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Review Article

The Content of Harmful and Potentially Harmful Constituents in Heated Tobacco Product: Systematic Review

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Abstract

According to World Health Organization (WHO), most of health hazards due to smoking comes from exposure to cigarette smoke (smoke aerosol), formed from the burning process of tobacco in conventional cigarettes. This propels the implementation of the concept of tobacco harm reduction by striving for products for those still craving for tobacco can still consume, but at a lower risk. This study aims to determine the difference in HPHC content between conventional cigarettes and HTP. The research method used was literature review. In the preliminary stage, the researchers carried out a process of screening titles and abstracts from studies and then independently filtered the text papers completely according to the objectives of this study. The review yielded 22 journals meeting with the rules and regulations in this research. The results showed that all 9 HPHCs recommended for reduction (nine TobReg priority constituent) were shown to be 90% lower in HTP compared to conventional cigarettes. The conclusion was that there were differences in the HPHC content between conventional cigarettes and HTP.

Keywords: HPHC; HTP; Conventional Cigarettes

1. INTRODUCTION

Indonesia is a home to 65 million smokers and one of the countries with the highest number of smokers in the world. A recent study of 2018 Basic Health Research by the Ministry of Health showed that the prevalence of smoking in Indonesia showed no sign of decline despite highly aggressive tobacco control policies in Indonesia. The astronomically high number of smokers in Indonesia calls for a new approach in dealing with the issue.

Smoking has long been associated scientifically with increased morbidity and premature mortality. most of health hazards due to smoking comes from exposure to cigarette smoke (smoke aerosol), formed from the burning process of tobacco in conventional cigarettes [1]. This propels the implementation of the concept of tobacco harm reduction by striving for products for those still craving for tobacco can still consume, but at a lower risk.

In terms of toxicology, health risks arising from toxic substances is largely determined by the exposure dose, that is, the amount of real toxic substances entering the body. Meanwhile, the exposure dose is largely determined by the level and duration of exposure. Thus, if the exposure level is lower, the exposure dose will also be lower, and in turn, the potential toxicity also decreases. Vice versa, the higher the exposure level, the higher the potential toxicity will be. Along with the concept of harm reduction, increased awareness of smoking-related health risks and technological developments, an innovation was born in the form of heated tobacco products as a lower risk alternative to conventional cigarettes. Heated tobacco product (HTP) is one instance of alternative tobacco products that do not undergo a burning or combustion process, but only a heating process.

When a cigarette burns, in many publications, about 6,000 - 8,000 kinds of chemical compounds in cigarette smoke are mentioned [2,3]. The chemical compounds in cigarette smoke are very complex and dynamic. Dynamic in this case means that the physicochemical properties of the compound contained can change rapidly and instantly, for example, the vapor generated from the combustion process immediately turns into particles, or vice versa. Also, the size of the existing particles can vary in size [4]. This is inversely proportional to HTP. Research by HTP producers and several independent institutions found that by eliminating the combustion process, there was a decrease in the levels of chemical compounds that can potentially cause health problems (Harmful an Potentially Harmful Constituents/HPHC) in HTP by up to 90% compared to the HPHCs produced by the 3R4F reference cigarette [5].

To date, there have been many foreign studies that have tried to analyze heated tobacco products. Previous studies are summarized briefly, including a brief discussion of the challenges with adapting standard analytical methods used to tobacco smoke. This literature review will discuss from the toxicological aspects whether there is a difference in the HPHC content between conventional cigarettes and HTP.

2. RESEARCH METHOD

The type of data used was secondary data in the form of quantitative data, qualitative data or a combination thereof. Textbooks underlying the theory in this study was also used. Study search and selection were performed using Medline, Scopus, PubMed and Database Web of Science, limited to studies conducted until July 2020 with a search period up to September 2020. The search included terms related to HnB in general ('Heat not burn', 'Tobacco Heating System', 'Electronic Nicotine Delivery System', 'Novel Tobacco Product') and brand names ('IQOS', 'Ploom', 'Heets', 'glo', 'PNV'), and were limited to studies published from 2010, thereby excluding obsolete or outdated papers on HnB devices. Prior to further discussion of papers to be used as reference, at the preliminary stage the researchers carried out a process of screening titles and abstracts from the study then independently filtered the papers completely in accordance with the objectives of this study.

The method used for this literature review was tradition review, that is a method of literature review on a topic selected based on the knowledge and experience possessed by the researcher. Systematic Literature Review is a literature review method that is used using predetermined stages. It identified, assessed, and interpreted the whole findings of a study topic, to answer predetermined research questions. The selection of papers was also not carried out subjectively by researchers, but using predetermined protocols and filters.

The use of publications in this study referred to inclusion and exclusion criteria. The inclusion criteria included literatures and publication journals focusing on the discussion of the use of heated tobacco technology and publications that have been peer-reviewed. Textbooks on basic theories of toxicology and disease risk assessment were also utilized. The publications that were directly related to studies on HPHCs in heated tobacco products were limited to those published after 2010. However, publications prior to 2010 were still used for supporting references. The exclusion criteria included publications that have not been peer-reviewed, did not focus on heated tobacco products, were not published in Englilsh and could no longer be downloaded or documented. Sources used in this study included publications containing subjects on HPHC emission both in HTPs or conventional cigarettes.

3. RESULTS AND DISCUSSIONS

The process of searching and filtering databases from journals or scientific publications on either heated tobacco products (HTP) or e-cigarettes were performed from July 2020 to September 2020. There were 248 publications from the initial searching which would be then narrowed to 22 scientific publications and become a reference in this study (Figure 1).

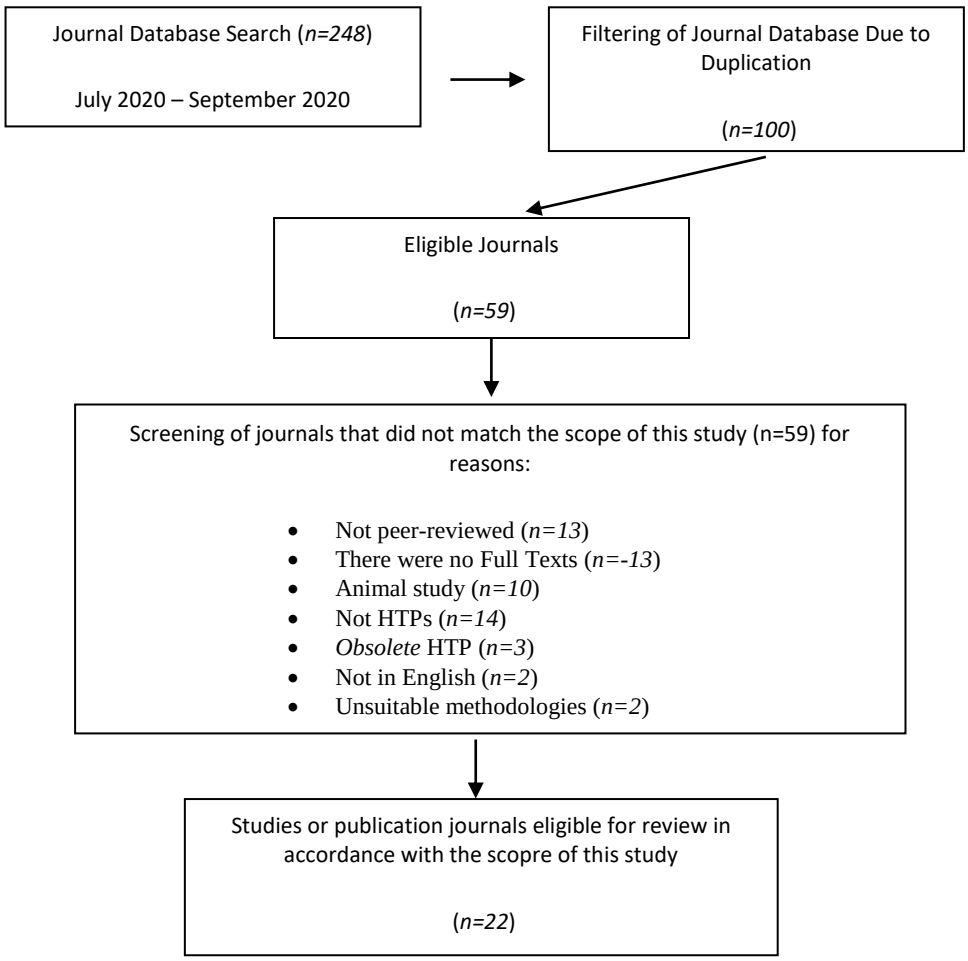

Figure 1: Schematic of the Process of Searching and Screening HTP-related Journals/Publications

3.1. HPHC Content in HTPs

The main driver of the conception of heated tobacco products is the need for an alternative for people who desire nicotine at lower risks. Health risks to smokers are caused more by exposure to HPHCs arising from the combustion process, not due to nicotine exposure. There was not enough evidence showing that nicotine is carcinogenic [3]. Several heated tobacco products, both ready-to-market or just prototypes, can be seen in table 1.

Table 1: Heated Tobacco Products That Are Ready to Market or Just Prototypes

Heated Tobacco Products (HTP) and Manufacturers	Marketing (Year and Region)	Product Description
IQOS®/THS 2.2 from PMI	2014, Japan, Italy and Switzerland	IQOS® consists of a holder, charger and tobacco plug (HEETS). The tobacco plug (about 320mg) is put into the holder and heated with an electronically-controlled heating knife inserted into the part of the tobacco plug. Operating heating temperature <350 °C. Single use for 6 minutes or up to 14 puffs.
iFuse® from BAT	2015, Romania	*iFuse*® includes electronic vapor device with a rechargeable Li-ion battery and integrated circuit power controller, on which Cartomizer (Neopod) is installed. This disposable *Neopod*® consists of an atomizer, liquid tank with 1.15 ml of unflavoured nicotine liquid and chamber containing a 130mg tobacco plug. When the user presses the button, a nicotine-containing vapor is generated, which is then pulled through the tobacco plug to absorb the flavour. Before reaching the tobacco plug, the aerosol reaches an average maximum temperature of <35 °C.
Glo®/THP 1.0 from BAT	2016, Japan	Glo® includes electronic devices with a rechargeable Li-ion battery and heating chamber and tobacco plug. A tobacco plug (about 260mg) is heated in the heating chamber from the periphery. Operating heating temperature <250°C. Reaches operating temperature after 30-40 seconds and a single use lasts 3 minutes.
Ploom Tech®/PNTV from JTI	2016, Japan	PNTV consists of a power supply, cartridges with heating and liquids, and capsules with a mixture of tobacco. Generates nicotine-free vapor by heating an unflavoured liquid; The steam then passes through the tobacco capsules to absorb the taste and nicotine.
Carbon-heated tobacco product (CHTP) from PMI	Not marketed	A specially designed electric lighter induces a carbon heating source which then heats up the tobacco plug.

Source: Simonavicius E. et al., 2018 [6]

The studies included in this literature review were reviewed with impartial view toward sources of funding. However, manufacturers who financed and report their own product findings were inherently bound by conflicts of interest. Table 2 is a summary of both independent or sponsor manufacturer studies.

Table 2: Summary of Independent and Sponsor Manufacturer Studies

Researcher, Year of Publication	Type of Research, Country	Study Design	Heated Tobacco Product and Reference Product	Objective
HTP Studies on Mainstream Smoke				
Auer et al., 2017 [7]	Independent, Switzerland	Comparative laboratory study using a smoking machine	IQOS® and Cigarettes	To compare HPHC levels in IQOS® mainstream aerosol emissions with mainstream smoke.
Farsalinos et al., 2018 [8]	Independent, Switzerland		IQOS®, Cigarettes, E-Cigarettes: (i) *Ciga-like* (ii) *eGo-style*, Second Generation (*pen-style tank*) (iii) *Variable wattage (tank model)*	To compare nicotine levels in the emission of IQOS® mainstream aerosol from the regular and menthol tobacco plug with nicotine in various types of e-cigarette aerosols and mainstream cigarette smoke.

Bekki et al., 2017 [9]	Independent, Japan		IQOS® and Cigarettes	To compare nicotine and HPHC levels in the IQOS® emission from a regular and menthol tobacco plug with mainstream cigarette smoke.
Schaller et al., 2016 [5]	PMI, Switzerland		THS 2.2/IQOS® and Cigarettes	To compare HPHC levels in IQOS® (mainstream) emissions with mainstream cigarette smoke.
Schaller et al., 2016 [5]	PMI, Switzerland		THS 2.2/IQOS® and Cigarettes	To compare HPHC levels in IQOS® emission (mainstream) from regular and menthol tobacco plugs (HEETS) with mainstream cigarette smoke.
HTP Studies on Mainstream Smoke				
Jaccard et al., 2017 [10]	PMI, Switzerland	Comparative laboratory study using a smoking machine	THS 2.2/IQOS® and Cigarettes	To compare HPHC levels in IQOS® (mainstream) emissions with mainstream cigarette smoke.
Pratte et al., 2017 [11]	PMI, Switzerland		THS 2.2/IQOS® and Cigarettes	To compare the number of solid particles in IQOS® emission (mainstream) with mainstream cigarette smoke.
Eaton et al., 2018 [12]	BAT, UK		THP 1.0/Glo® and Cigarettes	To compare HPHC levels of Glo® emission (mainstream) with mainstream cigarette smoke.
Forster et al., 2018 [13]	BAT, UK		THP 1.0/Glo® and Cigarettes	To compare HPHC levels of Glo® emission with IQOS emission and cigarette smoke.
Poynton et al., 2017 [14]	BAT, UK		iFuse® *Pen-style e-cigarette*	To compare HPHC levels of iFuse® emission (mainstream) with Vype ePen emission and cigarette smoke.
HTP Studies for clinical trials				
Kamada et al., 2016 [15]	Independent, Japan	*Case report*	IQOS®	To report cases of acute eosinophilic pneumonia after use.
Lopez et al., 2016 [16]	Independent, US	*Randomised crossover experimental trial*	*Pax LLTV Cigarette eGo e-cigarette (pen-style tank)*	To compare nicotine delivery, airborne CO concentration (expired), and suppression of symptoms due to cessation.
Brossard et al., 2017 [17]	PMI, Japan	*Randomised crossover experimental trial*	THS 2.2/IQOS®, Cigarettes and *Nicotine gum*	To compare nicotine delivery and effects on urge to smoke.
Haziza et al., 2016 [18]	PMI, Japan	RCT	THS 2.2/IQOS® and Cigarettes	To compare HPHC exposure over 5 days of use.
Haziza et al. 2016 [18]	PMI, Poland	RCT	THS 2.2/IQOS® and Cigarettes	To compare HPHC exposure over 5 days of use.
Lüdicke et al., 2017 [19]	PMI, Poland	RCT	THS 2.1 and Cigarettes	To compare HPHC exposure over 5 days of use.
Lüdicke et al., 2016 [20]	PMI, Poland	RCT	CHTP and Cigarettes	To compare HPHC exposure over 5 days of use.
Lüdicke et al., 2018 [21]	PMI, Japan	RCT	THS 2.2/IQOS® and Cigarettes	To compare HPHC exposure over 5 days of use in confinement and subsequent 85 days of use in outpatient setting.
Lüdicke et al., 2018 [21]	PMI, Japan	RCT	THS 2.2/IQOS® and Cigarettes	To compare the effects of biologically and clinically relevant risk markers over 90 days of use.
Picavet et al., 2016 [22]	PMI, UK	*Randomised crossover experimental*	THS 2.1 and Cigarettes	To compare nicotine delivery and effects on urge to smoke.

		trial		
Gee et al., 2018 [23]	BAT, Japan	*Randomised crossover experimental tria*	THP 1.0/Glo®, IQOS®, and Cigarettes	To compare the topography of puffs, mouth level exposure and average daily consumption.
Yuki et al., 2017 [24]	JTI, Japan	*Randomised crossover experimental trial*	PNTV®/*Ploom Tech*® and Cigarettes	To compare the pharmacokinetics of nicotine delivery.

CO, CO_2 and NO_x gases are markers of combustion. By eliminating the combustion process, the levels of CO, CO_2 and NO_x in HTP decreased significantly compared to conventional cigarette smoke [12,13].

Table 3: Mean Levels ± SD (Standard Deviation) of Combustion Marker Gases in Conventional Cigarettes Compared to HTPs

Marker (per stick)	**HTP**	**Conventional Cigarette**
CO, mg	NQ	32
CO2, mg	2.35	85.1
NO, µg	10.1	496
NO_x, µg	12.0	553

Source: Eaton, 2018 [12]

The data in table 3 shows that in the use of heated tobacco products, no combustion occurs, only heating. It is shown by the low levels of combustion markers namely CO, CO_2 and NO_x in HTPs. Low exposure to CO was also demonstrated by Caponneto et al. (2018) where the level of CO exhalation—as a biomarker of CO exposure in HTP users—was significantly lower compared to conventional cigarette consumers [25].

Mitoya et al. (2016), in their study showed a difference in HPHC levels of office space, residential air exposed to HTPs and conventional cigarettes [26]. In general, spaces exposed to HTP aerosols showed lover levels of HPHC compared to those exposed to cigarette smoke, except for a few compounds such as nicotine and acetaldehyde, which were similar to conventional cigarettes. In addition, it was shown that H_2O_2—one of free radical compounds in the ROS (reactive oxygen species) group—is 5 times lower in HTP aerosols than conventional cigarettes [27]. These studies corroborated existing studies concluding that the level of chemical compounds of mainstream smoke of conventional cigarettes largely is 90% higher than heated tobacco products [13, 5, 10, 28, 29]. Table 5 shows a decrease in the concentration of most of HPHCs in HTPs compared to conventional cigarettes [13].

Table 4: Content of HPHC Compounds in HTP Aerosols and Conventional Cigarettes and Their Decrease

Parameter	**Unit**	**Burnt Cigarette**	**HTP**	**Decrease (%)**
		Mean ± SD	**Mean ± SD**	
TPM	mg/stick	46.9 ± 2.8	26.1± 1.1	44.3
Water	mg/stick	15.1 ± 1.4	12.1 ± 1.1	20.1
NFDPM	mg/stick	29.8 ± 1.4	13.6 ±1.2	54.4
CO	mg/stick	32.0 ± 1.0	NQ (0.223)	99.8
CO_2	mg/stick	85.1 ± 4.0	2.05 ± 0.10	97.6
Ammonia	µg/stick	32.5 ± 3.5	4.01 ± 0.99	87.7
Hydrogen cyanide	µg/stick	343 ± 62	BDL (0.525)	99.9
Mercury	ng/stick	4.26 ± 0.50	1.28 ± 0.13	69.8
Cadmium	ng/stick	105.5 ± 5	BDL (0.162)	99.9
Black lead	ng/stick	28.7 ± 0.8	11.6 ± 8.7	59.5
Chromium	ng/stick	NQ (4.51)	4.34 ± 1.14	-22.7
Nickel	ng/stick	NQ (9.49)	NQ (0.878)	NC

Arsenic	ng/stick	8.01 ± 0.56	NQ (0.576)	94.6
Selenium	ng/stick	NQ (2.63)	NQ (0.731)	NC
Copper	ng/stick	24.8 ± 2.1	NQ (2.19)	91.5
Cobalt	ng/stick	BDL (0.893)	NQ (0.878)	NC
Beryllium	ng/stick	BDL (0.936)	NQ (0.024)	NC
Iron	ng/stick	38.1 ± 10.0	19.3 ± 5.4	49.3
Zinc	ng/stick	273 ± 17	21.5 ± 15.7	92.1
Lead	ng/stick	BDL (6.04)	NQ (0.876)	NC
NO	µg/stick	495 ± 16	9.60 ± 0.79	98.1
NO_x	µg/stick	555 ± 19	12.9 ± 0.8	97.2
Pyridine	µg/stick	28.6 ± 2.8	2.21 ± 0.29	92.3
Quinoline	µg/stick	0.389 ± 0.028	NQ (0.011)	98.5
Styrene	µg/stick	16.1 ± 2.0	NQ (0.039)	99.8
Nitrobenzene	µg/stick	BDL (0.038)	BDL (0.011)	NC
Benzo(b)furan	µg/stick	0.627 ± 0.067	NQ (O.016)	98.3
Hydroquinone	µg/stick	84.2 ± 1.8	0.347 ± 0.035	99.6
Resorcinol	µg/stick	1.57 ± 0.22	BDL (0.016)	99.5
Catechol	µg/stick	87.4 ± 3.4	3.11 ± 0.49	96.4
Phenol	µg/stick	13.5 ± 0.8	0.174 ± 0.022	98.7
p-Cresol	µg/stick	8.72 ± 0.38	BDL (0.010)	99.9
m-Cresol	µg/stick	3.48 ± 0.18	NQ (0.019)	99.6
o-Cresol	µg/stick	3.94 ± 0.16	NQ (0.026)	99.6
Propylene glycol	mg/stick	0.021 ± 0.005	0.390 ± 0.023	- 1724
Ethylene glycol	mg/stick	0.035 ± 0.001	0.011 ± 0.00	69.3
Diethillin glycol	mg/stick	BDL (0.004)	BDL (0.002)	NC
Glycidol	mg/stick	NQ (0.006)	0.044 ± 0.003	- 883
Glycerol	mg/stick	2.35 ± 0.05	3.02 ± 0.26	-28.4
Naphthalene	ng/stick	994 ± 94	2.2 ± 0.42	99.8
Pyrene	ng/stick	79.4 ± 7.5	8.97 ± 0.82	88.7
Benzo(a)anthracene	ng/stick	24.2 ± 2.4	1.54 ± 0.11	93.7
Chrysene	ng/stick	34.7 ± 3.2	2.61 ± 0.27	92.5
Benzo(a)pyrene	ng/stick	12.9 ± 1.3	NQ (0.354)	97.7
Indeno(1,2,3-cd)pyrene	ng/stick	4.19 ± 0.37	NQ (0.337)	97.2
Benzo(c) phenanthrene	ng/stick	8.32 ± 0.81	0.874 ± 0.171	89.5
Cyclopentane(c, d)pyrene	ng/stick	7.82 ± 1.12	0.515 ± 0.036	93.4
Benzo(j)aseantrilin	ng/stick	2.24 ± 0.43	BDL (0.104)	97.7
1,3 Butadiene	µg/stick	108 ± 4	BDL (0.029)	>99.9
Isoprene	µg/stick	887 ± 49	NQ (0.135)	>99.9
Acrylonitrile	µg/stick	19.5 ± 1.6	BDL (0.032)	99.9
Benzene	µg/stick	78.6 ± 4.6	NQ (0.056)	>99.9
Toluene	µg/stick	131 ± 5	NQ (0.204)	99.9
Ethylbenzene	µg/stick	13.4 ± 0.9	NQ (0.048)	99.8
Ethylene oxide	µg/stick	19.3 ± 2.0	BDL (0.036)	99.9

Vinyl chloride	ng/stick	95.6 ± 9.2	BDL (0.657)	99.7
Propylene oxide	ng/stick	903 ± 308	BDL (15.6)	99.1
Furan	µg/stick	61.9 ± 3.5	1.16 ± 0.01	98.1
Vinyl acetate	ng/stick	617 ± 20	BDL (11.0)	99.1
Nitromethane	ng/stick	690 ± 58	42.4 ± 1.5	93.9
2- Nitropropane	ng/stick	58.7 ± 6.1	BDL (1.45)	98.8
5-Methylchrysene	ng/stick	0.744 ± 0.205	BDL (0.028)	98.1
Benz(b)fluoranthene	ng/stick	12.3 ± 1.5	0.548 ± 0.091	95.5
Benz(k) fluoranthene	ng/stick	3.70 ± 0.49	0.225 ± 0.046	93.1
Dibenz(a,h)anthracene	ng/stick	0.915 ± 0.124	BDL (0.046)	95.8
Dibenz(a,l)pyrene	ng/stick	BDL (0.423)	BDL (0.254)	NC
Dibenz(a,e) pyrene	ng/stick	NQ (0.696)	BDL (0.125)	NC
Dibenz(a,i) pyrene	ng/stick	1.66 ± 0.41	BDL (0.132)	96.0
Dibenz(a,h) pyrene	ng/stick	BDL (0.236)	BDL (0.141)	NC
1-Aminonaphthalene	ng/stick	17.6 ± 0.6	NQ (0.027)	99.8
2-Aminonaphthalene	ng/stick	13.2 ± 0.8	NQ (0.012)	>99.8
3-Aminonaphthalene	ng/stick	3.49 ± 0.27	NQ (0.004)	>99.9
4-Aminobiphenyl	ng/stick	2.29 ± 0.12	NQ (0.005)	99.8
2,6- Dimethylaniline	ng/stick	6.11 ± 0.65	0.040 ± 0.004	99.4
Benzidine	ng/stick	BDL (0.010)	BDL (0.003)	NC
o-Anisidine	ng/stick	4.18 ± 0.23	0.244 ± 0.031	94.2
o- Toluidine	ng/stick	83.3 ± 2.1	0.371± 0.045	99.6
N-Nitrosonornicotine	ng/stick	263 ± 12	24.7 ± 2.5	90.6
N-Nitrosoanatabine	ng/stick	268 ± 20	37.7 ± 3.4	85.9
N-Nitrosoanabasine	ng/stick	24.1 ± 1.1	4.70 ± 0.39	80.4
4-(methylnitrosamino)-1-(3- pyridyl)-1- butanone	ng/stick	281± 16	6.61 ± 0.86	97.7
Acetamide	µg/stick	11.9 ±1.0	1.34 ± 0.05	88.7
Acrylamide	µg/stick	3.99 ± 0.39	1.04 ± 0.04	73.9
Caffeine acid	µg/stick	BDL (1.19)	BDL (0.478)	NC
Ethyl carbamate	ng/stick	BDL (6.43)	BDL (1.93)	NC
IQ	ng/stick	7.75 ± 1.07	BDL (0.164)	98.9
Glu-P-2	ng/stick	BDL (0.301)	BDL (0.120)	NC
Glu-P-1	ng/stick	BDL (0.239)	BDL (0.095)	NC
PhIP	ng/stick	BDL (0.365)	BDL (0.1460	NC
Trp-P-2	ng/stick	6.46 ± 1.0	BDL (0.113)	99.1
AαC	ng/stick	176 ± 16	NQ (0.443)	99.9
Trp-P-1	ng/stick	4.29 ± 0.52	BDL (0.098)	98.9
MeAαC	ng/stick	15.3 ± 2.1	BDL (0.115)	99.6
Hydrazine	ng/stick	NQ (12.2)	BDL (2.04)	NC
NDMA	ng/stick	14.2 ±1.3	BDL (0.178)	NC
NEMA	ng/stick	BDL (0.509)	BDL (0.254)	NC
NDEA	ng/stick	BDL (0.617)	BDL (0.308)	NC
NDiPA	ng/stick	BDL (0.540)	BDL (0.273)	NC

NDPA	ng/stick	BDL (0.150)	BDL (0.075)	NC
NDBA	ng/stick	NQ (1.11)	NQ (0.553)	NC
NPIP	ng/stick	BDL (0.172)	BDL (0.086)	NC
NPYR	ng/stick	17.6 ± 1.0	BDL (0.198)	99.4
NMOR	ng/stick	BDL (0.550)	BDL (0.275)	NC
NDELA	ng/stick	NQ (0.283)	0.576 ± 0.244	-163
Nornicotine	ng/stick	22117 ± 1351	NQ (47.6)	99.5
Anatabine	ng/stick	6218 ± 43	1157 ± 123	81.4
Anabasine	ng/stick	1030 ±120	408 ± 50	60.4
Myosmine	ng/stick	13226 ± 592	459 ± 36	96.5
Nicotine-N-oxide	ng/stick	NQ (291)	BDL (174)	NC
Cotinine	ng/stick	14320 ± 755	298 ± 43	97.9
β-Nicotyrene	ng/stick	7071± 125	NQ (127)	98.8
Formaldehyde	µg/stick	54.1 ± 6.0	3.29 ± 0.30	93.9
Acetaldehyde	µg/stick	2200 ± 103	111 ± 8	95.0
Acetone	µg/stick	660 ± 24	5.97 ± 0.66	99.1
Propionaldehyde	µg/stick	132 ± 3	5.31 ± 0.15	96.0
Acrolein	µg/stick	157 ± 9	2.22 ± 0.52	98.6
Isobutyraldehyde	µg/stick	45.7 ± 3.6	9.78 ± 0.46	78.6
Methyl ethyl ketone	µg/stick	192 ± 8	1.53 ± 0.20	99.2
n-Butyraldehyde	µg/stick	15.2 ± 1.5	BDL (0.088)	99.7
Crotonaldehyde	µg/stick	42.0 ± 6.2	0.567 ± 0.232	98.7
Acetoin	µg/stick	NQ (5.61)	5.78 ± 1.33	-0.14
Glyoxal	µg/stick	9.56 ± 1.68	BDL (0.063)	99.7
Methylglyoxal	µg/stick	26.2 ± 3.4	26.4 ± 2.4	-0.46
2,3-Butandion	µg/stick	260 ± 11	38.0 ± 4.4	85.4
2,3-Pentandion	µg/stick	35.0 ± 2.3	7.38 ± 1.07	78.9
Allyl alcohol	µg/stick	13.8 ± 2.3	1.24 ± 0.12	91.0

Source: Foster et al., 2018 [13]

As shown in table 4, all parameters in HTP have lower levels than conventional cigarettes, albeit with varying degrees. A small decrease is observed in TPM, water and tar (NFDPM). Meanwhile, other parameters are 70-99% lower for HTP.

A number of studies examining 9 TobReg priority constituents in conventional cigarettes and HTP showed that HPHC levels of HTP were largely lower than conventional cigarettes [13, 30, 12]. The decreases are shown in table 5.

Table 5: Content of 9 HPHCs Recommended in Mainstream Aerosols per Stick

Parameter	Unit	Cigarette	THP	% reduction
1,3-Butadiene	µg	108	BDL(0.029)	>99.9
Acetaldehyde	µg	2200	111	95.0
Acrolein	µg	157	2.22	98.6
Benzene	µg	78.6	NQ(0.056)	>99.9
Benzo[a]pyrene	Ng	12.9	NQ(0.354)	97.7
CO	Mg	32	NQ(0.223)	99.8
Formaldehyde	µg	54.1	3.29	93.9
NNK	Ng	281	6.61	97.7
NNN	Ng	263	24.7	90.6

Source: Foster et al., 2018 [13]

As shown in Table 5, all 9 HPHC compounds recommended for reduction (TobReg priority constituents) were shown to have 90% lower levels in HTP. The study by Poynton et al., 2017 on the 9 HPHC compounds and other toxic compounds also showed similar results, as presented in Table 6 [14].

Table 6: Levels of Several Compounds in HTP Aerosols Compared to Conventional Cigarettes (3R4F)

Toxicant	HTP		Conventional Cigarettes (3R4F)	
	Mean	Standard deviation	Mean	Standard deviation
Carbonyl compounds:				
Formaldehyde, µg	11.5	3.5	94,9	6.2
Acetaldehyde, µg	8.22	1.44	1732	43
Acetone, µg	7.09	2.48	726	16
Acrolein, µg	NQ	NQ	172	3
Methyl-ethyl-ketone, µg	NQ	NQ	202	7
Metal:				
Copper, ng	88.2	33.6	24.7	3.1
Zinc, ng	877	181	257	37
Iron, ng	260	48	34.5	13.9
Semi-volatile:				
Styrene, µg	0.50	0.34	17.4	1.7
PAH:				
Naphtalene, ng	8.54	2.21	1005	125
Chrysene, ng	1.86	0.82	36.8	3.6
TSNA:				
NNN, ng	NQ	NQ	265	22
Gases and volatile:				
CO, mg	4.74	0.00	29.6	1.5
Toluene, µg	NQ	NQ	116	9
Aromatic amine:				
2-amininaphtalene, ng	0.4	0.19	12.5	0.5
3-aminobiphenyl, ng	0.07	0.04	2.91	0.76
4-aminobiphenyl	0.06	0.04	2.14	0.50
o-toluidine	1.52	0.80	115	5
Volatile nitrosamine:				
NDMA, ng	15.7	2.7	6.95	1.4
NDEA, ng	13.4	4.6	BDL	BDL
NPYR, ng	15.1	1.3	BDL	BDL
NDELA, ng	7.67	1.82	4.79	3.19
Nicotine and nicotine impurity:				
Nicotine, mg	2.56	1.33	1.84	0.08
Myosmine, ng	5116	948	9809	701
Cotinin, ng	4824	916	50861	1912
β-nicotyrine, ng	926	410	9790	149

Source: Poynton et al., 2017 [14]

4. CONCLUSION

The results showed that all 9 HPHCs (nine TobReg priority constituent) were shown to be lower in HTP compared to conventional cigarettes.

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