, "The science basic of tobacco product regulation, https://www.who.int/tobacco/global_interaction/toberg/publications/tsr_951/en/

World Health Organization (2003), Health aspects of air pollution with particulate matter, ozone and nitrogen dioxide: Report on a WHO working group, https://apps.who.int/irls/handle/10665/107478

X. Liu, A Lugo, L Spizzichino, T Tabuchi, R Pacifici, S Gallus, (2019). Heat-not-burn tobacco products: concerns from the Italian experience, Tobacco Control, 28, 1 https://dx.doi.org/10.1136/tobaccocontrol-2017-054054