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Establishment of Toxic Metal Reference Range in Tobacco from U.S. Cigarettes

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Abstract

Smoking remains the leading cause of preventable death in the United States. There are numerous harmful substances in tobacco and tobacco smoke. Among the more than 4,000 identified compounds in smoke, many metals contribute to the health risks associated with tobacco use. Specific metals found in tobacco and tobacco smoke have been classified as carcinogens by the IARC. Exposures to toxic metals can cause outcomes including inflammation, sensitization, and carcinogensis. Metals in tobacco are transported in tobacco smoke proportionally with their concentrations in tobacco filler for a given cigarette design. To quantitatively examine metal content in numerous tobacco products, high throughput methods are desired. We developed a simple, rapid tobacco digestion method coupled with a sensitive analytical method using inductively coupled plasma-mass spectrometry (ICP-MS). Because of mercury's known memory effects and volatility, quantitative determinations of mercury were made with a direct combustion analyzer. The methods were utilized to examine arsenic, beryllium, cadmium, chromium, cobalt, lead, manganese, mercury, and nickel content in cigarette tobacco and to establish a reference range for the metals in 50 varieties of cigarettes available in the U.S. Our results are comparable to the limited datasets reported by others and with available standard reference material (SRM) values.

Keywords

Cigarette; Metals; Smoke; Tobacco

Introduction

Tobacco use continues to be the leading cause of preventable death and disease in the United States (1). Smoking prevalence has fallen in the U.S. since its peak in 1963, however the overall prevalence remains at approximately 20% of the U.S. population. Smoking prevalence is highest among a number of population subgroups: working adults ages 18–24 (24%); those who have completed less than a high school education (28%); those who are without health insurance (29%); and those living below the poverty level (28%) (2). Because of the established health risks associated with tobacco use, and the costs of treating

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individuals who have been diagnosed with life-threatening, disfiguring, and disabling diseases as a consequence of using these products, regulation of tobacco products by national governments is increasing globally. The United States (U.S.) passed legislation in 2009 to regulate tobacco products. Potential health risks from tobacco products and the expansion of global regulatory environment have necessitated the development of robust and accurate methods to examine the range or baseline concentrations of various toxicants present in tobacco products so that informed decisions can be made on setting regulatory limits to known toxicants from the products (3).

Among the numerous harmful and toxic constituents in tobacco and tobacco smoke, select metals may contribute to the overall harm. Many toxic metals are efficiently extracted from the soil by tobacco plants and accumulate in the lamina (4, 5). The concentrations and transfer efficiencies of toxic metals transferred during smoking from the tobacco filler to cigarette smoke depend on a number of factors: metal properties, their concentrations in the tobacco, filter type, cigarette design, rod length and diameter, mean mass of tobacco per rod, paper porosity, ventilation, and others. When all factors are constant, the concentrations of toxic metals that are transported in smoke are proportional to their concentrations in tobacco (2, 6, 7, 8). Peer reviewed literature on the metal content in cigarette tobacco filler and mainstream smoke from modern cigarettes is often limited in scope. Therefore, we sought to examine the concentrations of toxic metals in cigarette tobacco filler over a broad range of popular cigarette brands. The large number of commercial tobacco products available in the U.S. necessitate the development and utilization of robust, high throughput methods for tobacco analysis in order to quantitatively determine concentrations of toxic substances, particularly metals, found in cigarette filler, which are ultimately transported to cigarette smoke, and inhaled by smokers.

We targeted metals for analysis that have known toxic or harmful properties. Arsenic, beryllium, cadmium, and nickel are all IARC group 1 carcinogens (9, 10, 11). In addition to being a carcinogen, cadmium is associated with development of chronic obstructive pulmonary disease (COPD) and nephrotoxicity. Some metals have different toxicity depending on oxidation state. Though it is not apparent what proportions of chromium species exist in smoke, chromium (VI) is an IARC group 1 carcinogen (11). Chromium (III) has involvement in sensitization (12). Lead is an IARC group 2a carcinogen (13). Lead is also associated with neurotoxicity, including developmental neurotoxicity (14). Manganese is also neurologically toxic (15). Cobalt is a group 2b IARC carcinogen and may cause inflammation (16, 17, 18, 19). It is possible that different manganese and selenium oxidation states, along with iron and copper, may play a role in oxidation-reduction (redox) processes that contribute to pulmonary inflammation (20, 21, 22, 23).

Manganese was included in this method because it is redox active and has been shown to cause inflammation and sensitization (20, 21). Barium, which was included in a previously published method used for analysis of smokeless tobacco (24), was considered less relevant to analyses of cigarette filler tobacco because neither barium nor its oxide are volatile. Though barium and manganese concentrations in tobacco are readily measurable, neither is as efficiently transported into smoke as more volatile elements, such as cadmium and lead. Nevertheless, the concentrations of manganese in tobacco reported here are sufficiently high that even very low transport efficiency would result in measurable manganese in tobacco smoke. Preliminary experiments, however, showed that barium concentration in domestic tobacco smoke was near the LOD. Levels of other metals ranged from slightly below those of cadmium and lead to the same order of magnitude as these volatile elements. Thus some fraction of each of the metals will be transported to the smoke and inhaled by the smoker or partition to the sidestream smoke and potentially expose non-smokers via second hand smoke exposure.

Experimental

Cigarette samples

Fifty cigarette brands were purchased from retail outlets in the greater metropolitan Atlanta, Georgia, USA area in 2011. The samples were assigned unique identification numbers and logged into a database. Samples were stored in their original packaging until needed. Only authorized personnel had access to the samples.

Sample and blank preparation for analysis

Tobacco samples were dried in perfluoroalkoxy (PFA) containers for a minimum of 6 hours at 90°C. Dried cigarette filler tobacco was rendered more homogeneous by manual crushing with polypropylene / polystyrene tissue grinders (Thermofisher, Pittsburgh, PA, USA). Samples were tightly sealed until weighed for analysis. Drying and weighing were the only sample preparation steps for mercury analysis.

Samples were prepared for ICP-MS analysis by microwave digestion according to manufacturer-optimized recommendations for leaf materials in a CEM Discover SP-D Plus (Matthews, NC, USA) sequential microwave system. A measured amount of crushed filler tobacco (0.100 g to 0.190 g), was placed in teflon-lined quartz 30 mL digestion vessels. Double distilled nitric acid (5.0 mL, GFS, Powell, OH, USA) was added to each vessel prior to capping. The microwave heating profile was programmed to start at ambient temperature and increase to 200°C in 4 minutes, followed by a 3 minute digestion at 200°C. Cooling time to 80°C was 4 minutes. Pressure vents were programmed for a maximum of 2 releases at 13.6, 15.3, 17.0, 18.7 bars; and unlimited at 20.4 bars for safety. Digested samples were transferred to acid-cleaned 50.0 mL polypropylene graduated cylinders. Double distilled hydrofluoric acid (5.0 mL, 5% v/v) (GFS, Powell, OH, USA) was added to the digests. The digests were brought to 50.0 mL with ultrapure water rinses of the digestion vessel. Blanks were prepared by adding all reagents to the digestion vessels and proceeding through the digestion and dilution procedures without addition of tobacco. The microwave system, the digestion method, and the post-digestion addition of HF represent modifications to a previously published analytical method (24).

Mercury analysis

Mercury calibrations were performed using a mercury standard from Wako Pure Chemical Industries (Kawagoe, Japan) diluted into 0.2% v/v nitric acid and 0.01% w/v cysteine (Nacalai Tesque, Kyoto, Japan). Quantification was performed using five calibration standards diluted in this solution and the solvent blank included as a “0” calibration point.

Calibration was determined on the basis of mass of mercury pipetted into sample boats in 100 μL spikes. In addition to the "0" calibration point, the calibration range spanned from 0.100 ng to 5.00 ng mercury.

ICP-MS analytical parameters

Five calibration standard solutions were prepared by dilution of High Purity Standards (HPS, Charleston, SC, USA) arsenic, beryllium, cadmium, chromium, cobalt, manganese, nickel, and selenium, and National Institute for Standards and Technology lead standard (SRM 981) (NIST, Gaithersburg, MD, USA). Internal standard solutions were prepared by dilution of HPS rhodium, germanium, and iridium standards. Standards, solvent blanks, and digested tobacco samples (1.700 mL) were diluted 1:1 with 1.700 mL internal standard solution. Rhodium was assigned as the internal standard for cadmium in low resolution, and for chromium, manganese, cobalt, and nickel in medium resolution. Iridium (isotope 193) was assigned as internal standard for beryllium and lead in low resolution. Germanium (isotope 72) was assigned as internal standard for arsenic and selenium in high resolution and when quadrupole ICP-MS with reaction cell was used. The internal standards (2.00 μg/L Rh and Ir) were prepared in 1% v/v nitric acid for low and medium resolution ICP-MS analyses. The internal standard solution used for arsenic and selenium analyzed in high resolution (magnetic sector) or with argon collision gas (quadrupole) was 40 μg/L Ge dissolved in 1% v/v HNO_3 and 0.5% 2-propanol (Sigma, St. Louis, Mo, USA, semiconductor grade, VLSI). Addition of 2-propanol to the latter diluent, use of Ge as an internal standard, and the addition of manganese and selenium as analytes represent modifications to a previously published method.[24] Dilutions at both 1:1 and 1:5 were observed to have linear calibrations for all analytes.

Calibration ranges for all metals spanned the observed levels in the domestic cigarette filler analyzed, though the ranges were tighter than reported for a similar method previously published where it was used for smokeless tobacco analysis.[24] The following standard ranges, prior to dilution with internal standard solution, were used: ^{9}Be, 0.005 to 0.100 μg/L; ^{111}Cd, 1.000 to 20.0 μg/L; total lead (1.01446 × (^{206}Pb + ^{207}Pb + ^{208}Pb)), based on isotopic abundances of NIST lead standard (SRM 981) used for calibration to account for isotopic variations in different geographic areas), 0.500 μg/L to 10.00 μg/L; ^{52}Cr, 0.500 to 10.00 μg/L; ^{55}Mn, 50.0 to 1000. μg/L; ^{59}Co, 0.050 to 2.000 μg/L; ^{60}Ni, 0.050 to 10.00 μg/L; ^{75}As, 0.100 to 2.000 μg/L; ^{78}Se, 0.500 to 10.00 μg/L. The standards were prepared in 1% v/v nitric acid.

Quality control procedures

Reference tobacco 1S3 (North Carolina State University, Raleigh, NC, USA) and CTA-VTL-2 (Instytucie Chemii i Techniki Jądrowej, Warszawa, Poland) were used as quality control materials. Quality control samples were prepared for each run following the standard sample preparation procedure.

Instrumentation

Mercury analyses were performed using a Nippon MA3000 direct combustion mercury analyzer (Nippon North America, College Station, TX, USA). Oxygen combustion gas was controlled at 0.40 L/min. Temperature programs were the instrument defaults: standards and blanks were processed at 150°C for 60 s followed by 800°C for 120 s. The "Organism" program was used to process dried tobacco samples: 180°C for 120 s followed by 850°C for 120 s.

Analytical results for beryllium, cadmium, and lead were obtained in low resolution using a ThermoFisher (West Palm Beach, FL, USA) Element 2 magnetic sector ICP-MS with Spectron (Ventura, CA, USA) platinum-tipped nickel sampler and H skimmer cones. The introduction system consisted of an SC2-FAST autosampler and APEX-FAST HF desolvation unit (Elemental Scientific [ESI], Omaha, NE) and PFA-ST nebulizer fitted to an ESI high performance torch with a 1.8 mm sapphire injector. Results for chromium, manganese, cobalt, and nickel were obtained using medium resolution in the same method. Instrument parameters, including nitrogen addition via the Apex system, were optimized to maintain ^{98}Mo signal stability and intensity while bringing the ^{98}Mo^{16}O cps below 0.5% of total ^{98}Mo signal. Data was acquired with 3 runs of 10 passes at 25 samples per peak with 0.010 second sample time in "both" (counting and analog) mode except for beryllium. Beryllium signal was acquired by sampling 100 points across each peak. Mass windows were 100% in low resolution with the exception of beryllium which was assigned an 80% mass window. Mass windows in medium resolution were 120%. Search windows were 50% for all isotopes except ^{9}Be, which was assigned a 0% search window. Integration window widths were 20% for all isotopes in low resolution, 40% for ^{52}Cr, and 60% for all other isotopes in medium resolution. Mass offsets were acquired after mass calibrations and utilized along with the instrument's "Auto-Lock Mass" feature. The ^{9}Be isotopic peak was manually assigned a 0.0050 mass offset to avoid acquisition of a low intensity interference centered at an approximate mass of 8.98g. The manual mass offset, narrow integration window, and use of 100 samples per peak to offset the narrow mass range within which the beryllium peak was sampled permitted acquisition without contribution from the interference. Several of the above instrument parameters represent slight modifications to a method that has been described (24).

Arsenic and selenium were analyzed with a separate instrument method optimized specifically for arsenic with no nitrogen addition to the Apex desolvating introduction system. Mass windows in high resolution were 125%. Search and integration windows were 50% for ^{72}Ge and 20% for ^{75}As and ^{78}Se. Signal was acquired with 3 runs, 10 passes, 50 samples per peak in Fast Scan mode. Mass offsets were acquired after mass calibrations and utilized along with "Auto-Lock Mass" feature of the instrument's acquisition software.

The following were used for comparison of arsenic and selenium detection limits with those obtained with the magnetic sector instrument: Elan DRC2 (PerkinElmer, Shelton, CT, USA) with an ESI PC3 Peltier cooled introduction system; pfa-ST nebulizer; ESI high performance torch with a 1.8 mm sapphire injector; and Spectron (Ventura, CA, USA) platinum-tipped nickel sampler and skimmer cones. The instrument was optimized for maximum signal-to-background ratio using arsenic spiked into a diluted tobacco digest, while maintaining CeO/Ce ratios at ≤ 2%. Reaction cell conditions consisted of 0.5 rejection parameter quotient setting (RPQ), 0.4 mL/min argon cell gas, and 325 V axial field voltage optimum.

Method detection limits

The method detection limits (MDLs) were based on 3 times the total standard deviations (S_T) of the results of analyses of digest blanks where

$$\mathrm{MDL}=3\,\mathrm{x}\,S_T=3\,\mathrm{x}\left[\mathrm{S}^2{}_{\mathrm{within\ \ run}}+\mathrm{S}^2{}_{\mathrm{between\ \ run}}\right]^{1/2}$$

$S_{\text{within run}}$ is the standard deviation from analysis of 20 separate digest blanks in a single run. $S_{\text{between run}}$ is the standard deviation of the analysis of 20 separate digest blanks in 20 separate runs. As a conservative estimate, we calculated MDLs in µg/g tobacco based on the assumption of the minimum tobacco mass used for analysis (0.100g tobacco) which would yield the highest, most conservative MDL (even though a higher mass of tobacco would result in a lower MDL than calculated). The MDLs for mercury were obtained in the same manner, except that the “0” blank calibration solution was used.

Statistical analysis of data

Data were compared to determine a statistically significant difference with t test in Microsoft Excel 2010 (Microsoft, Redmond, WA, USA). The analytical QC samples were evaluated using a modified Westgard evaluation approach in SAS (25).

Results

High Throughput Preparations

The MA3000 mercury analyzer provides high throughput analytical capabilities with minimal sample preparation. The approach only requires weighing the dried tobacco samples prior to analysis. One analyst could run blanks, calibration standards, weigh and analyze quality controls and 50 samples per instrument in an 8-hour day.

The Discover SPD Plus digestion system was chosen because of short 10-minute digestion process (including cool-down to 80°C) and availability of PFA liners for the digestion vessels. After post-digestion addition of dilute hydrofluoric acid to dissolve silicate particulate, samples were colorless, indicating complete digestion. After samples were digested, preparation for analysis continued with dilution and addition of internal standards. The sequential digestion procedure made possible by this system allowed ICP-MS calibration and analyses to commence while the latter samples were still digesting, with no incurred dead time waiting for all samples to complete the preparation steps. The SC2-FAST rinse-out autosampler only required 20 seconds processing time between samples. Thus, these sample preparation and autosampling improvements dramatically improved our throughput for heptuplicate analyses of 50 samples, not counting blanks, calibration standards, and QCs compared to the previously published method (24).

We were able to weigh, digest, dilute, run calibration, and analyze 31 samples for arsenic and selenium, including necessary additional blanks, SRMs, and QCs, in a single 8-hour day. When a separate instrument was used for arsenic and selenium analyses, one person could separately dilute the digested samples and complete both instrumental analyses in the same day.

Method Detection Limits

Method improvements were intended to increase throughput and lower detection limits (Table 1) compared to our previously published magnetic sector method (24). However, comparison of MDLs from the analytes common to the present and former methods shows little difference in MDLs. Thus, MDLs appear to have reached instrument and method-limited concentrations. On the other hand, the lack of significant change in MDLs suggests two things. Long-term contamination control was excellent; and analytical performance was not compromised by modifications for faster throughput.

Arsenic, beryllium, cadmium, lead, chromium, manganese, cobalt, and nickel were all detectable in tobacco samples using the magnetic sector methods; mercury was detectable using the combustion mercury analyzer. The tobacco samples were also analyzed for arsenic and selenium with an Elan DRC2 quadrupole ICP-MS configured with a Peltier cooled introduction system and argon cell gas. A comparison of MDLs for arsenic and selenium analyzed in high resolution with a magnetic sector instrument versus the quadrupole with argon collision gas showed that the magnetic sector instrument had a lower MDL for ^{75}As, whereas the quadrupole had a lower MDL for ^{78}Se. An explanation for these results is that the ^{40}Ar^{35}Cl^{+} interference for ^{75}As^{+} was not as significant relative to the ^{75}As^{+} signal as was ^{40}Ar^{38}Ar^{+} to 78Se^{+}. While the interference for 75As^{+} was easily resolved in high resolution on the magnetic sector instrument, the intensity of 40Ar38Ar+ was very high compared to the intensity of ^{78}Se^{+}. Minor tailing of the interference peak into the analyte mass window caused a higher MDL. The ^{82}Se isotope was examined as an alternative, but its low isotopic abundance and consequential low intensity in high resolution made analysis impractical. Under the conditions used, the quadrupole instrument had less ion count sensitivity than the magnetic sector instrument, which made it less sensitive in the trace determination of ^{75}As. However, the capability to reduce the ^{40}Ar^{38}Ar^{+} interference with argon cell gas without generation of secondary interferences (26) made it superior to the magnetic sector instrument for determination of ^{78}Se. Nevertheless, selenium results for all tobacco filler samples were below both instrument MDLs, as was also observed for 247 cigarette brands tested in Canada (3).

Accuracy

Accuracy was assessed by comparing our results with certified or characterized values of SRMs, or with results obtained by others on these materials (Table 2). Good agreement exists between method results and SRM target ranges or previously reported results with only two minor exceptions. The manganese result for CTA-VTL-2 was slightly higher than the target value; and the lead result for CTA-OTL-1 was slightly lower than the target value, though there was overlap between the wide target error range of CTA-OTL-1 and one standard deviation above the mean of the results in the present method. INCT-OBTL-5 and INCT-PVTL-6 were only analyzed for mercury. The latter were obtained to replace CTA-OTL-1 and CTA-VTL-2, which are no longer commercially available.

Discussion

The primary goal of this work is to provide an overview of the concentration levels for select toxic and carcinogenic metals in tobacco filler used in modern domestic cigarettes. As cigarettes are an agriculturally based product and growing locations and conditions can influence metals uptake, the levels reported here relate to the cigarettes analyzed in this study (Table 3). Lot to lot or other seasonal variations could introduce considerable variation in specific products measured over time.

For this study, we quantitatively analyzed 50 different cigarette brands purchased in 2011 in the metro Atlanta area. All measurements were made in a strict QA/QC approach and the reported levels are an average obtained from heptuplicate (n=7) individual measurements of select metals (Table 3). Statistical comparisons of filler tobacco metals concentrations where the brand and variety were identical and differed only in hard or soft pack packaging (Basic Gold 100s, Kool Green, Marlboro 100s, Marlboro Gold 100s, Newport Green Menthol) showed that Marlboro Gold 100 soft pack differed slightly (but statistically significantly, $p < 0.05$) from the corresponding hard pack variant in terms of beryllium, chromium, lead, manganese, and nickel concentrations. This was also the case for the Newport Green Menthol King soft pack versus hard pack for beryllium and mercury concentrations ($p < 0.05$). Basic Gold soft pack filler was also slightly higher in mercury than the identical brand and variety in hard pack ($p < 0.05$). Other hard pack to soft pack comparisons showed that they were not significantly different at the 95% confidence interval. One possible explanation for the greater number of significant differences for Marlboro and Basic packaging than for other brands examined could possibly be the large market share for these varieties and the large amount of tobacco crop that would have to go into their manufacture, potentiating greater package to package or lot to lot variation.

Tobacco filler from the American Spirit Natural cigarettes was lower than other brands and varieties in mean beryllium, cobalt, and manganese concentrations, while the same brand had the highest mean concentrations for cadmium and mercury. This demonstrated that low concentrations of some toxic metals may not be an indication that all toxic metals are at low concentrations. Such differences likely arise from differences in tobacco varieties in the blend, differences in fertilization practices, or differences in soil concentrations between growing areas.

Nine of the ten varieties with highest arsenic concentrations were Marlboro varieties, though the other Marlboro varieties had arsenic concentrations at less than the 0.29 μg/g median concentration, indicating that not all products from the same manufacturer are identical in toxic metals concentrations. In contrast to Marlboro product arsenic characteristics, Marlboro product beryllium concentrations were clustered around the median of 0.031 μg/g and below. Much like the American Spirit example above, the levels of particular metals should not be interpreted as markers for all others.

Cadmium levels ranged from 1.0 to 1.7 μg/g dry tobacco; and lead levels ranged from 0.60 to 1.16 μg/g dry tobacco. Though cadmium and lead concentrations were not the highest metals concentrations in filler, it is well known that cadmium and lead are efficiently transported in smoke at higher concentrations than many metals (27, 28). Cadmium, as either the free metal, chloride, or oxide, and lead as the chloride are more volatile than many other metals or their oxides. Thus, concentration in tobacco may not be entirely predictive of the resulting concentrations of metals transported into smoke. The fact that cadmium and lead are carcinogens; that lead is neurodevelopmentally toxic; and that the half-life for pulmonary clearance for cadmium is 13 to 24 years (29) makes the facile transport of these toxic metals in smoke of particular concern.

The range of mean values for cobalt and nickel were respectively, 0.44 to 1.11 μg/g and 2.1 to 3.9 μg/g dry tobacco. Cobalt is found in the same concentration range, and nickel at higher concentrations than cadmium or lead, though reports typically find them transferred into mainstream smoke with much lower efficiency (27, 28). They are considered together here because they are classified by IARC for carcinogenicity, and because they share an inflammatory pathway and are potent sensitizers (19, 30, 31, 32, 33, 34, 35, 36, 37). Significant quantities of nickel are often found in tobacco, and the levels of cobalt are within the same order of magnitude as more volatile cadmium and lead. Fortunately, nickel and cobalt are not transferred as efficiently through the smoke as compared to the more volatile metals. Inhalation of nickel and cobalt pose a health threat, but the risk could be greater if they were more volatile.

Mean chromium levels ranged from 1.4 to 3.2 μg/g dry tobacco, also a higher range than for cadmium and lead. Chromium, like cobalt and nickel, is less efficiently transported in mainstream smoke due to lower volatility than cadmium or lead. Unless a tobacco crop was grown where a large amount of chromium (VI) existed in the soil, chromium in tobacco leaf would be expected to be predominantly in the chromium (III) oxidation state (38). Chromium and chromium speciation is of interest in tobacco because oxidation to higher oxidation states such as chromium (V) or (VI), as a result of smoking (38, 39) rendering these metals more carcinogenic, with higher redox activity, and with enhanced sensitizing and inflammatory properties (12). Though inefficiently transported in smoke, chromium accumulates in lung with an indeterminately long half-life for pulmonary clearance (40).

Mean values for manganese ranged from 131 to 245 μg/g dry tobacco. Manganese was included as an analyte of interest because it is redox active (41) and potentially neurotoxic. Manganese in airborne particulate has also been shown to be proinflammatory in pulmonary tissues, to induce or exacerbate asthma (20, 42), and is capable of oxidizing chromium (III) to chromium (VI) (41). Given the high concentrations of manganese in tobacco relative to other metals discussed, the smoke levels are apparently transferred with lower efficiency relative to other metals (43) because the metal or the oxide have lower volatility.

Selenium was included as an analyte of interest because it is a respiratory irritant, redox active and potentially neurotoxic. However, selenium was below the MDLs for both instrument methods described for all tobacco filler samples; thus its contribution to redox mechanisms of smoke-induced inflammatory potentiation is less than the contributions from other metals with redox potential, such as iron, copper, and manganese.

The importance of monitoring the concentrations of various toxicants present in tobacco becomes increasingly important as more jurisdictions pass and enforce the regulation of tobacco products. Solid science-based information is critical to help inform decisions on reducing or eliminating exposure to toxicants. In particular, the importance of monitoring metals concentrations in cigarettes has increased as the understanding of the contributions of metals to the pathologies caused by smoking has become more clear.

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Table 1

Method detection limits

Analyte	MDL (μg/g tobacco)
As (Magnetic Sector)	0.082
As (Quadrupole)	0.25
Be	0.0028
Cd	0.23
Co	0.05
Cr	0.16
Hg	0.00063
Mn	13
Ni	0.14
Pb	0.16
Se (Magnetic Sector)	0.69
Se (Quadrupole)	0.50

Table 2

Accuracy determined by analysis of certified reference materials (Mean ± standard Deviation).

μg/g	CTA-VTL-2 (n=20)	CTA-VTL-2 Target	CTA-OTL-1 (n=20)	CTA-OTL-1 Target	1S3 n=20	Previous Report[24]	INCT-OBTL-5	OBTL-5 Target	INCT-PVTL-6 (n=10)	PVTL-6 Target
As	1.044 ± 0.071	0.969 ± 0.072	0.613 ± 0.055	0.539 ± 0.060	0.314 ± 0.028	0.317 ± 0.041	NR		NR	
Be	0.094 ± 0.017	NA	0.109 ± 0.019	NA	0.044 ± 0.006	0.039 ± 0.001	NR		NR	
Cd	1.70 ± 0.17	1.52 ± 0.17	1.29 ± 0.15	1.12 ± 0.12	1.51 ± 0.11	1.51 ± 0.11	NR		NR	
Cr	0.437 ± 0.035	0.429 ± 0.026	0.930 ± 0.102	0.879 ± 0.039	1.39 ± 0.10	1.30 ± 0.07	NR		NR	
Cr	1.76 ± 0.21	1.87 ± 0.16	2.23 ± 0.45	2.59 ± 0.32	3.63 ± 0.39	3.75 ± 0.21	NR		NR	
Hg	0.044 ± 0.001	0.048 ± 0.009	NR	NA	0.023 ± 0.002	NR	0.019±0.001	0.021±0.001	0.021±0.001	0.024±0.002
Mn	93.8 ± 7.3	79.7 ± 2.6	431 ± 37	412 ± 14	391 ± 21	NR	NR		NR	
Ni	2.08 ± 0.13	1.98 ± 0.21	5.75 ± 0.55	6.32 ± 0.65	2.48 ± 0.16	2.73 ± 0.20	NR		NR	
Pb	20.1 ± 2.1	22.1 ± 1.2	3.95 ± 0.38	4.91 ± 0.80	1.98 ± 0.25	1.91 ± 0.10	NR		NR	

NA: Not available, NR: Not Run

Table 3

Mean concentrations of toxic metals from heptuplicate analyses of tobacco filler (μg/g ± standard deviation).

	As	Be	Cd	Co	Cr	Hg	Mn	Ni	Pb	Se
American Spirit Natural	0.31 ± 0.07	0.015 ± 0.003	1.7 ± 0.2	0.44 ± 0.09	1.9 ± 0.4	0.020 ± 0.001	131 ± 9	2.4 ± 0.3	0.73 ± 0.11	< 0.50
Basic Blue 100s HP	0.23 ± 0.06	0.031 ± 0.009	1.4 ± 0.4	0.93 ± 0.20	2.5 ± 0.6	0.013 ± 0.001	237 ± 57	3.1 ± 0.7	0.74 ± 0.27	< 0.50
Basic Green 100s HP Menthol	0.22 ± 0.05	0.027 ± 0.008	1.2 ± 0.2	0.78 ± 0.09	2.1 ± 0.2	0.013 ± 0.001	181 ± 20	2.5 ± 0.2	0.79 ± 0.19	< 0.50
Basic Gold 100s HP	0.23 ± 0.05	0.023 ± 0.003	1.2 ± 0.1	0.80 ± 0.23	2.1 ± 0.2	0.013 ± 0.001	172 ± 13	2.8 ± 0.4	0.77 ± 0.12	< 0.50
Basic Gold 100s SP	0.28 ± 0.07	0.021 ± 0.005	1.3 ± 0.2	0.80 ± 0.13	2.1 ± 0.4	0.014 ± 0.001	171 ± 26	2.9 ± 0.4	0.79 ± 0.11	< 0.50
Benson & Hedges Luxury Gold 100s SP	0.25 ± 0.05	0.022 ± 0.003	1.3 ± 0.2	0.69 ± 0.08	2.4 ± 0.3	0.015 ± 0.001	166 ± 15	2.8 ± 0.1	0.74 ± 0.16	< 0.50
Benson & Hedges Green 100s HP Menthol	0.26 ± 0.08	0.029 ± 0.007	1.3 ± 0.2	0.79 ± 0.11	2.4 ± 0.4	0.015 ± 0.001	195 ± 20	2.8 ± 0.3	0.80 ± 0.25	< 0.50
Camel Blue Turkish Domestic Blend HP	0.30 ± 0.05	0.026 ± 0.005	1.2 ±0.1	0.69 ± 0.07	2.7 ± 0.5	0.016 ± 0.001	174 ± 20	3.2 ± 0.1	0.82 ± 0.17	< 0.50
Camel Turkish Domestic Blend HP	0.30 ± 0.04	0.021 ± 0.003	1.1 ± 0.1	0.61 ± 0.07	1.8 ± 0.2	0.015 ± 0.001	151 ± 14	3.0 ± 0.2	0.74 ± 0.09	< 0.50
Capri Magenta HP	0.30 ± 0.05	0.041 ± 0.014	1.4 ± 0.4	0.78 ± 0.16	2.5 ± 0.5	0.015 ± 0.001	214 ± 43	3.6 ± 0.7	0.68 ± 0.26	< 0.50
Carlton White 100s HP	0.25 ± 0.07	0.020 ± 0.004	1.5 ± 0.2	0.68 ± 0.06	1.4 ± 0.3	0.017 ± 0.001	189 ± 26	2.1 ± 0.1	1.06 ± 0.25	< 0.50
Doral Silver 100s HP	0.30 ± 0.06	0.049 ± 0.017	1.3 ± 0.4	0.98 ± 0.23	3.1 ± 0.9	0.014 ± 0.001	224 ± 61	3.7 ± 1.2	0.83 ± 0.35	< 0.50
Doral Gold HP	0.30 ± 0.06	0.041 ± 0.011	1.1 ± 0.2	0.87 ± 0.09	2.4 ± 0.2	0.015 ± 0.001	193 ± 14	3.2 ± 0.4	0.78 ± 0.11	< 0.50
Kent Golden SP	0.25 ± 0.04	0.026 ± 0.004	1.3 ± 0.2	0.73 ± 0.09	1.6 ± 0.2	0.014 ± 0.000	187 ± 24	2.7 ± 0.2	0.81 ± 0.22	< 0.50
Kool Green Menthol SP	0.29 ± 0.06	0.040 ± 0.014	1.4 ± 0.3	0.73 ± 0.12	2.8 ± 0.4	0.014 ± 0.001	192 ± 31	3.5 ± 0.6	0.74 ± 0.26	< 0.50
Kool Green Menthol HP	0.29 ± 0.05	0.037 ± 0.012	1.4 ± 0.4	0.77 ± 0.16	2.7 ± 0.5	0.014 ± 0.001	215 ± 46	3.4 ± 0.6	0.75 ± 0.33	< 0.50
Marlboro Red SP	0.33 ± 0.07	0.031 ± 0.007	1.3 ± 0.2	0.80 ± 0.08	3.0 ± 0.3	0.015 ± 0.001	194 ± 18	3.9 ± 0.5	0.73 ± 0.15	< 0.50
Marlboro Silver 100s HP	0.30 ± 0.07	0.029 ± 0.007	1.4 ± 0.4	0.82 ± 0.20	2.6 ± 0.6	0.016 ± 0.001	210 ± 57	3.3 ± 0.9	0.81 ± 0.36	< 0.50
Marlboro Gold SP	0.35 ± 0.06	0.030 ± 0.006	1.3 ± 0.1	0.81 ± 0.08	3.0 ± 0.1	0.015 ± 0.001	183 ± 14	3.7 ± 0.5	0.75 ± 0.12	< 0.50
Marlboro Gold 100s SP	0.32 ± 0.07	0.027 ± 0.006	1.3 ± 0.1	0.71 ± 0.04	2.7 ± 0.2	0.014 ± 0.001	169 ± 10	3.5 ± 0.1	0.72 ± 0.13	< 0.50
Marlboro Gold 100s HP	0.35 ± 0.04	0.035 ± 0.005	1.2 ± 0.1	0.70 ± 0.07	3.1 ± 0.3	0.015 ± 0.001	169 ± 12	3.5 ± 0.2	1.16 ± 0.26	< 0.50
Marlboro Gold HP	0.36 ± 0.02	0.032 ± 0.004	1.1 ± 0.1	0.71 ± 0.08	2.9 ± 0.3	0.015 ± 0.001	175 ± 18	3.6 ± 0.3	0.87 ± 0.14	< 0.50
Marlboro Red HP	0.33 ± 0.04	0.033 ± 0.004	1.2 ± 0.1	0.71 ± 0.07	2.9 ± 0.1	0.015 ± 0.001	170 ± 10	3.5 ± 0.1	0.83 ± 0.14	< 0.50
Marlboro 100s HP	0.36 ± 0.04	0.032 ± 0.006	1.3 ± 0.1	0.71 ± 0.05	2.7 ± 0.3	0.015 ± 0.001	175 ± 11	3.4 ± 0.3	0.77 ± 0.14	< 0.50
Marlboro 100s SP	0.34 ± 0.05	0.030 ± 0.006	1.2 ± 0.1	0.74 ± 0.08	2.7 ± 0.3	0.015 ± 0.001	171 ± 17	3.7 ± 0.8	0.77 ± 0.17	< 0.50
Marlboro Silver HP	0.34 ± 0.06	0.028 ± 0.006	1.2 ± 0.1	0.71 ± 0.04	2.8 ± 0.5	0.015 ± 0.001	175 ± 12	3.3 ± 0.3	0.74 ± 0.11	< 0.50
Marlboro Gold Menthol HP	0.29 ± 0.06	0.023 ± 0.005	1.2 ± 0.2	0.65 ± 0.05	2.4 ± 0.2	0.015 ± 0.001	154 ± 11	3.3 ± 0.3	0.77 ± 0.18	< 0.50

	As	Be	Cd	Co	Cr	Hg	Mn	Ni	Pb	Se
Marlboro Green Menthol HP	0.28 ± 0.04	0.023 ± 0.004	1.1 ± 0.1	0.62 ± 0.04	2.2 ± 0.3	0.015 ± 0.001	166 ± 11	2.8 ± 0.2	0.73 ± 0.08	< 0.50
Marlboro HP	0.32 ± 0.05	0.025 ± 0.004	1.3 ± 0.1	0.71 ± 0.03	2.6 ± 0.4	0.014 ± 0.001	171 ± 10	3.6 ± 0.3	0.75 ± 0.15	< 0.50
Maverick Gold 100s HP	0.30 ± 0.05	0.026 ± 0.004	1.0 ± 0.1	0.84 ± 0.10	1.9 ± 0.3	0.016 ± 0.001	169 ± 17	3.7 ± 0.9	0.64 ± 0.18	< 0.50
Merit Gold HP	0.23 ± 0.05	0.035 ± 0.010	1.2 ± 0.2	0.77 ± 0.04	2.4 ± 0.2	0.014 ± 0.001	207 ± 24	2.7 ± 0.2	0.82 ± 0.23	< 0.50
Misty Blue Slims	0.30 ± 0.06	0.046 ± 0.014	1.0 ± 0.1	0.76 ± 0.05	2.3 ± 0.3	0.015 ± 0.001	189 ± 18	3.0 ± 0.2	0.99 ± 0.32	< 0.50
Newport Green King SP Menthol	0.23 ± 0.04	0.039 ± 0.011	1.4 ± 0.4	1.11 ± 0.21	2.0 ± 0.5	0.017 ± 0.002	245 ± 49	3.3 ± 0.7	0.62 ± 0.28	< 0.50
Newport Green Menthol HP	0.23 ± 0.04	0.025 ± 0.005	1.2 ± 0.1	0.93 ± 0.14	1.8 ± 0.5	0.014 ± 0.001	205 ± 30	2.9 ± 0.3	0.60 ± 0.05	< 0.50
Newport Green Menthol 100s HP	0.22 ± 0.05	0.023 ± 0.004	1.1 ± 0.1	0.97 ± 0.15	1.4 ± 0.1	0.015 ± 0.001	187 ± 14	2.6 ± 0.3	0.65 ± 0.13	< 0.50
Now Gold 100s SP	0.23 ± 0.06	0.018 ± 0.003	1.6 ± 0.2	0.67 ± 0.12	1.4 ± 0.3	0.017 ± 0.001	184 ± 30	2.2 ± 0.1	0.88 ± 0.18	< 0.50
Pall Mall Blue	0.32 ± 0.06	0.035 ± 0.005	1.1 ± 0.1	0.80 ± 0.09	2.3 ± 0.3	0.013 ± 0.001	178 ± 19	3.5 ± 0.4	0.84 ± 0.14	< 0.50
Parliament Blue HP	0.23 ± 0.06	0.034 ± 0.010	1.5 ± 0.3	0.81 ± 0.11	2.7 ± 0.5	0.014 ± 0.001	214 ± 37	2.9 ± 0.6	0.74 ± 0.29	< 0.50
Salem Gold 100s	0.30 ± 0.06	0.037 ± 0.011	1.2 ± 0.1	0.75 ± 0.04	2.1 ± 0.1	0.014 ± 0.001	183 ± 12	2.8 ± 0.1	0.77 ± 0.17	< 0.50
Salem Gold HP	0.31 ± 0.04	0.040 ± 0.010	1.3 ± 0.1	0.75 ± 0.03	2.2 ± 0.2	0.014 ± 0.001	198 ± 23	3.0 ± 0.2	0.77 ± 0.17	< 0.50
Salem Silver 100s HP Menthol	0.33 ± 0.07	0.036 ± 0.010	1.4 ± 0.4	0.81 ± 0.18	3.2 ± 1.8	0.015 ± 0.001	197 ± 50	3.6 ± 0.8	0.88 ± 0.33	< 0.50
Salem Green HP Menthol	0.31 ± 0.05	0.036 ± 0.010	1.4 ± 0.3	0.81 ± 0.16	2.4 ± 0.5	0.015 ± 0.001	207 ± 45	3.3 ± 0.8	0.93 ± 0.37	< 0.50
True Silver SP	0.25 ± 0.06	0.045 ± 0.014	1.2 ± 0.3	0.95 ± 0.18	2.3 ± 0.5	0.014 ± 0.001	226 ± 42	3.6 ± 0.8	0.70 ± 0.22	< 0.50
USA Gold 100s SP	0.26 ± 0.05	0.023 ± 0.004	1.2 ± 0.1	0.71 ± 0.05	1.4 ± 0.2	0.015 ± 0.001	163 ± 13	2.4 ± 0.2	0.80 ± 0.17	< 0.50
Vantage Multicolor SP	0.29 ± 0.07	0.041 ± 0.009	1.2 ± 0.2	0.84 ± 0.07	2.7 ± 0.4	0.014 ± 0.002	207 ± 25	3.4 ± 0.4	0.87 ± 0.25	< 0.50
Virginia Slims Gold 100s HP	0.25 ± 0.04	0.035 ± 0.012	1.3 ± 0.3	0.77 ± 0.13	2.6 ± 0.5	0.014 ± 0.000	218 ± 48	3.0 ± 0.7	0.71 ± 0.24	< 0.50
Winston Gold HP	0.28 ± 0.06	0.023 ± 0.005	1.5 ± 0.2	0.74 ± 0.07	1.8 ± 0.2	0.017 ± 0.001	184 ± 26	3.1 ± 0.2	0.82 ± 0.15	< 0.50
Winston Red 100s HP	0.29 ± 0.05	0.038 ± 0.013	1.5 ± 0.5	0.92 ± 0.21	2.2 ± 0.7	0.018 ± 0.002	218 ± 61	3.4 ± 0.9	0.75 ± 0.35	< 0.50
Winston White 100s HP	0.28 ± 0.06	0.042 ± 0.013	1.6 ± 0.5	0.90 ± 0.27	2.5 ± 0.8	0.016 ± 0.001	232 ± 72	3.6 ± 1.0	1.1 ± 0.5	< 0.50
Winston Red HP	0.28 ± 0.06	0.028 ± 0.005	1.3 ± 0.1	0.70 ± 0.05	2.1 ± 0.4	0.017 ± 0.001	190 ± 14	3.2 ± 0.2	0.79 ± 0.10	< 0.50
2R4F	0.35 ± 0.05	0.020 ± 0.001	1.4 ± 0.1	0.81 ± 0.29	1.3 ± 0.3	0.019 ± 0.001	198 ± 17	2.6 ± 0.2	0.70 ± 0.09	< 0.50
3R4F	0.33 ± 0.05	0.019 ± 0.002	1.3 ± 0.1	0.56 ± 0.04	1.3 ± 0.3	0.021 ± 0.002	202 ± 10	2.2 ± 0.2	0.64 ± 0.05	< 0.50