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Clove cigarette smoking: biochemical, physiological, and subjective effects

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Abstract

Alternative tobacco products such as clove (kreteks) and bidi cigarettes have become increasingly popular among US smokers. The nicotine content of a popular clove cigarette (Djarum Special) filler averaged 7.4 mg; conventional cigarettes contained 13.0 mg. However, smoke yields from standardized machine-smoking analysis indicated it delivered more nicotine, carbon monoxide (CO), and tar than conventional cigarettes. In a clinical study, nicotine delivery, physiologic, and subjective effects of the clove cigarette were compared to their own brand of cigarette in 10 adult smokers (7 males). Average time to smoke the clove cigarette (549 s) and number of puffs (15.1) were significantly greater than own brand (314 s and 9.4 puffs). Increases in venous plasma nicotine and exhaled CO after smoking the clove cigarette (17.4 ng/ml; 6 ppm) were similar to those after own brand (17.6 ng/ml; 4.5 ppm). Maximal changes in heart rate (HR), systolic, and diastolic blood pressures (BP) did not differ significantly between the clove and own brand of cigarette. Compared to their own brand of cigarette, the clove cigarette was rated as better tasting and being distinctly different. Our findings indicate that clove cigarettes deliver significant quantities of nicotine, CO, and presumably other toxic components of tobacco smoke. Taste satisfaction, aromatic odor, and novelty may contribute to their appeal to young smokers.

Keywords: Kreteks; Alternative cigarettes; Nicotine; Smoking

1. Introduction

The Federal Trade Commission (FTC) periodically publishes nicotine, carbon monoxide (CO), and tar delivery yields from machine smoking of domestic cigarettes (Federal Trade Commission, 2000); however, no such data are readily available for foreign cigarettes that penetrate the US market. Bidis and clove cigarettes are imported tobacco products popular among US smokers. In previous reports, the physical composition and clinical effects of bidi cigarettes have been described (Malson and Pickworth, 2002; Malson et al., 2001, 2002). However, no clinical reports on the effects of clove cigarette smoking have been published.

Clove cigarettes are produced in Indonesia and exported throughout the world. They are composed of a mixture of tobacco (60–80%) and ground clove buds (20–40%), available with or without filters, and are usually machine rolled in white, brown, or black paper (California State Department of Health Services, 1988). The cigarettes are usually marketed in brightly colored packaging and have a distinctly different aroma than traditional cigarettes because of the cloves. Eugenol, an analgesic, is naturally occurring in cloves and is present in milligram quantities in the clove cigarette filler (Claus and Tyler, 1965). Like menthol, eugenol may diminish the harshness of the tobacco smoke (American Academy of Pediatrics Committee on Substance Abuse, 1991; Centers for Disease Control and Prevention (CDCP), 1985). In fact, clove cigarettes are referred to as "trainer cigarettes," implying that the use of clove cigarettes may prove to be a gateway product to conventional cigarettes (American Academy of Pediatrics Committee on Substance Abuse, 1991; Guidotti and Laing, 1992).

A significant proportion of young smokers in the United States use clove cigarettes. A 1999 national survey found

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that 1.9% of middle school students and 5.8% of high school students currently smoked clove cigarettes (CDCP, 2000). However, there have been no prevalence rates published for clove smoking among adults.

Although clove smoking has been documented in epidemiological studies and in survey data, there are no clinical studies of their acute physiological and subjective effects. In the present report, the nicotine content of the filler rod and smoking machine estimates of nicotine and tar delivery from a popular brand of clove cigarette were determined. The clove cigarette was then used in a clinical study to compare changes in plasma nicotine levels, exhaled CO, cardiovascular, and subjective effects with a conventional cigarette.

2. Methods

2.1. In vitro studies

2.1.1. Physical composition

The clove cigarette used in the present study was Djarum Special, manufactured for Kretek International (Moorpark, CA) by PT Djarum (Kudos, Indonesia) and was obtained from a local tobacco outlet. The nicotine content of the clove cigarettes was determined by methods described in Malson et al. (2001). Briefly, rod filler and cigarette weight were determined from an average of 10 cigarettes. The rod filler (“tobacco”) was removed, weighed and pooled for chemical analysis. Nicotine concentration was determined using gas chromotographic techniques. Using this method, the limit of detection was 300 pg and the limit of quantitation was 4.5 ng. For the purposes of comparison, a similar analysis was conducted on the four popular conventional cigarettes usually smoked by the participants.

2.1.2. FTC smoke analysis

Delivery of nicotine, tar, and CO from the clove cigarette was measured using machine-smoking methods based on those developed by the FTC (Federal Trade Commission, 2000; Federal Register, 1967; Pillsbury, 1996) and outlined by the International Standards Organization (ISO) in ISO methods 3308, 3402, 10362-1, and 10315. Clove cigarettes were smoked onto a single 44-mm diameter glass fiber filter commonly referred to as a Cambridge filter pad (Fidus Instrument, Richmond, VA) using an automated Filtrona SM342 smoking machine (Filtrona Instruments & Automation, Milton Keynes, UK) equipped with a CO analyzer. Before smoking, the cigarettes and the Cambridge filter pads were conditioned at 22 °C and 60% relative humidity for at least 24 h.

According to standardized smoking practices, the smoking machine was calibrated to take one puff of 2-s duration and 35-ml volume every 60 s and to maintain an average airflow velocity over the cigarettes of 200±30 mm/s (Pillsbury, 1996). The puff volume (35.0±0.1 ml) was measured using a 50-ml soap film glass burette (Filtrona Instruments, Richmond, VA). Airflow velocity (200±50 mm/s) at the individual ports was measured using a Filtrona VMD100 velocity measurement digitizer (Filtrona Instruments & Automation) connected to a Schiltknecht ThermoAir2 Thermoelectric anemometer equipped with an omnidirectional probe (Schiltknecht Messtechnick, Gossau, Switzerland).

CO was measured from the vapor phase portion of the mainstream cigarette smoke and nicotine was measured from the CFP using gas chromotography techniques. Total particulate matter (TPM) was obtained by calculating the weight difference in the CFP after the smoking process. Tar is calculated by subtracting the water and nicotine from the TPM. All analyses were done in triplicate. A University of Kentucky reference cigarette (1R4F) and a blank cigarette (no nicotine) were run in triplicate with the clove cigarette analysis.

2.2. Clinical study

2.2.1. Participants

Ten (10) research volunteers participated in the study; 7 males and 3 females. The average age of the participants was 30.3 years (range=19–46) and their average weight was 78.5 kg (range=51.8–106.4 kg). Participants smoked an average 21.3 cigarettes a day (range=13–30) for 13.4 years (range=5–25). The participants regularly smoked filtered, conventional cigarettes with an average FTC-yield of 1.1 mg nicotine (range=0.7–1.4) and 14.5 mg of tar (range=9–19) (Federal Trade Commission, 2000). Their scores on the Fagerström Test for Nicotine Dependence averaged 5.4 (range=3–9; Heatherton et al., 1991); scores above five indicate a high degree of nicotine dependence (Fagerström et al., 1990). Participants were required to have previously smoked either clove or bidi cigarettes without adverse reactions. Four participants self-reported previous clove cigarette smoking; all participants had smoked bidis.

Participants were recruited from the local community by advertisements in newspapers, radio, coffee shops, and tobacco shops where alternative cigarettes are sold. They underwent medical and psychological screening approved by the NIDA, Institutional Review Board (IRB) to verify their good health and ability to safely participate in the study. Prior to participation in the study, subjects signed an informed consent document approved by the local IRB. The consent form met guidelines established by the US Department of Health and Human Services. Volunteers were paid for their participation in the study.

2.2.2. Design and procedures

The study was performed on an outpatient basis at NIDA, Intramural Research Program (IRP). Participants reported to the laboratory for two experimental sessions between 9:00 a.m. and 3:00 p.m. Participants were not asked to maintain tobacco abstinence on experimental days

and the experimental cigarette was not the first cigarette of the day. This was an open-label, within-subject design comparing two cigarette conditions: a clove cigarette (Djarum Special) and the participant's own brand of a filtered conventional cigarette. The data for the present report were taken from two sessions of a study that consisted of six experimental sessions; presentation of the conditions was randomized. Data from the other four experimental days were used to determine the effects of Eclipse (Philip Morris, Richmond, VA) cigarettes (Pickworth et al., 2002a). The researchers supplied the clove cigarette and the subjects brought a cigarette of the brand that they ordinarily smoked. Subjects were instructed to smoke ad libitum to a line of 50 mm on the tobacco rod of each cigarette.

2.2.3. Dependent measures

2.2.3.1. Plasma nicotine levels. Blood samples were collected before smoking, and 2, 5, 10, 15, 30, and 60 min after smoking and were kept on ice until centrifugation and separation of plasma. Plasma was frozen (−20 °C) until the time of analysis. Plasma nicotine was measured using a thermoionic specific detector (Labstat Kitchner, Ontario, Canada). The lower limit of quantification was 1 ng/ml.

2.2.3.2. Exhaled carbon monoxide. Exhaled CO was measured in parts per million (ppm) with a CO monitor (Vitalograph, Lenexa, KS). Exhaled CO was measured before and 15, 30, and 60 min after smoking.

2.2.3.3. Cardiovascular measures. Systolic and diastolic blood pressure (BP) and heart rate (HR) were measured using an automated cardiovascular monitor (Datascope, Paramus, NJ). Cardiovascular measures were collected before and 2, 5, 10, 15, 30, and 60 min after smoking.

2.2.3.4. Substance delivery measures. As the subject smoked ad libitum, time to smoke (seconds) and the number of puffs per cigarette were recorded by a research assistant.

2.2.3.5. Subjective measures. Twenty minutes after smoking, subjects completed two questionnaires about the overall cigarette smoking experience. This interval was used in previous research on nonconventional cigarettes (Malson et al., 2002; Pickworth et al., 1999). Cigarette satisfaction was evaluated with the Cigarette Evaluation Scale (CES; Rose et al., 2000; Westman et al., 1992) and sensory effects were determined using the Duke Sensory Questionnaire (DSQ; Behm and Rose, 1994). Both questionnaires employ an anchored, seven-point Likert scale where 1="Not At All" and 7="Extremely". Individual items from the CES were collected and composites of several items were created to measure characteristics such as Satisfaction (satisfaction, good taste), Psychological Reward (calm, concentration, wakefulness, reduction of hunger, irritability), and Aversion (dizziness, nausea) (Brauer et al., 2001). The Enjoyment of Sensation (sensations in throat and chest) and Craving Reduction items were analyzed separately.

Individual items from the DSQ were collected, and a composite of several items was created to measure overall cigarette strength (puff strength on tongue, nose, mouth and throat, windpipe, and chest; maximum score=35; range 7–35) (Malson et al., 2002).

2.2.4. Data analysis

To adjust for baseline differences among subjects, the baseline BP, HR, and plasma nicotine levels were subtracted from subsequent measures. Statistical analyses were conducted using repeated-measures analysis of variance (ANOVA) (Winer et al., 1991). The within-subject factors were cigarette condition (two levels: clove and own brand) and time (six levels; 2, 5,10, 15, 30, 60 min). The Greenhouse–Geisser epsilon was used in the ANOVA to adjust for degrees of freedom in within-subject analyses. Post hoc dependent *t* tests were used when the ANOVA revealed significant main effects of time or cigarette or the interaction. Subjective effects of the cigarettes were analyzed using dependent *t* tests. Data are presented as mean±S.D. unless otherwise indicated.

3. Results

3.1. In vitro studies

Table 1 provides physical characteristics of the clove cigarette and the average of four popular US cigarettes (Malson et al., 2001). The total nicotine content of filler in the rod of the clove cigarette averaged 7.39 mg. The manufacturer acknowledges that 60% of the rod is composed of tobacco and 40% is ground clove buds.

Table 2 provides standardized machine-smoking yields for the Djarum Special clove cigarette and the average FTC yields of four popular US cigarettes. Compared to the

Table 1
Physical characteristics of a popular clove cigarette

	Cigarette weight (mg)	Rod filler weight (mg)	Nicotine filler concentration (mg/g)	Nicotine per cigarette rod (mg)	Concentration of nicotine in tobacco* (mg/g)
Djarum Special	1071.2	869.6	8.5	7.39	14.2
Conventional cigarette	925.8	713.2	18.3	13.0	N/A

* Assumes that the tobacco weight is approximately 60% of the rod filler weight and that all of the nicotine is in the tobacco component of the filler. Conventional cigarette is an average of four filtered US cigarettes: Marlboro, Newport, Camel, and Kool (Malson et al., 2001). N/A=not available.

Table 2
FTC values of a popular clove cigarette

	Puffs	TPM	Nicotine	CO	Tar
Djarum Special	19.4±0.5	53.7±8.0	2.0±0.2	28.3±0.4	46.8±6.6
Conventional cigarette	10.3*	N/A	1.1±0.1	15.5±1.7	16.3±1.3
University of Kentucky (1R4F)	N/A	11.4±0.5	0.8±0.05	14.3±1.6	9.9±0.6

Values are mean±S.D. of measures: puffs to consume cigarette rod at 2 s/puff, 35 ml/puff. Values for TPM (total particulate matter), nicotine, CO, and tar are milligrams per cigarette. Conventional cigarette is an average of four filtered US cigarettes: Marlboro, Newport, Camel, and Kool (Federal Trade Commission, 2000).

* Puff values based on an average of three filtered US cigarettes: Marlboro, Newport, Kool (Pickworth et al., 2002b). N/A=not available.

conventional cigarettes, the clove cigarettes delivered more tar, nicotine, and CO under machine-smoking conditions. The data from the University of Kentucky reference cigarette (1R4F) are also presented in Table 2. These values are within 1 S.D. of the FTC standards for that cigarette—indicating the validity of the analysis.

3.2. Clinical study

3.2.1. Plasma nicotine

Plasma levels of nicotine increased after smoking both the clove and their own brand of cigarette (Fig. 1). The increase was greatest 2 min after smoking, thereafter plasma levels of nicotine diminished over the course of the 1-h session. The ANOVA indicated no significant effect of cigarette, but a significant main effect of time [$F(54,6)=46.6$, $P<.001$]. There was no significant cigarette×time interaction.

3.2.2. Heart rate

As shown in the lower panel of Fig. 1, heart rate increased after smoking either the clove or the own brand of cigarette. The increase was greatest 2 min after smoking and the decrease to baseline levels occurred within 15 min. The ANOVA revealed no significant effect of cigarette but a significant main effect of time [$F(54,6)=12.9$, $P<.001$). There was no significant cigarette×time interaction.

3.2.3. Blood pressure

Systolic BP increased transiently after smoking both cigarettes. The ANOVA indicated a significant main effect of time [$F(5,45)=4.32$, $P<.01$], but not a significant difference between cigarettes or a cigarette time interaction. Diastolic BP was not significantly changed after smoking either of the cigarettes.

3.2.4. Exhaled CO

Exhaled CO increased after smoking each of the cigarettes. Maximum increase in CO occurred 15 min after smoking. The CO boost averaged 6.0 (±3.4) ppm after the clove cigarette and 4.5 (±3.1) ppm after own brand. The ANOVA indicated that there was no significant main effect of cigarette, but there was a significant effect of time [$F(27,3)=17.2$, $P<.001$]. There was no significant cigarette×time interaction.

3.2.5. Substance delivery factors

As shown in the upper panel of Fig. 2, participants took an average of 549.6 (±57.6) s to smoke the clove cigarette, but 314.3 (±33.4) s to smoke their own brand of cigarettes; a difference that was significant [$t(9)=5.20$, $P<.01$]. In the lower panel of Fig. 2, puffs per cigarette are illustrated. Subjects took significantly more puffs to consume the clove cigarette (15.1±1.2) than their own brand of cigarette [9.4±0.9; $t(9)=8.33$, $P<.001$].

3.2.6. Subjective measures

Analyses of the CES indicated that subjects liked the taste of the clove cigarette (6.1±0.5) significantly more than their usual brand of cigarette (4.8±0.4) [$t(9)=2.25$, $P<.05$]. Clove cigarette smoking also caused a greater reduction in hunger for food (2.1±1.5) than their own brand (3.0±1.9) [$t(9)=2.1$, $P<.10$]. On the DSQ, subjects rated the clove cigarette (1.9±1.2) as significantly different from their own brand of cigarette (6.5±1.3) [$t(9)=10.2$, $P<.001$]. All other

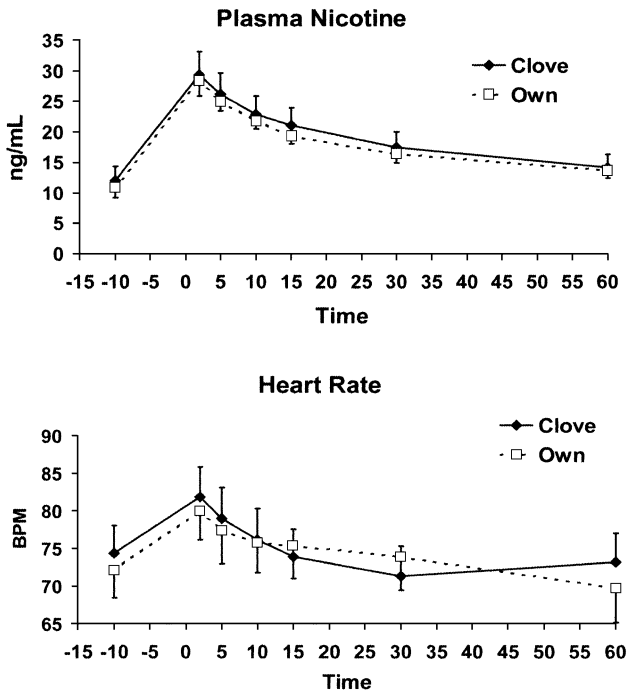

Fig. 1. Plasma nicotine levels (upper panel) and heart rate (lower panel) before (−10 min) and for 60 min after smoking a clove (Djarum Special) or the participant's usual brand of cigarette. Subjects (n=10) smoked a single cigarette ad libitum. Values represent mean (±S.E.M.) of plasma nicotine (ng/ml) and heart rate in beats per minute (BPM).

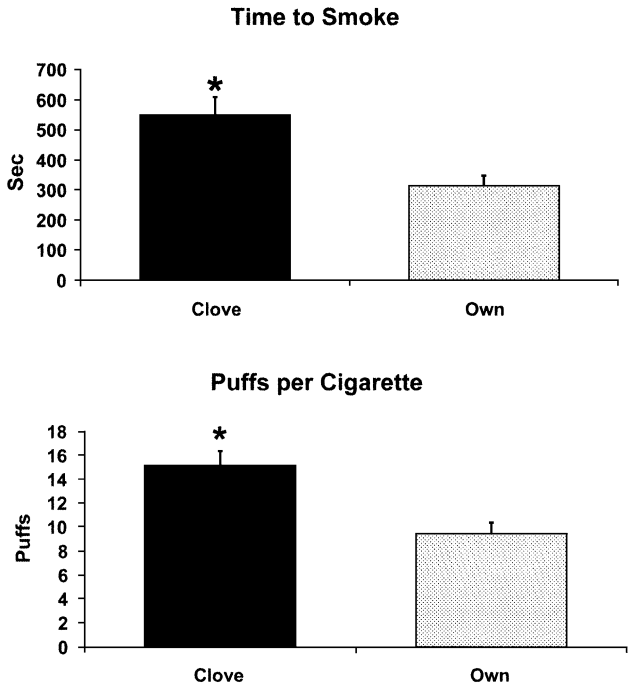

Fig. 2. Substance delivery factors, time to smoke (upper panel), and puffs per cigarette (lower panel), from 10 participants smoking either the clove cigarette (Djarum Special) or their usual brand of cigarette (Own). Values are mean (±S.E.M.). * indicates significant difference between clove and own brand (paired *t* test).

differences in subjective items were not statistically significant.

4. Discussion

Although the cigarettes most often consumed by teenagers are the heavily advertised brands, such as Marlboro, Camel, and Newport (Cummings et al., 1997), cigarettes sold by importers and small manufacturers retain a small but significant market share. Niche products such as bidis, cloves, and additive-free cigarettes are often sold in health food stores, ethnic groceries, head shops, and on the internet (Fisher, 2000). Although clove cigarettes are widely used, very little is known of their physical composition and delivery characteristics by either machine smoking or clinical observations. In the present report, clove cigarettes contained less nicotine and tar than conventional cigarettes; however, FTC smoking indicated more nicotine and tar delivery than conventional cigarettes. In a small-sample clinical study, there was equal delivery of nicotine and CO from a clove and conventional cigarette.

The clove cigarette rod contained 7.39 mg of nicotine in the rod filler, which was less than that reported for conventional cigarettes (13 mg). However, the filler of the rod is 40% dried clove buds and 60% tobacco. If the entire rod were filled with tobacco, it would contain about 12.7 mg of nicotine. Thus, the nicotine concentration in the tobacco of this clove cigarette (14.2 mg/g) is similar to conventional cigarettes (18.2 mg/g; Malson et al., 2001).

The clove cigarette was machine smoked using modified FTC procedures (Federal Register, 1967; Pillsbury et al., 1996). Compared to an average of typical conventional cigarettes, the clove cigarette yielded more nicotine, more tar, and more CO. The higher smoke delivery of the clove cigarette, under machine-smoking conditions, results in part from the lack of filter ventilation holes, which are present on most conventional cigarette brands. Although not measured in this study, the lower porosity of the thicker paper wrapper used in clove cigarettes might also result in higher smoke delivery. Furthermore, more standard machine puffs were needed to consume the clove cigarette than a conventional cigarette. As estimated by machine smoking, clove cigarettes have the potential to deliver nicotine, tar, CO, and other products of mainstream smoke in quantities that equal or possibly exceed those of conventional cigarettes. However, estimates from machine smoking are not reliable indicators of delivery (Sweeney and Kozlowski, 1998). Therefore, in vivo effects of a clove cigarette were determined in a small-sample, within-subject clinical study.

After smoking both the clove and conventional cigarette, there were significant increases in heart rate, systolic BP, plasma levels of nicotine, and exhaled CO. Generally, the effects of the clove cigarette were similar to those of the participant's own brand. Thus, while the clove cigarette contained considerably less nicotine than their own brand, participants were able to extract equal amounts of nicotine.

Although the physiologic effects were comparable, there were some differences in smoking behavior. Compared to their own brand, the clove cigarette was smoked significantly slower and more puffs were needed. Slower smoking rates may have occurred because the rods of the clove cigarette are more firmly packed than the tobacco of a conventional cigarette. Similarly, more puffs and more time were needed to consume an additive-free and bidi cigarette (Malson et al., 2002).

Findings from the clinical study of the clove cigarettes are similar to those of bidis—another alternative tobacco product (Malson and Pickworth, 2002; Malson et al., 2002). Smoking a bidi cigarette that contained less tobacco and nicotine in its rod increased plasma nicotine to levels that were equivalent to those seen after smoking a conventional cigarette. Smoking a nonfilter, high nicotine content, additive-free cigarette, American Spirit, increased plasma levels of nicotine, but to a lesser extent than would be expected from their FTC values. These data support the notion that when individuals smoke novel cigarettes, they will adjust their cigarette smoking behavior to achieve plasma levels of nicotine comparable to their own brand of cigarette (Russell, 1990). When plasma nicotine levels were increased by the application of nicotine patches (Benowitz et al., 1998;

Pickworth et al., 1994) or by intravenous nicotine infusions (Benowitz and Jacob, 1990), smoking behavior was changed to diminish nicotine delivery. Interestingly, smoking behavior during the consumption of cigarettes containing no nicotine was determined by sensory qualities and other components of the smoke (Pickworth et al., 1999; Robinson et al., 2000; Rose et al., 2000).

Although there have been no specific studies on consumer perceptions of clove cigarette safety, smokers consistently judge that additive-free cigarettes and other alternative tobacco products are safer than conventional cigarette products (Arnett, 1999). Data from the present study and from existing literature refute the notion that clove cigarettes are a safe alternative. Thirteen cases of serious acute respiratory distress following clove cigarette smoking led to hospitalization (CDCP, 1985; Guidotti et al., 1989). Among the people that experienced severe distress from smoking cloves were those that smoked in the presence of or immediately following acute respiratory infections.

There are limitations to this study that may diminish the generalizibility of our results. There were only 10 participants in the clinical study and 7 of them were males. Participants smoked only one cigarette of their own brand and a single brand of a clove cigarette in a laboratory environment in the presence of the investigators. These conditions may have affected their smoking behavior. Furthermore, all of the participants had a history of bidi smoking, four self-reported previously smoking clove cigarettes, none were current smokers of clove cigarettes. The limited exposure to clove cigarettes among these participants may have caused a novelty condition that impacted subjective responses and smoking behavior.

The results of the study have practical and theoretical importance. To our knowledge, this is the first study where nicotine delivery from clove cigarettes has been directly estimated in human subjects. The data from this clinical laboratory study could be used by regulatory agencies to objectively determine health risks and addiction liability from smoking clove cigarettes. Finally, differences between nicotine content of filler rods, machine estimates of smoke delivery and actual delivery in the clinical study illustrate the discrepancies between in vivo and in vitro methods of smoke exposure.

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