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Research Article

A Randomized Multi-Location Puffing Topography Study using Heated Tobacco Products and Conventional Cigarettes by Chinese Adult Smokers

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Abstract

Objectives: Heated tobacco products (HTPs) are emerging novel tobacco products. The aim of this study was to collect and compare usage behavioral data on HTPs and conventional cigarettes (CCs) by recording their puffing topographic parameters under laboratory conditions. Methods: 200 adult cigarette users (164 male, 36 female) from four cities of China were recruited and randomly divided into three groups: a tobacco flavor HTP (coded as Original-HTP) group, a menthol flavor HTP (coded Menthol-HTP) group, and a cigarette group (CCs). The volunteers in the two HTP groups were given 1-week acclimatization to the HTP products which had a nicotine content of 1.0 mg/stick. Their puffing parameters were collected via a commercial calibrated puff behavior recorder. The puffing topography of every participant included their puffing duration, interval, puffing flow rate and puff volume. These data were analyzed together with urinary nic-otine metabolites post product usage. Results: When using the same nicotine stick, the volunteers in the two HTPs groups showed statistically more puff numbers and puff volume, also faster flow velocity and peak flow rates. In comparison, the CCs group showed longer inter-puff intervals and higher levels of nicotine in the urine. The differences on the puffing topography in four cities were not significant. Conclusions: There were substantial differences in the puffing topography between HTPs and CCs users by Chinese smokers. The implication of these findings was that in order to compare the nicotine and toxicant exposures between HTPs and CCs, preclinical emission test conditions should reflect the usage patterns of the two types of tobacco products for more accurate risk assessment.

Keywords: Heated Tobacco Product; Conventional Cigarette; Puffing Topography; Demographic Characteristics; Standardized Testing Conditions;

Introduction

The use of tobacco products contributes to the development of a number of pre-ventable diseases, however, there are still many smokers who are not or unable to quit [1]. All tobacco products use can become an addiction for some users. The effects of nicotine intake and exposures to harmful substances from tobacco products on the human body are complex, and the assessment of such effects needs to be conducted on different aspects of the product use [2].

The risks of cigarette smoking to health are well known, in recent years many to-bacco companies have developed alternative tobacco and nicotine products, such like electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs) [3]. HTPs were first launched in Japan and then European markets in 2014 [4], with their claimed benefits of harm reduction and aiding smoke cessation their use have increased in re-cent years [5].

HTPs are designed to heat tobacco below the ignition temperature and deliver aerosolized nicotine and other tobacco constituents for inhalation [6]. Based on con-trolled heating technologies, different HTPs are now available for producing aerosols containing nicotine without burning tobacco [7].

As a new form of nicotine delivery, HTPs have significantly different smoke gen-eration principles and smoke components from CCs [8]. According to data from the tobacco industry, the toxicant contents in the aerosols of some commercial HTPs are about 90-95% lower than that of conventional cigarette smoke, the levels of harmful and potentially harmful components (HPHCs) such as aldehydes and volatile organic compounds in heated cigarette smoke are also significantly reduced [9]. A review in-cluding 25 relevant studies published in English between 2015 and 2021 suggests that exclusive HTP use over smoking may reduce the risk of some chronic diseases, includ-ing respiratory disease, cardiovascular diseases and cancer, although they may pose a risk for those that are non-smokers, so HTPs have been intended to be an alternative to CCs for heavy smokers who had failed comprehensive treatment for nicotine addiction [8]. In addition, HTPs do not emit 2nd hand smoke and may reduce environmental pol-lution [3].

Several types of HTPs have been introduced into the market so far, including brands such as iQOS, Glo, Ploom, Pax and iFuse and are sold in more than 40 countries [8]. A recent market research found that a large number of Chinese smokers are in-terested in HTPs [10], either in combination with other tobacco products or as quitting aids. However, some studies found that these types of novel tobacco products can also attract young generation users who never smoke [11].

As a newly developed alternative nicotine products, emission analysis of the chemical composition of HTPs aerosol is an important step in determining whether HTPs offer both individual and population-level harm reduction potential. In fact, some studies reported the levels of harmful and potentially harmful constituents (HPHCs) in the emissions from HTPs are significantly reduced as compared to CCs [1, 12]. Emission data from chemical analysis are typically collected under standard machine-smoking regimens defined by the International Organization for Standardi-zation (ISO) or the Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) [13]. However, the standardized regimens are intended for product com-parison purposes and do not necessarily reflect human puffing behavior. To estimate the real emissions or the levels of chemicals inhaled by their users from HTPs, which are more relevant to assess these products' true harm reduction potential, puffing topographic parameters close to real-world usage have to be gathered.

Puffing topography of a tobacco product is influenced by the design and specifica-tions of the product, and the smoking habits of the user. There is also a correlation with user preferences, etc. Puffing topography data not only reflect personal preferences and smoking habits of smokers to a considerable extent, but also significantly affects the toxicant intake by the tobacco users [14, 15]. Harsher puffing conditions such as more, longer, and larger puffs yield higher levels for most toxicant emissions [16]. For instance, a lot of researches have reported puffing topographic data among smokers using different generations of e-cigarettes [13, 17, 18], most of them showed that puff duration, inter-puff interval and puff volume among e-cigarette users varied from conventional cigarettes. In addition, different flavors of e-cigarettes could also result in different puff durations and different levels of plasma nicotine as measured in clinical studies [14]. There is evidence that both the levels and forms of nicotine affects the user's puffing topography.

With the rapid development of HTPs, it is important to study the puffing topog-raphy of HTPs for smokers of different demographics. So far few studies on puffing topographies of HTPs compared to CCs have been reported for Chinese smokers [19]. Cigarettes available in China are predominantly a local Virginia blends, which are quite different to the dominant tobacco varieties outside China. Transition patterns by Chinese smokers to use HTPs may be different to those seen in other parts of the world where HTPs are available. We therefore conducted a randomized experiment to meas-ure the puffing topographic behavior by using two differently flavored HTPs (one to-bacco and one menthol) and compared those to CCs under similar standardized condi-tions, in order to further understand the nicotine exposure and metabolism of heated cigarettes on the human body. The results of this study were expected to provide in-sights on potential risk in the switching of Chinese smokers from conventional ciga-rettes to HTPs. An understanding of any product characteristics that pertain to HTPs use may also facilitate the development of a standard protocol for HTPs testing and clinical studies [13]. In addition, it can also provide a basis for the experimental design of evaluating the exposure of heated cigarette smoke.

Materials and Methods

Devices and Products

PuffmanTM puff behavior recorders (Puffman automation and instruments com-pany, China) were used to measure the parameters of puffing topography of every participant in this study. The technical specifications are shown Table 1.

No.	Technical Parameter	Values
1	Puff volume range	0-150 mL
2	Precision of puff volume	± 2%
3	Flow velocity range	10 - 50 mL/s
4	Precision of flow velocity	± 2%
5	Puff duration range	0 - 99 s
6	Precision of puff duration	± 100 ms
7	Inter-puff interval range	0 - 10 Min
8	Precision of inter-puff interval	± 100 ms
9	Pressure drop range	1 kPa
10	Precision of pressure drop	± 1%
11	Data collection frequency	100 Hz

Table 1: The technical parameters of puff behavior recorder used in this research.

Before using each puff behavior recorder in this test, trial runs were performed to compare the recorded data and to ensure they were within the specified ranges. Dur-ing the experiment, care was taken to wipe any aerosol residuals within the product adaptation hole every half hour of usage.

All of the HTP devices and consumable tobacco sticks, and test cigarettes in the experiment were provided by Shanghai New Tobacco Product Research Institute Co., Ltd. As shown in Figure 1, the HTP device had a maximum heating temperature of 350?. The nicotine content of the HTP consumable sticks (both original tobacco and menthol flavor) was 1.0 mg per stick. CCs were commercially available with a nicotine content of 1.0 mg/stick and a tar content of 11 mg/stick.

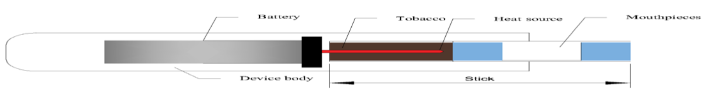

Figure 1: The schematic of the tested HTP device with a tobacco stick inserted.

Human Subjects and Study Groups

Subjects were selected from four cities, including Shanghai and Suzhou in Eastern China, Hefei in Central China, and Guiyang in Western China. We used the simple random sampling method to select 50 participants in each city totaling 200, and then divided them randomly into three groups. Tests were run from July to August 2022.

The inclusion criteria of participants included: aged 19–65 years, without cardio-vascular, respiratory or reproductive diseases, no psychiatric and other serious psy-chiatric disorders, no pregnancy or breastfeeding, not taking any medication in the past week that could be considered interference to the test purpose. Volunteers smoked 5–20 cigarettes with ISO tar yield between 10–12 mg, nicotine level of 1.0 mg daily for at least 2 years (current brand for >6 months) [20]. The exclusion criteria included: ev-er or known illicit drug abuse, current or former mental disorders, diagnosed cardio-vascular diseases, chronic obstructive pulmonary disease, other respiratory diseases or cancer of any kind, or any other reasons that could be considered noncompatible with the purpose of the study. The investigators of the study also evaluated the participants' adherence of the experimental protocol. Informed consent was obtained from all the subjects after explaining the purpose of the study. The Biomedical Ethics Review Committee of Tongren Traditional Chinese Medicine Hospital approved the study (Approval number: TRSZYY-2022-02).

Experimental Methods

All the subjects were allowed to familiarize themselves with the usage of the HTP products and also the puff behavior recorder. Efforts were made to encourage them puff naturally and to reproduce their usual puff behaviors as needed. The adaptation period lasted six days, during which each participants were provided with an average of 5 cigarettes and HTP sticks. Instructors were on hand when needed to guide the par-ticipants to custom their stable puffing behaviors.

In the first round of the experiment starting from July 2022, the three groups of participants were randomly assigned to puff CCs (group 1, n = 72), the Original- HTPs (group 2, n = 68), and the Menthol- HTPs (group 3, n = 60) respectively. On the seventh day, they were required to smoke one single cigarette sample which they had been as-signed within 5 minutes in very similar experimental environments including atmos-pheric pressure, temperature and indoor ventilation. Throughout the entire process of puffing, we recorded their smoking behavioral parameters including puff number, puff volume, puff duration, inter-puff interval, flow velocity, peak flow rate, peak time us-ing the puff behavior recorder as well as atmospheric pressure at the same time. The process was video recorded in order to verify each participant's compliance and en-sure that all of data had been correctly recorded.

In the second round beginning at the eighth day, the participants in group 1, group 2 and group 3 were switched to puff Original-HTPs, Menthol- HTPs and CCs respectively. In the last round beginning at the fifteenth day, participants in group 1, group 2 and group 3 were switched to puff Menthol- HTPs, CCs and Original-HTPs respectively. Similar to the first round, we also set a six-day adaptation period for the second and the third round, as well as required each participant to smoke a cigarette sample assigned to them within 5 minutes and recorded the above smoking behavioral parameters at the same time (Figure 3).

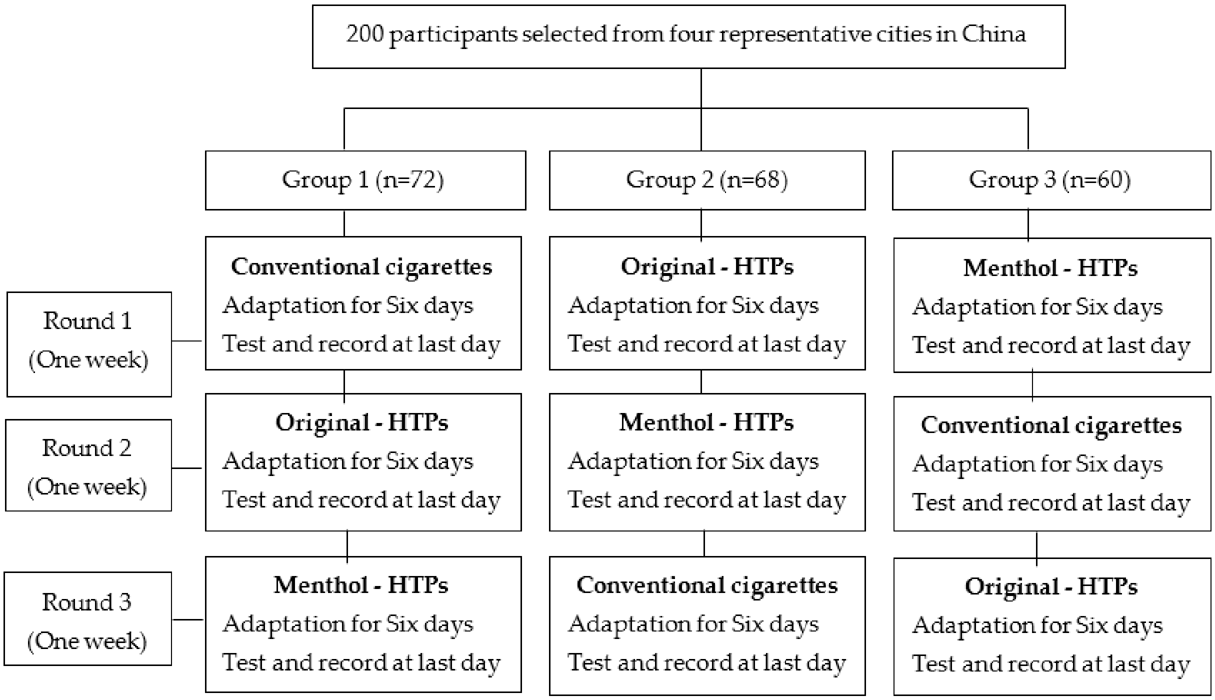

Figure 2: The flowchart of the experiment.

On the last day of each round, urine samples in the morning and 8 hours after smoking cigarette sample were collected to assess the individual's nicotine exposure level from the sample cigarette. During this period, all volunteers freely drunk water to facilitate the elimination of nicotine. The following eight nicotine metabolites in urine will be primarily tested: nicotine (NIC), cotinine (COT), cotinine-N-ß-D-glucuronide (COTG), (1'S, 2'S)-nicotine-1'-oxide (NNO), (S)-cotinine N-oxide (CNO), trans-3-hydroxycotinine (OHCOT), nornicotine (NNIC), and norcotinine (NCOT). The urine sample was labeled and once collected, it was stored in liquid nitrogen for testing as soon as possible using the method reported before [10].

Data collection and statistical analysis

Participants' smoking history and demographic information were collected before the first round of experiment using a self-administered questionnaire designed in the study (see later).

Puff number was defined as the total number of puffing one single cigarette or single HTP stick. Puff volume was continuously recorded in unit of mL during a single mouth puffing process. Puff duration time refers to the duration of a single mouth puffing process. Inter-puff interval was defined as the time interval between two ad-jacent mouth puffing behaviors. Flow velocity, peak flow rate and peak time were rec-orded or calculated based on one single cigarette which the participants puffed in the experiment.

We calculated the means of the above puffing parameters and atmospheric pres-sure in three repeats of the experiment to describe the puffing topographies after ex-cluding the influence of puff order.

Data were checked for consistency and any abnormality. Characteristics of the participants were described as mean and standard deviation (SD) for continuous var-iables if normally distributed or as median and interquartile range (IQR) if non-normally distributed. Categorical variables were presented as number and per-centages (%). We compared continuous variables using One-way analysis of variance (ANOVA) among the three groups divided by different types of tobacco sticks includ-ing CCs, Original - HTPs and Menthol - HTPs if the data are normally distributed. In the case of a significant difference had been found between the groups, Tukey's post-hoc test was applied to examine the source of the difference. For non-normally distributed data or the data with heterogeneity in variance, Kruskal-Wallis test was used to compare average differences between multiple groups. For categorical variable data, Chi-square test was used to compare proportions' differences. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 23.0.

Results

Throughout the entire experimental phase, all the participants reported no ad-verse reactions or physical discomfort during or 1-week after the study.

Demographic characteristics and smoking history

The average age of the participants was 34.04 ± 10.52 years old, ranging from 19 to 65 years old, 164 (82.0%) participants were male, all the participants were current smokers, of which 96 (48.0%) had been smoking for more than 10 years, the average duration of cigarette smoking was 10.65 ± 8.38 years. Participants' average body mass index (BMI) was 22.95 ± 3.04 kg/m2, of which 14.0%, 54.5%, 25.0%, 6.5% were under-weight, normal weight, overweight and obesity respectively. The proportions of daily cigarette consumption, Intention to quit smoking and occupation among the partici-pants were presented in Table 2.

		N	%
Gender	Male	164	82
	Female	36	18
Duration of cigarette smoking(ys)	＜10	104	52
	10～	96	48
Daily cigarette consumption	≤10/d	107	53.5
	11～20/d	79	39.5
	≥21/d	14	7
Body weight	Underweight	28	14
	Normal weight	109	54.5
	Overweight	50	25
	Obesity	13	6.5
Intention to quit smoking	Yes	95	47.5
	No	105	52.5
Occupation	Civil servant	1	0.5
	Professional and technical personnel	16	8
	Staff member	58	29
	Enterprise management personnel	51	25.5
	Worker	22	11
	Student	12	6
	Self-employed	18	9
	Unemployed personnel	3	1.5
	Retired (resigned) personnel	9	4.5
	Others	10	5
Total		200	100

Table 2: Demographic characteristics of the participants.

Except for daily cigarette consumption, there were no statistically significant differences in the demographic characteristics of participants from the four representa-tive cities, including gender, age, weight status and duration of cigarette smoking (Table 3), indicating that there were few differences in the demographic composition be-tween the participants from the four cities.

	Guiyang	Hefei	Shanghai	Suzhou	$\chi^2/F^*/H^{**}$	*P*
Gender: Male (%)	82	86	74	86	3.252	0.354
Age: ys (mean±SD)	32.64±10.50	35.66±9.73	33.40±10.61	34.22±10.50	0.781^*	0.506
Weight Status: Underweight (%)	16	8	16	16	5.011^{**}	0.171
Normal (%)	48	68	38	64		
Overweight (%)	32	18	34	16		
Obesity (%)	4	6	12	4		
Duration of cigarette smoking: ＜10ys (%)	56	50	50	52	0.481	0.923
Daily cigarette consumption: ≤10/d (%)	64	34	82	34	35.656^{**}	＜0.001
11～20/d (%)	32	62	18	46		
≥21/d (%)	4	4	0	20		
Note: *Represents F value in ANOVA, **Represents H value in Kruskal-Wallis test.						

Table 3: Demographic characteristics of the participants among the four cities.

Differences of puffing topography

We compared the means of puff number, puff volume, puff duration, inter-puff interval, flow velocity, peak flow rate, peak time among the three groups of partici-pants who smoked different types of tobacco sticks, there were significant differences on all of the above variables (Table 4).

During the experiment, no statistical differences were found in the average at-mospheric pressure of the three groups of participants, which indicates that the levels of puffing parameters would not be affected by atmospheric pressure (Table 4).

When we compared the above puffing parameters in each city, we found that the puffing characteristics in each city were not similar except for flow velocity (Figure 3). The differences of puffing topography in the four cities between the Original- HTPs and Menthol-HTPs was subtle. However, the overall trend in variances between HTPs and CCs remained consistent.

Variables	Types of cigarettes	n	Means	SD	SE	F/H	*P*
Puff number	CCs	200	18.98	6.484	0.458	12.94	＜0.001
(per session)	Original- HTPs	200	21.88	7.199	0.509		
	Menthol- HTPs	200	22.1	6.835	0.483		
Puff volume (mL)	CCs	200	39.636	14.575	1.031	155.090*	＜0.001
	Original- HTPs	200	65.639	21.303	1.506		
	Menthol- HTPs	200	58.838	22.44	1.587		
Puff duration (s)	CCs	200	1.877	0.612	0.043	4.366	0.013
	Original- HTPs	200	2.048	0.642	0.045		
	Menthol- HTPs	200	1.889	0.679	0.048		
Inter-puff interval (s)	CCs	200	12.47	3.73	0.264	26.423	＜0.001
	Original- HTPs	200	10.283	3.163	0.224		
	Menthol- HTPs	200	10.3	3.464	0.245		

Flow velocity (mL/s)	CCs	200	22.106	7.529	0.532	127.849	＜0.001
	Original- HTPs	200	33.55	8.094	0.572		
	Menthol- HTPs	200	31.978	7.642	0.54		
Peak flow rate (mL/s)	CCs	200	34.321	13.123	0.928	202.548*	＜0.001
	Original- HTPs	200	56.036	15.873	1.122		
	Menthol- HTPs	200	51.112	14.794	1.046		
Peak time (s)	CCs	200	0.764	0.339	0.024	8.099*	0.017
	Original- HTPs	200	0.859	0.436	0.031		
	Menthol- HTPs	200	0.745	0.371	0.026		
Atmospheric pressure (kPa)	CCs	200	98.181	6.108	0.432	0	＞0.999
	Original- HTPs	200	98.181	6.108	0.432		
	Menthol- HTPs	200	98.184	6.11	0.432		
Note: *Represents H value in Kruskal-Wallis test due to heterogeneity in variance.							

Table 4: Comparisons on the means of puffing parameters and atmospheric pressure among different types of cigarettes.

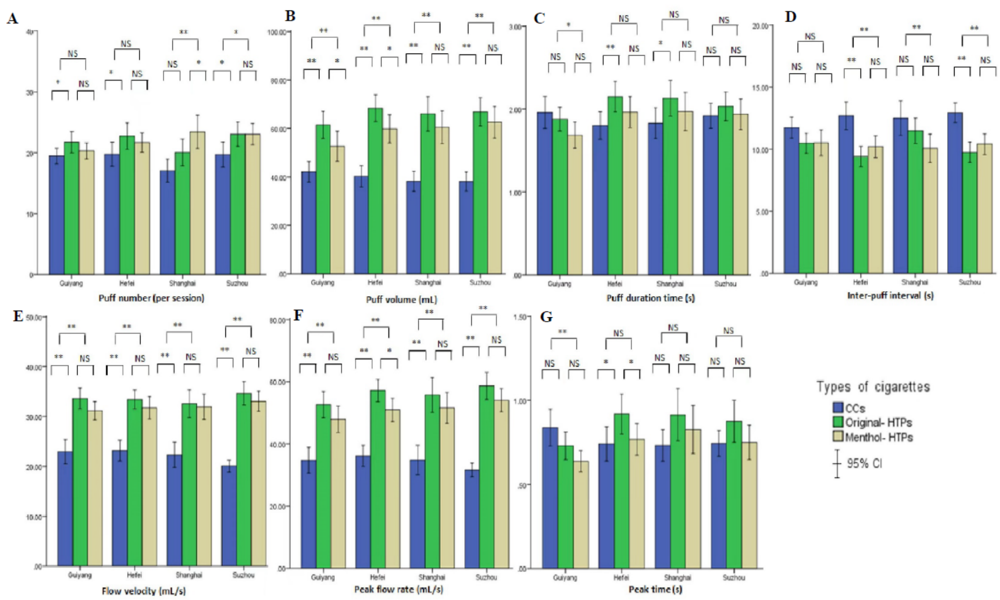

Figure 3: Comparison of puffing parameters differences among different types of cig-arettes divided by cities. A. Puff number. B. Puff volume. C. Puff duration. D. Inter-puff interval. E. Flow velocity. F. Peak flow rate. G. Peak time. (NS: no significance; * p<0.05; ** p<0.01, respectively)

Differences in urinary nicotine metabolites levels

There were statistically significant differences in the average levels of all kinds of urinary nicotine metabolites among CCs, Original- HTPs and Menthol- HTPs, whether in urine samples in the morning or 8 hours after smoking cigarette sample (Table 5). In all the HTPs group, the total urinary nicotine metabolites content were lower than that of the CCs group (Figure 4).

Nicotine metabolites	**Urine samples**	**In the morning**		**8 hours after puffing one stick**		***P***
		Mean	**SD**	**Mean**	**SD**	
NIC	CCs	30.39	12.26	87.17	14.03	<0. 01
	Original- HTPs	21.76	5.08	49.09	12.31	
	Menthol- HTPs	26.68	7.87	67.55	14.39	
COT	CCs	4.62	0.87	49.04	5.64	<0. 01
	Original- HTPs	3.45	0.95	41.98	7.97	
	Menthol- HTPs	4.25	0.98	26.92	5.04	
COTG	CCs	27.01	5.76	289.5	85.49	<0. 01
	Original- HTPs	18.44	5.1	186.6	31.24	
	Menthol- HTPs	14.85	3.12	166.6	33.25	
NNIC	CCs	0.58	0.15	3.89	1.05	<0. 01
	Original- HTPs	0.55	0.19	1.87	0.47	
	Menthol- HTPs	0.41	0.1	1.47	0.58	
NCOT	CCs	5.04	1.69	21.81	2.92	<0. 01
	Original- HTPs	2.38	0.62	19	3.64	
	Menthol- HTPs	3.79	1.71	21.72	4.75	
NNO	CCs	4.1	0.66	16	2.42	<0. 01
	Original- HTPs	3.58	0.69	15.08	2.49	
	Menthol- HTPs	3.53	0.53	10.23	1.83	
CNO	CCs	1.86	0.35	4.89	0.9	<0. 01
	Original- HTPs	1.42	0.41	2.51	0.5	
	Menthol- HTPs	1.22	0.28	2.65	0.49	
OHCOT	CCs	49.45	10.48	165.9	19.26	<0. 01
	Original- HTPs	26.95	5.42	49.68	9.61	
	Menthol- HTPs	42.98	9.72	95.87	18.31	

Table 5: Comparisons on 8 urinary nicotine metabolites among test products (ng/L).

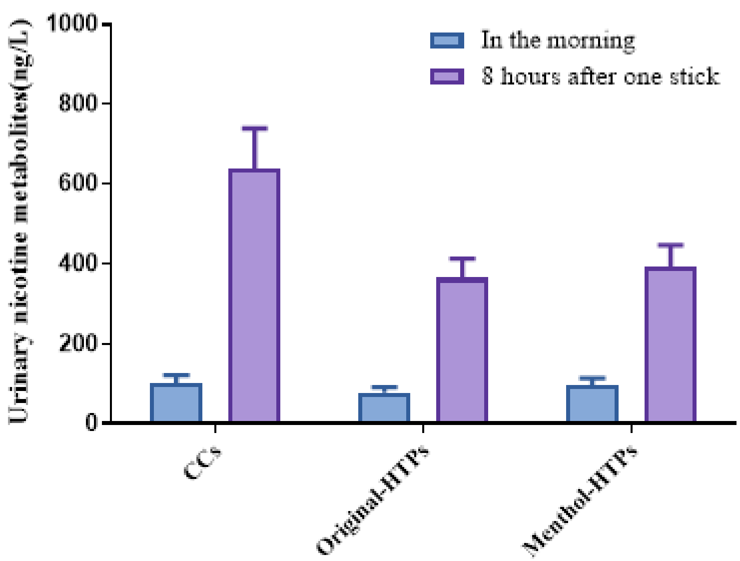

Figure 4: Comparison of total urinary nicotine metabolites.

Discussion & Conclusion

China has 341 million smokers whose consumption accounted for one-third of the world's cigarette consumption and 740 million non-smokers are estimated to be ex-posed to second-hand smoke [21, 22]. The smoking rates for men and women were 49.7% and 3.54%, respectively [23]. The participants in this study came from four sam-pling cities of wide geographical regions of China, thus could provide a window to witness the general smoking population.

The results of this study found that different characteristics could be observed between the HTPs and CCs users in all the measured puffing parameters, which is somewhat similar to the previously reported differences between e-cigarettes and CCs users [24]. In addition, except for flow velocity, the HTPs users from the different re-gions also exhibited different characteristics in their puffing topographies.

The average puff numbers and puff volumes in the Original- HTPs group and in the Menthol- HTPs group were both significantly higher than those in the CCs group, one of the possible explanations may be HTPs users needed to draw larger puffs to ob-tain similar amount of aerosol from the HTP consumables due to the lower average aerosol delivery ability of HTPs compared to CCs [25]. This finding is different from that by Sheng et al's study conducted in Henan, China which showed that the puff volume did not change significantly among cigarette smokers switching to HTPs [26]. While, the means puff volume in the Original- HTPs group and in the Menthol- HTPs group were both very similar to those in Sheng W et al's study and Murphy et al's study [27]. The reason for this discrepancy may be related to the number of subjects, also the accuracy of the instruments used in the different experiments.

Our study also found that the average urine nicotine metabolites levels in the us-ers of Original- HTPs and Menthol- HTPs were both lower than those in the users of CCs, whether in the urine samples in the morning or 8 hours after smoking; these findings were consistent with the increment of average puff number and puff volume among the users of Original- HTPs and Menthol- HTPs. It suggests that when smokers switch to smoke HTPs, they may increase puff number and puff volume due to the decrease in nicotine intake per puff.

We also found that the inter-puff intervals in the users of Original- HTPs and Menthol- HTPs were both significantly shorter than those of the CCs group. Jones J et al. also reported similar results, they found that the oral exposure level of nicotine in the smoke of HTPs was lower than that of CCs [25]. The shortening of the inter-puff intervals of HTPs may be related to lower smoke and nicotine produced by each HTPs puff behavior compared to CCs. When using HTPs, the participants have to inhale more aerosol and nicotine to meet their own needs within the same time by shortening the inter-puff interval. Similar to HTPs, in some studies the nicotine delivery efficiency of e-cigarettes was lower than that of CCs as well, Norton et al. and Wagener et al. re-ported that consumers of e-cigarettes also shorten the inter-puff interval to improve satisfaction [17, 28].

The average flow velocities and peak flow rates in the users of Original- HTPs and Menthol- HTPs were both significantly higher than those in the users of CCs. These results may be related to the compensatory smoking behaviors by the HTPs users, they needed to compensate for the low nicotine release to increase air flow rate and increase puff frequency [29]. There is research data showing that the draw resistance of HTPs was significantly lower than that of CCs. Therefore, it was reasonable to assume that smokers might compensate by increasing their puffing frequency of low draw re-sistance cigarette products [30]. In our previous research, we also found that the draw resistance of HTPs was significantly lower than that of CCs. Therefore, it may be rea-sonable to conclude that smokers obtained puffing compensation by increasing the puffing intensity of low draw resistance cigarette products in this study. In addition to the compensatory effect of nicotine, there was evidence to suggest that lower tar pro-duction can also have a compensatory effect in cigarette smoking [31]. When nicotine yield is reduced in a product, for example with a lower tar content, similar to the users of HTPs, the users could compensate for the decrease in tar obtained by inhaling larger amounts of aerosol.

At the same nicotine content, the nicotine transfer efficiency of HTPs may be low-er. That is, when smoking cigarettes with the same stick nicotine content, the nicotine content in the body of HTPs users is lower. This was confirmed in our previous studies that lower levels of nicotine and its metabolic markers in the HTPs users' urine com-pared to CCs users' [10, 32].

In conclusion, our study explored substantial differences in the puffing topogra-phy of the HTPs and CCs users. When using cigarettes with the same nicotine content, the HTP users showed more puff numbers and puff volume, also faster flow velocity and peak flow rates. While, the CCs users showed longer inter-puff interval. A possible explanation is that consumers of HTPs need to ensure satisfactory levels of smoke and nicotine from HTPs by increasing puff number and puff volume, as well as shortening the inter-puff interval.

The cotinine content in the urine showed that the conventional cigarettes users showed higher levels of nicotine intake compared to the HTP users. It is speculated that the differences may be due to the nicotine content, tar content, and flavor differ-ences of the tobacco sticks. When comparing the differences between the four cities, the general differences of puffing topography remained the same, but there were subtle differences between the cities. However, the relationship between the types of tobacco sticks and the puffing topography of different users need more exploration. The find-ings in this research provided evidence that smokers switch to use HTPs adopt differ-ent puffing behaviors to those used in smoking cigarettes, which will have implications for risk assessment of the different types of tobacco products.

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