

# Estimation of the Retention of Menthol in the Respiratory Tract of Menthol Cigarette Smokers: A Pilot Study \*

by

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## SUMMARY

Menthol has been measured in cigarettes, in cigarette smoke preparations, and in smokers' blood and urine, but the efficiency of retention of smoke-delivered menthol by the smoker has not previously been reported. Thirteen smokers participated in a study designed to determine the deposition and retention efficiency of menthol in cigarette smoke in the respiratory tract when smoking mentholated cigarettes. This paper describes the results obtained during the measurement of analytes in exhaled cigarette smoke. Solanesol, nicotine, and menthol in exhaled smoke were collected using a vacuum-assisted pump during the smoking session in which each participant smoked three mentholated cigarettes within one hour. The analytes were quantified using a high-performance liquid chromatography (HPLC) method for solanesol and a gas chromatography-flame ionization detection (GC-FID) method for nicotine and menthol. Cigarette butts were collected after smoking and compared against those from machine-smoked cigarettes to provide an estimate of mouth-level exposures to the smoke constituents during normal smoking. An average of 93% of smoke-delivered menthol, 97% of nicotine and 64% of solanesol was retained by smokers of a mentholated cigarette. The results for solanesol and nicotine in this study were in agreement with prior published values for smokers of non-mentholated cigarettes. The findings of this study confirm the general utility of the mouth-level exposure technique to estimate smokers' exposures to mainstream smoke constituents, and are consistent with a considerable body of evidence from investigations of cigarette smoke exposure biomarkers indicating that exposures of smokers to major smoke constituents from menthol and non-menthol cigarettes are essentially identical. [Beitr. Tabakforsch. Int. 26 (2014) 26–33]

## ZUSAMMENFASSUNG

Der Mentholgehalt ist bereits in Zigaretten, in Zigarettenrauchextrakten sowie im Blut und Urin von Rauchern bestimmt worden, zur Effizienz der Retention von über den Rauch abgegebenem Menthol beim Raucher wurden bisher jedoch noch keine Daten vorgelegt. Es nahmen dreizehn Raucher an einer Studie zur Ermittlung der Deposition und Retentionseffizienz in den Atemwegen von im Zigarettenrauch enthaltenen Menthol beim Rauchen mentholhaltiger Zigaretten teil. Dieser Artikel beschreibt die Ergebnisse der Messung der Analyten in exhalierendem Zigarettenrauch. Während der Rauchsitzung rauchte jeder Teilnehmer drei mentholhaltige Zigaretten innerhalb einer Stunde und es wurden Solanesol, Nikotin und Menthol im exhalierten Rauch mithilfe einer vakuumunterstützten Pumpe gesammelt. Zur Quantifizierung der Analyten wurde bei Solanesol die Methode der Hochleistungsflüssigchromatografie (HPLC) eingesetzt sowie bei Nikotin und Menthol die Methode der Gaschromatografie mit Flammenionisationsdetektor (GC-FID). Die Zigarettenstummel wurden nach dem Rauchen gesammelt und mit denen maschinell abgerauchter Zigaretten verglichen, um eine Schätzung der Exposition des Mundbereichs mit Rauchbestandteilen beim normalen Rauchen abzugeben. Im Durchschnitt lag bei Rauchern einer mentholhaltigen Zigarette die Retention des über den Rauch abgegebenen Menthols bei 93%, für Nikotin lag sie bei 97% und für Solanesol bei 64%. Die Ergebnisse dieser Studie für Solanesol und Nikotin stimmten mit bereits veröffentlichten Werten für Raucher nicht mentholhaltiger Zigaretten überein. Die Erkenntnisse dieser Studie bestätigen den generellen Nutzen der Untersuchungsmethode der Exposition im Mundbereich, um die Exposition des Rauchers mit Bestandteilen des Hauptstromrauchs zu schätzen. Sie decken sich zudem mit den Ergebnissen einer Vielzahl von Untersuchungen zu Biomarkern der

Rauchexposition, aus denen hervorgeht, dass bei mentholhaltigen und nicht mentholhaltigen Zigaretten die Exposition des Rauchers mit wesentlichen Bestandteilen des Rauchs weitestgehend identisch ist. [Beitr. Tabakforsch. Int. 26 (2014) 26–33]

## RESUME

Le menthol a été mesuré dans des cigarettes, dans des préparations de fumée de cigarettes ainsi que dans le sang et l'urine de fumeurs, mais l'efficacité de rétention par le fumeur du menthol délivré dans la fumée n'a fait l'objet d'aucun rapport jusqu'à présent. Treize fumeurs ont participé à une étude destinée à déterminer l'efficacité de dépôt et de rétention du menthol de la fumée de cigarette dans les voies respiratoires lors du fumage de cigarettes mentholées. Le présent document décrit les résultats obtenus pendant la mesure des analytes dans la fumée de cigarette exhalée. Le solanésol, la nicotine et le menthol dans la fumée exhalée ont été collectés en utilisant une pompe assistée par dépression pendant la session de fumage, au cours de laquelle chaque participant a fumé trois cigarettes mentholées en l'espace d'une heure. Les analytes ont été quantifiés en utilisant une méthode de chromatographie en phase liquide à haute performance (CLHP) pour le solanésol et une méthode de chromatographie en phase gazeuse avec détection par ionisation de flamme (CPG-DIF) pour la nicotine et le menthol. Les mégots de cigarette ont été collectés après le fumage et comparés à ceux des cigarettes fumées par machine pour fournir une estimation des expositions au niveau de la bouche aux composants de la fumée pendant un fumage normal. Une moyenne de 93% du menthol, 97% de la nicotine et 64% du solanésol délivrés dans la fumée ont été retenus par les fumeurs d'une cigarette mentholée. Les résultats pour le solanésol et la nicotine dans cette étude concordaient avec des valeurs précédemment publiées pour des fumeurs de cigarettes non-mentholées. Les résultats obtenus dans cette étude confirment l'utilité générale de la technique d'exposition au niveau de la bouche pour évaluer les expositions des fumeurs aux composants du flux principal de la fumée et concordent avec un ensemble considérable de données probantes issues d'études sur les marqueurs biologiques d'exposition à la fumée de cigarette, indiquant que les expositions des fumeurs aux principaux composants de la fumée de cigarettes mentholées et non-mentholées sont essentiellement identiques. [Beitr. Tabakforsch. Int. 26 (2014) 26–33]

## INTRODUCTION

The deposition and retention of smoke constituents in the respiratory tract of smokers is one of the primary factors that determine the nature and the site of the well-known biological and pathological consequences of cigarette smoking. The smoker's inhalation/exhalation pattern, the physical and chemical properties of the cigarette smoke aerosol, and the genetic and constitutional characteristics of the smoker all appear to play some role in the

determination of disease risks for individual smokers or smoking populations. The cigarette smoke aerosol is an exceedingly complex mixture of both particulate/droplet phase and gas/vapor phase constituents whose deposition and retention efficiencies are determined by an incompletely understood interplay among their chemical and physical properties and of the aerosol droplet concentration in the inhaled smoke (1, 2). There has been considerable interest in studying the respiratory retention of both particulate phase and gas/vapor phase smoke constituents and various techniques have been employed (3). Two of the most studied constituents are nicotine, the major alkaloidal component of tobacco leaf and smoke, and solanésol, a nonvolatile natural leaf constituent that has been widely employed as a marker for the smoke particle/droplet phase. For example, SINCLAIR and coworkers (4) studied the behavior of nicotine within the respiratory tracts of four smokers and observed approximately 90% nicotine retention following even a very shallow inhalation (< 100 mL). Since the apparent retention efficiency of nicotine exceeds that typically estimated for smoke particle retention, the authors concluded that nicotine evaporates from the smoke particle during inhalation and is absorbed in the airways as a vapor. In another study, ROSE and colleagues (5) reported the delivery of nicotine into arterial blood following cigarette smoke inhalation was substantially less and slower than had previously been assumed. The authors postulated that nicotine initially distributes into the upper respiratory tract tissue, thus slowing its entry into the arterial circulation, a phenomenon also observed in clinical studies of nicotine vapor inhaler devices (5). The retention of solanésol has been previously studied with results showing retention values between 20% and 57% (with an average of  $40 \pm 20\%$ ) in males, and between 10% and 58% (with an average  $27 \pm 14\%$ ) in females (6).

Menthol, used as a flavoring ingredient, has been measured in cigarettes, in cigarette smoke preparations, and in smokers' blood and urine, but the efficiency of retention by the smoker of smoke-delivered menthol from mentholated cigarettes has not previously been reported. NELSON *et al.* (7) reported very similar mouth level exposures from menthol and non-menthol cigarettes in a large national survey of U.S. smokers, in agreement with both experimental and population studies that have reported similar levels of exposure biomarkers for smokers of cigarettes with and without menthol as a characterizing flavoring ingredient (8, 9). Nevertheless, and despite a number of epidemiologic investigations that have reported no increased occurrence of diseases such as lung cancer among smokers who prefer mentholated cigarettes (10), speculation has persisted that menthol in cigarette smoke may affect smoking behaviors, smoking exposures or smoking harms. One element of a better understanding of menthol's role - if any - in affecting smoking behavior is an accurate estimate of the efficiency of the delivery of cigarette menthol from the cigarette into the smoke and its subsequent retention in the smoker's respiratory tract. Prior calculated estimates of local and systemic exposures to menthol have by necessity relied upon default assumptions to approximate menthol retention from cigarette smoking exposures. The present study sought to provide a

**Table 1. Smoking parameters used in the development of the calibration curves (from 3 cigarettes per pad).**

Puff volume (mL)	Puff duration (seconds)	Puff interval (seconds)
10	1	60, 240
25	1	60, 120, 240
35	1	60, 120, 180, 240
35	1.5	75, 85, 95, 105, 115
35	2	60, 80, 95, 105, 115
45	1.5	40
45	2	30
50	2	30
55	2	80
60	2	30, 60

science-based estimate of menthol retention in the context of cigarette smoking.

The objective of this pilot study was to evaluate the total respiratory tract retention of solanesol and nicotine by smokers of a conventional mentholated cigarette, compare those values to published retention values by smokers of otherwise-similar non-mentholated cigarettes, and evaluate the total retention of menthol by smokers of a conventional mentholated cigarette.

## METHODS

To achieve the objectives of the study it was necessary to determine solanesol, nicotine, and menthol on Cambridge filter pads and in cigarette filter butts following mechanical and human smoking. The analysis of solanesol on the pads generated by the smoke collection and from the 1 cm cut portion of the cigarette filter butts was performed by an HPLC method and the analysis of nicotine and menthol in the pads and butts was performed by GC-FID methods. The HPLC method was similar to that reported in the literature for solanesol analysis (11, 12), and the GC-FID method for nicotine/menthol analysis was developed by Lorillard Research and Development for this pilot study.

The experimental component of the study comprised several steps, including: 1) collection of particulate matter on Cambridge filter pads using a linear smoking machine under several smoking regimes to calibrate the collections from human smoking, 2) collection of particulate matter from the exhaled cigarette smoke generated by the smokers, 3) measurement of solanesol, nicotine, and menthol, in the pads and in the cigarette butts, and 4) calculation of the results. The steps are described in detail in sections that follow.

### *Human subjects*

Fifteen adult smokers (7 males, 8 females; 12 black, 3 white) were provided with details of the study prior to giving their written consent to participate. The study protocol was reviewed and approved for conformance with applicable human research studies regulations by Quorum Review Inc., Seattle, WA, USA. Subjects were between

24–51 years of age and had identified themselves as smokers of 10–20 full flavored menthol cigarettes per day for at least one year. Subjects did not have any clinically significant diseases or health conditions and smoking status was confirmed by a  $\text{piCO}^+$ ™ Smokerlyzer® (Bedfont Scientific Ltd., Rochester, United Kingdom). Participants were asked to refrain from smoking for a minimum of one hour before the smoking session. The smoking session was performed in an environment familiar to the smoker in order to provide comfortable, natural smoking conditions. No physiological parameters of the smoking process (i.e., puffing, inhalation or exhalation patterns) were measured. Protocol deviations occurred with two smokers because of smoking and/or filter butt processing errors, reducing the number of smokers to thirteen in the final analysis.

### *Cigarettes*

For this study a commercially available, full flavored menthol cigarette was used. The test cigarette's mainstream smoke yields under International Organization for Standardization (ISO) conditions were: 13.5 mg "tar" (nicotine-free dry particulate matter), 1.0 mg nicotine, and 15.6 mg carbon monoxide. The filter type was cellulose acetate and the cigarette length was 80 mm. Preliminary results showed that aged cigarettes resulted in poor machine curve correlations for menthol, likely due to menthol migration and equilibration within the sealed pack. For the purpose of this study, fresh, unopened cigarette packs, which were stored in a -60 °C freezer on the same day in which they were produced, were used.

### *Machine regime curve*

Particulate matter was collected from three cigarettes on 44 mm Cambridge pads using a 20 port Cerulean SM 450 (Molins PLC, Milton Keynes, United Kingdom) linear smoking machine. Table 1 shows the 25 smoking conditions used. The smoking conditions were selected in order to cover a range of flow rates through the cigarette filter intended to span the range of smoking behaviors exhibited by human smokers. Immediately after each cigarette was machine smoked, the used filter butts were extinguished in sand, cut 1 cm from the mouth end, longitudinally quartered, and added to 20 mL of 0.1% v/v anethole (internal standard) in methanol. The analytes were extracted by shaking for 35 min on a wrist action mechanical shaker. Concurrently, the Cambridge pads were immediately added to vials with 20 mL of the extraction solution, followed by 35 min of shaking. An aliquot was injected into the GC-FID for nicotine/menthol analysis and into the HPLC for solanesol analysis. Preliminary analyses of the sample matrices spiked with known quantities of the authentic compounds of interest had confirmed the adequacy of the extraction and analyses to quantify the target analytes. Average recovery for three levels of analyte fortification was 96.9% for menthol, 85.9% for nicotine, and 96.1% for solanesol on the 44 mm Cambridge pad and 95.9% for menthol, 88.6% for nicotine, and 98.7% for solanesol from the cigarette filters. The trapping efficiency and capacity of the 44 mm Cambridge pads was tested by smoking three cigarettes at the most intense smoking

regime used to develop the machine calibration curve with effluent smoke passed through three -70 °C chilled impingers filled with 20 mL of extraction solution in series behind the Cambridge pad. The trapping efficiency of the pad was 98.1%, 100%, and 100% for menthol, nicotine, and solanesol, respectively.

#### *Exhaled smoke collection*

The collection of the exhaled smoke was done using a simple device modeled after the apparatus developed by MOLDOVEANU and COLEMAN (13). We modified the device by adding a second 92 mm Cambridge pad in series behind the primary Cambridge pad. The handheld device used in this study consisted of two 92 mm Cambridge pads, and a pad having at one opening a replaceable mouth piece, and at the other opening a connection to a diaphragm vacuum pump (aspiration was set to  $200 \pm 10$  mL/s). The tube connecting the pad holder to the pump had two large ports to the exterior and these flow bypass ports were occluded by the subjects' fingers during exhalation. The vacuum-assisted flow through the apparatus was calibrated so that each subject's exhalation of smoke through the replaceable mouth piece and onto the pads was sensed to be effectively neutral. Three mentholated cigarettes were smoked within one hour down to 3 mm from the tipping paper with 15 min breaks between cigarettes. The cigarette filter was immediately processed after smoking with a 1 cm portion being cut from the mouth end of the cigarette. The filter was cut into longitudinal quarters and added to 20 mL of the extraction solution followed by 35 min of shaking. The pad-collected exhalate was immediately processed with the addition of 60 mL of extraction solution followed by 35 min of shaking.

#### *HPLC analysis of solanesol*

The analysis of solanesol was done on an Agilent® (Santa Clara, CA, USA) 1100 Series HPLC with UV-VIS detection at 205 nm. The HPLC columns used were a Phenomenex (Torrance, CA, USA) C-18 Security Guard Column ( $3.5 \mu\text{L} \times 4 \text{ mm} \times 3.0 \text{ mm}$ ) and a Waters (Milford, MA, USA) Symmetry Analytical column ( $3.5 \mu\text{m} \times 4.6 \text{ mm} \times 75 \text{ mm}$ ) with the column temperature set to 40 °C. The sample injection volume was 20  $\mu\text{L}$  with a column flow rate of 1.5 mL/min. The mobile phase was isocratic and was 90% acetonitrile: 10% methanol. Solanesol retention time was 15.3 min. An external calibration curve was used with 7 standards ranging from 0.0063–0.3258 mg/mL; the Instrument Limit of Quantification (ILOQ) was 0.000041 mg/mL. The calibration curve for solanesol quantification was linear with  $R^2 = 0.99$ , and the line intercept was zero.

#### *GC-FID analysis of menthol and nicotine*

The menthol and nicotine analysis was done on an Agilent® (Santa Clara, CA, USA) 6890 GC-FID equipped with a Phenomenex (Torrance, CA, USA) Rtx-5 column ( $15 \text{ m} \times 0.25 \text{ mm} \times 0.25 \mu\text{m}$ ) set to ramped pressure. An internal standard (anethole) calibration curve was used with 11 standards covering 0.00052 to 3.232 mg/mL. The

calibration curves for nicotine and menthol were both linear with a  $R^2 = 0.99$ . The retention time for menthol, nicotine, and anethole was 3.01, 3.82, and 3.53 min, respectively.

## RESULTS AND DISCUSSION

The analysis of solanesol, nicotine, and menthol was done initially for machine smoked cigarettes using different smoking conditions (shown in Table 1) with concurrent analysis of the smoked Cambridge filter pad and the cut portion of the cigarette butt. Correlations between the levels of solanesol, nicotine, and menthol in smoke as a function of the level in the cigarette butts were obtained. Using these charts the levels of solanesol, nicotine, and menthol in the cigarette smoke delivered to the subjects were calculated based on the measured level of solanesol, nicotine, and menthol in the cigarette butt produced by the smoker. After this part of the study was completed, the subjects smoked the cigarettes and the exhaled smoke collected as previously described was analyzed for solanesol, nicotine, and menthol. The level of solanesol, nicotine, and menthol in exhaled smoke was then compared with that in the smoke delivered to the subjects. The amount of solanesol, nicotine, and menthol retained by the smoker was calculated as the following difference:

$$\text{Retention amount} \left( \frac{\mu\text{g}}{\text{cig}} \right) = \text{Delivered level} - \text{Exhaled level} \quad [1]$$

The amount retained (%) was also calculated for each smoker using the following expression:

$$\text{Retention \%} = \left( \frac{\text{Delivered} - \text{Exhaled}}{\text{Delivered}} \right) \times 100 \quad [2]$$

In order to determine the amount of solanesol, nicotine, and menthol in the smoke delivered to the subjects, a regression line was calculated between the level of the solanesol, nicotine, and menthol in smoke as a function of solanesol, nicotine, and menthol in 1 cm cut portion of the cigarette butts. Correlation charts were calculated using the 25 smoking conditions. The graphs showing the calibration curves for solanesol, nicotine and menthol are shown in Figures 1, 2 and 3, respectively. Our results show a linear dependence for solanesol ( $R^2 = 0.98$ ) and for nicotine ( $R^2 = 0.98$ ). The linear dependence reported in this study is consistent with nicotine and solanesol values in the literature. MOLDOVEANU and COLEMAN (13) reported a linear dependence for solanesol of  $R^2 = 0.98$  and MOLDOVEANU and ST. CHARLES (14) reported a linear dependence for nicotine of  $R^2 = 0.95$ .

Menthol did not fit well with a linear regression but was better modeled with fourth-order polynomials as shown in Figure 3. The origin of this apparent curvature was not investigated further. The reason for this apparent curvature is not known, and further work is indicated to gain a better understanding of this nonlinear relationship.

Table 2 shows the results of the levels of solanesol, nicotine, and menthol in the exhaled smoke as collected from the smoker; the delivered amount as determined from the cigarette butt and compared to the machine curve

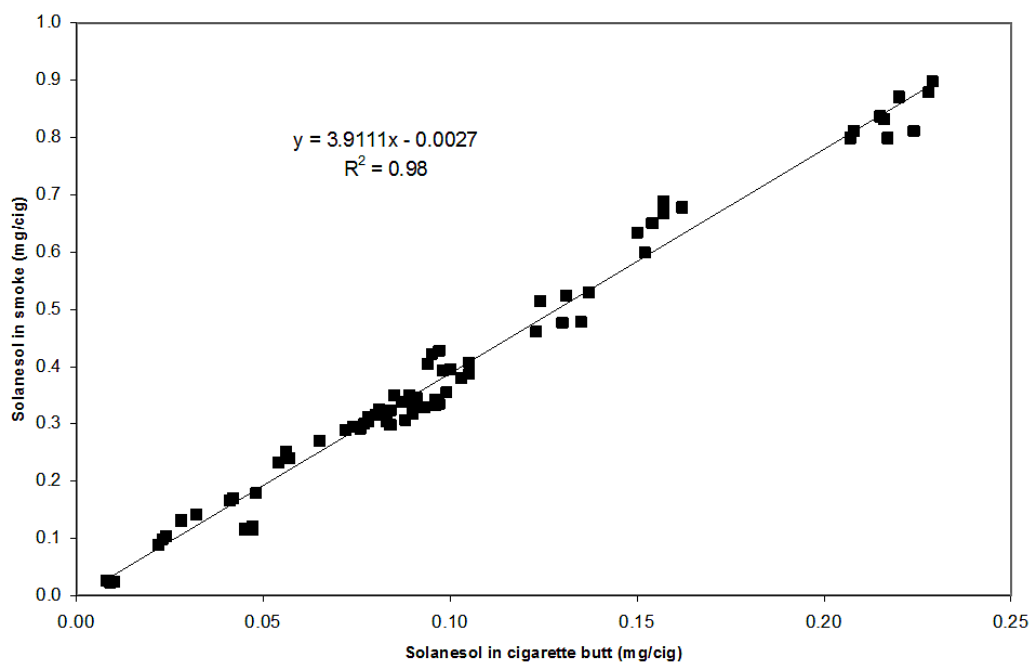


Figure 1. Calibration line of solanesol level in smoke vs in the cigarette butt.

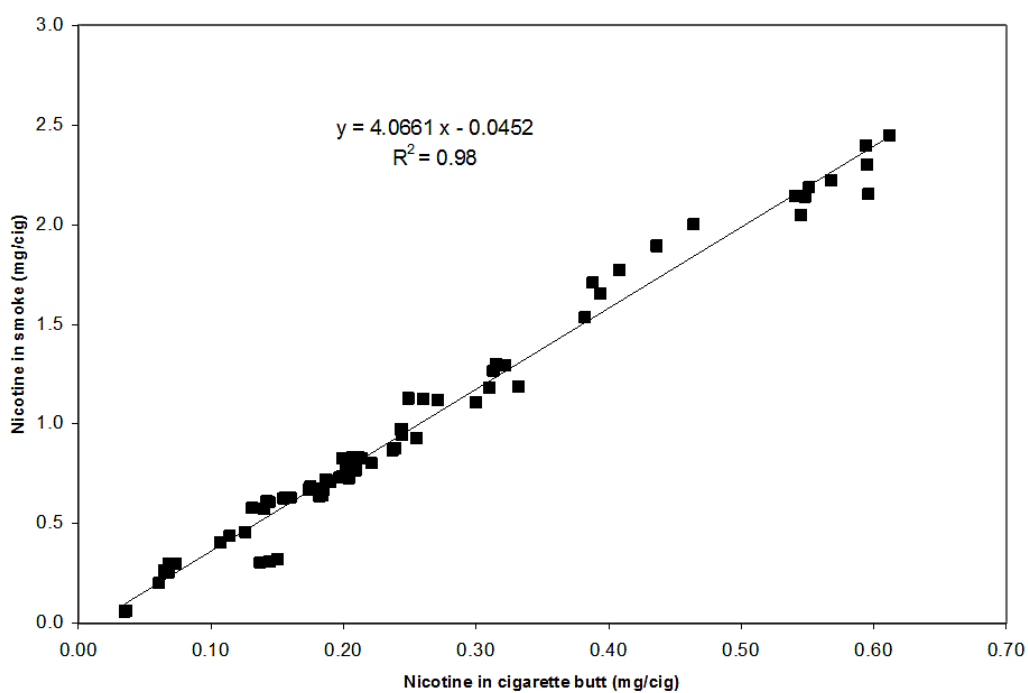


Figure 2. Calibration line of nicotine level in smoke vs in the cigarette butt.

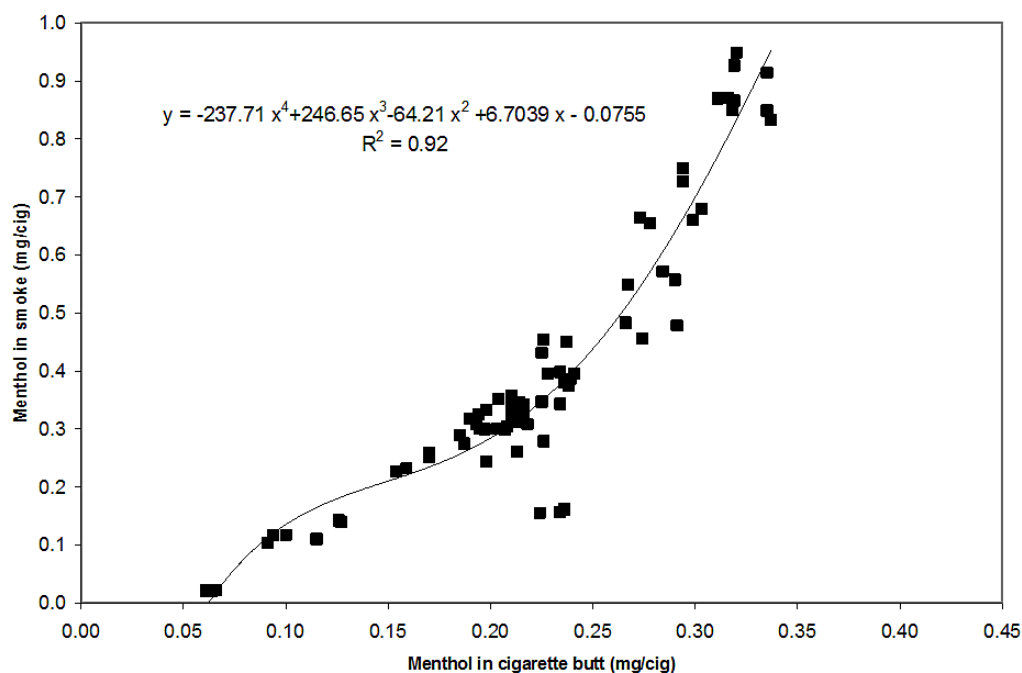


Figure 3. Calibration line of menthol level in smoke vs in the cigarette butt.

results; the retained amount calculated using expression [1]; and the percent retained using expression [2]. For each analyte the mean and range are shown. Our reported values for nicotine and solanesol are consistent with the reported literature values in smokers of a non-mentholated cigarette. For example, ARMITAGE and colleagues (15) examined in ten smokers the influence of inhalation depth and breath-hold duration on the retention of nicotine and nicotine uptake. The cigarette used by ARMITAGE *et al.* (15) was a 9.6 mg "tar" non-mentholated cigarette and the cigarettes were smoked through a cigarette holder attached to a smoking analyzer which recorded puff volumes, puff durations, and puff times. The authors found that nicotine retention increased from 46.5% at zero inhalation volume to 99.5% at

1000 mL inhalation (2 s breath-hold) and from 98.0% at zero breath-hold to 99.9% at 10 s breath hold (500 mL inhalation). MOLDOVEANU and ST. CHARLES (14) investigated nicotine retention in eight smokers of a 10.6 mg "tar" non-mentholated cigarette. They found that their smokers retained approximately 84.6% nicotine. ARMITAGE and colleagues (15) also evaluated solanesol in their 2004 inhalation studies. They found in smokers of a 10 mg "tar" cigarette that solanesol retention increased from 34.2% at zero inhalation volume to 71.9% at 1000 mL (2 s breath-hold) and from 51.8% at zero breath-hold to 87.6% at 10 s breath-hold (500 mL inhalation). In another study, MOLDOVEANU and COLEMAN (12) examined solanesol retention in ten smokers of non-mentholated cigarettes with "tar" values

Table 2. The levels of analytes in exhaled smoke, the delivered levels to the smoker, the amount retained, and retention (%).

Analyte	Exhaled mean (µg/cig) (range)	Delivered mean (µg/cig) (range)	Retained mean (µg/cig) (range)	Retention mean (%) (range) RSD (%)
Solanesol	107 (39–182)	302 (219–518)	195 (119–376)	64.0 (46–86) 23.1
Nicotine	13 (4–35)	488 (346–832)	474 (342–809)	97.3 (93–99) 1.8
Menthol	15 (9–22)	206 (168–271)	189 (147–256)	92.7 (87–96) 2.5

**Table 3. Comparison of retention values in the literature (Mean, SD shown).**

	Lorillard pilot study	MOLDOVEANU AND COLEMAN (13)	ARMITAGE <i>et al.</i> (15)	MOLDOVEANU AND ST. CHARLES (14)	MOLDOVEANU AND COLEMAN (13)
Cigarette	Menthol	Non-menthol	Non-menthol	Non-menthol	Non-menthol
"Tar" (ISO/FTC)	13.5 mg	5.0 mg	9.6 mg	10.6 mg	16.2 mg
# Smokers	13	10	10	8	10
Solanesol retention (%)	64.0 (± 14.8)	59.0 (± 5.9)	68.0 (± 7.5) *	Not analyzed	71.3 (± 7.2)
Nicotine retention (%)	97.3 (± 1.8)	Not analyzed	99.0 (± 0.5) *	84.6 (± Not reported)	Not analyzed
Menthol retention (%)	92.7 (± 2.3)	Not analyzed	Not analyzed	Not analyzed	Not analyzed

\* Data shown for 2 s breath-hold and 500 mL inhalation air

of 5.0 mg, 10.6 mg, and 16.2 mg. The exhaled smoke was collected using a vacuum-assisted procedure intended to provide neutral exhalation effort, and solanesol was analyzed using an HPLC method. Solanesol retained by smokers of the 5.0 mg "tar" product ranged from 53% to 70%; from 60% to 72% for the 10.6 mg cigarette; and from 62% to 82% for the 16.2 mg cigarette. As shown in Table 3, the results from our preliminary investigation in a mentholated cigarette were in good agreement with the aforementioned published values in a non-mentholated cigarette.

Since smoking behavior (i.e., puff volume, puff frequency, puff duration, potential vent-blocking, and other various inhalation behaviors) can vary from person to person, this pilot study only provides a "snap shot" of smoker retention efficiencies. A subsequent study involving a considerably larger number of subjects may show if this finding is valid for a larger population. This observation that the cigarette flavor ingredient menthol does not appear to substantively affect the retention of other smoke constituents is consistent with a number of published investigations of smoke exposure biomarkers that have reported essentially identical exposures for smokers of menthol and non-menthol cigarettes (8, 9). The present study appears to be the first to have reported an estimate of the respiratory tract retention of menthol by smokers of a mentholated cigarette. The average retention value of 93% estimated for menthol here is similar to that reported by numerous authors for nicotine and other semi-volatile smoke constituents and is in good agreement with the value predicted by the model recently described by ST. CHARLES (16, 17) which generally provides accurate estimates of smoke constituent retention across diverse chemical classes based upon the vapor pressure of the compounds of interest and a growing body of empirical data provided by techniques similar to those employed in this study.

## CONCLUSIONS

This pilot study reports the levels of solanesol, nicotine, and menthol estimated to have been inhaled during realistic smoking, and then measured in exhaled breath from each puff taken from a mentholated cigarette. We

found that solanesol was retained at 64%; nicotine was retained at approximately 97%, and menthol at 93%. The study's findings of retention values of 64% and 97% for solanesol and nicotine, respectively, for this commercial menthol cigarette were in good agreement with previously-published values for non-mentholated cigarettes. This study extends the knowledge of retention of solanesol and nicotine by smokers, and provides a science-based estimation of the respiratory tract retention of cigarette smoke-delivered menthol to replace default assumptions that have been employed in previous studies of menthol and cigarette smoke.

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