Original investigation

Flavored Versus Nonflavored Waterpipe Tobacco: A Comparison of Toxicant Exposure, Puff Topography, Subjective Experiences, and Harm Perceptions

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Abstract

Introduction: Flavored waterpipe (WP) tobacco is the main type of tobacco used by young WP smokers, and a major factor attracting youth to smoke. However, evidence regarding the effect of limiting flavor on WP smokers' experience continues to be lacking. This study aims at evaluating the effect of flavor restriction on WP smokers' toxicant exposure, smoking topography, subjective experiences and harm perception.

Methods: Thirty-two WP smokers completed two, 45-minute ad libitum smoking sessions (preferred flavor vs non-flavored tobacco) in a crossover design pilot study. Plasma nicotine concentration and exhaled carbon monoxide (eCO) were measured before and after each smoking session. Puff topography was recorded throughout the smoking session. Participants completed survey questionnaires assessing subjective smoking experiences and harm perception.

Results: Significant differences were observed in plasma nicotine concentration between the two WP tobacco conditions, with a higher increase in plasma nicotine concentration following the flavored tobacco session. There were no significant differences between the two WP tobacco conditions for eCO and smoking topography measures. Compared with the non-flavored WP tobacco, we documented enhanced subjective smoking measures of satisfaction, calmness, taste, puff liking and enjoyment following the preferred flavored WP tobacco session. Cigarette harm perception was significantly higher among participants after smoking their preferred flavor compared with non-flavored WP tobacco.

Conclusions: Limiting tobacco flavor has a substantial effect on WP smokers' nicotine exposure, subjective experience and harm perception. Therefore, eliminating or restricting WP flavors could be an essential element of comprehensive tobacco control policies to reduce the appeal of WP tobacco products for youth.

Implications: This study highlights the important role of flavor in shaping WP smokers' experiences and exposures and the potential impact that regulating flavored WP tobacco may have on curbing WP use among youth in the US. Such regulations may reduce the appeal and the interest in WP smoking initiation and continued use.

Introduction

Water pipe (WP) smoking (aka hookah, shisha, narghile) is becoming increasingly popular in the United States, especially among youth. Time-trends in tobacco use among high-school students based on 2011–2016 US National Youth Tobacco Survey show a significant increase in WP use, whereas most of other tobacco use has declined.¹ In fact, data from the first wave (2014) of the Population Assessment of Tobacco and Health (PATH) study, the first population-based survey designed to guide the US Food and Drug Administration's tobacco regulatory efforts, show that WP smoking is becoming a main tobacco use method in the United States that is particularly common between 18 and 34 years.² Moreover, WP smoking is widespread among college students in the United States; in 2016, a survey conducted by the American College Health Association reveals that 23% of college students in the United States were current (past month) WP smokers.³ A growing body of evidence suggests that similar to cigarettes, WP smoking can lead to nicotine dependence^{4,5} and many other known smoking-related illnesses such as cancer, cardiovascular and respiratory diseases.⁶

The introduction of manufactured flavored tobacco is a major factor in the global resurgence of WP among young people.^{7,8} Flavored WP tobacco is a wet mixture of tobacco, sweeteners, and a variety of flavors that come with both ordinary (eg, fruits) and exotic names (eg, Pirate's Cave, Sex on the Beach), which produces an appealing, aromatic, and smooth smoking experience.⁹ It is well established that tobacco flavoring is a strategy that has been used by the tobacco industry to attract youth and to increase the appeal of smoking.^{10,11} Quantitative and qualitative studies show that flavored WP tobacco is the main attractant for new smokers and a key component of the "WP experience" in established smokers.^{12–14} For example, in a study of a sample of adult WP smokers in the United States, the major motivating factors related to using flavored WP tobacco were the smoke's taste, smell, and smoothness.¹⁵ Moreover, a national study that examined flavored tobacco products use among youth in the United States in 2013–2014 showed that among ever users of tobacco, 89% reported using WP as their first flavored tobacco product.¹⁶

In an effort to control flavored tobacco products, Congress banned flavored cigarettes as part of the Family Smoking Prevention and Tobacco Control Act (FSPTCA), but this ban does not currently include flavored WP tobacco. In 2016,¹⁷ the Food and Drug Administration extended its regulatory authority to include WP products under the FSPTCA.¹⁸ This important development creates the need for evidence to guide the Food and Drug Administration and other policy bodies to create effective regulations for flavored WP tobacco. Yet, research regarding the effects of restricting flavor on WP smoking experience is very limited.

To the best of our knowledge, only one study examined the effect of flavor preference (preferred vs. nonpreferred flavor) on smoking behavior among WP smokers.¹⁹ Results of this study indicated that flavor manipulation resulted in significant changes in subjective experience and suggested a possible need for regulations restricting

flavored WP tobacco.¹⁹ However, empirical evidence of the effects of eliminating flavor on WP smoker's experiences and behavior is still lacking. Our study aims to generate such evidence by comparing flavored WP tobacco with nonflavored WP tobacco in terms of the following: (1) toxicant exposure (plasma nicotine and exhaled carbon monoxide [eCO]), (2) puff topography, (3) users' subjective smoking experiences, and (4) harm perception using a crossover experimental design. We hypothesized that smoking flavored WP tobacco is associated with an enhanced smoking experience, greater satisfaction, intense buffering behavior, and longer smoking session resulting in increased levels of nicotine exposure compared with nonflavored tobacco. Finding from this pilot study may bring novel insights regarding the effect of eliminating flavor on WP smokers and could inform flavor-based regulations for WP use in the United States.

Methods

Participants

Thirty-two participants were recruited from the metropolitan area surrounding Miami, Florida, via flyers, word of mouth, and online advertisements (eg, Craigslist). Participants provided informed consent and attended two laboratory sessions. Participants were healthy, between the ages 18 and 30 years, and WP smokers who smoked flavored WP tobacco. Exclusion criteria included self-reported history of chronic health problems or psychiatric conditions, regular use of prescription medications (other than vitamins or birth control), and self-reported current use of more than 5 cigarettes/month or other tobacco/nicotine products (>5 times in the past month). Females were excluded if they were pregnant (verified by urinalysis), or breast feeding. This study was approved by Florida International University Institutional Review Board.

Procedure

Participants completed two sessions (participants' preferred flavor and nonflavored WP tobacco), separated by a 48-hour wash-out period to avoid carryover effects and preceded by greater than or equal to 12-hour tobacco/nicotine abstinence. Session order was counterbalanced. Before each session, the WP head was filled with 15 g of the assigned tobacco preparation and covered with perforated aluminum foil.²⁰ The assigned tobacco was also weighed following the end of the smoking session. Tobacco was heated with quick-light charcoal disks (33 mm diameter; 6.2 g; Three Kings, Holland, or similar brand). For standardization, only one type of WP device was used (Khalil Mamoon 27 in, Egypt). Participants were then instructed to use the WP *ad libitum* for 45-minute WP use session. Blood samples and eCO measurements were collected before the 45-minute WP use session began and immediately after it ended.²¹ Subjective responses were assessed after the smoking session. During each session, participants were seated in a comfortable recliner chair and were given the choice to watch movies while smoking.

For participants' preferred brand, the most commonly used tobacco-based brands were Al Fakher (United Arab Emirates; $n = 25$), followed by Starbuzz (United States; $n = 6$), and Haze (United States; $n = 1$). For participants' most preferred flavors, refer to Table 1. For the nonflavored condition, all participants smoked Zaghoul Nakhla (Egypt; $n = 32$), nonflavored WP tobacco. Payments were provided to compensate for participants' time, effort, and expense of attending sessions.

Measures

Plasma Nicotine

Blood was drawn during presmoking and postsmoking sessions at each lab visit. Blood samples were centrifuged, plasma was stored at -80°C and analyzed for nicotine concentration. Consistent with previous literature,²² plasma nicotine samples were analyzed using the gas chromatography–mass spectrometry method. The assay's limit of detection was 0.2 ng/mL and limit of quantitation was 1.0 ng/mL.

Subjective Measures

Participants responded to three self-administered subjective measures: the Duke Sensory Questionnaire (DSQ), the Cigarette/WP Evaluation Scale (WES), and harm perception. Below are additional details about these measures.

The WES is a 11-item questionnaire that was adapted from studies of cigarettes^{23,24} and modified for the WP (replacing the

word “cigarette” with “water pipe”). This scale assesses participants' perception of the smoked WP (eg, satisfying, tastes good, makes you dizzy); each WES item was rated on a seven-point Likert scale (“Not at all” to “Extremely”). The DSQ has nine items that assess participants' sensory experience of the inhaled product (eg, How satisfying were the puffs?); all questions were rated on a seven-point Likert scale (“Not at all” to “Extremely”).²⁵ Harm perception was assessed by using a three-item scale adapted from previous literature.²⁶ The direct measure was “Compared to your usual flavored brand, this WP is...” with answers on a seven-point scale ranging from -3 , a lot less harmful; to 0 , equally as harmful; to $+3$, a lot more harmful. To measure perceptions of WP's relative risk compared to cigarettes (relative harm perception), we asked two separate questions: (1) “In your opinion, how harmful is the WP to general health?” and (2) “In your opinion, how harmful is smoking cigarettes for health?” The answers to both were rated on a seven-point scale ranging from 1 (not at all harmful) to 7 (extremely harmful).

WP Smoking Topography

WP smoking topography was measured during each session. Smoking topography was assessed using a validated equipment.^{27,28} Inhalation-induced pressure changes were amplified, digitized, and sampled. Software converts signals to air flow (mL/sec) and integrates the flow data, producing measures of total smoking time, total puff time, puff duration, interpuffing interval, number of puffs, total volume inhaled, and average puff volume.

Exhaled Carbon Monoxide

eCO was measured before and immediately after WP use via BreathCO monitor (Vitalograph, Lenexa, KS).

Data Preparation and Analysis

As in other studies,^{21,29} plasma nicotine concentration values below the limit of quantitation were replaced with the limit of quantitation (1 ng/mL) because this approach is more conservative than assuming that values below the limit of quantitation were zero. Data for subjective measures and topography were missing for one participant, whereas for plasma nicotine data were missing for two participants. Accordingly, analyses for subjective measure and topography outcomes were based on 31 participants and for plasma nicotine outcomes were based on 30 participants. Descriptive statistics for the characteristics of the study sample were summarized with means and SDs or proportions. Means for subjective measures, eCO, and topography were compared by tobacco condition (flavored and nonflavored). For eCO measures, eCO boost was calculated by subtracting the pre-session measurement from the postsession measurement.¹⁹ To compare the effects of WP tobacco condition on plasma nicotine levels, data were entered into a repeated model analysis of variance with two within-subject factors: time (presmoking and postsmoking sessions) and WP tobacco condition (flavored and nonflavored). Huynh–Feldt corrections were used to adjust for violations of the sphericity assumption.³⁰ The analysis was controlled for age of initiating WP smoking, number of WPs smoked in the past month, duration of smoking session, and amount of tobacco consumed. Planned comparisons using two-tailed paired samples t tests were used to examine differences between means for which p values $<.05$ were reported as significant. All analyses were performed in IBM SPSS Version 21.0.³¹

Table 1. Baseline Characteristics for the Overall Sample ($n = 32$)

Variables	Overall sample
Gender (male) (%)	53.1
Race (%)	
White	78.1
Nonwhite	21.9
Hispanic (%)	53.1
Age (in years) ^a	22.4 (3.2)
Age at first smoking of water pipe ^a	17.4 (2.4)
Student status (%)	53.1
Water pipe uses/month ^a	13.8 (15.8)
Screening eCO ^a	2.1 (1.6)
Average time spent smoking water pipe (%)	
Less than 30 min	3.1
30–60 min	40.6
More than 60 min	56.3
Cigarettes use (%) ^b	31.3
Sharing water pipe with others (%)	81.3
Location of water pipe smoking (%)	
At home	37.5
At friends' place	25.0
At a public place	37.5
Preferred flavors (%)	
Grape	28.1
Apple	25
Mint	18.7
Watermelon	9.4
Mixed fruits	9.4
Other ^c	9.4

eCO = exhaled carbon monoxide.

^aData presented as mean (SD).

^bLess than 5 cigarettes/month.

^cOther includes cherry, orange, and blueberry.

Results

Study participants ($n = 32$) had a mean age of 22.4 (SD = 3.2) years and ranged from 18–30 years. Participants were mainly males ($n = 17$; 53.1%). Twenty-five participants (78.1%) self-identified as white, two as African American/black (6.3%), one as Asian (3.1%), and four as other (14.5%). Seventeen participants were college students (53.1%). Most participants ($n = 20$; 62.5%) reported smoking WP at least once a week, whereas the rest of the participants ($n = 12$; 37.5%) reported smoking WP every day or on most days during the past 6 months. The mean age for starting smoking WP was 17.4 (SD = 2.4). The mean eCO level at screening was 2.1 ppm (SD = 1.6). See Table 1 for full details. There was a significant difference in the amount of consumed tobacco following the smoking session with a greater amount of nonflavored tobacco consumed (5.3 g) compared with flavored (4.5 g; $p < .05$).

Plasma Nicotine

A significant time by condition interaction was observed for plasma nicotine ($F = 5.0$, $p < .05$; Figure 1) meaning that changes in nicotine levels across time depended on the smoked tobacco condition. Mean presession plasma nicotine concentration for the flavored tobacco condition was 1.5 ng/mL (SEM = 0.5) and increased to 14.2 ng/mL (SEM = 1.8) postsession. For the nonflavored tobacco condition, mean presession plasma nicotine concentration was 1.4 ng/mL

(SEM = 0.6) and increased to 11.1 (SEM = 1.2) postsession. As the figure shows, average plasma nicotine levels at postsmoking time-points were significantly different between the flavored and nonflavored tobacco conditions ($p < .05$).

WP Smoking Topography

WP smoking topography data are shown in Table 2. Results did not reveal any significant differences between the flavored and nonflavored tobacco conditions for any topography measure.

Exhaled Carbon Monoxide

Mean eCO levels for the flavored tobacco condition increased from 2.1 ppm (SD = 1.6) presession to 35.5 ppm (SD = 36.2) postsession resulting in an overall change of 33.4 ppm (SD = 36.3). For the nonflavored tobacco preparation, the mean eCO increased from 2.0 ppm (SD = 1.5) presession to 39.3 ppm (SD = 30.1) postsession resulting in an overall change of 37.3 ppm (SD = 29.8). Although there was a trend toward higher levels of eCO following the non-flavored tobacco condition, the difference between the two tobacco conditions was not significant ($p > .05$).

Subjective Measures

Subjective measures revealed significant differences between the two conditions. Figures 2 and 3 depict mean ratings for WES and DSQ,

Figure 1. Means ($\pm$ SEM) for plasma nicotine concentration presmoking and postsmoking sessions by tobacco condition (flavored and nonflavored) ($n = 30$, two participants were missing data for nicotine concentration). Controlled for age of start smoking water pipe (WP) and number of WPs smoked in the past month, duration of smoking session, and amount of tobacco consumed. *Indicates significant differences.

Table 2. Water pipe Smoking Topography Measures by Tobacco Condition ($n = 31$)^a

	Flavored		Nonflavored		<i>t</i>	<i>p</i>
	Mean	SD	Mean	SD		
Total smoke time (min)	42:02	8:09	42:06	7:49	-0.05	.95
Total puffing time (min)	6:15	3:34	5:26	3:32	1.64	.11
Average puff duration (s)	3.36	1.93	3.26	1.72	0.38	.70
Average IPI (s)	21.3	11.7	24.4	17.1	-1.14	.26
Total number of puffs	134.5	119.2	122.6	115.7	1.19	.24
Total inhaled volume (L)	79.5	50	82.8	55.3	-0.52	.60
Average puff volume (L)	0.68	0.40	0.83	0.50	-1.70	.09

IPI = interpuffing interval.

^aOne participant was missing data for topography.

[†]One participant was missing data for the flavor tobacco session. * indicates significant differences.

Figure 2. Means (±SEM) for postsession subjective responses for Water Pipe Evaluation Scale by tobacco condition (flavored and nonflavored) ($n = 31$, one participant was missing data for the flavor tobacco session). *Indicates significant differences.

[†]One participant was missing data for the flavor tobacco session. * indicates significant difference.

Figure 3. Means (±SEM) for postsession subjective responses for Duke Sensory Questionnaire by tobacco condition (flavored and nonflavored) ($n = 31$, one participant was missing data for the flavor tobacco session). *Indicates significant difference.

respectively. For the WES, significant differences were observed between groups for the following indices: satisfying product, liking the taste of the product, calmness, enjoyment of smoke sensation in the mouth and throat, feeling nauseous after using the product, and reduced craving for WP. For each of these items, values were greater after smoking the preferred flavor tobacco condition (p values $<.01$) compared with the nonflavored condition, except for feeling nauseous after using WP, which was greater after smoking the nonflavored tobacco condition (p value $<.05$). For the DSQ, significant differences were observed between groups for the following indices: puff likeness, puff satisfaction, and similarity of product to smoker's own used brand. For each of these items, values were greater after smoking the preferred tobacco flavor condition (p values $<.01$) compared with the nonflavored condition.

For both tobacco conditions, there was no significant differences in harm perception among participants toward WP smoking in general and while comparing the smoked WP at the laboratory with the participant's usual flavored brand (p values $>.05$). However, for cigarette smoking harm perception, participants scored significantly higher following smoking the flavored tobacco condition than following smoking the nonflavored tobacco condition (p value $<.05$).

Discussion

This is the first clinical laboratory study to compare the effect of flavored and nonflavored WP tobacco use on smokers' toxicant exposure, puff topography, subjective responses, and harm perception. The results show that compared with nonflavored tobacco, smoking flavored tobacco was associated with a greater increase in

plasma nicotine concentration. Results also show that smoking flavored WP tobacco enhanced the subjective experience of WP smoking. This study highlights the important role of flavor in shaping WP smokers experience and exposures and the potential that regulating flavored WP tobacco may have for curbing WP use among youth in the United States.

Although there were no differences in topography measurements and average smoking time between the two tobacco conditions, participants had higher concentrations of plasma nicotine after smoking their preferred WP tobacco flavor. This finding highlights the impact of flavored tobacco on nicotine exposure, which can influence the development and maintenance of nicotine dependence among WP smokers.⁵ Flavoring may also influence WP dependence through nonnicotine mechanisms, as WP smokers are attracted to distinct features attributable to WP-specific characteristics such as the taste and smell of flavored WP smoke.^{15,32} Although this finding provides insight on the possible influence of flavored tobacco on plasma nicotine, a more in-depth examination is needed to explain the role of flavoring and its related additives (eg, glycerol) on nicotine delivery and absorption.

Most importantly, in this study, participants generally found smoking their preferred flavored WP tobacco preparation more satisfying, calming, good tasting, and well liked. Our findings are in line with those of Leavens et al.¹⁹ who compared the effect of flavored tobacco variations (preferred vs. nonpreferred) and found that smoking the preferred flavor preparation was associated with an enhanced subjective experience. In addition, our study shows that smoking nonflavored tobacco was associated with a negative subjective experience (feeling nauseous). This can be explained by the higher levels of eCO recorded among participants following smoking nonflavored tobacco compared with flavored. High levels of eCO have been shown to be associated with dizziness and feeling nauseous.^{33,34}

Studies that evaluated the relationship between subjective responses and smoking trajectories among cigarettes smokers show that smokers who endorse negative subjective effects have a reduced likelihood of becoming regular smokers or developing nicotine dependence.^{35,36} However, high rates of satisfaction reflect reward obtained from smoking that has been associated with experimentation and progression to regular smoking among cigarettes smokers.^{37–39} Thus, similar to cigarettes,^{10,17} regulatory actions that eliminate or restrict flavoring in WP tobacco may reduce initiation and continued use of WP smoking among youth.

Another interesting finding in our study is how participants perceived risk regarding cigarette smoking. Contrary to our expectation, following smoking each tobacco condition (flavored and nonflavored), we observed no difference in harm perception for WP smoking. However, following smoking the preferred flavored WP tobacco condition, participants perceived smoking cigarettes as more harmful compared to following smoking the nonflavored tobacco condition. This difference can be explained by the common misconception that the cooled and sweetened taste of flavored WP tobacco makes it less harmful.⁷ The flavor can mask the harsh taste of tobacco, making flavored tobacco products easier to use and increasing its appeal.¹⁰ Future Food and Drug Administration regulations should address misperceptions associated with WP flavored tobacco smoking and should provide health warning labels that highlight the comparative harm of WP smoking to cigarettes.⁴⁰

Although our study addresses important gaps in the WP smoking literature, our results should be considered in the context of the study

limitations. This pilot study is limited in scope, using a small sample of mostly college students. However, WP smoking is very common among this age group.³ Moreover, given the nature of the study's objective, comparing flavored with nonflavored tobacco preparations, our study was designed as an open-label. Accordingly, blinding the participants was not feasible. Additionally, the laboratory environment unavoidably differs from the typical WP smoking atmosphere. However, to mimic the WP café environment, our laboratory was furnished with a reclining chair, and participants could watch movies if they chose. These features made the session area more relaxing and entertaining to facilitate a natural smoking experience. In fact, although participants were informed that they may stop the smoking session at any point, most participants completed the full smoking session (average smoking time = 42 minutes). In addition, participants smoked WP alone rather than in a group setting as is typically done. In our sample, over 80% report sharing a WP when they smoke, therefore the results may differ outside the laboratory environment when a WP is shared with peers during the smoking session.⁴¹ However, since both sessions share the same lab environment, and only differed by the tobacco flavor condition, the observed differences likely reflect the potential effect of flavor on WP smokers.

Nevertheless, given the current limited knowledge regarding the effect of flavor elimination on WP smoking experiences and toxicant exposure, our preliminary data represent a crucial first step in exploring the effects of regulating flavored tobacco on WP smoking. In a laboratory crossover design study, we were able to demonstrate that flavored WP tobacco smoking produces a greater increase in plasma nicotine concentration, an enhanced effect on subjective smoking experiences, and a higher harm perception of smoking cigarettes compared with nonflavored WP tobacco. In light of our results, restricting WP flavors could be an essential element of comprehensive tobacco control policies designed to reduce the appeal of WP tobacco products for youth.

Future research could test multiple tobacco conditions (eg, preferred flavors vs. nonpreferred flavor vs. nonflavored tobacco) and incorporate subjective questions regarding interest in continued use and future willingness of using these products. Such comparisons would allow for a complete understanding of the impact of flavoring on WP smoking behavior and experience. Furthermore, as we gain more insights about the role of flavored tobacco in shaping WP smokers' experience, we may be able to disentangle its effect on various levels of WP use. Such information can provide important evidence regarding the expected effects of flavor regulation on WP smokers at different stages of their smoking trajectories.

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Declaration of Interests

TE is a paid consultant in litigation against the tobacco industry and is named on a patent application for a device that measures the puffing behavior of electronic cigarette users.

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