The effect of flavoured and non-flavoured tobacco on subjective experience, topography and toxicant exposure among waterpipe smokers

Ziyad Ben Taleb [ORCID],[1] Mayra Vargas,[2] Mohammad Ebrahimi Kalan [ORCID],[2] Alison Breland,[3] Thomas Eissenberg,[4] David Brown,[5] Wasim Maziak[6]

ABSTRACT

Introduction Flavoured waterpipe (WP) tobacco is a major factor in the resurgence of WP smoking and a main attractant of WP use among youth. Yet, evidence of the effects of limiting flavour on WP smoker's experiences and exposures is limited. This study examined the impact of flavour manipulation on WP smokers' toxicant exposure and smoking experiences.

Method A total of 144 WP smokers attended two, 45 min ad libitum smoking sessions (flavoured vs non-flavoured tobacco) in a crossover design study. Participants completed a battery of questions assessing subjective smoking experiences. Exhaled carbon monoxide (eCO) and plasma nicotine concentrations were measured before and after the smoking sessions. Puff topography was recorded throughout the smoking sessions.

Results Compared with the non-flavoured WP tobacco, participants reported enhanced subjective smoking measures of satisfaction and enjoyment following smoking flavoured WP tobacco (ps <0.05). Although participants spent a longer time smoking flavoured tobacco, they took on average larger puffs while smoking the non-flavoured tobacco (ps <0.05). Greater levels of eCO were recorded following the non-flavoured tobacco session (p<0.05) compared with flavoured tobacco. No significant differences were observed in plasma nicotine concentrations between the two tobacco conditions. WP harm perception was higher among participants after smoking non-flavoured WP tobacco compared with their preferred flavour (p<0.05).

Conclusion Smoking the flavoured tobacco product was associated with enhanced subjective experiences compared with the non-flavoured, suggesting a potential role for flavour regulation in reducing WP use. Mixed results were observed for toxicants exposure in relation to smoking flavoured compared with non-flavoured products suggesting the need for a more comprehensive assessment of the effects of other tobacco constituents and additives on toxicant exposure in WP smokers.

INTRODUCTION

During the last two decades, waterpipe (WP) tobacco smoking has gained popularity both in the USA and globally.[1 2] Data from the 2014 Population Assessment of Tobacco and Health estimated that 10.7% of young adults between the ages of 18 and 24 currently (last 30 days) smoke WP in the USA.[3] Additionally, recent data from the 2018 National College Health Assessment showed that 14.7% of college students have ever used WP.[4] A growing body of evidence suggests that WP use can lead to nicotine dependence and many of the known smoking-related illnesses such as cancer, cardiovascular disease and a variety of respiratory diseases.[5 6] Additionally, by providing a gateway to cigarette smoking, WP smoking also threatens to undermine success in curbing cigarette smoking in the USA.[7]

Several factors may have contributed to the surge in popularity of WP smoking, including the flavouring of WP tobacco, perception of reduced-harm and the promotion and marketing of WP tobacco products and venues on the internet and social media.[1 8 9] Flavoured tobacco products are widely available, and are commonly used by youths.[10] A national study examining flavoured tobacco product use among youth in 2013–2014 showed that the majority of youth tobacco users (81%) reported that the first tobacco they ever used was flavoured, with WP having the highest rate of flavoured tobacco use (89%).[10] Flavoured WP tobacco is usually manufactured by mixing tobacco with honey (molasses), glycerin and fruit-based additives and flavours.[11 12]

While some local jurisdiction in the USA (eg, the city of San Francisco) do ban retail sales of flavoured WP tobacco, a similar regulation on the national level does not exist. In 2016, the Food and Drug Administration (FDA) extended its regulatory authority over tobacco products to include WP.[13] This development creates an opportunity to provide evidence to inform the FDA on the potential of flavour regulation to curtail WP use among youth in the USA. Yet, empirical evidence of the effects of eliminating flavours on WP smokers' experiences and behaviour is limited. Two studies to date have investigated the effect of flavour variations on young WP smokers' (18–38 years old) experiences and exposures. The first showed that even a minor manipulation of flavour preference has a significant effect on smoking subjective experiences, and suggested the need to study the impact of completely eliminating flavour on the overall smoking experience and toxicant exposure.[14] As a proof of concept of the effect of eliminating flavour on WP smokers' experience, we conducted a pilot study involving 32 WP smokers, who were compared when smoking their preferred flavour versus non-flavoured tobacco.[15] Our preliminary findings indicated that compared with non-flavoured tobacco, study participants reported an enhanced smoking experience while using flavoured WP tobacco with no changes in puffing

behaviour. The current study expands this work by utilising a larger sample size (n=144) and assessing additional outcomes including nicotine withdrawal symptoms and urges to smoke. Accordingly, this study aims at comparing the effect of limiting flavour on (1) puffing behaviour, (2) exposure to nicotine and carbon monoxide, (3) subjective measures and (4) nicotine withdrawal symptoms and urges to smoke. We hypothesised that in comparison with flavoured WP tobacco, smoking non-flavoured tobacco will be associated with a reduced satisfactory smoking experience, less intense puffing and shorter smoking sessions resulting in reduced exposure to nicotine and carbon monoxide.

METHODS
Participants
A total of 144 participants were recruited from the metropolitan area surrounding Miami, Florida by placing flyers around WP venues, word of mouth and internet advertisements. Participants were healthy and smoked flavoured WP at least once/month in the last 6 months. Participants were between the ages of 18 and 30 years and provided informed consent for study participation. Exclusion criteria included: (1) self-reported history of health problems or psychiatric diseases; (2) regular use of medications; (3) self-reported current use of >5 cigarettes/month or other tobacco/nicotine products; and (4) currently pregnant or breast feeding.

Procedure
Eligible participants completed two counterbalanced 2-hour sessions that differed by tobacco condition (preferred flavour vs non-flavoured WP tobacco) separated by a 48-hour washout period to avoid carryover effect. Participants who had a specific preference were asked to bring their own preferred flavour/brand. Otherwise, participants were offered a variety of flavours at the lab to choose from. Prior to smoking, the WP head was filled with 15 g of session-specific tobacco product and covered with perforated foil.[16] Two pieces of quick-lighting charcoal were lit by study staff and placed on top of the foil. During each session, participants were seated in a comfortable recliner chair and were permitted to watch a movie of their choice. Participants were instructed to use WP ad libitum for up to 45 min, while puff topography was measured. Subjective effects were assessed, blood was sampled and exhaled carbon monoxide (eCO) concentration was measured before and after the 45-min WP use session.[17]

Measures
Demographics
Participants completed questionnaires assessing age, gender, ethnicity and student status.

WP smoking frequency and patterns
Participants self-reported their WP smoking frequency by responding to the following question: '*On average how many hookahs (heads/bowels) you usually smoke per month?*'.[18] Participants self-reported their WP smoking patterns by responding to the following questions: '*At what age did you smoke hookah for the first time in your life?*', '*What is the average time you usually spend during a hookah smoking session?*', '*Do you usually share the same hookah with others?*', '*Where do you usually smoke hookah?*'.[18] To assess flavour preference, participants were asked to '*specify the type of tobacco flavour you usually smoke*'.

Other tobacco product use
Participants self-reported use of any tobacco products (≤5 times/month) by answering the following question 'Do you regularly use any of the following tobacco/nicotine products?': *cigarettes, electronic cigarettes, cigar, Cigarillos/Little cigars, smokeless tobacco, other* and *none*.

WP puff topography
Puff topography was assessed using a validated instrument[15] with software that converted pressure signals to air flow (mL/s) data, producing measures of total time spent smoking, cumulative puffing time, puff duration, interpuff interval, number of puffs, total volume inhaled, average puff volume and maximum puff volume.

Plasma nicotine
Blood samples were centrifuged and plasma stored at −80℃, to be analysed later for nicotine concentration. The analysis was conducted using gas chromatography-mass spectrometry (GC-MS).[19] The assay's *limit of quantitation* (LOQ) was 1.0 ng/mL. LOQ is defined as the lowest concentration of nicotine that can be precisely determined using the GC-MS method. For nicotine analysis in our study, the LOQ was 1.0 ng/mL. Accordingly, any sample analysis yielding less than the LOQ was replaced with 1.0 ng/ mL. This approach is more conservative than assuming values below the LOQ were zero. Additional analyses were conducted to measure nicotine content in flavoured and non-flavoured tobacco products using GC-MS.

Exhaled carbon monoxide
Measurements of eCO were recorded before and 5 min after WP use via BreathCO monitor (Vitalograph, Lenexa, Kansas, USA).

Subjective measures
The WP Evaluation Scale
The WP Evaluation Scale (WES) is an 11-item questionnaire that was adapted from a scale used for cigarettes.[20 21] This scale assesses participants' perception of the smoked WP. For example, to assess satisfaction, participants were asked to evaluate the hookah they just smoked by answering the following question: 'Was it satisfying?'. Each item was rated on a 7-point Likert scale ('not at all' to 'extremely'). WES was administered post-WP smoking.

The Duke Sensory Questionnaire
The Duke Sensory Questionnaire (DSQ) has nine items that assess participants' sensory experience of the inhaled product. For example, participants were asked to evaluate the WP they just smoked by answering the following question: 'How much did you like the puffs?' All questions were rated on a 7-point Likert scale (not at all to extremely).[22] DSQ was administered post-WP smoking.

Harm perception
Harm perception was assessed using a 3-item scale.[23] The direct measure was; 'Compared with your usual flavoured brand, this WP is…' with answers on a 7-point scale ranging from 'a lot less harmful' to 'a lot more harmful'. To measure perceptions of WP's relative risk compared with cigarettes, we asked two questions: (1) 'How harmful is the WP to health?' (2) 'How harmful is smoking cigarettes for health?'. The answers to both were rated on a 7-point scale ranging from 1 (not at all harmful) to 7

(extremely harmful). Harm perception was measured post-WP smoking.

Minnesota Nicotine Withdrawal Scale

Minnesota Nicotine Withdrawal Scale (MNWS) consists of 11 items: (1) urges to smoke, (2) irritability/frustration/anger, (3) anxious, (4) difficulty concentrating, (5) restlessness, (6) hunger, (7) impatient, (8) craving nicotine, (9) drowsiness, (10) depression/feeling blue and (11) desire for sweets.[24] Items were presented as Visual Analogue Scales with the item centred above a horizontal line. Participants clicked a mouse to mark anywhere along the horizontal line, where the score is the distance between the mark and the left anchor, expressed as a percentage of total line length. The MNWS was measured pre-WP and post-WP smoking.

Questionnaire of Smoking Urges-Brief

Questionnaire of Smoking Urges-Brief (QSU) consists of 10 items that were adapted to WP smoking and rated on a 7-point Likert scale ranging from 0 (strongly disagree) to 6 (strongly agree).[25] Items are: (1) I have a desire to smoke now; (2) nothing better than smoking now; (3) if it were possible, I probably would smoke now; (4) I could control things better now if I could smoke; (5) all I want now is to smoke; (6) I have an urge for a WP; (7) a WP would taste good now; (8) I would do almost anything for a WP now; (9) smoking would make me less depressed; and (10) I am going to smoke WP as soon as possible. The 10 items form two factors: factor I (intention to smoke) and factor II (anticipation of relief from withdrawal). The QSU was assessed pre-WP and post-WP smoking.[26]

During each flavoured tobacco smoking session, the brand and flavour of the tobacco used, were recorded. In addition, following completion of all smoking sessions, participants were asked to evaluate the amount of smoke produced after each session by responding to this question 'Which waterpipe tobacco produced the greater amount of smoke during your smoking session' with the following answer options (1) flavoured tobacco, (2) non-flavoured tobacco and (3) no difference.

Data preparation and analysis

Characteristics of the study sample were summarised with means and SDs or proportions. Means were calculated for all subjective measures and compared by tobacco condition using two-tailed paired samples t-tests. Similar to previous studies,[15 27] plasma nicotine concentration values below LOQ were replaced with the LOQ (1 ng/mL), which is more conservative than assuming values below the LOQ were zero. Consumed tobacco for each condition was calculated by subtracting the remaining tobacco weight after each smoking session from the baseline tobacco weight (15 g). Sensitivity analysis was performed to evaluate whether results were influenced by using the complete dataset (n=144) with our pilot study data included vs excluding data from our pilot study (n=112). This analysis revealed that retaining data from the pilot study did not affect the direction of results, therefore we utilised the complete dataset for final analyses (n=144) (supplementary tables 1 and 2). Data for subjective measures were missing for one participant. Data for plasma nicotine samples were missing for 13 participants due to the inability to draw blood. The mean of the data from the other 131 participants at that time point was substituted and, when the data were analysed with and without these 13 participants, the results were unchanged. Therefore, all results for plasma nicotine concentration are reported with n=131. In order to

compare the effects of WP tobacco condition on nicotine withdrawal symptoms and plasma nicotine and eCO concentration, data were entered into a repeated measures ANOVA with two within-subject factors: time (pre-WP and post-WP) and WP tobacco condition (flavoured and non-flavoured). Huynh-Feldt corrections were used to adjust for violations of the sphericity assumption.[28] Pearson's correlation coefficients were calculated to assess the strength of the relationship between nicotine boost (change in plasma nicotine concentration pre–post) and nicotine withdrawal symptoms. Significance was set at $p < 0.05$. All analyses were performed in IBM SPSS V.21.[29]

RESULTS

Table 1 shows a detailed description of study participants' baseline characteristics. Study participants had a mean age of 21.8 (SD=2.9) years and the majority were men (n=85; 59%). The mean age for starting WP smoking among participants was 17.7 (SD=2.4) years. For participants' preferred brand, the most commonly used tobacco bands were Al Fakher (n=134), followed by Starbuzz (n=9), and Haze (n=1). For the non-flavoured condition, all participants smoked Zaghloul Nakhla, a non-flavoured WP tobacco preparation. There was a significant difference in the amount of consumed tobacco following the

Table 1 Baseline characteristics for the overall sample (n=144)

Variables	Overall sample
Gender (%)	
Female	41
Male	59
Race (%)	
White	67.4
Non-white	32.6
Hispanic (%)	58.3
Age (in years)*	21.8 (2.9)
Age of first smoking of waterpipe*	17.7 (2.4)
Student status (%)	67.4
Waterpipe uses/month*	6.1 (9.2)
Screening eCO*	2 (1.3)
Average time spent smoking waterpipe (%)	
Less than 30 min	9
30–60 min	60.4
More than 60 min	30.6
Tobacco use (%)†	
Cigarettes	37.5
E-cigarettes	1.3
Cigars	0.6
Sharing waterpipe with others (%)	91.6
Location of waterpipe smoking (%)	
At home	22.2
At friends' place	27.1
At a public place	50.7
Preferred flavours (%)	
Mixed fruits	33.5
Apple	31.9
Mint	22.2
Grape	10.4
Other‡	2

*Data presented as mean (SD).
†Tobacco use of ≤ 5 times/month.
‡Other includes mango, watermelon and blueberry.
eCO, exhaled carbon monoxide.

Table 2 Waterpipe smoking topography measures by flavour condition conditions (n=143)*

Topography parameters	Flavoured tobacco		Non-flavoured tobacco		P value
	Mean	SD	Mean	SD	
Smoking time, min	42:23	7:52	40:32	9:22	0.01
Cumulative puffing time, min	5:37	3:36	4:48	2:56	0.003
Puff duration, s	3.4	1.5	3.2	1.4	0.32
Interpuff interval, s	27	17.4	29.7	19.6	0.06
Number of puffs	109.1	76.7	101	77.3	0.09
Total volume, L	66.8	48.3	66.7	45.6	0.97
Puff volume, L	0.68	0.41	0.79	0.48	0.01
Maximum puff volume, L	1.64	0.79	2.05	1	<0.001

*One participant was missing data for topography.

smoking session with a greater amount of non-flavoured tobacco consumed (5.3 g) compared with flavoured (4 g) (p<0.05). Nicotine content analysis of tobacco used in both conditions revealed that on average, every 1 g of non-flavoured tobacco has 0.45 mg of nicotine, while every 1 g of flavoured tobacco has 0.22 mg of nicotine.

WP smoking topography
Significant differences were observed between the two conditions for the following measures: smoking time, puffing time, puff volume and maximum puff volume (table 2). Longer mean smoking and longer mean cumulative puffing time were observed for the flavoured tobacco smoking session compared with non-flavoured (42:23 vs 40.32 min and 5:37 vs 4:48 min, respectively; p<0.05). However, during the non-flavoured tobacco smoking session, greater puff volume and greater maximum puff volume were observed compared with flavoured tobacco (0.79 vs 0.68 L and 2.05 vs 1.64 L, respectively; p<0.01).

Plasma nicotine
There was no significant time by condition interaction for mean plasma nicotine concentration (F<1, p>0.05) demonstrating that changes in plasma nicotine concentration across time did not depend on the tobacco flavour condition. Mean pre-WP plasma nicotine concentration for the flavoured tobacco condition was 1 ng/mL (SEM=0.06) and increased to 8.5 ng/mL (SEM=0.7) post-WP resulting in a nicotine boost of 7.5 ng/mL (SEM=0.7). For the non-flavoured tobacco condition, mean pre-WP plasma nicotine concentration was 1 ng/mL (SEM=0.05) and increased to 8.4 (SEM=0.8) post-WP resulting in a nicotine boost of 7.4 ng/mL (SEM=0.6). Average plasma nicotine levels at post-smoking time points were not significantly different between flavoured and non-flavoured tobacco conditions (p>0.05; see supplementary figure).

Exhaled carbon monoxide
A significant time by condition interaction was observed for eCO level (F (1, 142)=5.3, p<0.05) demonstrating that changes in eCO level across time depended on tobacco condition. Mean eCO level for the flavoured condition increased from 1.8 ppm (SEM=0.1) pre-WP to 22.8 ppm (SEM=2.1) post-WP with an overall change of 21 ppm (SEM=2). For the non-flavoured condition, the mean eCO level increased from 2 ppm (SEM=0.1) pre-WP to 27.7 ppm (SEM=1.9) post-WP with an overall change of 25.7 ppm (SEM=1.9). As figure 1 shows, there
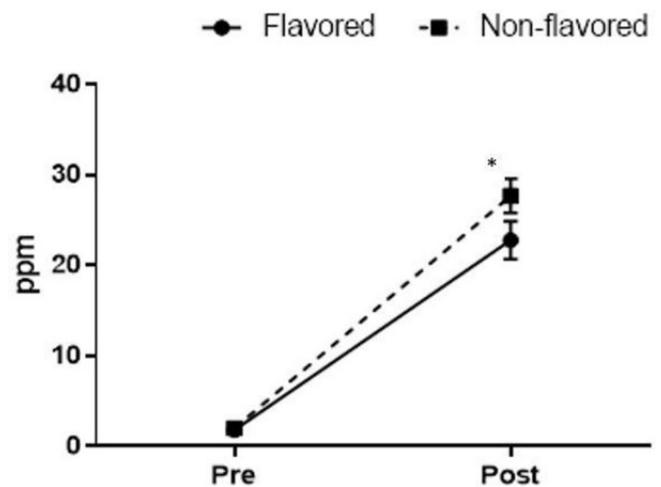
† One participant was missing data for eCO. * indicates significant differences.

Figure 1 Means (±SEM) for exhaled carbon monoxide levels pre/post-WP by flavour condition (n=143).† WP, eCO, exhaled carbon dioxide; WP, waterpipe.

was a higher boost in eCO for non-flavoured tobacco compared with flavoured tobacco (p>0.05).

Subjective measures
Participants' assessment of each tobacco product's ability to generate smoke showed that 69.8% of participants believed that flavoured tobacco produced more smoke, while 20.9% believed that non-flavoured tobacco produced more smoke and 9.3% believed there was no difference (p<0.05).

Figures 2 and 3 depict mean ratings for WES and DSQ, respectively. For the WES, significant differences were observed between the two tobacco conditions for all indices except for 'did it reduce your craving?'. For all items, values were greater after smoking flavoured tobacco compared with non-flavoured tobacco (p<0.01), except for 'Did it make you feel nauseous?' which was greater after smoking the non-flavoured tobacco (p<0.05). For the DSQ, significant differences were observed between the two tobacco conditions for the following indices: 'How much did you like the puffs?', 'How satisfying were the puffs?', 'How similar to your own brand/flavour were the puffs?', 'Rate the strength of the puffs on the windpipe' and 'How high in nicotine were the puffs?'. For each of these items, scores were greater after smoking flavoured tobacco (p<0.01), except for 'How high in nicotine were the puffs?' which was greater after smoking non-flavoured tobacco (p<0.05).

For both tobacco conditions, there were no significant differences in harm perception among participants towards cigarette, and WP smoking in general (p>0.05). However, harm perception scores were significantly higher for non-flavoured tobacco when compared with the participant's usual flavoured brand (p<0.05) (figure 4).

Table 3 shows detailed results for MNWS. Across all items, there was no significant interaction between condition and time, demonstrating that changes in MNWS across time did not depend on the tobacco flavour condition. There was a significant effect for time across the following MNWS items: 'Urges to smoke a waterpipe', 'Difficulty concentrating', 'Hunger', 'Craving a waterpipe/Nicotine' and 'Drowsiness'. Mean scores
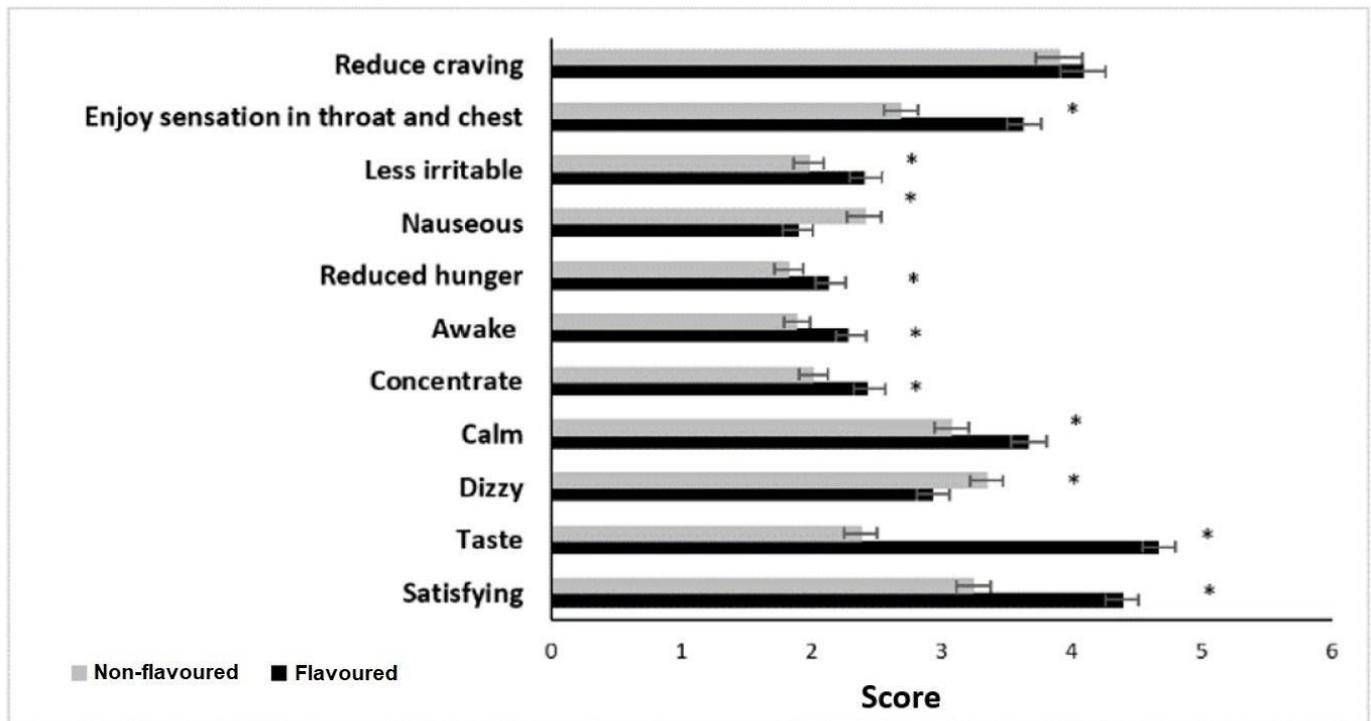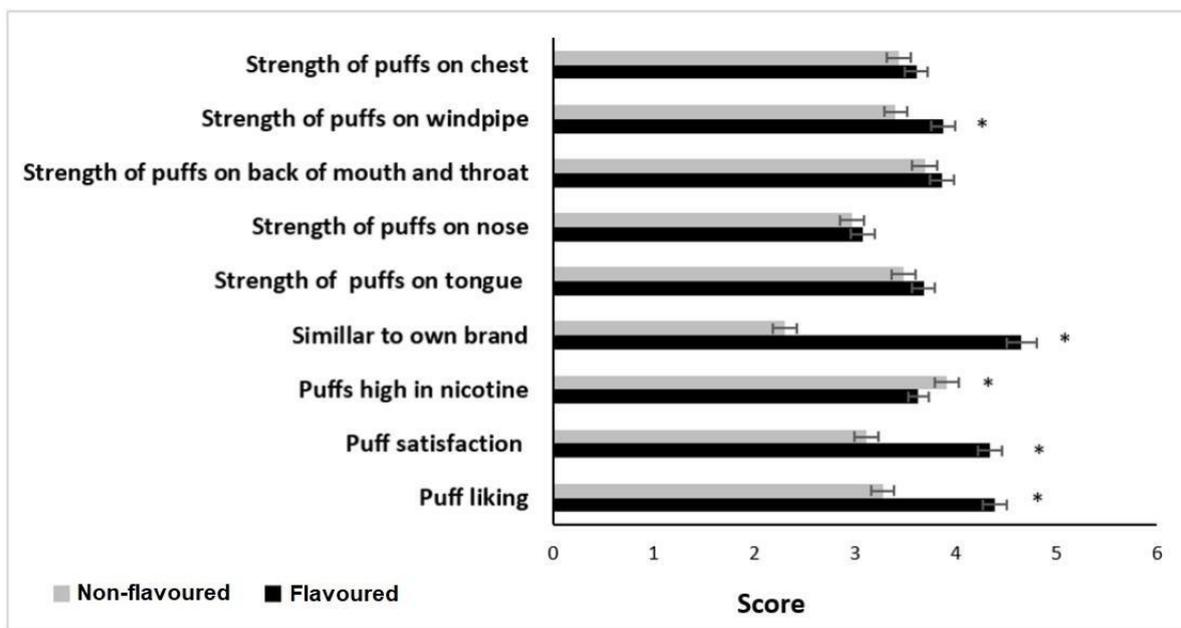
† One participant was missing data for the flavoured tobacco sessions. * indicates significant differences.

Figure 2 Means (±SEM) for post-WP subjective responses for Waterpipe Evaluation Scale by flavour condition (n = 143).† WP, waterpipe.

for all the above-mentioned items reduced significantly from presmoking to post-WP except for 'hunger' which increased from pre-smoking to post-WP. For factors I and II of the QSU-Brief (table 3), there was no significant interaction between condition and time, demonstrating that changes in factors I and II across time did not depend on the tobacco condition. There was a significant effect of time observed for both factors, in which scores were reduced significantly from pre-WP to post-WP.

Following the flavoured tobacco smoking session, plasma nicotine boost was correlated with pre-WP urges to smoke ($r=0.28$, $p \leq 0.05$), craving ($r=0.18$, $p \leq 0.05$) and with QSU factor I ($r=0.29$, $p \leq 0.05$) and factor II ($r=0.20$, $p \leq 0.05$). Similarly, following the non-flavoured smoking session, plasma nicotine boost was correlated with pre-WP urges to smoke ($r=0.26$, $p \leq 0.05$), craving ($r=0.20$, $p \leq 0.05$) and with QSU factor I ($r=0.20$, $p \leq 0.05$) and factor II ($r=0.19$, $p \leq 0.05$).

† One participant was missing data for the flavoured tobacco sessions. * indicates significant differences.

Figure 3 Means (±SEM) for post-WP subjective responses for Duke Sensory Questionnaire by flavour condition (n = 143).† WP, waterpipe.
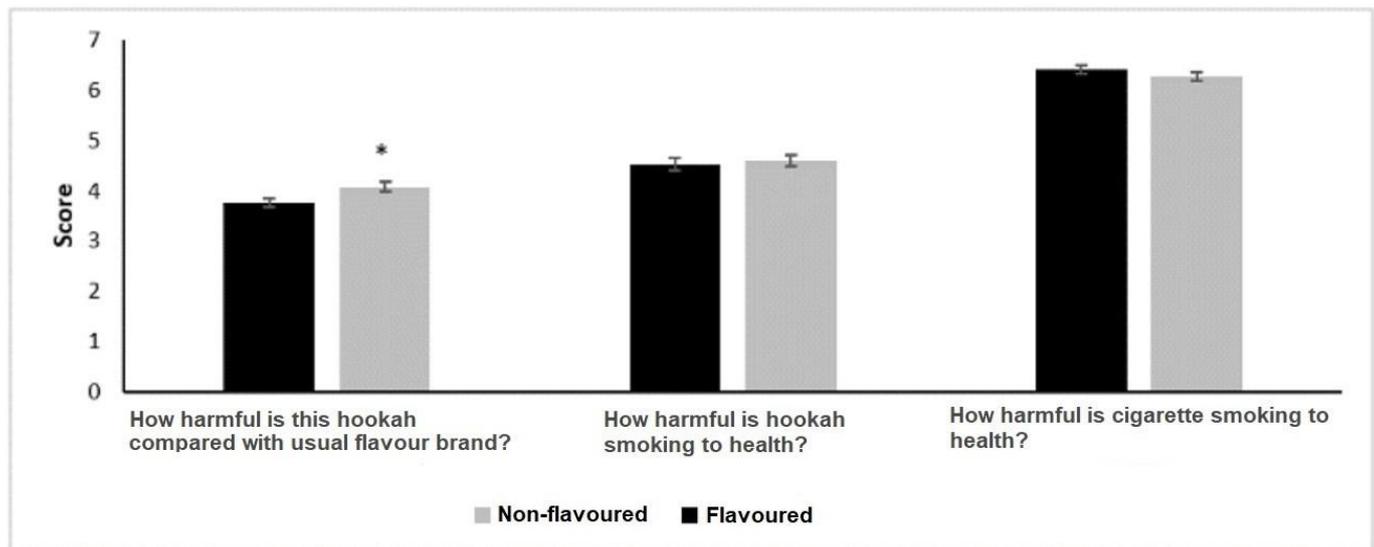
† **One participant was missing data for the flavoured tobacco sessions.** * **indicates significant differences.**

Figure 4 Means (±SEM) for post-WP harm perception responses by flavour condition (n = 143).† WP, waterpipe.

DISCUSSION

This study demonstrates the substantial effects of eliminating tobacco flavour on puffing behaviour, toxicant exposure and subjective experiences among young adult WP smokers. Following smoking flavoured tobacco, WP smokers reported an overall enhanced smoking experience with higher levels of enjoyment and satisfaction and lower harm perception. While there was no difference in plasma nicotine concentration among participants following smoking both tobacco products, greater

Table 3 ANOVA results for withdrawal symptoms/smoking urges by time (pre vs post) and condition (flavoured vs non-flavoured) (n=143)

	Condition		Time		Condition × time	
	F	P value	F	P value	F	P value
Minnesota Nicotine Withdrawal Scale						
Urges to smoke a waterpipe	<0.1	n.s	66.4	<0.01	0.4	n.s
Irritability/ frustration/anger	<0.1	n.s	1.1	n.s	0.1	n.s
Anxious	1.2	n.s	2.4	n.s	0.4	n.s
Difficulty concentrating	2.1	n.s	7.2	<0.01	1.5	n.s
Restlessness	1.8	n.s	0.2	n.s	0.5	n.s
Hunger	4.4	<0.05	22.5	<0.01	0.6	n.s
Impatient	2.5	n.s	0.4	n.s	0.2	n.s
Craving a waterpipe/ nicotine	0.3	n.s	37.8	<0.01	<0.1	n.s
Drowsiness	1.8	n.s	40.4	<0.01	2.7	n.s
Depression/ feeling blue	1.4	n.s	<0.1	n.s	0.4	n.s
Desire for sweets	1.6	n.s	3.9	n.s	0.5	n.s
Questionnaire of Smoking Urges (QSU)						
Factor 1*	0.4	n.s	148.8	<0.01	1	n.s
Factor 2†	1.2	n.s	43.2	<0.01	0.2	n.s

*Intention to smoke.
†Anticipation of relief from withdrawal.
ns, non-significant.

levels of eCO were recorded among participants following smoking the non-flavoured tobacco.

In line with our pilot study,[15] the results show that subjective positive and negative smoking experiences were dependent on the flavour condition, where smoking flavoured WP tobacco enhanced positive experiences and reduced negative responses. For example, participants found the flavoured tobacco to be more satisfying, calming, good tasting, well-liked and experienced less dizziness and nausea compared with the non-flavoured tobacco. This is likely because flavouring and other additives in WP tobacco reduce and mask the harsh taste of raw tobacco, facilitating a more positive WP smoking experience.[10] In contrast, non-flavoured tobacco has a low amount of humectant (glycerin) and molasses, which is associated with a higher burning temperature of tobacco and low production of particulate matter (PM).[30 31] Indeed, our study participants reported that non-flavoured tobacco is less efficient in generating the usual smoke cloud, for which PM is a major source. It is likely that in their attempt to produce the usual smoke, the participants were taking deeper puffs that enhanced the combustion process leading to more eCO production, and nausea associated with higher levels of exposure to CO.[31 32] Our data support such a possible scenario, where the non-flavoured condition was associated with larger puff volumes and higher eCO boosts compared with the flavoured condition. These findings validate our pilot work that showed a trend towards larger puffs and greater eCO levels among participants following smoking non-flavoured tobacco.[15] Accordingly, merely eliminating flavour may lead to compensating smoking behaviour, which in turn can increase exposure to some toxicants.

Another important piece of this puzzle is offered by the unexpected equal levels of nicotine exposure in the flavoured versus non-flavoured conditions, which mirrored the similarity in the level of suppression of nicotine withdrawal symptoms and urges to smoke between the two conditions. When we planned the study, we hypothesised that because the flavour condition would be more enjoyable, participants would likely get more nicotine smoking the flavoured products and accordingly greater suppression of withdrawal symptoms. However, what we are learning—and this knowledge is still unfolding—is that many

factors likely will influence drug self-administration including degree of nicotine dependence, composition of the product itself other than flavour (eg, concentration of humectant), puffing behaviour, exposure to other toxicants, nicotine content in the product itself and nicotine yields in the mainstream smoke. These factors will influence nicotine exposure in different directions. For example, in our study, nicotine content in non-flavoured tobacco was higher than in the flavoured tobacco. On the other hand, flavoured WP tobacco has higher levels of humectant which has been shown to be associated with higher nicotine yields in WP mainstream smoke.[30] It seems, however, that nicotine dependence level will likely balance out these factors so smokers will adapt their smoking to self-administer their usual dose of nicotine. This assumption is supported by our findings showing a positive correlation of urges to smoke and craving with nicotine boost regardless of tobacco condition and other factors.

While this study addresses important gaps in the literature, it has some limitations. The laboratory setting inevitably is different from the typical WP lounge vibe. However, to simulate the WP café environment, our laboratory was furnished with a reclining chair, and participants were invited to choose a movie to watch while smoking. These features made the session area more relaxing and entertaining to mimic a natural smoking experience. Additionally, in our study, participants smoked WP alone in a laboratory environment. Therefore, the results may differ outside the laboratory as WP is commonly shared with peers.[33] Nevertheless, our research represents a critical step in understanding the effects of flavour and tobacco composition in shaping the overall WP smoking experience.

In this laboratory crossover design study, we were able to demonstrate that flavoured WP tobacco smoking is associated with enhanced subjective smoking experiences, and lower harm perception compared with non-flavoured WP tobacco. On the other hand, eliminating flavour was associated with taking larger puffs and greater exposure to CO. Our findings suggest a complex influence of flavour and other tobacco additives on smokers, and how changes in one or more can lead to a cascade of compensatory and adaptive behaviours by smokers who influence exposure to toxicants. For example, glycerin is commonly added to flavoured WP tobacco because of its humectant, sweetening and preservative properties.[34–36] It is also added to flavoured WP tobacco to increase smoke production since glycerin produces mist when heated.[37] This was perhaps reflected in our study participants reporting greater smoke production following smoking the flavoured WP tobacco compared with non-flavoured. This indicates the need for a more comprehensive assessment of the effects of tobacco constituents and additives, specifically on the use of humectants and its effect on smoking behaviour and toxicant exposure. This is also in line with recent policy guidance released by the FDA. The guidance highlighted remaining issues that need to be addressed before updating regulations for WP tobacco products, which include how WP might be used in the absence of flavours.[38] While providing strong evidence on the potential of flavour limitation on users' experience, our study results also can frame the parameters of future studies needed by the FDA to regulate flavoured WP tobacco. These can include comparing multiple tobacco compositions in terms of flavours, and humectant contents (eg, high glycerin vs low glycerin). Such comparisons will lead to a better understanding of how flavouring and other additives are shaping the overall WP smoking experiences and exposures.

What this paper adds

- ► Flavoured tobacco has a substantial effect on enhancing the waterpipe (WP) smoking expierence.
- ► This study demonstrates that flavoured WP tobacco smoking is associated with enhanced subjective smoking experiences, and lower harm perception compared with non-flavoured WP tobacco.
- ► Eliminating one component of the tobacco (flavour) will lead to a cascade of compensatory and adaptive behaviours by smokers who influence exposure to toxicants.

Key messages

What is the key question?
- ► What is the main impact of flavour manipulation on waterpipe (WP) smokers' behaviour, toxicant exposure and subjective experiences?

What is the bottom line?
- ► Despite the clear association between flavour and enhanced subjective experiences, smoking flavoured tobacco was not associated with higher exposure to toxicants compared with non-flavoured tobacco.

Why read on?
- ► This study provides critical information for regulatory actions regarding the substantial effects of eliminating tobacco flavour on the overall smoking experiences among young adult WP smokers.

ORCID iDs
Ziyad Ben Taleb http://orcid.org/0000-0001-6894-5535
Mohammad Ebrahimi Kalan http://orcid.org/0000-0001-7709-5392

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