

Review of cigars and cigar-type products as potential sources of consumer exposure to heavy metals

Paweł Jacek Hać, Bartłomiej Michał Cieślik, Piotr Konieczka*

Faculty of Chemistry, Department of Analytical Chemistry, Gdańsk University of Technology, 11/12 Gabriela Narutowicza Street, 80-233 Gdańsk, Poland

*Corresponding author: Piotr Konieczka, e-mail: piotr.konieczka@pg.edu.pl

Table of Contents

| | |
|---|-----------|
| INTRODUCTION..... | 3 |
| TRENDS IN CIGAR SMOKING | 5 |
| ELEMENTAL CONTAMINATION OF CIGARS..... | 7 |
| TOXICITY OF HEAVY METALS PRESENT IN CIGARS | 8 |
| METHODOLOGY | 13 |
| METHODS OF HEAVY METAL DETERMINATION IN CIGAR SAMPLES | 13 |
| RESULTS..... | 19 |
| ELEMENT CONTENT ANALYSIS | 19 |
| DISCUSSION..... | 25 |
| CONCLUSIONS | 30 |
| ACKNOWLEDGEMENTS | 31 |
| DECLARATION OF INTEREST STATEMENT | 32 |
| REFERENCES | 32 |

Highlights

- Despite the increased interest of consumers, research on the elemental analysis of cigars is rare
- Based on the analysis of the literature, it was noticed cigar tobacco may differ significantly in heavy metals content such as: Pb, Cd, Ni, Cr
- The level of metal contamination is likely related to the origin and growth environment of the tobacco
- Monitoring the level of heavy metal contamination of all tobacco products is important for the health of their consumers

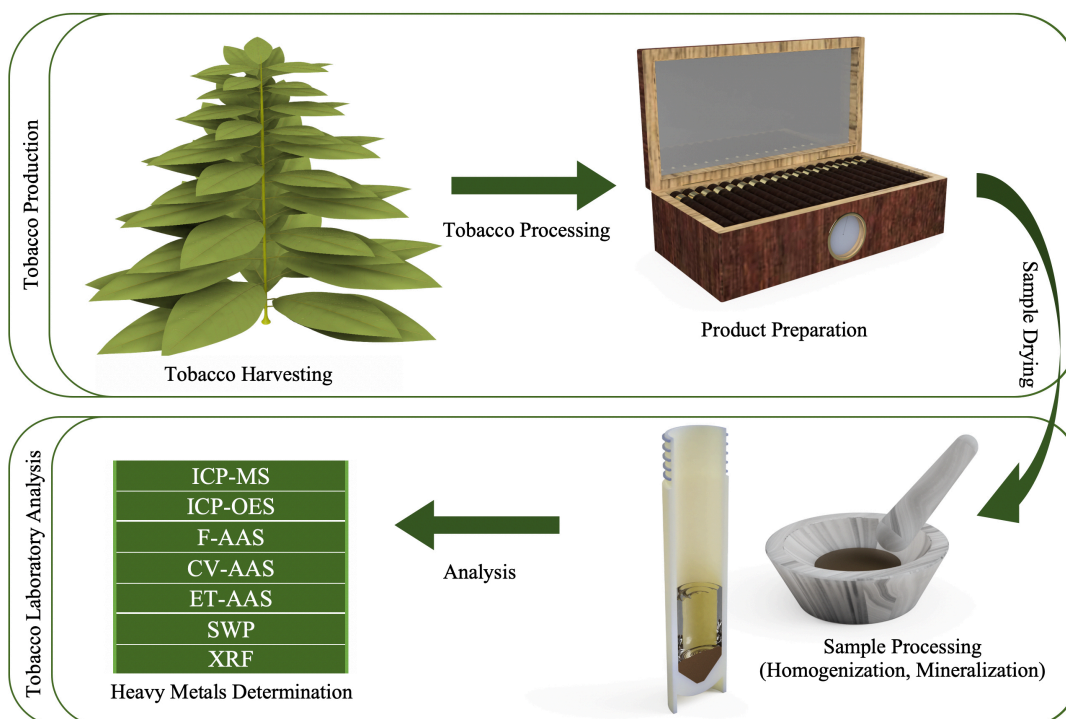
Review of cigars and cigar-type products as potential sources of consumer exposure to heavy metals

Abstract

The popularity of cigars, growing since 1993, has not gone hand in hand with the increased interest of researchers in these products. Although the literature widely describes the harmfulness of tobacco and the content of toxic substances in tobacco products, the topic is often treated selectively as relating primarily to cigarettes and rarely extends to other products of the broadly defined tobacco industry. However, there is no reason to marginalize the harmful effects of other nicotine products, (which include tobacco products such as cigars). The study analyzed the available literature on the content of selected heavy metals in cigar tobacco. Among the heavy metals, the following contents of elements content in tobacco were recorded in cigars: Fe (420-2200 $\mu\text{g/g}$), Mn (100-370 $\mu\text{g/g}$), Zn (14-180 $\mu\text{g/g}$), Cu (15-140 $\mu\text{g/g}$), Pb (not detected-32 $\mu\text{g/g}$), Cd (nd-19 $\mu\text{g/g}$), Ni (nd-13 $\mu\text{g/g}$), Cr (nd-10 $\mu\text{g/g}$), Co (0.65-1.0 $\mu\text{g/g}$), As (nd-0.66 $\mu\text{g/g}$), Hg (18-25 ng/g). Importantly, the values often differ between cigars of different origins and types, indicating the need for more extensive research.

Keywords: cigars, heavy metals, tobacco, trace analysis

Graphical Abstract



Introduction

The oldest tobacco (*Nicotiana tabacum*) consumption artifacts found are those related to snuff, and therefore it is believed that ingestion was the first method of tobacco consumption¹. Later, tobacco also began to be smoked, chewed, drunk as a brew, eaten or smeared on the body (to kill insects)^{1,2}. It was appreciated for its analgesic, antiseptic and insecticidal properties¹.

The globalization of tobacco has contributed to the emergence of a number of new ways of using this stimulant, and the isolation of nicotine has allowed the development of non-tobacco products delivering the substance to the human body. Owing to this, the market now has a wide range of nicotine products³. Due to their large number, it is worth making the first division here, concerning the manner of use. In the literature, the term "combustible tobacco" (CT) can be found in opposition to smokeless tobacco (ST). One of the CT products is a cigar.

Cigars are cylindrical products made entirely of tobacco leaves. In the cross-section, three layers can be distinguished: filler, binder and wrapper, as shown in Figure 1. The quality of the cigar is mostly dependent on the filler, which is both the core and the main component of the cigar, i.e. about 94 % of the weight. The outermost layer, wrapper, is about 2 % (the rest of the mass is contained in the binder, which is between the wrapper and the filler). Consequently, the most visible leaf is responsible for the strength (amount of tar, nicotine, and carbon monoxide⁴) of the cigar to a very small extent; thus a very mild cigar may be wrapped in a dark leaf and vice versa.

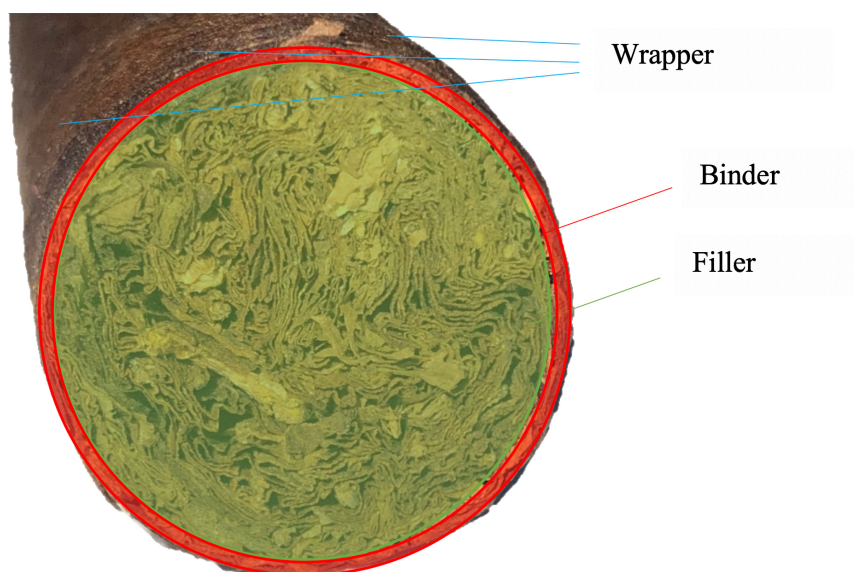


Fig. 1. Cross-section of an Alec Bradley American Sungrown Gordo cigar with a long filler (handmade) with marked layers.

As early as 1899, the author of the book *Curing and Fermentation of Cigar Leaf Tobacco*⁵ drew attention to the specific properties that must be met by a tobacco leaf used to produce a high-quality cigar. First of all, he emphasizes the importance of taste, aroma and flammability, and then the nicotine content, which by itself does not determine the quality of a cigar, just as the content of ethanol does not determine the quality of wine.

It is the climate, soil characteristics and experience of the growers that make it possible to obtain high-quality leaves, which, however, do not have a specific cigar smell or taste. For that, the crop requires three-stage processing – broadly speaking: (1) curing process; (2) fermentation; and (3) after-fermentation or aging. During these stages, among other things, the loss of nicotine occurs. The entire leaf preparation process can take up to several years⁵.

Cigars can come in a variety of sizes and shapes, and take about one to two hours to smoke. Three types of products can be classified as cigars: "large cigars", "little

cigars" and "cigarillos". Little cigars are defined as a "roll of tobacco wrapped in leaf tobacco or any substance containing tobacco (...) and as to which one thousand units weigh no more than three pounds" (about 1.36 kg). They can also be equipped with a filter and a mouthpiece. In recent years (in the United States), however, a tax on little cigars has been introduced that has become equal to the tax on cigarettes. As a consequence, some producers increased the weight of tobacco in these products and thus changed their tax category (in the US). Cigarillos do not have a separate definition (and thus no separate tax category in the US). They weigh more than little cigars and less than large cigars (premium cigars). The latter are tobacco products larger than little cigars and cigarillos, which can be divided into hand-made (with a long filler) and machine-made (with a short filler). By comparison, cigarettes are most simply classified as a "roll of tobacco wrapped in paper" and are often subject to regulations, such as banning of distinguishing flavors, prohibition of descriptors such as "light" or "ultralight". These regulations usually, to a limited extent, also apply to products referred to as "cigars" ⁶⁻¹¹.

Trends in cigar smoking

At the beginning of the 20th century, when cigarette smoking was not yet very common, cigars and pipes were the most popular forms of consumption of CT products. Almost a hundred years later, exactly in 1991, cigars already accounted for only about 1.5 % of the tobacco market ². They had definitely been superseded by cigarettes and never returned to their former dominance over the CT products market.

In the studies published in 2003, attention was drawn to a clear increase in interest in cigars in the years 1993-2000. Until 1993, the consumption of cigars in the US was steadily falling. This trend changed with the arrival of a "cigar lifestyle magazine" *Cigar Aficionado*. Smoking cigars in the United States (US) was previously



an obscure activity that was practiced mainly by blue collar workers smoking inexpensive, machine-made cigars. By 1995, *Cigar Aficionado* was already the most popular lifestyle magazine in the United States with a readership of over 400,000 per single issue. One of the largest international cigar companies, Consolidated Cigar Holdings Inc., has credited the magazine with an improved image of cigar smoking, which resulted in a significant increase in their consumption and sales ¹². The authors of this paper do not specify, however, whether they consider little cigars and cigarillos as "cigars".

Similar observations are reported by Baker et al. in the publication from 2000. In it, it was specified that in the years 1993-1997 the consumption of all types of cigars rose rapidly after a period of decline (in the years 1964-1993). According to that study, however, "premium" cigars accounted for a small share, compared to "small cigars" or "cigarillos" ¹³.

A study published in 2021 noted that in the following years, i.e. 2000-2016, the consumption of cigars in the US doubled (from 6.2 to 12 billion items per year). However, the authors point out that the products referred to in the US as "Cigar" come in the three forms mentioned. In the conducted research, large cigars accounted for about half of the consumed products ¹⁴.

In a 2019 review, the authors showed that cigar smoking among adolescents is a growing problem. These products have been shown to be harmful to health, albeit to a lesser extent than cigarettes. It was pointed out that in 37 studies a wide range of products (large cigars, little cigars and cigarillos) were considered cigars, in 7 it was not specified what constitutes a cigar, and in 4 only cigarillos were examined. This is problematic, since these products have different characteristics, which should be taken into consideration ⁷.



In fact, cigars are more harmful than cigarettes, and their long-term use causes cancer of the lung and upper gastrointestinal tract ^{13,14}. Consumers of cigars, constitute a significant and, since 1993, a growing number.

Elemental contamination of cigars

Environmental pollution with heavy metals is a serious global problem. They are not biodegradable and tend to accumulate in the environment. They can also accumulate in body tissues (bioaccumulation), and their content may increase with subsequent trophic levels (biomagnification). Heavy metals can be classified, in the context of their biological role, as essential and nonessential. The former are required, in low concentrations, by living organisms for physiological and biochemical functions, while the latter are redundant or even toxic.

The concentration of these metals in the body above a certain limit causes severe health effects. Important metals (biologically active) include, among others: Fe, Zn, Mn, Ni, Cu, Co and Cr, while non-essential metals, therefore considered absolutely harmful, e.g. Pb, Hg and Cd ¹⁵⁻¹⁷. Scientists are divided as to the importance of chromium in living organisms. An element also classified as nonessential is arsenic (As), which, however, is a metalloid, therefore calling it "heavy metal" could be considered erroneous ¹⁸.

The possibility of inhalation of these heavy metals is largely dependent on the temperature of the cigars during smoking. According to Shikata's tests from 1926, carried out with an iron-constantan enameled thermocouple placed in the middle of a cigar, the average temperature was 646.6 °C. The researcher noted the key role played by airflow in the achieved temperature, therefore the mean was determined on the basis of the collected maximum stable measured values without or with slow suction.

Oriental cigars (Japanese Tobacco Monopoly Bureau) were used in the research ¹⁹.



The humidity of a cigar may vary depending on its type and storage conditions. Accounting for the water content is important, as it can reach up to 10-15% for tobacco stored in a humidor^{20,21}. The determination of metals in cigars should always be carried out on tobacco samples with known moisture content at the time of measurement. These can be lyophilized samples or, alternatively, part of the matrix samples can be directed for parallel testing using a moisture analyzer.

Toxicity of heavy metals present in cigars

All heavy metals in sufficiently large amounts are harmful, and when they enter the body they produce toxicity by forming complexes with cellular compounds containing sulfur, nitrogen or oxygen. In this way, they inactivate enzyme systems or modify key protein structures, leading to dysfunction and death of cells^{22,23}.

As shown in Figure 2, the contents of the determined heavy metals often varied considerably. With such a wide range of places and years of research and sample purchase, when discussing the toxicity of cigar contamination with these elements, it is most sensible to refer to the highest marked contents, since for consumers, the highest possible risk is crucial.

Arsenic (classified as a metalloid) is present in cigars in trace amounts. Compared to other heavy metals determined in tobacco, there was little of it, the content did not exceed 0.7 µg/g. Arsenic in nature can occur in three oxidation states: trivalent arsenite, pentavalent arsenate, and elemental arsenic (nontoxic). It is also present in the form of organic and inorganic compounds, and also as a gas, arsane, with arsane and inorganic arsenic compounds being the most toxic. Most cases of arsenic (III) oxide poisoning involve accidental ingestion of arsenic-containing pesticides. On the contrary, the main cause of chronic arsenic toxicity in humans is geological contamination^{18,22,24}.



Compared to other determined heavy metals, mercury was present in cigars at approximately one order of magnitude less; therefore, the studies gave its content in ng/g of tobacco". In tobacco products, mercury exists in inorganic, organic, and elemental forms. The inorganic form is easily absorbed in many ways: from the gastrointestinal tract, by inhalation or dermally, while the organic form is very well absorbed from the digestive system, which may be associated with an increased risk for consumers of chewing tobacco. The toxic effect of elemental mercury is caused by inhaling its vapors, due to its good absorption into the pulmonary circulation. The metal is transported in the blood to the kidneys, intestines, lungs, and brain, where it easily crosses the blood-brain barrier and is deposited ²².

Lead has numerous industrial uses, however it has no physiological significance and any traces of lead in the human body can be considered contamination. As a consequence, lead contamination of cigars can have catastrophic health effects, especially in the case of CT products. In the latest publications (published after 2000 ²⁵⁻²⁸), the content of this element slightly exceeds 3 µg/g, however in 1977 it was measured at 30.80 µg/g. Due to the harmfulness of Pb, it is necessary to monitor its content in tobacco products. Furthermore, adults are often exposed to lead poisoning through the respiratory system ²², which only confirms the key role of the mentioned analysis of CT products. The toxic effect of lead is related to, inter alia, disruption of the activity of neurotransmitters and their receptors, which in turn leads to the disruption of synapse formation and their destruction ²².

Cadmium is one of the most important environmental pollutants, as it can cause many toxic effects. At the same time, it demonstrates the ability to accumulate in plant and animal tissues, influencing their growth and development, and posing a huge threat to human health. Therefore, tobacco products are naturally exposed to the accumulation



of Cd, and cigar consumers can inhale smoke rich in this element. From all the examined heavy metals, cadmium was determined in the greatest number of works, seven out of ten. In the latest publications, its highest recorded content is 2.24 $\mu\text{g/g}$ ²⁵⁻³⁴; however, similarly to lead, in 1977 the recorded values were much higher, reaching even 18.80 $\mu\text{g/g}$ ³⁰. The most important mechanisms of cadmium toxicity include changes in gene expression and inhibition of damaged DNA repair, disrupting apoptosis and autophagy, causing oxidative stress and interaction with bioelements^{35,36}.

In cigars, Co occurs in trace amounts, not much greater than As, although it should be noted that its content was determined only in two studies: in 2015²⁶ and 2019³⁴. The highest determined content of Cr was as much as 9.75 $\mu\text{g/g}$, Chromium and cobalt in trace amounts are needed in the human body due to their involvement in metabolic processes. The former is involved in glucose metabolism, while the latter (Co (III)) takes up the active site of vitamin B12 and is essential for its activity. The toxicity of Cr and Co is related to their oxidation state. Cr appears in a wide variety of oxidation states, the most common of which are Cr (III) and Cr (VI). Co also occurs in different oxidation states, of which Co (II) and Co (III) are the most common. While chromium in the sixth oxidation state is classified by the International Agency for Research on Cancer (IRAC) as a group 1 carcinogen (carcinogenic for humans), Cr (III) and metallic Cr are classified in group 3 (impossible to classify due to lack of relevant evidence). Cobalt, on the other hand, is classified as possibly carcinogenic to humans and it has been shown that occupational exposure to this element is associated with cardiomyopathy and neurological damage¹⁶.

Nickel is a heavy metal present in the environment at very low levels in the form of oxides or sulfides. It was noted that vegetables may contain more nickel than other foods, however it was not specified which vegetables or where they come from.



Environmental sources with lower concentrations of Ni are reported to include tobacco, but the authors did not specify which tobacco. As shown in Table S1, presented in Supplementary Materials where all data collected during presented review are shown in details, the nickel contents in cigar tobacco can be as high as 12.53 $\mu\text{g/g}$ ²⁵. This is approximately three times higher than the upper end of the nickel concentration range for tobacco indicated by the authors. From the point of view of the consumer's health, it is therefore important to monitor the amount of this element in various cigars. The most common toxicity caused by nickel compounds is an allergic skin reaction that occurs in part of the population. Nickel has also been shown to be a potential immunomodulatory and immunotoxic agent, independent of its allergic properties. Nickel compounds have also been classified as carcinogenic to humans and animals²³. Nickel is also an essential element for both animal and plant life. It has been reported to interact with iron found in hemoglobin to aid oxygen transport, stimulate metabolism, and is considered a key metal in many plant and animal enzyme systems¹⁷.

Iron homeostasis is an essential biological process that ensures the distribution of this element into tissues for a variety of cellular processes³⁷. However, iron overload and consequent transferrin saturation and accumulation of non-transferrin bound iron (NTBI) are possible. Uncontrolled iron deposition in organs leads to progressive tissue damage and consequent organ failure. NTBI is presumed to play a major role in various pathological conditions that are dominated by iron overload^{38,39}. Among the heavy metals, it is Fe that is present in the cigars in highest concentrations^{25,28,34}. The studies reported its content to be as high as 2.17 mg/g. Although the human body may have a high iron tolerance due to the biological role of these element, it is still important that compared to other tested heavy metals, Fe is present in significantly higher amounts in



tobacco. The effect of iron absorbed from the digestive system can be radically different from the effect it has on the respiratory system ⁴⁰.

Zinc is an essential micronutrient for human health, especially for the elderly ⁴¹. All major metabolic pathways are regulated by zinc metalloenzymes. However, zinc overload is associated with health consequences, e.g., damage to neurons. Moreover, the route of administration can make a difference in toxicity ⁴². In the works on the determination of selected heavy metals in cigars, the zinc content was up to 176 $\mu\text{g/g}$ ³⁰. The toxicity related to Zn overload and the toxicity related to the form of administration (in the gas fraction, with the smoke) can be taken into consideration. Although few people are exposed to zinc poisoning due to their diet or exposure to this element in their environment, there can be some danger in the growing popularity of additives to, among others, food, supplements, or drugs ⁴². Zinc additives are used in food preparation, processing and preservation ⁴². It is not unlikely that this trend will spread to tobacco manufacturers.

Manganese is an essential element for intracellular activities, because it acts as a cofactor for some enzymes and thus plays an important role in the processes of digestion, energy production, and immune response ⁴³. This metal can be absorbed quickly from the digestive or respiratory tract and tends to accumulate in organs such as liver and brain. Right after iron, the manganese content is the highest in cigars (up to 374 $\mu\text{g/g}$ ²⁶). The high content of Mn in tobacco, compared to other examined heavy metals, combined with rapid absorption by the respiratory system, may lead to poisoning with this element ⁴⁴. Patients with such a diagnosis exhibited, among other, Parkinson's-like symptoms ⁴⁴. The source of exposure may be contaminated food, water, soil, or air ^{43,44}. Growing tobacco in soil contaminated with manganese or in an environment with contaminated air, or watering it with contaminated water, can



increase the content of this element in cigars due to *Nicotiana tabacum* ability to accumulate this element ⁴⁵.

Copper is one of the heavy metals essential for the proper functioning of living organisms due to the role it plays in proteins and other biomolecules ⁴⁶. An excess of Cu can cause oxidative stress in tissues and their subsequent damage ⁴⁷. Inhalation of metal vapors, including copper, can result in severe respiratory health consequences ⁴⁸. The highest Cu content recorded in the examined studies was 138 $\mu\text{g/g}$ ³⁰. Compared to elements such as Hg, As, or Cd, the levels of Cu in cigars are significantly higher.

Methodology

As part of this study, the information available in databases (including ACS, Nature, Oxford Journals, PubChem, Scopus and Taylor & Francis) was analyzed in terms of contamination of cigars with harmful elements. Keywords such as cigars, cigar tobacco, tobacco contamination, cigar contamination, heavy metals in cigar tobacco and the like were used in the search. The search was limited to the areas of chemistry and medicine. Boolean operators such as AND and NOT were also used ("cigar NOT cigarette", "cigar AND heavy metals", "cigar NOT lake", "cigar AND elemental contamination", "cigar AND tobacco contamination", "cigar tobacco AND heavy metals", "cigar AND contamination"). The results and methods of sample preparation described in the works published in the years 1972-2021 were analyzed. As the number of studies on the elemental contamination of cigars is small and there is a lack of new scientific reports on this subject, there is both need and space for further research.

Methods of heavy metal determination in cigar samples

Various analytical procedures were used to determine the heavy metal content in the tested tobacco. The information mentioned is presented in Table S1 in the



Supplementary Materials section. The content ranges of selected heavy metals, the determination methods used, countries and years of research are listed in brief in Table 1.

Table 1. A list of content ranges of selected heavy metals in the studied works, determination methods used, countries and years of research.

| Country | Element, content, content range [µg/g] | Determination method | Years of Research |
|-------------------------------|---|---|-----------------------|
| United States of America | Zn 51* | Atomic absorption spectroscopy (AAS) | 1972 ²⁹ |
| | Cd 1.9* | | |
| German Democratic Republic | Zn 97-176 | Square-Wave | 1977 ³⁰ |
| | Cu 42 – 138 | Polarography (SWP) | |
| | Pb 16 – 32 | | |
| | Cd 7.9 – 19 | | |
| United States of America | Cd 0.33 – 2.2 | Inductively Coupled Plasma – Mass Spectrometry (ICP-MS) | 2016 ** ³¹ |
| United States of America | Hg 21*** | Cold Vapor – Atomic Absorption Spectrometry (CV-AAS) | 2008 ³² |
| India | Fe 530 – 2200 | Inductively Coupled Plasma – Optical Emission Spectrometry (ICP-OES) | 2010 ²⁵ |
| | Zn 14 – 56 | | |
| | Ni 6.1 – 13 | | |
| | Cu 15 – 38 | | |
| | Cr 2.7 – 9.8 | | |
| | Pb 1.1 – 3.1 | | |
| | Cd 0.29 – 1.2 | | |
| United States of America | Mn 140 – 370 | Inductively Coupled Plasma – Mass Spectrometry (ICP-MS) | 2015 ²⁶ |
| | Ni 1.5 – 4.4 | | |
| | Co 0.65 – 1.00 | | |
| | Cr 0.88 – 6.46 | | |
| | Pb 0.46 – 1.23 | | |
| | Cd 0.752 – 1.74 | | |
| United States of America | Hg 17.9 – 24.9*** | Cold Vapor – Atomic Absorption Spectrometry (CV-AAS) | 2015 ³³ |

| | | | |
|-----------------------|--------------------|---|--------------------|
| United Kingdom | Ni nd – 1.4 | X-ray fluorescence (XRF) | 2015 ²⁷ |
| | Cr nd – 3.4 | | |
| | Pb nd – 1.2 | | |
| | Cd nd – 1.7 | | |
| | As nd – 0.5 | | |
| Poland | Fe 660 – 420 | X-ray fluorescence (XRF) | 2018 ²⁸ |
| | Zn 50 – 65 | | |
| | Mn 100 – 160 | | |
| | Ni 2.8 – 3.0 | | |
| | Cu 22 – 29 | | |
| | Cr 1.4 (LOD) – 1.6 | | |
| | Pb 0.31 – 0.57 | | |
| | As <LOD | | |
| Brazil | Fe 880 | Inductively Coupled Plasma – Optical Emission Spectrometry (ICP-OES) | 2019 ³⁴ |
| | Zn 43 | | |
| | Mn 220 | | |
| | Ni 8.2 | | |
| | Cu 16 | | |
| | Co 0.99 | | |
| | Cd 0.96 | | |
| | As <LOQ | | |

*Values per unit [$\mu\text{g}/\text{cigar}$], ** the samples were leaves from which cigars could be made,

***Values per unit [ng/g].

Menden et al. in 1972 published the results of an analysis of the content of cadmium, nickel, and zinc in cigarettes, which they compared with the content of these elements in pipe and cigar tobacco. As reported, they used one brand of cigar, purchased on the market. The country of origin of this cigar is unknown; however, research has been conducted in the United States. Tobacco samples were prepared for testing using dry and wet ashing. No significant differences were observed in the results obtained using these two methods. Wet ashing consisted of boiling the samples until dissolution and oxidation in concentrated HNO_3 , evaporating to a volume of 1 ml and then dissolving with hot 10 % HNO_3 for analysis. Dry ashing was performed by placing samples wetted with concentrated nitric acid (V) in a muffle furnace ($400\text{--}450^\circ\text{C}$). What remained was dissolved in 2 ml of concentrated HNO_3 , evaporated, and the residue was



dissolved in 10 % HNO₃ for analysis, which was performed with 10% nitric acid solutions (V) using atomic absorption spectroscopy (AAS) by aspirating samples directly into a Perkin-Elmer Model 303 ²⁹.

Franzke et al. in 1977 determined the content of zinc, copper, lead, and cadmium in five cigars or cigarillos. The research was carried out in the GDR (German Democratic Republic), and the products were also most likely purchased in this country. It was decided that the method would be wet tobacco combusting to avoid cadmium losses in dry incineration. The sample preparation included digestion of 2.0 g of tobacco in a mixture of HNO₃ / HClO₄ (4: 1) and heating until clarification. The contents of the examined heavy metals were determined using square wave polarography³⁰.

Lugon-Moulin et al. in the paper from 2006 analyzed 755 leaf samples of three major types (Flue-cured, Burley and Oriental) obtained from 13 countries on four continents between 2001 and 2003. The sampling method involved acquiring leaves from one farmer's field (s) and from different plants at random. The samples were oven dried at 60–70 °C and 500 mg of each were digested in 10 ml of concentrated HNO₃ in a microwave-accelerated digestion system. The solution was transferred to 200 ml volumetric flasks and brought to a final volume with deionized water. To specify the content of Cd, ICP-MS was used. Although this is not strictly on cigars, the tested tobacco leaves could have been used in cigar production ³¹.

In Panta et al. research from 2008 on mercury content in tobacco, the AMA-254 advanced mercury analyzer was used. It included a system for sample pyrolysis, Hg trapping by amalgamation with gold, and detection by an in-line atomic absorption spectrometer. Only one brand of cigars was analyzed, measuring 12.7 cm in total length and 1 cm in diameter. Whole cigars, after removing the plastic tip, were simply placed directly into a quartz pyrolysis tube using Teflon coated tweezers after weighing. The



mean moisture (6.2%) of a cigar was defined as the weight difference before and after drying it for 3 h at 100 °C ³².

In a 2010 publication, Verma et al. described some heavy metal concentrations in different Indian tobacco products, including five brands of cigars. The research was carried out in Rohtak, located in India. Samples were purchased in local markets according to their availability and use by smokers in and around the city. Tobacco samples were taken from cigar filler and ground to ~200 mesh size using an agate mortar and pestle. One gram (accurately weighed in the fifth decimal place) of each homogenized sample was digested using a combination of mineral acids (HF, HNO₃ and HClO₄) supported by high temperature. Subsequently, the solution was evaporated to dryness, recovered with 2 mol/dm³ HNO₃ and kept in the laboratory systematically for elemental analysis using ICP-OES ²⁵.

Pappas et al. in 2015 studied levels of content of some heavy metals in little cigars that were purchased domestically (USA) in 2014. All 17 brands of cigars were selected based on their availability. Filler samples were dried for a minimum of 1 h at 90 ° C and then ground for 20 s to improve homogenous in a Smart Grind coffee grinder. Weighed sample portions (0.100-0.150 g) were digested with double-distilled nitric acid, hydrofluoric acid and 35 % hydrogen peroxide, supported with microwaves. The digested samples were diluted with ultrapure water to a volume of 100 ml. An S.C.-DX FAST autosampler was used to eliminate carryover and guarantee high sample throughput. Metal concentrations were measured with an ICP MS ²⁶.

In 2015 Fresquez et al. studied the mercury content in the same 17 brands of cigars as Pappas et al. The tobacco drying and homogenizing methods were also identical. However, samples were purchased from online retail outlets and approximately 0.050 ± 0.010 g of dry tobacco filler was taken for analysis instead of



0.100-0.150 g. Mercury concentration was determined by UV absorption at 253.7 nm with a cold vapor – atomic absorption technique ^{26,33}.

Caruso et al. in 2015 analyzed As, Pb, Cr, Ni, and Cd concentrations in 23 filtered cigars. Samples consisted of seven brands and were purchased in June 2013 from a retail website. The researchers had chosen the products according to their availability and popularity. Cigars from each brand were purchased in flavored and unflavored variants for comparison. Cigar packs were conditioned at $22.0 \pm 2.0^\circ\text{C}$ and $60.0 \pm 2.0\%$ relative humidity in an environmental chamber before testing. Metal content testing was performed at the University of St. Andrews (Scotland, UK). The sample preparation included tobacco drying, powdering, and pressing into pellets. 25 elements concentrations were measured with polarized energy-dispersive x-ray fluorescence (XRF), but the authors focused on the five most toxic ²⁷.

Majewska et al. in 2018 measured levels of 18 elements in some tobacco products that had been purchased from local markets (Poland). Cigar fillers were carefully separated, dried, and ground with the ultrapure mill. 0.2 g of tobacco powder was mixed with high purity HNO_3 (Merck Surapur 65%, 6 mL) and 200 μL of 100 ppm water solution of $\text{Ga}(\text{NO}_3)_2$ (Merck). The solution was mineralized in a microwave oven. To measure the concentrations of the elements tested, a S2 Picofox spectrometer was used, equipped with a 30 W X-ray tube with a Mo anode working at 50 kV and 600 A. The paper does not present the exact contents; however, charts illustrating them were presented. The data was therefore obtained from the charts using the GetData Graph Digitizer program ²⁸.

Ferreira et al., in 2019 studied the mineral composition of some tobacco products. The authors had bought 22 samples (eight cigars) at the fairs in the city of Salvador, Bahia, Brazil, from specific tobacco stores. The tobacco products were cut



into smaller pieces and dried by lyophilization (Liotop Model L10) for 72 h, after which the samples were powdered for 10 minutes in a ball mill (PM 100, Retsch, Düsseldorf, Germany). Approximately 200 mg of homogenized samples were transferred to polytetrafluoroethylene (PTFE) digestion vessels and 2.1 ml of HNO₃ (65%) 1.2 mL H₂O₂ (30% m m⁻¹) and 6.7 mL of deionised water was added. The samples were digested in closed vessels kept at a temperature of 180 °C for 2 h. After the process, a solution was filled to 15 mL with deionized water. An inductively coupled plasma optical emission spectrometer (model E720, Agilent, Varian, Mulgrave, Australia) was used for analysis³⁴.

Results

In this work, the content of selected heavy metals was analyzed in ten papers published between 1972 and 2019 (no data were available between 2020-2021). In some of these papers, other CT products were referred to as "cigars", which was noted in the *Discussion*. For the purposes of determining the content of the 11 selected heavy metals in this work, no distinction was made as to exactly which product, referred to as a "cigar", was examined by the authors, or whether they were only leaves from which cigars can be made. The results are shown in Table 1 and Table S1 and summarized in the graphs in Figures 2 and 3.

Element content analysis

First of all, it should be noted that most studies used the unit "µg/g of tobacco", and only in one, from 1972, the content was defined as "µg/cigar". Figure 2 presents graphs that compare the content of individual heavy metals in cigar tobacco from the cited works. Their contents in tobacco differ from each other and are distributed as follows (according to average values): Fe>Mn>Zn>Cu>Pb>Ni>Cr>Cd>Co>As>Hg.

When analyzing the values presented in Figures 2 and 3, and in Tables 1 and S1, it can be noticed that tobacco has the highest content of iron and manganese. Heavy metals such as Pb, Cd, Ni, and Cr are usually found in small amounts, and Co and As can be regarded as trace elements. Mercury at cigars occurs in the lowest concentrations, on average around 21 ng/g of tobacco. The graphs should be interpreted so that most of the results are within the boxes, that is, between the first and third quartiles and around the median (horizontal line inside the box). The points outside the boxes and whiskers are diverging points.

As evidenced in Figure 2, the reported concentrations of several heavy metals cover a wide range of values, with some concentrations being significantly higher than the average value. Analysis of Table 1 shows that the deviating values often originate from specific works. For example, in the case of lead, values an order of magnitude greater than in the rest of the works come from Franzke et al. from 1977³⁰. The authors of the study specify neither the place of origin of the tobacco from which the products were made nor the method of production. A similar observation, relating to the same work, can be made for copper, cadmium, and zinc. Although here the values are not always an order of magnitude higher, they are still clearly higher than in the other works.



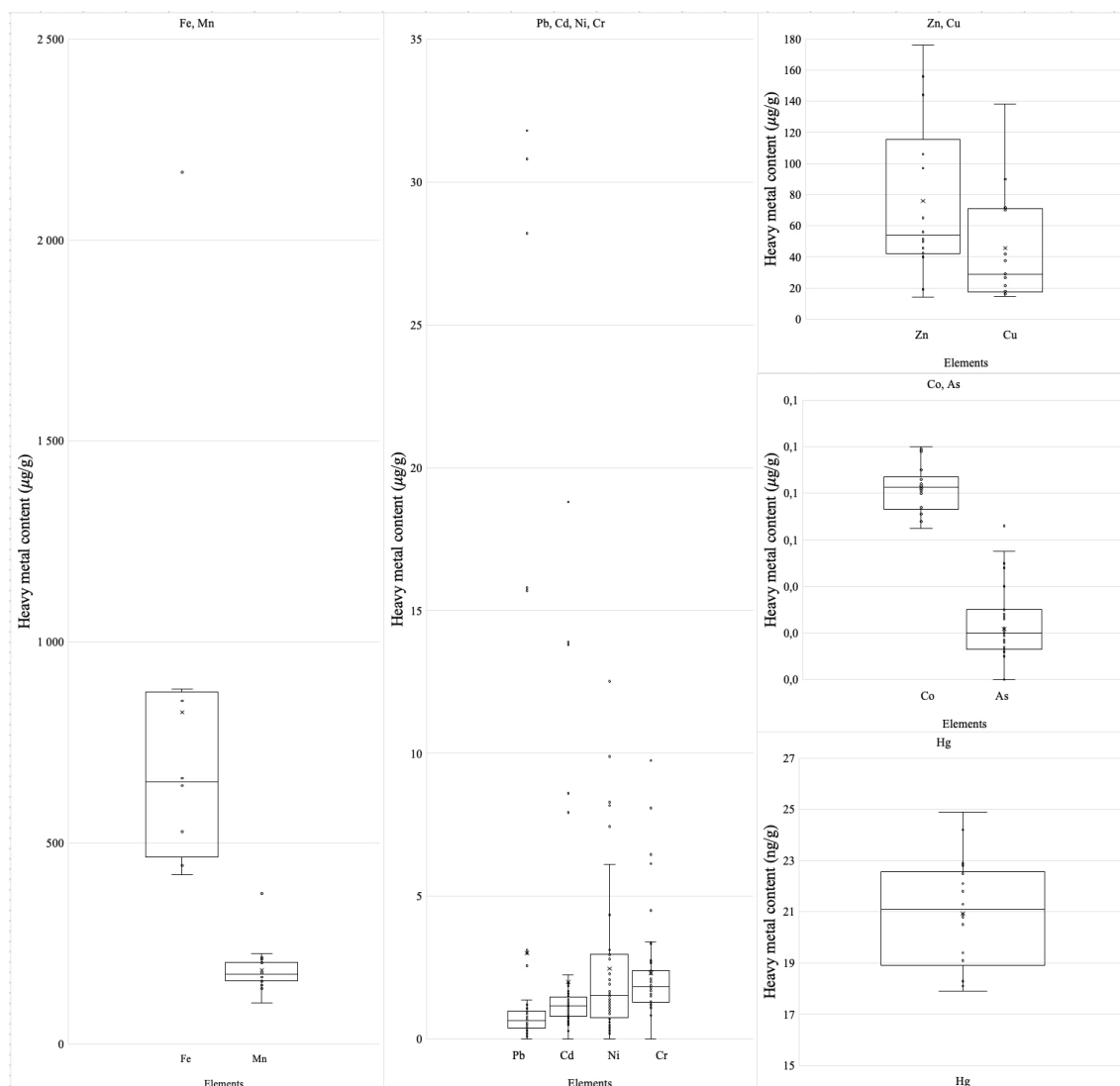


Fig. 2. Box and whiskers plots with the results of the determination of the heavy metals in cigars. The boxes contain most of the results for a given element, the horizontal segment inside them determines the location of the median, and "x" shows the mean ²⁵⁻³⁴.

A similar situation occurs in the results of the work of Verma et al. from 2010 ²⁵ where the nickel and chromium content is noticeably higher than in other studies. However, this relationship cannot be observed for other heavy metals. The lead content in the results of Verma et al. ²⁵ is higher than in later analyzed works of other authors, but lower than in the earlier work of Franzke et al. ³⁰. Copper, on the other hand, occurs here at the lowest concentration of all studies (except for one result), as does cadmium. The iron content generally, apart from one significantly different result, corresponds to

the values of the other cited works. In addition, it is not stated in this paper that the test tobacco had been dried. If the moisture was not truly eliminated from the sample, the values would be higher when converted to the dry matter content.

It is interesting that the values from the work of Menden et al. from 1972²⁹, which are defined as the content of an element per the whole cigar, are contained within the boxes. Although the weight of the product tested is unknown, cigars usually weigh from about one and half to several grams⁴⁹. Assuming a similar weight range to convert the content reported per cigar to the unit of $\mu\text{g/g}$ of tobacco would result in an even lower value.

When considering why in some studies the content of heavy metals is higher, two reasons can be taken into account: the impact of year of the study (the awareness of elemental impurities has developed over the years) or the type of samples. Although there are few works available, it would seem that the first factor is not likely to be the cause of such a phenomenon. In the case of the heavy metals whose contents are higher, the analysis of the results from other, both earlier and later works, shows no dependence on the sampling time. The influence of the broadly understood "sample type" is more likely. This includes both the origin of the tobacco and the method of preparation (machine or manual) and the effect of any additives. Unfortunately, there have been few works on this subject, which makes it difficult to determine the cause of this phenomenon with certainty. There is a probability that random batches of products had been contaminated. It may even be associated with a limited number of samples or with tobacco growing in only one season. A broader analysis involving more products, brands, variants, and countries of origin would provide valuable information. Regular research would help determine the trend in the content of the heavy metals in tested cigars.



By analyzing the graph of normalized values (according to Equation 1) values in Figure 3, it is possible to see how the contents of the heavy metals in tobacco are distributed in the examined works. In the case of the elements Zn, Co and Hg, a narrow scatter of the results was observed. In the case of other elements, some values are much higher than others, sometimes even thirty times.

$$n = \frac{x - \min}{\max - \min} \quad (1)$$

Where:

n – normalized value,

x – value subject to normalization,

\min – minimum value in the data set,

\max – maximum value in the data set.

The work of Verma et al.²⁵ presents a summary of the the results of elemental analyses of 22 studies and the results of the elemental analysis of cigarettes from the authors' own research. These and other^{28,29} results from the analyzed works are shown in Figure 4 and the results obtained for cigarettes are summarized.



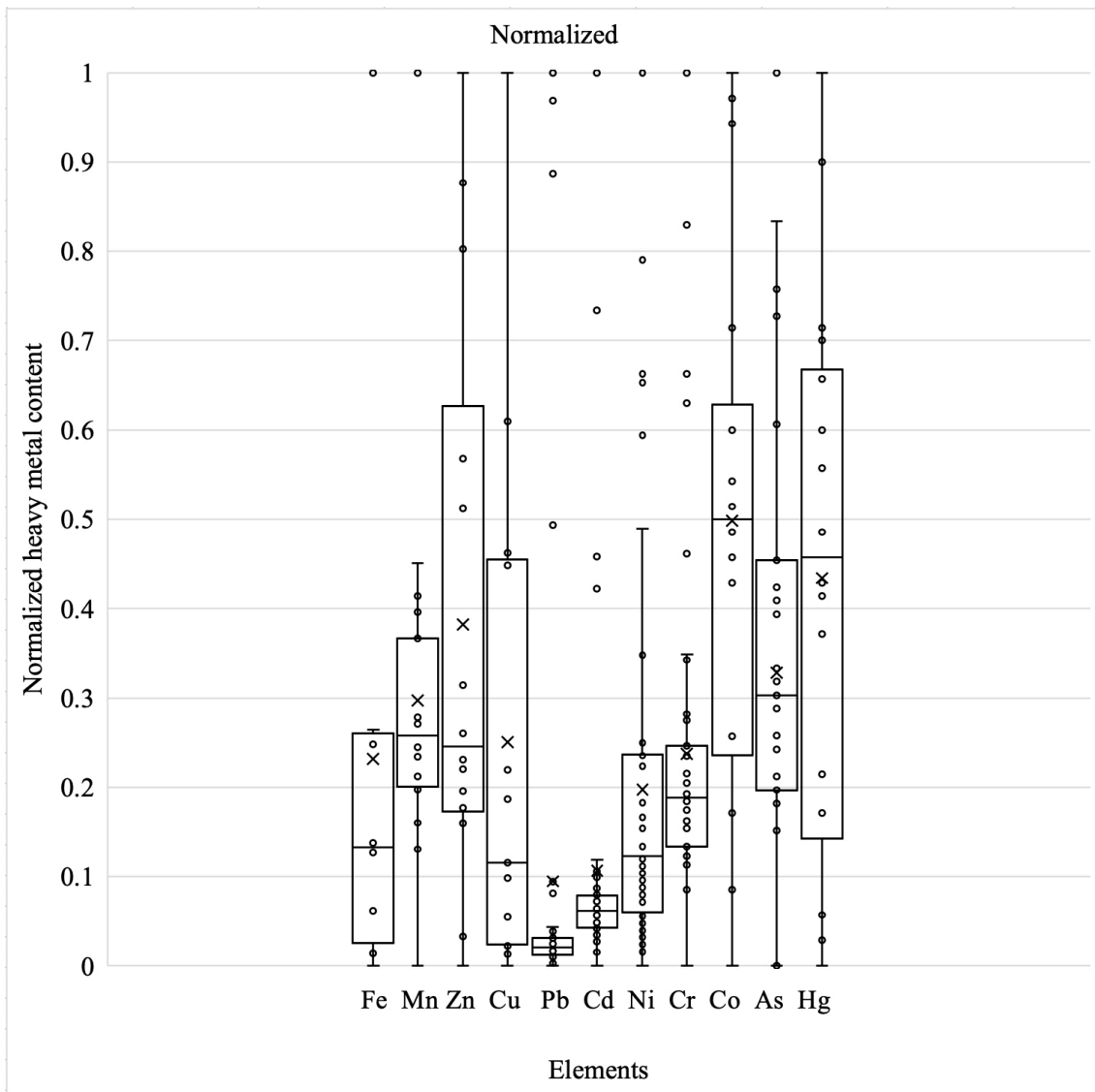


Fig. 3. Box and whiskers plots with normalized contents of all determined elements. The values on the vertical axis are not concentration values. The boxes contain most of the results for a given element, the horizontal segment inside them determines the location of the median, and "x" shows the mean²⁵⁻³⁴.

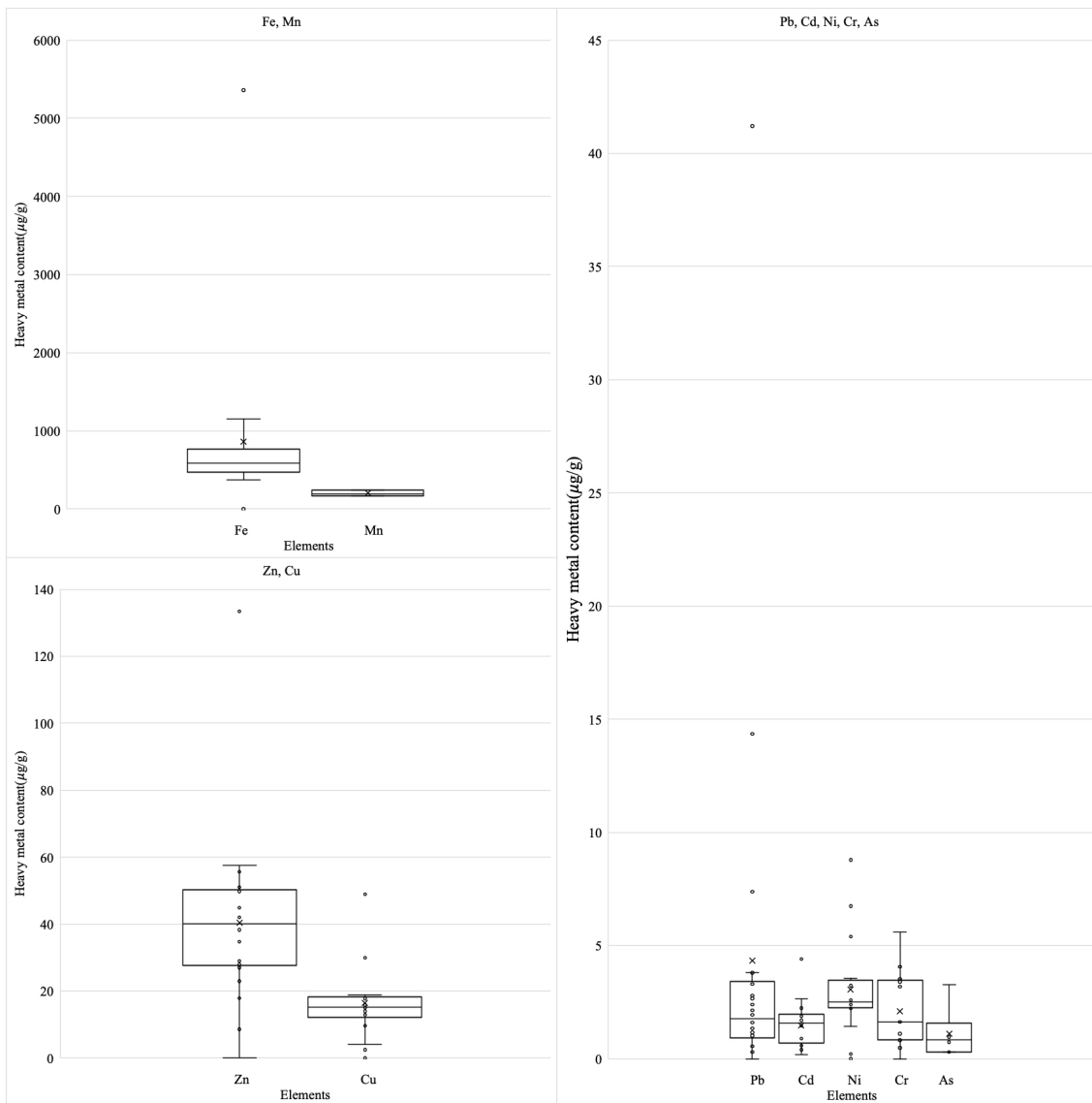


Fig. 4. Box and whiskers plots with the results of the determination of the selected heavy metals in cigarettes. The boxes contain most of the results for a given element, the horizontal segment inside them determines the location of the median, and "x" shows the mean. The values are from the works of Verma, Menden and Majewska et al. 25,28,29

Discussion

Analyzing the literature data on cigars, it can be concluded that despite the growing popularity of these products since 1993, they have not been as widely described by researchers as cigarettes. This is confirmed by the comparison in the work of Verma et

al.²⁵, in which the authors compared the results of their own research on selected products with the data in the literature. The authors cited as many as 25 references for cigarettes, 2 for bidi (a cigar-like product, but the wrapper is made of Tendu leaf), 4 for chewing tobacco, and 3 for snuff. However, they did not cite any work on the content of the tested metals in cigars.

Often such studies are not strictly focused on cigars. In two of the studies^{29,32} they were tested only for comparison with the results obtained for cigarettes, and in another one³¹ it was not finished products that were tested, but leaves from which cigars could be made. In the oldest of the cited works, the authors wrote: "For comparison, we determined the metal content of one brand of cigar and one brand of pipe tobacco, which were purchased on the market." When choosing a cigar for comparison, the authors do not state that they were guided by the origin of the leaves or other factors that may have turned out to be crucial for the content of the heavy metals being determined.

The relatively small number of items and often secondary importance of cigars in the literature prove that these products are not a popular subject of research and that they are not given due attention, despite their popularity growing for almost thirty years. Thus, it can be concluded that further research on cigars will be scientifically valuable.

Another piece of evidence of the lack of proper attention to cigars is the issue of inconsistent naming, as noted by researchers^{7,13,14}. There is a distinction between traditional, premium quality *large cigars*, smaller *little cigars* and *cigarillos*. The works often refer to them all generally as "cigars", which is unjustified and confusing as these products differ in the way they are made, and often also in the type of tobacco. When starting research, the tested material should be defined as precisely as possible, not only classifying it, for example, within the scope of tobacco products but also, if possible,



specifying the place and time of purchase, the origin of leaves, etc. Calling various products collectively *cigars* in the works makes it difficult to compare them with each other.

Expanding beyond the scope of this work the issue of nomenclature, it is worth noting that some inhaled nicotine products no longer contain tobacco, thus it is worth implementing the term *nicotine products* to which tobacco products belong. It is also worth noting that some new systems have been developed to heat tobacco instead of burning it⁵⁰⁻⁵². The mentioned feature makes it impossible to qualify such systems as combustible tobacco – CT. It is interesting to note that the so-called "hookah" or "shisha", which has been known for a long time as popular "wet" tobacco products, cannot also be called a CT because the tobacco in it is heated instead of burned. The use of the correct nomenclature is essential for the correct description and comparison of the nicotine products tested.

The authors of one of the works on nickel toxicity²³ report that environmental sources of lower levels of nickel include, inter alia, tobacco. However, smoking cigarettes has been found to be a non-occupational source of nickel exposure due to the fact that each cigarette contains 1.1-3.1 µg of nickel and up to 20 % of it may occur in the gaseous phase. The authors summarized this paragraph with the words: "pipe tobacco, cigarettes and other types of tobacco products do not greatly differ from one another in terms of nickel content", following Cempel and Nikel⁵³, whose study they refer to. At the same time, however, they note that: "(...) vegetables usually contain more nickel than do other food items ", and that the element in question can be leached from pipes and containers for drinking water and carbonated drinks. The authors provided imprecise information, as it is not known what plant products (when and where they were taken) were compared. However, it should be noted that the indicated



range of nickel content in the products generally corresponds to the values collected from the analyzed works. Nevertheless, as can be seen in Table S1, in the work of Verma et al.²⁵ the nickel content is at least two and sometimes even three times higher. This could confirm the importance of the origin of the samples, their preparation and the growing environment of the tested plants.

Heavy metals have been shown to be taken up by tobacco plants and accumulated in them⁵⁴. Although in the conducted studies the transfer of nickel to plants was the lowest among the examined heavy metals, in general terms, the content of nickel in plant tissues always increased along with the increase in the content of metal in the soil⁵⁴.

Proper preparation of samples for elemental analysis is crucial. For example, it is worth noting that while tobacco was dried in the other works²⁶⁻³⁴, in the work of Verma et al.²⁵ – it was not. Cigar tobacco has a certain amount of moisture that ensures flexibility of the leaves and thus prevents them from crumbling when stored or used. A crumbling cigar is practically unfit for consumption. Not taking into account the influence of water makes it impossible to compare the test results. Good practice, as evidenced by the authors of other publications²⁶⁻³⁴, is to determine the content of heavy metals in a dried or lyophilized product. Despite the lack of such information, it can be assumed that Verma et al. had dried the tested tobacco some extent, which is supported by the fact that they homogenized the sample in a mortar. This would have been very difficult with moist tobacco. However, it is necessary to dry the tobacco prior to wet ashing. Alternatively, it is possible to perform a parallel water content analysis for a statistically significant number of samples to provide the data needed for calculation adjustment.



Menden et al.²⁹ stated in their description of the preparation of analytical samples: "The samples of tobacco, ash, or TSC (tobacco smoke condensate) were either wet ashed or dry ashed. The two methods were used as convenience dictated, since no evident difference in results could be associated with these procedures.". However, there is no information that researchers had optimized mineralization methods, which would clearly show whether it was possible to observe differences between the methods used. For dry ashing, the authors moistened the sample with concentrated nitric acid. These conditions appear to be sufficient for the quantitative sequestration of nickel and cadmium, consistent with the researchers' finding of no apparent difference in results associated with the use of different ashing procedures. Franzke et al.³⁰ expected cadmium losses during dry ashing and therefore only used wet ashing.

Elemental analysis requires attention to every detail that could constitute a potential source of contamination of the sample with the tested heavy metals. Ferreira et al.³⁴ report that the tobacco was homogenized in a ball mill (PM 100, Retsch, Düsseldorf, Germany). A ball mill with metal balls can contaminate the sample with metals that the balls are made of. For comparison, Verma et al.²⁵ precisely indicated that an agate mortar and pestle were used to homogenize the samples. Careful preparation of samples reduces the possibility of their contamination, and precisely describing the optimal procedure allows others to apply it in their research.

In some studies, the tested products were compared with each other. For example, in the work of Panta et al.³² it is easy to notice that the tested cigar contained on average significantly more mercury than the tested cigarettes. In another publication, seven years prior³³, the determined mercury content was of a similar order of magnitude.



Conclusions

In studies comparing the content of tested metals in cigars and cigarettes^{25,29,30} or cigarillos²⁸, in most cases the cigars were characterized by a higher content of the toxic heavy metals. This may indicate a greater harmfulness of cigars than of cigarettes, as mentioned before. Smoke, whether exhaled or sidestream, pollutes the atmosphere around the smoker. Therefore, regardless of the product and the smoking method, passive smoking is always a source of exposure. In this approach, the exposure can be estimated regardless of the smoking method. After analyzing the available literature on heavy metal content in cigars, the following directions of future research have been identified:

First, due to the small number of studies on the content of heavy metals in cigars and inaccuracies related to the nomenclature of these products, a need for a wide range of research on this subject has been identified. It is necessary to improve analytical procedures and perform basic tests for samples from different regions. Thanks to extensive research on cigars, but also on other nicotine products, it will be possible to compare product groups and, consequently, exposure of their consumers to the toxic substances contained in the products.

Secondly, based on the literature data collected from 1972 to 2019, it is not possible to clearly determine trends in the content of determined heavy metals in the discussed tobacco products. Therefore, there is a pressing need for long-term analyses of cigars for selected heavy metals. Although the lack of a noticeable trend in the literature to date in the content of the selected heavy metals over time does not exclude the existence of such a relationship, the time factor may be less important than the origin of the leaves. In addition, consumers of cigars attach great importance to the origin of the leaves from which the cigar is made, unlike, for example, cigarette consumers. Therefore, sellers present such information in the product specification,



thanks to which cigars can be treated as a probe for testing the degree of contamination of tobacco crops in individual countries of leaf origin.

Thirdly, the analysis of the collected data shows that the concentrations of one analyzed heavy metal may vary vastly within different origin samples. Therefore, it is impossible to fully agree with the authors^{23,53} who indicate that tobacco belongs to environmental sources of lower levels of nickel. This is a generalization, and when analyzing Table 1, it is not difficult to notice that the nickel content in the work of Verma et al.²⁵ is higher than in the other works. The metal content in tobacco can be determined by the tobacco growing environment and the environment and method of cigar production. Important information can be provided by testing samples that differ in terms of their production and country of origin (tobacco growing). The problem may also concern other elements from a wide spectrum of those potentially harmful to consumers.

Fourthly, as can be seen in Figure 4, the average marked content of selected heavy metals in cigarettes in the works selected by the authors generally corresponds to the content of these elements in cigars (presented in Figure 2). However, when comparing these values with the data presented in supplementary materials, it turns out that some of the heavy metals concentrations in analyzed cigars could be considered as higher. Therefore it is advisable to develop research into cigars, cigarillos and little cigars.

Acknowledgements

We would like to thank Dr. Richard J. O'Connor, Professor of Oncology at Roswell Park Comprehensive Cancer Center, a co-author of one of the works, for providing accurate results of the research used in the publication.



We would like to thank MSc Ilona Stabrawa from the Institute of Physics of Jan Kochanowski University in Kielce for help in obtaining accurate research results from publications.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interest statement

Authors have no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

References

- 1 Musk AW, De Klerk NH. History of tobacco and health. *Respirology*. 2003. doi:10.1046/j.1440-1843.2003.00483.x.
- 2 Orleans CT, Slade J, Slade JD. Nicotine Addiction: Principles and Management. *J Am Med Assoc*. 1994;272. doi:doi:10.1001/jama.1994.03520150095047.
- 3 O'Connor RJ. Non-cigarette tobacco products: What have we learnt and where are we headed? *Tob Control*. 2012. doi:10.1136/tobaccocontrol-2011-050281.
- 4 Braun M, Koger F, Klingelhöfer D, Müller R, Groneberg DA. Particulate matter emissions of four different cigarette types of one popular brand: Influence of tobacco strength and additives. *Int J Environ Res Public Health*. 2019;16:1–11. doi:10.3390/ijerph16020263.
- 5 Loew O. Curing and Fermentation of Cigar Leaf Tobacco. US Government Printing Office; 1899.
- 6 Young D, Borland R, Hammond D, Cummings KM, Devlin E, Yong HH, O'Connor RJ. Prevalence and attributes of roll-your-own smokers in the International Tobacco Control (ITC) Four Country Survey. *Tob Control*. 2006. doi:10.1136/tc.2005.013268.
- 7 Kong G, Creamer MLR, Simon P, Cavallo DA, Ross JC, Hinds JT, Fishbein H, Gutierrez K. Systematic review of cigars, cigarillos, and little cigars among adolescents: Setting research agenda to inform tobacco control policy. *Addict*



- Behav.* 2019. doi:10.1016/j.addbeh.2019.04.032.
- 8 Pickworth WB, Rosenberry ZR, O'Grady KE, Koszowski B. Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure. *Tob Regul Sci.* 2017. doi:10.18001/trs.3.2(suppl1).8.
- 9 Koszowski B, Rosenberry ZR, Kanu A, Viray LC, Potts JL, Pickworth WB. Nicotine and carbon monoxide exposure from inhalation of cigarillo smoke. *Pharmacol Biochem Behav.* 2015. doi:10.1016/j.pbb.2015.10.007.
- 10 Rosenberry ZR, Pickworth WB, Koszowski B. Large cigars: Smoking topography and toxicant exposure. *Nicotine Tob Res.* 2018. doi:10.1093/ntr/ntw289.
- 11 Pickworth WB, Rosenberry ZR, Koszowski B. Toxicant exposure from smoking a little cigar: Further support for product regulation. *Tob Control.* 2017. doi:10.1136/tobaccocontrol-2015-052633.
- 12 DeSantis AD, Morgan SE. Sometimes a Cigar [Magazine] is More Than Just a Cigar [Magazine]: Pro-Smoking Arguments in Cigar Aficionado, 1992-2000. *Health Commun.* 2003;15:457–80. doi:10.1207/S15327027HC1504_05.
- 13 Baker F, Ainsworth SR, Dye JT, Crammer C, Thun MJ, Hoffmann D, Repace JL, Henningfield JE, Slade J, Pinney J, Shanks T, Burns DM, Connolly GN, Shopland DR. Health risks associated with cigar smoking. *J Am Med Assoc.* 2000. doi:10.1001/jama.284.6.735.
- 14 Chen-Sankey JC, Mead-Morse EL, Le D, Rose SW, Quisenberry AJ, Delnevo CD, Choi K. Cigar-Smoking Patterns by Race/Ethnicity and Cigar Type: A Nationally Representative Survey Among U.S. Adults. *Am J Prev Med.* 2021;60:87–94. doi:https://doi.org/10.1016/j.amepre.2020.07.005.
- 15 Devi P, Kumar P. Concept and Application of Phytoremediation in the Fight of Heavy Metal Toxicity. *J Pharm Sci Res.* 2020;12:795–804.
- 16 Scharf B, Clement CC, Zolla V, Perino G, Yan B, Elci SG, Purdue E, Goldring S, MacAluso F, Cobelli N, Vachet RW, Santambrogio L. Molecular analysis of chromium and cobalt-related toxicity. *Sci Rep.* 2014. doi:10.1038/srep05729.
- 17 Poonkothai M, Vijayavathi BS. Nickel as an essential element and a toxicant. *Int J Environ Sci.* 2012.



- 18 Li J, Chen J, Chen S. Supercritical water treatment of heavy metal and arsenic metalloid-bioaccumulating-biomass. *Ecotoxicol Environ Saf.* 2018. doi:10.1016/j.ecoenv.2018.03.069.
- 19 Shikata M. On the combustion temperature of cigars and cigarettes. *Bull Agric Chem Soc Japan.* 1926. doi:10.1271/bbb1924.2.90.
- 20 Ng LK, Hupé M. Effects of moisture content in cigar tobacco on nicotine extraction: Similarity between Soxhlet and focused open-vessel microwave-assisted techniques. *J. Chromatogr. A,* 2003. doi:10.1016/S0021-9673(03)01178-6.
- 21 Garner WW, Bacon CW, Bowling JD. Cigarette and Cigar Tobaccos: Relationship of Production Conditions to Chemical and Physical Characteristics. *Ind Eng Chem.* 1934. doi:10.1021/ie50297a015.
- 22 Ibrahim D, Froberg B, Wolf A, Rusyniak DE. Heavy metal poisoning: Clinical presentations and pathophysiology. *Clin Lab Med.* 2006. doi:10.1016/j.cll.2006.02.003.
- 23 Das KK, Reddy RC, Bagoji IB, Das S, Bagali S, Mullur L, Khodnapur JP, Biradar MS. Primary concept of nickel toxicity - An overview. *J Basic Clin Physiol Pharmacol.* 2019. doi:10.1515/jbcpp-2017-0171.
- 24 Gorby MS. Arsenic poisoning. *West J Med.* 1988;149:308–15.
- 25 Verma S, Yadav S, Singh I. Trace metal concentration in different Indian tobacco products and related health implications. *Food Chem Toxicol.* 2010. doi:10.1016/j.fct.2010.05.062.
- 26 Pappas RS, Martone N, Gonzalez-Jimenez N, Fresquez MR, Watson CH. Determination of toxic metals in little cigar tobacco with “Triple Quad” ICP-MS. *J Anal Toxicol.* 2015. doi:10.1093/jat/bkv016.
- 27 Caruso R V., O’Connor RJ, Travers MJ, Delnevo CD, Edryd Stephens W. Design characteristics and tobacco metal concentrations in filtered cigars. *Nicotine Tob Res.* 2015. doi:10.1093/ntr/ntu341.
- 28 Majewska U, Piotrowska M, Sychowska I, Banaś D, Kubala-Kukuś A, Wudarczyk-Moćko J, Stabrawa I, Gózdź S. Multielemental analysis of tobacco plant and tobacco products by TXRF. *J Anal Toxicol.* 2018.

- doi:10.1093/jat/bky016.
- 29 Menden EE, Elia VJ, Michael LW, Petering HG. Distribution of Cadmium and Nickel of Tobacco During Cigarette Smoking. *Environ Sci Technol*. 1972. doi:10.1021/es60068a008.
- 30 Franzke C, Ruick G, Schmidt M. Untersuchungen zum Schwermetallgehalt von Tabakwaren und Tabakrauch. *Food / Nahrung*. 1977. doi:10.1002/food.19770210507.
- 31 Lugon-Moulin N, Martin F, Krauss MR, Ramey PB, Rossi L. Cadmium concentration in tobacco (*Nicotiana tabacum* L.) from different countries and its relationship with other elements. *Chemosphere*. 2006. doi:10.1016/j.chemosphere.2005.09.005.
- 32 Panta YM, Qian S, Cross CL, Cizdziel J V. Mercury content of whole cigarettes, cigars and chewing tobacco packets using pyrolysis atomic absorption spectrometry with gold amalgamation. *J Anal Appl Pyrolysis*. 2008. doi:10.1016/j.jaap.2008.05.006.
- 33 Fresquez MR, Gonzalez-Jimenez N, Gray N, Watson CH, Pappas RS. High-throughput determination of mercury in tobacco and mainstream smoke from little cigars. *J Anal Toxicol*. 2015. doi:10.1093/jat/bkv069.
- 34 Ferreira HS, Oliveira SS, Santos DCMB, Fontana KB, Maranhão TA, Almeida TS, Araujo RGO. Characterisation of the mineral composition of tobacco products (cigar, shredded and rope). *Microchem J*. 2019. doi:10.1016/j.microc.2019.104196.
- 35 Đukić-Ćosić D, Baralić K, Javorac D, Djordjevic AB, Bulat Z. An overview of molecular mechanisms in cadmium toxicity. *Curr Opin Toxicol*. 2020;19:56–62. doi:https://doi.org/10.1016/j.cotox.2019.12.002.
- 36 Chen H, Li Y, Ma X, Guo L, He Y, Ren Z, Kuang Z, Zhang X, Zhang Z. Analysis of potential strategies for cadmium stress tolerance revealed by transcriptome analysis of upland cotton. *Sci Rep*. 2019. doi:10.1038/s41598-018-36228-z.
- 37 Huang H, Zuzarte-Luis V, Fragoso G, Calvé A, Hoang TA, Oliero M, Chabot-Roy G, Mullins-Dansereau V, Lesage S, Santos MM. Acute invariant NKT cell

- activation triggers an immune response that drives prominent changes in iron homeostasis. *Sci Rep.* 2020. doi:10.1038/s41598-020-78037-3.
- 38 Das SK, Wang W, Zhabyeyev P, Basu R, Mclean B, Fan D, Parajuli N, Desaulniers J, Patel VB, Hajjar RJ, Dyck JRB, Kassiri Z, Oudit GY. Iron-overload injury and cardiomyopathy in acquired and genetic models is attenuated by resveratrol therapy. *Sci Rep.* 2015. doi:10.1038/srep18132.
- 39 Brissot P, Ropert M, Le Lan C, Loréal O. Non-transferrin bound iron: A key role in iron overload and iron toxicity. *Biochim Biophys Acta - Gen Subj.* 2012. doi:10.1016/j.bbagen.2011.07.014.
- 40 Morgan J, Bell R, Jones AL. Endogenous doesn't always mean innocuous: a scoping review of iron toxicity by inhalation. *J Toxicol Environ Heal - Part B Crit Rev.* 2020;23:107–36. doi:10.1080/10937404.2020.1731896.
- 41 Cabrera ÁJR. Zinc, aging, and immunosenescence: an overview. *Pathobiol Aging Age-Related Dis.* 2015. doi:10.3402/pba.v5.25592.
- 42 Nriagu J. Zinc toxicity in humans. *Encycl. Environ. Heal.*, 2019. doi:10.1016/B978-0-12-409548-9.11836-6.
- 43 Chen P, Bornhorst J, Aschner M. Manganese metabolism in humans. *Front Biosci - Landmark.* 2018. doi:10.2741/4665.
- 44 O'Neal SL, Zheng W. Manganese Toxicity Upon Overexposure: a Decade in Review. *Curr Environ Heal Reports.* 2015;2:315–28. doi:10.1007/s40572-015-0056-x.
- 45 Hiatt AJ, Ragland JL. Manganese Toxicity of Burley Tobacco. *Agron J.* 1963;55:47–9. doi:10.2134/agronj1963.00021962005500010017x.
- 46 Dameron CT, Harrison MD. Mechanisms for protection against copper toxicity. *Am. J. Clin. Nutr.*, 1998. doi:10.1093/ajcn/67.5.1091S.
- 47 Uriu-Adams JY, Keen CL. Copper, oxidative stress, and human health. *Mol Aspects Med.* 2005. doi:10.1016/j.mam.2005.07.015.
- 48 Nemery B. Metal toxicity and the respiratory tract. *Eur Respir J.* 1990. doi:10.1097/00043764-199012000-00003.
- 49 Delnevo CD, Hrywna M, Giovenco DP, Lo EJM, O'Connor RJ. Close, but no



- cigar: Certain cigars are pseudo-cigarettes designed to evade regulation. *Tob Control*. 2017;26:349–54. doi:10.1136/tobaccocontrol-2016-052935.
- 50 Caputi TL. Heat-not-burn tobacco products are about to reach their boiling point. *Tob Control*. 2017. doi:10.1136/tobaccocontrol-2016-053264.
- 51 Tran CT, Bosilkovska M, de La Bourdonnaye G, Blanc N, Haziza C. Reduced levels of biomarkers of exposure in smokers switching to the Carbon-Heated Tobacco Product 1.0: a controlled, randomized, open-label 5-day exposure trial. *Sci Rep*. 2020;10:19227. doi:10.1038/s41598-020-76222-y.
- 52 Phillips BW, Schlage WK, Titz B, Kogel U, Sciuscio D, Martin F, Leroy P, Vuillaume G, Krishnan S, Lee T, Veljkovic E, Elamin A, Merg C, Ivanov N V., Peitsch MC, Hoeng J, Vanscheeuwijck P. A 90-day OECD TG 413 rat inhalation study with systems toxicology endpoints demonstrates reduced exposure effects of the aerosol from the carbon heated tobacco product version 1.2 (CHTP1.2) compared with cigarette smoke. I. Inhalation exposure, clinical p. *Food Chem Toxicol*. 2018. doi:10.1016/j.fct.2018.04.015.
- 53 Cempel M, Nikel G. Nickel: A review of its sources and environmental toxicology. *Polish J Environ Stud*. 2006.
- 54 Saha N, Rahman MS, Jolly YN, Rahman A, Sattar MA, Hai MA. Spatial distribution and contamination assessment of six heavy metals in soils and their transfer into mature tobacco plants in Kushtia District, Bangladesh. *Environ Sci Pollut Res*. 2016. doi:10.1007/s11356-015-5575-3.



Table S1. Results of heavy metals determination in cigar tobacco available in the literature (the presented results are in the form as in the source materials)

| Product | Year | Method | Fe $\mu\text{g/g}$ tobacco | Zn $\mu\text{g/g}$ tobacco | Mn $\mu\text{g/g}$ tobacco | Ni $\mu\text{g/g}$ tobacco | Cu $\mu\text{g/g}$ tobacco | Co $\mu\text{g/g}$ tobacco | Cr $\mu\text{g/g}$ tobacco | Pb $\mu\text{g/g}$ tobacco | Cd $\mu\text{g/g}$ tobacco | As $\mu\text{g/g}$ tobacco | Hg ng/g tobacco | Author |
|--|------|---------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-----------------------------|--------------|
| "One brand of cigar(...)" | 1972 | AAS | x | 51.40 | x | x | x | x | x | x | 1.86 | x | x | Menden |
| Stadtwappen Halle | 1977 | SWP | x | 144.00 | x | x | 71.70 | x | x | 30.80 | 13.90 | x | x | Franzke* |
| Bode-Spitzen | 1977 | SWP | x | 97.00 | x | x | 41.80 | x | x | 15.70 | 7.94 | x | x | Franzke* |
| Medianos | 1977 | SWP | x | 176.00 | x | x | 89.90 | x | x | 31.80 | 18.80 | x | x | Franzke* |
| Swirtigal 40 | 1977 | SWP | x | 156.00 | x | x | 138.00 | x | x | 28.20 | 13.80 | x | x | Franzke* |
| Nestor | 1977 | SWP | x | 106.00 | x | x | 70.00 | x | x | 15.80 | 8.61 | x | x | Franzke* |
| India. Mysore (Karnatak state). Flue-cured. | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.33 ± 0.17 | x | x | Lugon-Moulin |
| The Philippines. Ilocos region and Cagayan Valley. Burley | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 2.24 ± 0.75 | x | x | Lugon-Moulin |
| Thailand. Province of Lampang - Flue-cured tobacco and Sukhothai - Burley tobacco. | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 1.99 ± 0.75 | x | x | Lugon-Moulin |
| Turkey. Bergama. Kale and Karacasu. Oriental | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.56 ± 0.68 | x | x | Lugon-Moulin |
| Albania. Korce and Elbadan. Oriental | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 1.64 ± 1.35 | x | x | Lugon-Moulin |
| Bulgaria. several tobacco-producing regions in the south of the country. Oriental | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 1.06 ± 0.87 | x | x | Lugon-Moulin |
| France. Alsace. Midi-Pyrenees. Rhone-Alpes and Pays de la Loire. Flue-cured | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 1.46 ± 0.73 | x | x | Lugon-Moulin |
| Greece. Elassona. Oriental | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.77 ± 0.46 | x | x | Lugon-Moulin |
| Italy. Vento and Umbria for Flue-cured. Campania - Burley | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.82 ± 0.27 | x | x | Lugon-Moulin |
| Argentina. Tucman and Misiones - Burley. Salta and Jujuy - Flue-cured | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.65 ± 0.45 | x | x | Lugon-Moulin |
| Brazil. Rio Grande do Sul and Santa Catarina - both Flue-cured and Burley tobacco; Parana - Flue-cured tobacco | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.75 ± 0.61 | x | x | Lugon-Moulin |
| Ecuador. Guayas. Burley and Flue-cured | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 1.95 ± 0.67 | x | x | Lugon-Moulin |
| USA. 10 processed Flue-cured. Collected at random from a processing plant | 2006 | ICP-MS | x | x | x | x | x | x | x | x | 0.51 ± 0.05 | x | x | Lugon-Moulin |
| One brand of cigar | 2008 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 20.8 ± 1.0 | Panta |
| King's Adward | 2010 | ICP-AES | 528.31 ± 28.1 | 39.84 ± 2.32 | x | 9.90 ± 0.99 | 17.87 ± 1.58 | x | 2.68 ± 0.57 | 1.08 ± 0.62 | 0.75 ± 0.07 | x | x | Verma |
| Café Cream | 2010 | ICP-AES | 444.27 ± 40.05 | 45.66 ± 7.55 | x | 12.53 ± 1.31 | 26.83 ± 2.07 | x | 4.50 ± 0.87 | 3.01 ± 0.77 | 1.22 ± 0.21 | x | x | Verma |



| Product | Year | Method | Fe $\mu\text{g/g}$ tobacco | Zn $\mu\text{g/g}$ tobacco | Mn $\mu\text{g/g}$ tobacco | Ni $\mu\text{g/g}$ tobacco | Cu $\mu\text{g/g}$ tobacco | Co $\mu\text{g/g}$ tobacco | Cr $\mu\text{g/g}$ tobacco | Pb $\mu\text{g/g}$ tobacco | Cd $\mu\text{g/g}$ tobacco | As $\mu\text{g/g}$ tobacco | Hg ng/g tobacco | Author |
|---------------------------|------|---------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------|----------|
| Olympic | 2010 | ICP-AES | 2168.44 \pm 128.76 | 13.91 \pm 1.14 | x | 6.13 \pm 1.19 | 14.72 \pm 0.58 | x | 9.75 \pm 0.53 | 1.38 \pm 0.42 | 0.29 \pm 0.1 | x | x | Verma |
| Phillies | 2010 | ICP-AES | 642.56 \pm 35.42 | 56.15 \pm 1.3 | x | 7.44 \pm 1.80 | 37.75 \pm 1.23 | x | 6.14 \pm 0.65 | 3.11 \pm 0.68 | 0.70 \pm 0.11 | x | x | Verma |
| Imperial | 2010 | ICP-AES | 853.34 \pm 54.21 | 19.21 \pm 0.78 | x | 8.30 \pm 069 | 17.48 \pm 1.39 | x | 8.09 \pm 0.78 | 2.58 \pm 0.59 | 0.58 \pm 0.07 | x | x | Verma |
| Hav-A-Tampa | 2015 | ICP-MS | x | x | 202 \pm 15 | 4.36 \pm 0.45 | x | 0.80 \pm 0.07 | 6.46 \pm 0.90 | 0.69 \pm 0.05 | 1.24 \pm 0.05 | 0.17 \pm 0.02 | x | Pappas |
| Muriel Sweets | 2015 | ICP-MS | x | x | 138 \pm 12 | 1.58 \pm 0.08 | x | 0.71 \pm 0.05 | 1.24 \pm 0.30 | 0.70 \pm 0.12 | 1.31 \pm 0.05 | 0.13 \pm 0.01 | x | Pappas |
| Winchester | 2015 | ICP-MS | x | x | 202 \pm 6 | 1.67 \pm 0.15 | x | 0.68 \pm 0.05 | 0.88 \pm 0.19 | 0.54 \pm 0.06 | 1.69 \pm 0.08 | 0.14 \pm 0.01 | x | Pappas |
| Vaquero | 2015 | ICP-MS | x | x | 160 \pm 13 | 1.97 \pm 0.26 | x | 0.81 \pm 0.03 | 1.58 \pm 0.23 | 0.78 \pm 0.05 | 1.06 \pm 0.87 | 0.55 \pm 0.03 | x | Pappas |
| Santa Fe | 2015 | ICP-MS | x | x | 139 \pm 11 | 2.80 \pm 0.28 | x | 0.65 \pm 0.03 | 2.29 \pm 0.16 | 1.00 \pm 0.08 | 0.808 \pm 0.027 | 0.17 \pm 0.01 | x | Pappas |
| Phillies (Regular) | 2015 | ICP-MS | x | x | 146 \pm 11 | 2.29 \pm 0.49 | x | 0.71 \pm 0.07 | 1.84 \pm 0.53 | 0.78 \pm 0.03 | 1.36 \pm 0.02 | 0.12 \pm 0.01 | x | Pappas |
| Captain Black | 2015 | ICP-MS | x | x | 210 \pm 11 | 1.50 \pm 0.06 | x | 0.82 \pm 0.04 | 0.88 \pm 0.53 | 0.46 \pm 0.05 | 1.74 \pm 0.13 | 0.14 \pm 0.01 | x | Pappas |
| Wswisher Sweets | 2015 | ICP-MS | x | x | 166 \pm 20 | 3.14 \pm 0.29 | x | 0.84 \pm 0.07 | 3.34 \pm 0.65 | 1.23 \pm 0.16 | 0.910 \pm 0.042 | 0.26 \pm 0.02 | x | Pappas |
| Cheyenne | 2015 | ICP-MS | x | x | 156 \pm 9 | 4.37 \pm 0.19 | x | 0.82 \pm 0.03 | 1.88 \pm 0.14 | 0.81 \pm 0.05 | 1.06 \pm 0.03 | 0.66 \pm 0.03 | x | Pappas |
| Murano (Regular) | 2015 | ICP-MS | x | x | 202 \pm 8 | 1.93 \pm 0.10 | x | 0.98 \pm 0.06 | 1.26 \pm 0.04 | 0.59 \pm 0.02 | 1.21 \pm 0.04 | 0.16 \pm 0.01 | x | Pappas |
| Clipper Black (Red) | 2015 | ICP-MS | x | x | 374 \pm 27 | 1.69 \pm 0.13 | x | 0.74 \pm 0.07 | 1.83 \pm 0.05 | 0.57 \pm 0.10 | 1.12 \pm 0.04 | 0.19 \pm 0.01 | x | Pappas |
| Vendetta (9 mm) | 2015 | ICP-MS | x | x | 169 \pm 14 | 1.97 \pm 0.07 | x | 0.86 \pm 0.05 | 1.33 \pm 0.05 | 0.62 \pm 0.03 | 1.17 \pm 0.09 | 0.28 \pm 0.01 | x | Pappas |
| Al Capone (Sweets Filter) | 2015 | ICP-MS | x | x | 225 \pm 12 | 2.97 \pm 0.17 | x | 1.00 \pm 0.08 | 1.92 \pm 0.19 | 0.74 \pm 0.05 | 1.68 \pm 0.09 | 0.21 \pm 0.03 | x | Pappas |
| Smoker's Best (Light) | 2015 | ICP-MS | x | x | 177 \pm 10 | 3.13 \pm 0.15 | x | 0.83 \pm 0.02 | 2.74 \pm 0.17 | 0.910 \pm 0.057 | 0.788 \pm 0.040 | 0.20 \pm 0.01 | x | Pappas |
| Smoker's Best (Menthol) | 2015 | ICP-MS | x | x | 176 \pm 10 | 2.96 \pm 0.20 | x | 0.84 \pm 0.05 | 2.42 \pm 0.14 | 0.88 \pm 0.04 | 0.752 \pm 0.035 | 0.21 \pm 0.01 | x | Pappas |
| Remington (Full Flavor) | 2015 | ICP-MS | x | x | 166 \pm 10 | 2.08 \pm 0.08 | x | 0.86 \pm 0.04 | 1.54 \pm 0.17 | 0.59 \pm 0.02 | 1.16 \pm 0.07 | 0.16 \pm 0.01 | x | Pappas |
| Prime Rime (Blueberry) | 2015 | ICP-MS | x | x | 178 \pm 10 | 3.15 \pm 0.25 | x | 0.90 \pm 0.05 | 2.75 \pm 0.13 | 0.96 \pm 0.04 | 1.20 \pm 0.05 | 0.22 \pm 0.01 | x | Pappas |
| Al Capone | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 21.3 \pm 0.6 | Fresquez |
| Captain Black | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 22.8 \pm 0.8 | Fresquez |
| Cheyenne Full Flavor | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 20.5 \pm 1.0 | Fresquez |
| Clipper Black Red | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 21.8 \pm 0.7 | Fresquez |
| Hav-A-Tampa Natural | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 24.9 \pm 0.7 | Fresquez |
| Murano Regular | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 21.3 \pm 0.4 | Fresquez |
| Muriel Sweets | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 22.9 \pm 0.6 | Fresquez |
| Phillies | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 24.2 \pm 0.7 | Fresquez |



| Product | Year | Method | Fe $\mu\text{g/g}$ tobacco | Zn $\mu\text{g/g}$ tobacco | Mn $\mu\text{g/g}$ tobacco | Ni $\mu\text{g/g}$ tobacco | Cu $\mu\text{g/g}$ tobacco | Co $\mu\text{g/g}$ tobacco | Cr $\mu\text{g/g}$ tobacco | Pb $\mu\text{g/g}$ tobacco | Cd $\mu\text{g/g}$ tobacco | As $\mu\text{g/g}$ tobacco | Hg ng/g tobacco | Author |
|---|------|--------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------|----------|
| Prime Time Blueberry | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 19.4 \pm 0.9 | Fresquez |
| Remington Full Flavor | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 18.1 \pm 0.8 | Fresquez |
| Santa Fe Original | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 22.5 \pm 0.6 | Fresquez |
| Smokers Best Lights | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 22.1 \pm 0.5 | Fresquez |
| Smokers Best Menthol | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 20.9 \pm 0.5 | Fresquez |
| Swisher Sweets | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 19.1 \pm 0.8 | Fresquez |
| Vaquero Natural | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 17.9 \pm 0.8 | Fresquez |
| Vendetta (9 mm) | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 18.1 \pm 0.8 | Fresquez |
| Winchester Classic | 2015 | CV-AAS | x | x | x | x | x | x | x | x | x | x | 18.3 \pm 0.8 | Fresquez |
| Muriel Menthol | 2015 | XRF | x | x | x | 0.2 | x | x | 1.5 | 0.3 | 1.3 | 0.1 | x | Caruso |
| Muriel Sweets | 2015 | XRF | x | x | x | 0.3 | x | x | 1.1 | 0.1 | 1.3 | 0.1 | x | Caruso |
| Swisher Sweet Mild | 2015 | XRF | x | x | x | 0.9 | x | x | 1.6 | 0.5 | 1.4 | 0.2 | x | Caruso |
| Swisher Sweets Grape 100's | 2015 | XRF | x | x | x | 0.7 | x | x | 2 | 0.4 | 1.1 | 0.2 | x | Caruso |
| Swisher Sweets Regular 100's | 2015 | XRF | x | x | x | 1.2 | x | x | 2.1 | 0.4 | 1.1 | 0.2 | x | Caruso |
| Swisher Sweets Regular 84's Little Cigars | 2015 | XRF | x | x | x | 1.3 | x | x | 2 | 0.7 | 1.1 | 0.3 | x | Caruso |
| Cheyenne Classic 100's | 2015 | XRF | x | x | x | 0.6 | x | x | 1.2 | 0.1 | 1.4 | 0.2 | x | Caruso |
| Cheyenne Full Flavor 100's | 2015 | XRF | x | x | x | 0.4 | x | x | 1.7 | 0.2 | 1 | 0.3 | x | Caruso |
| Cheyenne Grape 100's | 2015 | XRF | x | x | x | 0.5 | x | x | 1.3 | 0.3 | 1 | 0.2 | x | Caruso |
| Double Diamond Full Flavor 100's | 2015 | XRF | x | x | x | 0.9 | x | x | 2.3 | 0.5 | 1.5 | 0.3 | x | Caruso |
| Double Diamond Grape | 2015 | XRF | x | x | x | 1.4 | x | x | 2.3 | 0.7 | 1.6 | 0.3 | x | Caruso |
| Double Diamond Milds | 2015 | XRF | x | x | x | 1 | x | x | 3.4 | 1.2 | 1.7 | 0.3 | x | Caruso |
| Phillies Menthol | 2015 | XRF | x | x | x | 0.3 | x | x | 1.3 | 0.3 | 1.4 | nd | x | Caruso |
| Phillies Sweet | 2015 | XRF | x | x | x | 0.3 | x | x | 1.2 | 0.3 | 1.3 | nd | x | Caruso |
| Remington Full Flavor | 2015 | XRF | x | x | x | 0.7 | x | x | 1.5 | 0.2 | 1.1 | 0.5 | x | Caruso |
| Remington Grape | 2015 | XRF | x | x | x | 0.6 | x | x | 1.7 | 0.5 | 1 | 0.4 | x | Caruso |
| Remington Lights | 2015 | XRF | x | x | x | 0.4 | x | x | 1.2 | 0.7 | 1.4 | 0.3 | x | Caruso |
| Santa Fe Menthol | 2015 | XRF | x | x | x | 0.9 | x | x | 2 | 0.6 | 0.6 | 0.1 | x | Caruso |
| Santa Fe Original | 2015 | XRF | x | x | x | 1 | x | x | 1.8 | 0.7 | 0.8 | 0.2 | x | Caruso |
| Santa Fe Sweet Cherry | 2015 | XRF | x | x | x | 1.2 | x | x | 2.1 | 0.5 | 1.2 | 0.2 | x | Caruso |



| Product | Year | Method | Fe $\mu\text{g/g}$ tobacco | Zn $\mu\text{g/g}$ tobacco | Mn $\mu\text{g/g}$ tobacco | Ni $\mu\text{g/g}$ tobacco | Cu $\mu\text{g/g}$ tobacco | Co $\mu\text{g/g}$ tobacco | Cr $\mu\text{g/g}$ tobacco | Pb $\mu\text{g/g}$ tobacco | Cd $\mu\text{g/g}$ tobacco | As $\mu\text{g/g}$ tobacco | Hg ng/g tobacco | Author |
|--|------|---------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------|----------|
| Santa Fe White | 2015 | XRF | x | x | x | 1 | x | x | 2.4 | 0.1 | 0.7 | 0.1 | x | Caruso |
| Santa Fe White Menthol | 2015 | XRF | x | x | x | 1.1 | x | x | 2 | 0.3 | 0.9 | 0.1 | x | Caruso |
| Swisher Sweet Regular Filter Tip Cigar | 2015 | XRF | x | x | x | nd | x | x | nd | nd | nd | 0 | x | Caruso |
| Cigars | 2018 | XRF | 661 \pm 34 | 64.9 \pm 3.2 | 160.6 \pm 8.0 | 2.95 \pm 0.57 | 29.0 \pm 1.9 | x | < 0.83 | 0.31 \pm 0.27 | x | 0.48 \pm 0.28 | x | Majewska |
| Cigarillos | 2018 | XRF | 420 \pm 22 | 49.6 \pm 2.7 | 102.5 \pm 6.4 | 2.81 \pm 0.55 | 21.5 \pm 1.4 | x | < 0.83 | 0.57 \pm 0.29 | x | < 0.27 | x | Majewska |
| Cigars | 2019 | ICP-OES | 883.00 | 42.6 | 215 | 8.18 | 16.35 | 0.99 | x | x | 0.96 | < LOQ | x | Ferreira |

* Unit $\mu\text{g/cigar}$

References

- Franzke C, Ruick G, Schmidt M. Untersuchungen zum Schwermetallgehalt von Tabakwaren und Tabakrauch. *Food / Nahrung*. 1977;21(5):417-428. doi:10.1002/food.19770210507.
- Majewska U, Piotrowska M, Sychowska I, Banaś D, Kubala-Kukuś A, Wudarczyk-Močko J, Stabrawa I, Gózdź S. Multielemental analysis of tobacco plant and tobacco products by TXRF. *J Anal Toxicol*. 2018;42(6):409-416. doi:10.1093/jat/bky016.
- Caruso R V., O'Connor RJ, Travers MJ, Delnevo CD, Edryd Stephens W. Design characteristics and tobacco metal concentrations in filtered cigars. *Nicotine Tob Res*. 2015;17(11):1331-1336. doi:10.1093/ntr/ntu341.
- Lugon-Moulin N, Martin F, Krauss MR, Ramey PB, Rossi L. Cadmium concentration in tobacco (*Nicotiana tabacum* L.) from different countries and its relationship with other elements. *Chemosphere*. 2006;63(7):1074-1086. doi:10.1016/j.chemosphere.2005.09.005.
- Menden EE, Elia VJ, Michael LW, Petering HG. Distribution of Cadmium and Nickel of Tobacco During Cigarette Smoking. *Environ Sci Technol*. 1972;6(9):830-832. doi:10.1021/es60068a008.
- Verma S, Yadav S, Singh I. Trace metal concentration in different Indian tobacco products and related health implications. *Food Chem Toxicol*. 2010;48(8-9):2291-2297. doi:10.1016/j.fct.2010.05.062.
- Ferreira HS, Oliveira SS, Santos DCMB, Fontana KB, Maranhão TA, Almeida TS, Araujo RGO. Characterisation of the mineral composition of tobacco products (cigar, shredded and rope). *Microchem J*. 2019;151:1-7. doi:10.1016/j.microc.2019.104196.
- Pappas RS, Martone N, Gonzalez-Jimenez N, Fresquez MR, Watson CH. Determination of toxic metals in little cigar tobacco with "Triple Quad" ICP-MS. *J Anal Toxicol*. 2015;39(5):347-352. doi:10.1093/jat/bkv016.
- Fresquez MR, Gonzalez-Jimenez N, Gray N, Watson CH, Pappas RS. High-throughput determination of mercury in tobacco and mainstream smoke from little cigars. *J Anal Toxicol*. 2015;39(7):1-6. doi:10.1093/jat/bkv069.
- Panta YM, Qian S, Cross CL, Cizdziel J V. Mercury content of whole cigarettes, cigars and chewing tobacco packets using pyrolysis atomic absorption spectrometry with gold amalgamation. *J Anal Appl Pyrolysis*. 2008;83(1):7-11. doi:10.1016/j.jaap.2008.05.006.

