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Determination of the Transfer Efficiency of *d*-Nicotine to Mainstream Smoke*

by

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SUMMARY

Experiments were conducted to independently determine the mainstream smoke transfer efficiency of *d*-nicotine and *l*-nicotine. Two types of cigarettes (University of Kentucky 2R1 reference cigarette and a cigarette prepared from reconstituted sheet material, TS1) were employed in the study. A chiral-gas chromatography–selected ion monitoring–mass selective detection analysis was used to separate and determine *d*- and *l*-nicotine. The two types of cigarettes were injected with varying levels of *d*- or *l*-nicotine (0–20 mg). The tobacco was removed from the nicotine-injected cigarettes and analyzed for total nicotine and *d*- and *l*-nicotine. The cigarettes were smoked under FTC (Federal Trade Commission) conditions, and the Cambridge pad extracts were analyzed for total nicotine and *d*- and *l*-nicotine. The total nicotine transfer efficiency and the transfer efficiencies of *d*- and *l*-nicotine were determined. Nicotine transfer efficiency is dependent on the type of tobacco employed in a blend and the configuration of the cigarette. As a result, the total nicotine transfer efficiency for the 2R1 cigarettes was different than for the TS1 cigarettes. Likewise, the independently measured transfer efficiencies for *d*- and *l*-nicotine were different between the two cigarettes. The transfer efficiencies of *d*- and *l*-nicotine were not found to be different within a cigarette type. The average transfer efficiency for *d*-nicotine in a 2R1 cigarette was determined to be 19.25%. The average transfer efficiency for *l*-nicotine in a 2R1 cigarette was 16.05%. The average transfer efficiency for *d*-nicotine in a TS1 cigarette was 10.15% and 10.65% for *l*-nicotine. These differences between *d*- and *l*-nicotine were determined not to be statistically significant and are of no practical consequence. [Beitr. Tabakforsch. Int. 19 (2001) 237–244]

ZUSAMMENFASSUNG

Es wurden Untersuchungen durchgeführt, um unabhängig voneinander die Effizienz des Übergangs von *d*-Nikotin und *l*-Nikotin in den Hauptstromrauch von Cigaretten zu bestimmen. In dieser Studie wurden zwei Cigarettentypen (Kentucky 2R1 Referenzcigaretten und Cigaretten, TS1, die aus Tabakfolie hergestellt wurden) untersucht. Mittels chiraler Gaschromatographie–Massenspektrometrie im SIM (Selected Ion Monitoring) Modus wurden *d*- und *l*-Nikotin voneinander getrennt. Den zwei Cigarettentypen wurden unterschiedliche Mengen an *d*- und *l*-Nikotin zugesetzt (0–20 mg). Der Tabak wurde aus den mit Nikotin angereicherten Cigaretten entfernt und auf den Gesamtgehalt an *d*- und *l*-Nikotin analysiert. Die Cigaretten wurden unter FTC (Federal Trade Commission)-Bedingungen abgeraucht und die Cambridgefilterextrakte hinsichtlich des Gesamtnikotins sowie des *d*- und *l*-Nikotins analysiert. Die Effizienz des Übergangs des gesamten Nikotins sowie des *d*- und *l*-Nikotins wurde bestimmt. Die Effizienz des Nikotinübergangs hängt vom Tabak in der Mischung ab und vom Design der Cigarette. Folglich bestand ein Unterschied bei der Effizienz des Übergangs des Gesamtnikotins zwischen den 2R1 und den TS1 Cigaretten. Gleichfalls war die unabhängig voneinander gemessene Effizienz des Übergangs von *d*- und *l*-Nikotin bei den zwei Cigarettentypen unterschiedlich. Innerhalb eines Cigarettentyps wurden keine Unterschiede hinsichtlich der Effizienz des Übergangs von *d*- und *l*-Nikotin gefunden. Die durchschnittliche Effizienz des Übergangs von *d*-Nikotin in einer 2R1 Cigarette lag bei 19,25%. Die durchschnittliche Effizienz des Übergangs von *l*-Nikotin in einer 2R1 Cigarette betrug 16,05%. Die durchschnittliche Effizienz des Übergangs von *d*-Nikotin in einer TS1 Cigarette lag bei 10,15% und

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betrug für *l*-Nikotin 10,65%. Die gemessenen Unterschiede zwischen *d*- und *l*-Nikotin waren statistisch nicht signifikant und haben keine praktischen Konsequenzen. [Beitr. Tabakforsch. Int. 19 (2001) 237–244]

RESUME

Des essais ont été menés pour déterminer de manière indépendante l'efficacité du transfert de la *d*- et *l*-nicotine vers la fumée du courant principal. Deux types de cigarettes (une cigarette de référence Kentucky 2R1 et une cigarette confectionnée avec du tabac reconstitué, TS1) ont été utilisés. *d*- et *l*-nicotine ont été séparées et déterminées par chromatographie en phase gazeuse chirale–contrôle ionique spécifique–spectrométrie de masse. Des quantités différentes en *d*- et *l*-nicotine (0–20 mg) ont été apportées aux deux types de cigarette. Le tabac a été retiré des cigarettes auxquelles on avait apporté de la nicotine et la teneur en nicotine et en *d*- et *l*-nicotine a été dosée. Les cigarettes ont été fumées selon les recommandations de la FTC (Federal Trade Commission), et le rendement en nicotine totale et en *d*- et *l*-nicotine retenu sur les filtres Cambridge a été analysé. L'efficacité du transfert de la nicotine totale et l'efficacité du transfert de la *d*- et *l*-nicotine ont été déterminées. L'efficacité du transfert de la nicotine dépend du type de tabac utilisé dans le mélange et de la configuration de la cigarette. On observe que l'efficacité du transfert de la nicotine totale mesurée pour les cigarettes 2R1 est différente de celle obtenue pour les cigarettes TS1. De même, les efficacités du transfert de *d*- et *l*-nicotine déterminées de manière indépendante sont différentes pour les deux cigarettes. Aucune différence n'a pu être trouvée entre les efficacités du transfert de *d*- et *l*-nicotine pour le même type de cigarette. L'efficacité moyenne du transfert de la *d*-nicotine dans une cigarette 2R1 est de 19,25%; celle du transfert de la *l*-nicotine dans une cigarette 2R1 est de 16,05%. L'efficacité moyenne du transfert de la *d*-nicotine dans une cigarette TS1 est de 10.15% et de 10.65% pour la *l*-nicotine. Ces différences entre la *d*- et la *l*-nicotine ne sont pas significatives statistiquement et n'amènent pas de conséquences pratiques. [Beitr. Tabakforsch. Int. 19 (2001) 237–244]

INTRODUCTION

For many years there has been scientific discussion and work published surrounding two questions concerning *d*-nicotine (1,2,4,6,8,9,11–13,15–17): Is *d*-nicotine naturally present in tobacco? If *d*-nicotine is present in tobacco, does it transfer to smoke like *l*-nicotine?

Based on recent studies employing sensitive liquid chromatographic techniques (1,12) it seems clear that small levels of *d*-nicotine (0.1–0.6% of the total nicotine) are naturally present in tobacco (13). Previous reports in the literature (8) indicated that *d*-nicotine was not found in tobacco. Most likely this is because experimenters employed analytical methodologies that were either not sensitive enough to find low levels of *d*-nicotine or the analytical method employed was not suitable for the difficult separation of *d*-nicotine from *l*-nicotine (12). For example, PERFETTI and COLEMAN, who used chiral-gas chromatography–selected ion monitoring–mass selective detection analysis for the separation and analysis of *d*- and *l*-nicotine (8) stated, "essentially no *d*-nicotine (was) found in any of the tobacco samples" they analyzed.

In recent studies, small but quantifiable levels of *d*-nicotine have been found in mainstream cigarette smoke condensate (4,6,8,9,11,12). Conversely, in earlier work, scientists were unable to detect even the slightest amount of *d*-nicotine in mainstream cigarette smoke condensate (2). Advances in analytical chemistry have become more sophisticated and our ability to delve deeper into tobacco and smoke chemistry has improved (14). It seems very clear today that *d*-nicotine is a verifiable component of mainstream cigarette smoke.

As *d*-nicotine is naturally present in tobacco and is a verifiable mainstream smoke component, the question of whether the two enantiomers of nicotine transfer to mainstream smoke at the same rate has been of interest (15–17). Prior work by HOUSEMAN (17) employed *d*-[2'-^{14}C]nicotine di-(*p*-toluoyltartrate) injected into 70-mm cigarettes to determine the transfer rate of *d*- and *l*-nicotine. HOUSEMAN concluded that the transfer characteristics of exogenous *d*- and endogenous *l*-nicotine were similar. JENKINS and COMES performed nicotine transfer efficiency experiments with uniformly (U) *l*-nicotine-^{14}C-injected into University of Kentucky 1R1 70-mm reference cigarettes (16). JENKINS' data indicated that there was about a 4% increase in the transfer of exogenously applied *l*-nicotine-^{14}C-(U) compared to the endogenous *l*-nicotine in the tobacco. JENKINS calculated from HOUSEMAN's data that there was also a 4% increase in the transference of exogenously applied *d*-nicotine from the *d*-nicotine salt injected into the cigarette. JENKINS argued that the 4% difference in transfer was small when considering the variability in cigarette-to-cigarette smoke yields (16). The studies of HOUSEMAN and JENKINS indicate that *d*- and *l*-nicotine have very similar nicotine transfer efficiencies to mainstream smoke. It should be kept in mind that their experiments, although highly sensitive, were based on single point determinations. PERFETTI *et al.* (15) have recently reported on results of mainstream nicotine transfer efficiency experiments for a variety of *d*- and *l*-nicotine salts and neat *d*- and *l*-nicotine. They concluded that salts of *d*- and *l*-nicotine and neat *d*- and *l*-nicotine have essentially the same mainstream smoke nicotine transfer efficiency. This conclusion was based on the hypothesis that there was no practical or statistical significance in the total nicotine transfer efficiencies measured when either *d*-nicotine or *l*-nicotine were injected into cigarettes and their mainstream smoke nicotine transfer efficiencies were measured. The individual transfer efficiencies of *d*-nicotine and *l*-nicotine were not determined as they did not analytically separate and quantify the amount of *d*- and *l*-nicotine in tobacco and mainstream smoke condensate.

Additionally, there has been interest in whether *l*-nicotine racemizes during the smoking process (4,8,9,12) to produce *d*-nicotine, if natural *d*-nicotine alone transfers to smoke, or if a combination of these thermochemical events take place (8,12). Recently, evidence has been reported that indicates that naturally occurring *d*-nicotine not only transfers to mainstream smoke, but that additional *d*-nicotine is formed through racemization/pyrosynthesis during the smoking process and then transfers to mainstream smoke (12).

PERFETTI *et al.* recently described a technique for the detection, separation and quantification of *d*- and *l*-nicotine based on a novel chiral-gas chromatography–mass selective detection analytical approach (8,9,11). PERFETTI *et al.* have recently completed work on the transfer efficiency of nicotine from salts prepared with *d*- and *l*-nicotine (15). Those experiments showed that the total nicotine delivered to mainstream smoke, whether it was from *l*-nicotine salts, *d*-nicotine salts, *l*-nicotine or *d*-nicotine, was the same for cigarettes of a particular configuration and tobacco type.

Even with all of this information, no definitive study on the direct measurement of the transfer of *d*-nicotine to mainstream smoke, or a determination of the transfer efficiency of *d*-nicotine across a set of products containing a range of *d*-nicotine, has been published. This report describes the results of the analysis of tobacco extracts and mainstream smoke nicotine collected from specially prepared cigarettes for the determination of the transfer efficiency of *d*-nicotine to mainstream smoke.

EXPERIMENTAL

Reagents

The (*S*)-(–)-isomer of nicotine (*l*-nicotine) was purchased from Eastman Kodak (Rochester, NY, USA). The (*R*)-(+)-nicotine (*d*-nicotine) was prepared by T.D.C. Research (Blacksburg, VA) using an established method (3). Standard solutions were prepared in methylene chloride (Burdick and Jackson, Muskegon, MI).

Cigarettes

Reference cigarettes with and without additives

The reference cigarette 2R1 was purchased from the University of Kentucky Tobacco and Health Research Institute (Lexington, KY). The 2R1 cigarettes are described in detail by DIANA *et al*. (5). The 85-mm non-filtered cigarettes were prepared by uniformly syringe injecting various quantities of *d*- or *l*-nicotine into the cigarette rods. The 2R1 reference cigarette was used as a control.

TS1 cigarettes

Non-filtered cigarettes (70-mm tobacco rod length, 24.8 mm circumference) were prepared. The paper-type reconstituted tobacco sheet (RTS) used in this study was previously described by PERFETTI and COLEMAN (8). TS1 corresponds to Samples A (8). The stem and leaf content of the RTS samples were 62% and 38%, respectively.

The reconstituted tobacco sheet (TS1) was cut to a standard width (28 cuts per inch) without casing or added glycerin. Cigarettes were made to a constant tobacco rod firmness and rod weight. The cigarette paper for the TS1 cigarette was obtained from Ecusta Division of P. H. Glatfelter (Pisgah Forest, NC) and had a CORESTA porosity of 24 cm/min and contained 0.55% citrate burn chemical. The citrate burn chemical was a mixture of sodium and potassium citrates.

Cigarettes prepared with d- *or* l-*nicotine for determination of nicotine transfer efficiency*

2R1 reference cigarettes and the single grade cigarette TS1 were injected with varying levels of either *d*- or *l*-nicotine. Three levels of neat *l*-nicotine (5, 10 and 20 mg) and three levels of neat *d*-nicotine (5, 10 and 20 mg) were injected into the cigarette rods of both types of cigarettes. The injected nicotine was centered in the smoked portion of the 2R1 or the TS1 cigarettes. For the 2R1 cigarette, the injected nicotine was centered (longitudinally and laterally) over a 55-mm segment of the 62-mm portion of the rod, which was smoked. For the TS1 cigarette, the injected nicotine was centered (longitudinally and laterally) over a 40-mm segment of the 47-mm portion of the rod, which was smoked. After injection of the various additives, the cigarettes were aged for a week prior to analyses. Tobacco nicotine analyses and FTC (Federal Trade Commission) smoke analyses were conducted on each cigarette type. The 2R1 and the TS1 control cigarettes were also analyzed employing the same procedures. In this experiment, the 2R1 reference cigarettes and the TS1 cigarettes (control and injected cigarettes) were smoked to a butt length of 23 mm.

Instrumentation

Separations were performed on a Hewlett Packard (HP) 6890 gas chromatograph (GC) equipped with a HP 5973 mass selective detector and a HP 6890 autoinjector. Automatic injections, 0.2 μL, were made in the split mode with a split ratio of 60 to 1. The mass selective detector was configured in the selected ion monitoring mode (SIM) with m/z set at 84 and 133.

The GC column was a J&W Scientific (Folsom, CA) Cyclodex B, 30-m, 0.25-mm i.d., 0.25-μm film thickness fused silica column. The initial oven temperature was 50 °C. After holding at 50 °C for 0.5 min the oven was temperature programmed to 108 °C at 30 °C/min. The oven was then held at 108 °C for 31 min. Next, the oven was temperature programmed to 220 °C at 20 °C/min and held there for 5 min. Throughout the entire chromatographic run the flow was held constant at 1.0 mL/min. The injection port and MSD transfer line were held at 250 °C and 240 °C, respectively.

Smoke collection

Cigarette smoke samples were obtained by employing the FTC (19) smoking method described by OGG (18), in accordance with accepted procedures (7).

Tobacco extractions

Nicotine in tobacco was quantitatively extracted from the samples and analyzed in accordance with accepted procedures (7,10). The presence of *d*-nicotine in the smoke and tobacco samples was confirmed by the addition of small quantities (μL) of a *d*-nicotine standard solution to the sample matrices and confirming the increase in abundance of m/z = 84 and 133 at the correct retention time. In addition, the response of m/z = 84 and 133 for both isomers at equal concentrations was found to be identical.

Method for statistical analysis of data

Data were analyzed using SAS software (SAS Institute, Cary, NC). Regression models were fit to each data set to predict the amount of nicotine transferred to mainstream smoke (mg/cig) from the nicotine available in unburned tobacco. Slopes for regression models fit to data sets were compared using a *t*-test. Microsoft Excel 97-SR1 (Redmond, WA) was used for editing, formatting, and printing tables and figures.

RESULTS AND DISCUSSION

Table 1 contains the results of the physical, tobacco and cigarette smoke chemistry for 2R1 reference cigarettes and the TS1 cigarettes. The 2R1 reference cigarettes were injected with *l*-nicotine or *d*-nicotine at three levels. The TS1 cigarettes were treated in the same manner. The length and weight for the two cigarette types were different. The 2R1 cigarettes were 85 mm in length and approximately 1.2 g in weight. The TS1 cigarettes were 70 mm in length and approximately 0.89 g in weight. These differences in configuration, packing density, and tobacco type have an effect on the generation and transfer of mainstream smoke constituents. The tobacco types employed in the cigarettes (American blend [2R1] *vs.* reconstituted tobacco sheet [TS1]) exhibit differences in burn rate and puff count and the inherent physical and chemical properties of each tobacco are different.

The level of total nicotine in the 2R1 and TS1 cigarettes increased as the amount of either *l*- or *d*-nicotine injected into the cigarettes increased. The increase in total nicotine (5, 10, or 20 mg) associated with each of the test 2R1 and TS1 cigarettes corresponded well to the applied amount of *l*- or *d*-nicotine in each test cigarette. Total mainstream smoke nicotine yields are highly correlated with the total amount of tobacco nicotine in each cigarette within each of the 2R1 and TS1 series of products (R^2 = 0.98, for 2R1, and R^2 = 0.99, for TS1).

Total mainstream smoke nicotine transfer efficiencies are calculated values, obtained from mainstream smoke nicotine yields divided by the total nicotine available in the portions of the tobacco rods that are consumed during puffing and smolder. Nicotine transfer efficiencies or more appropriately, apparent nicotine transfer efficiencies, calculated in this manner reflect differences in the amount of tobacco burnt during puffs. The range in the total nicotine transfer efficiencies for the 2R1 cigarettes was 15.96–19.29% and for the TS1 cigarettes was 9.83–11.38%. The objective of this study was to determine the mainstream transfer efficiencies for *l*- and *d*-nicotine, independently. The percentage of *d*-nicotine present in tobacco was obtained from GC–MSD (gas chromatography–mass spectrometry detection) analysis of the tobacco extracts obtained from the nicotine injected cigarettes and the control cigarettes of each set of products (2R1 and TS1). The level of *d*-nicotine in the control 2R1 and TS1 cigarettes and the test cigarettes injected with *l*-nicotine was below the detection limit (BLD = 2%) of the GC–MSD method (8). The quantity of *d*-nicotine in the *d*-nicotine injected test products was well within the detection range of the GC–MSD method. The range of *l*-nicotine on the tobacco from the 2R1 cigarettes was 41.2% to 100% of the total nicotine. The range of *d*-nicotine on the tobacco from the 2R1 cigarettes was BLD to 58.9% of the total nicotine. The range of *l*-nicotine on the tobacco from the TS1 cigarettes was 20.6% to 100% of the total nicotine. The range of *d*-nicotine on the tobacco from the TS1 cigarettes was BLD to 79.4% of the total nicotine. The quantity of either *d*- or *l*-nicotine present in the tobacco extracts was calculated based on the determined percentages of each isomer found via the GC–MSD analysis divided by the total nicotine found by GC analysis of the extract.

The range of *l*-nicotine in the mainstream smoke from the 2R1 cigarettes was 35.3% to 100% of the total mainstream nicotine. *d*-Nicotine in the mainstream smoke from the 2R1 cigarettes ranged between BLD to 64.8% of the total mainstream nicotine. The range of *l*-nicotine in the mainstream smoke from the TS1 cigarettes was 18.3% to 100% of the total mainstream nicotine. *d*-Nicotine in the mainstream smoke from the TS1 cigarettes ranged between BLD to 81.7% of the total mainstream nicotine. The percentage of *d*- or *l*-nicotine present in the mainstream smoke was calculated based on the determined percentages of each isomer found on the extracted Cambridge pads via the GC–MSD analysis divided by the total nicotine found by GC analysis of the Cambridge pads employing the FTC analysis procedure.

The total weight (mg) of nicotine available for transfer to

Table 1.
Physical analyses and tobacco and smoke chemistry on Reference cigarettes and cigarettes made from single grade tobacco components injected with *d*- or *l*-nicotine

Cigarette or smoke parameter	2R1	2R1 + 5 mg *l*-nic	2R1 + 10 mg *l*-nic	2R1 + 20 mg *l*-nic	2R1 + 5 mg *d*-nic	2R1 + 10 mg *d*-nic	2R1 + 20 mg *d*-nic	TS1	TS1 + 5 mg *l*-nic	TS1 + 10 mg *l*-nic	TS1 + 20 mg *l*-nic	TS1 + 5 mg *d*-nic	TS1 + 10 mg *d*-nic	TS1 + 20 mg *d*-nic
Cigarette length (mm)	85	85	85	85	85	85	85	70	70	70	70	70	70	70
Cigarette weight (g)	1.1911	1.1961	1.2011	1.2111	1.1961	1.2011	1.2111	0.8832	0.8882	0.8932	0.9032	0.8882	0.8932	0.9032
Nicotine %	1.438	2.101	2.657	3.852	2.096	2.701	3.814	0.854	1.663	2.08	3.563	1.552	2.399	3.885
Puffs/cig (butt length = 23 mm)	12.2	12.4	12.4	12.7	12.9	12.9	12.7	4.9	4.9	4.9	5.1	5.1	4.9	5
Nicotine (mg/cig)	2.41	3.22	4.12	5.43	3.25	3.9	5.86	0.53	1.03	1.42	2.18	0.91	1.43	2.32
Weight of tobacco burned during smoking (mg)	868.8	872.4	876.1	883.4	872.4	876.1	883.4	593.0	596.4	599.7	606.4	596.4	599.7	606.4
Total nicotine (*d* and *l*) available for transfer to MSS[a] (mg)	12.49	18.33	23.28	34.03	18.29	23.66	33.69	5.06	9.92	12.47	21.61	9.26	14.39	23.56
Total nicotine transfer efficiency (%)	19.29	17.57	17.70	15.96	17.77	16.48	17.39	10.47	10.39	11.38	10.09	9.83	9.94	9.85
l-Nicotine in tobacco (%)	100	100	100	100	74.15	60	41.15	100	100	100	100	57.75	34.8	20.6
d-Nicotine in tobacco (%)[b]	0.00	0.00	0.00	0.00	25.85	40	58.85	0.00	0.00	0.00	0.00	42.25	65.2	79.4
l-Nicotine in smoke (%)	100	100	100	100	71.1	51.8	35.3	100	100	100	100	48.7	32.2	18.3
d-Nicotine in smoke (%)[b]	0.00	0.00	0.00	0.00	28.9	48.3	64.8	0.00	0.00	0.00	0.00	51.3	67.8	81.7
l-Nicotine in tobacco available for transfer to MSS[a] (mg)	12.49	18.33	23.28	34.03	13.56	14.20	13.86	5.06	9.92	12.47	21.61	5.35	5.01	4.85
d-Nicotine in tobacco available for transfer to MSS[a] (mg)[b]	0.00	0.00	0.00	0.00	4.73	9.47	19.83	0.00	0.00	0.00	0.00	3.91	9.38	18.71
l-Nicotine in smoke (mg)	2.41	3.22	4.12	5.43	2.31	2.02	2.01	0.53	1.03	1.42	2.18	0.44	0.46	0.42
d-Nicotine in smoke (mg)[b]	0.00	0.00	0.00	0.00	0.94	1.88	3.80	0.00	0.00	0.00	0.00	0.47	0.97	1.90
l-Nicotine transfer efficiency (%)[b]	19.29	17.57	17.70	15.96	17.04	14.23	14.92	10.47	10.39	11.38	10.09	8.29	9.20	8.75
d-Nicotine transfer efficiency (%)[b]	0.00	0.00	0.00	0.00	19.87	19.90	19.15	0.00	0.00	0.00	0.00	11.94	10.34	10.13

[a]MSS = mainstream smoke.
[b]A value of zero means below detection limit (BLD = 2%).

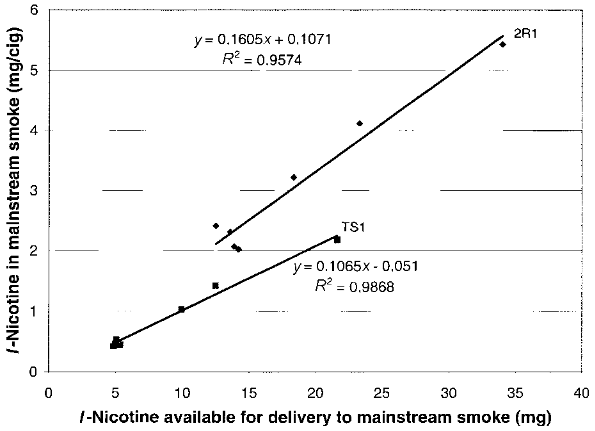

Figure 1.
***l*-Nicotine in mainstream smoke *vs.* *l*-nicotine in tobacco available for delivery**

mainstream smoke was calculated based on the total weight of the tobacco consumed during puffing and smolder multiplied by the percentage of total nicotine in the tobacco. The total weight of the tobacco consumed during smoking was calculated by multiplying the total weight of the tobacco rod by the ratio of the length burned during smoking to the total length of the tobacco rod. The 2R1 cigarettes were 85 mm in length and 62 mm of the rod was consumed during smoking. The TS1 cigarettes were 70 mm in length and 47 mm of the rod was consumed during smoking. *l*-Nicotine available for transfer to mainstream smoke for the 2R1 cigarettes ranged from 12.49 to 34.03 mg. The range in *d*-nicotine available for transfer to mainstream smoke for the 2R1 cigarettes was BDL to 19.83 mg. The range in *l*-nicotine available for transfer to mainstream smoke for the TS1 cigarettes was 5.01–21.61 mg. *d*-Nicotine available for transfer to mainstream smoke for the TS1 cigarettes ranged from BDL to 18.71 mg.

The weight of *d*- or *l*-nicotine found in mainstream smoke was calculated by multiplying the total FTC mainstream nicotine by the percentage of *d*- or *l*-nicotine found in the extracted Cambridge pads as analyzed by GC-MSD. The range in *l*-nicotine transferred to mainstream smoke for the 2R1 cigarettes was 2.02–5.43 mg. *d*-Nicotine transferred to mainstream smoke for the 2R1 cigarettes ranged from BDL to 3.08 mg. The range in *l*-nicotine transferred to mainstream smoke for the TS1 cigarettes was 0.42–2.18 mg. *d*-Nicotine available for transfer to mainstream smoke for the TS1 cigarettes ranged from BDL to 1.90 mg.

The mainstream smoke transfer efficiency for *l*-nicotine was calculated from mainstream smoke yield of *l*-nicotine divided by the available *l*-nicotine in the portion of the tobacco rod that was consumed during puffing and smolder. The transfer efficiency for *d*-nicotine was calculated in the same manner. The range in the mainstream smoke transfer efficiency for *l*-nicotine in the 2R1 cigarettes was 14.23–19.29% (average = 16.67%). The

Table 2.
***l*-Nicotine *vs.* *d*-nicotine transfer efficiency in 2R1 and TS1 blends, comparison of regression coefficients**

Cig. type	Regression results	*l*-Nicotine	*d*-Nicotine	Total nicotine
2R1	*n*	7	7	7
	Intercept	0.1071	0.0104	0.4575
	Slope	0.1605	0.1925	0.1526
	Slope Std. Err.	0.0151	0.0016	0.0091
	R^2	0.9574	0.9997	0.9824
	l-Nicotine slope *vs.* *d*-Nicotine slope			
	t = 2.10			
	p = 0.062			
TS1	*n*	7	7	7
	Intercept	-0.0510	0.0121	0.0637
	Slope	0.1065	0.1015	0.0974
	Slope Std. Err.	0.0055	0.0028	0.0044
	R^2	0.9868	0.9985	0.9897
	l-Nicotine slope *vs.* *d*-Nicotine slope			
	t = 0.82			
	p = 0.432			

mainstream smoke transfer efficiency for *d*-nicotine in the 2R1 cigarettes ranged between 19.15–19.90% (average = 19.64%). The range in the mainstream smoke transfer efficiency for *l*-nicotine in the TS1 cigarettes was 8.29–11.38% (average = 9.79%). The mainstream smoke transfer efficiency for *d*-nicotine in the 2R1 cigarettes ranged from 10.13–11.94% (average = 10.80%).

Figure 1 is a plot of the *l*-nicotine in tobacco available for delivery to mainstream smoke *vs.* the yield of *l*-nicotine in mainstream smoke. Table 2 presents results of linear regression models fit to the data. The slopes of the regression lines are estimates of the average nicotine transfer efficiencies for the 2R1 and the TS1 cigarette series. These estimates for the 2R1 and the TS1 cigarette series are quite different, 16.05% *vs.* 10.65%, respectively. The regression equations for the 2R1 and the TS1 cigarette series have R^2 values of 0.96 and 0.99, respectively. The differences in apparent mainstream nicotine transfer efficiencies for these two series of cigarettes are due to inherent differences in the chemical properties of the tobaccos used in the cigarettes and to differences in the materials used to construct the cigarettes (15). These differences in the 2R1 and TS1 cigarettes contribute to the changes observed in the smoke composition, which in large part are due to the inherent burn rates associated with the two types of cigarettes (15).

Figure 2 is a plot of the *d*-nicotine in tobacco available for delivery to mainstream smoke *vs.* the yield of *d*-nicotine in mainstream smoke. The slopes of the regression lines are estimates of the average nicotine transfer efficiencies for the 2R1 and the TS1 cigarette series. These estimates

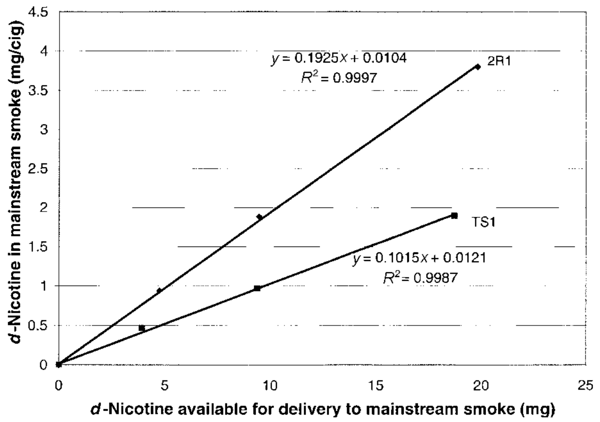

Figure 2.
***d*-Nicotine in mainstream smoke *vs.* *d*-Nicotine in tobacco available for delivery**

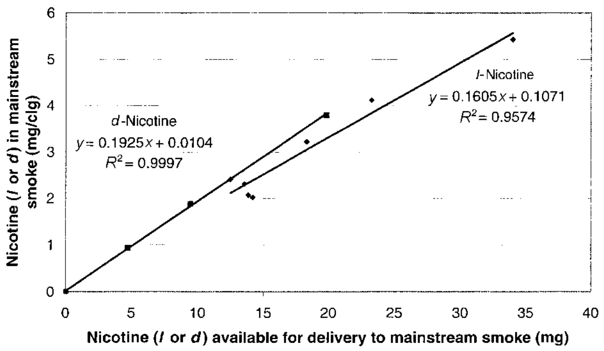

Figure 3.
Nicotine in mainstream smoke *vs.* nicotine in tobacco available for delivery for 2R1 cigarettes

for the 2R1 and the TS1 cigarette series are again quite different, 19.25% *vs.* 10.15%, respectively. The regression equations for average nicotine transfer efficiencies for the 2R1 and the TS1 cigarette series have R^2 values of 0.99 and 0.99, respectively.

Figure 3 is a plot of the nicotine transfer efficiencies for *l*- and *d*-nicotine in 2R1 cigarettes. The individual regression equations for the *l*- and *d*-nicotine appear to be very similar. A *t*-test comparing the slopes for *d*- and *l*-nicotine was not significant ($p = 0.06$). When all of the data (total *d*- and *l*-nicotine) is plotted together, the estimated average nicotine transfer rate for both the *d*- and *l*-nicotine was 15.25%, with the regression equation having $R^2 = 0.98$.

Figure 4 is a plot of the nicotine transfer efficiencies for *l*- and *d*-nicotine in TS1 cigarettes. Again, the individual regression equations for the *l*- and *d*-nicotine appear very similar. A *t*-test comparing the slopes for *d*- and *l*-nicotine was not significant ($p = 0.43$). When all of the data (total *d*- and *l*-nicotine) is plotted together, the estimated average nicotine transfer rate for both the *d*- and *l*-nicotine was 9.74%, with the regression equation having $R^2 = 0.99$.

The results of the experiments of this report clearly show that *d*-nicotine and *l*-nicotine in tobacco have mainstream

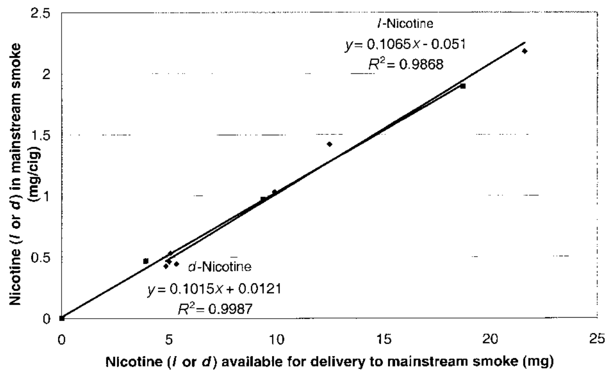

Figure 4.
Nicotine in mainstream smoke *vs.* nicotine available for delivery for TS1 cigarettes

transfer efficiencies that are not different. Differences in total nicotine transfer efficiencies exist for cigarettes having different tobacco types and/or a different cigarette construction. For a specified cigarette, the transfer efficiency of *d*-nicotine is not significantly different from that of *l*-nicotine.

CONCLUSIONS

Experiments were conducted to independently determine the mainstream smoke transfer efficiency of *d*-nicotine and *l*-nicotine. Two types of cigarettes (University of Kentucky 2R1 reference cigarette and a cigarette prepared from reconstituted sheet material, TS1) were employed in the study. A chiral-gas chromatography–selected ion monitoring–mass selective detection analysis was used to separate and determine *d*- and *l*-nicotine. The two types of cigarettes were injected with varying levels of *d*- or *l*-nicotine (0–20 mg). The tobacco was removed from the nicotine-injected cigarettes and analyzed for total nicotine and *d*- and *l*-nicotine. The cigarettes were smoked under FTC conditions and the Cambridge pad extracts were analyzed for total nicotine and *d*- and *l*-nicotine. The total nicotine transfer efficiency and the transfer efficiencies of *d*- and *l*-nicotine were determined. Nicotine transfer efficiency is dependent on the type of tobacco employed in a blend and the configuration of the cigarette. As a result, the total nicotine transfer efficiency for the 2R1 cigarettes was different than the TS1 cigarettes. Likewise the independently measured transfer efficiencies for *d*- and *l*-nicotine were different between the two cigarettes. The transfer efficiencies of *d*- and *l*-nicotine were not found to be different within a cigarette type. The average transfer efficiencies for *d*-nicotine and *l*-nicotine in a 2R1 cigarette were 19.25% and 16.05%, respectively. The average transfer efficiencies for *d*-nicotine and *l*-nicotine in a TS1 cigarette were 10.15% and 10.65%, respectively. These differences were determined not to be statistically significant and are of no practical consequence.

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