Market Survey of Modern Oral Nicotine Products: Determination of Select HPHCs and Comparison to Traditional Smokeless Tobacco Products

Martin, A.M.; Jablonski, J.J.; Cheetham, A.G.; Enthalpy Analytical, LLC, Richmond, VA, USA

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Abstract

In an effort to combat the risks associated with use of traditional tobacco products, tobacco science and product innovation has been redirected towards providing the consumer with products that deliver nicotine while potentially limiting their exposure to harmful or potentially harmful constituents (HPHCs). Among these product innovations are modern oral nicotine products (MONPs), or tobacco-free nicotine products (TFNPs).

This body of work sought to investigate the potential for select HPHC exposure (tobacco-specific nitrosamines (TSNAs), carbonyls, benzo[a]pyrene, nitrite, metals) from MONPs and to compare it to that from traditional smokeless tobacco products. Given the recent push towards reducing the consumer's potential risk, this work expands on previously published studies both in terms of diversity of products assessed and analytes tested[1,2]. In total, twenty-one unique MONPs were assessed and compared to four traditional tobacco products.

We found that there was a difference in the potential exposure based on the MONP filler—plant material vs granulate/powder. Typically, the HPHC levels observed in plant-based MONPs were higher than those observed for granulate/powder products with this trend most significant within the metals analysis. Here, the observed levels of select metals were generally higher in plant-based MONPs, the levels for which were, in some instances, also greater than those seen in traditional smokeless tobacco products. Generally, the overall HPHC levels observed in MONPs were at or below those levels observed in traditional tobacco products.

Study Overview

For this work, twenty-five (25) different products from nine individual manufacturers were assessed. Of these twenty-five, four were traditional smokeless tobacco products tested for comparative purposes: two CORESTA reference products (CRP1.1 and CRP2.1) and two commercial smokeless tobacco products (Long Cut and Snus). Of the twenty-one MONP tested, thirteen were powder-based and eight were plant-based. All modern oral nicotine products were purchased by the authors through online retailers or directly from the manufacturer. The goal was to obtain products from a range of manufacturers that also varied in flavors and product type (pouch vs. long cut). All test articles were stored refrigerated until use.

The compounds to be analyzed were selected based upon the FDA HPHC list for smokeless tobacco and the IARC class. One goal of study was to determine whether select methods, developed for smokeless tobacco products, would be suitable to novel tobacco-free products.

All samples were extracted in triplicate. Results are reported on a per gram basis.

Table 1. Products tested

Code	Form	Filler	Flavor
A1	Pouch	powder	Wintergreen
A2	Pouch	powder	Black Cherry
A3	Pouch	powder	Mint
A4	Pouch	powder	Citrus
B1	Pouch	powder	Wintergreen
B2	Pouch	powder	Citrus
B3	Pouch	powder	Berry
C1	Pouch	powder	Mango
C2	Pouch	powder	Honey Lemon
C3	Pouch	powder	Wintergreen
D1	Pouch	powder	Lush
E1	Pouch	powder	Citrus
E2	Pouch	powder	Wintergreen
F1	Pouch	plant	Wintergreen
F2	Pouch	plant	Straight
F3	Long Cut	plant	Peach
F4	Long Cut	plant	Berry
G1	Long Cut	plant	Blood Orange
G2	Long Cut	plant	Peach
G3	Pouch	plant	Straight
G4	Pouch	plant	Wintergreen
Snus	Pouch	tobacco	Wintergreen
Long Cut	Long Cut	tobacco	Wintergreen
CRP1.1	Pouch	tobacco	Straight
CRP2.1	Long Cut	tobacco	Straight

Methodology

Table 2. Analytes tested and LOQs

		In-house	CORESTA		IARC
Compound	Units	LOQ	LOQ	Method No	Class
NAB	ng/g	3.3	3.8	CRM-72	3
NAT	ng/g	13	15	CRM-72	3
NNK	ng/g	13	15	CRM-72	1
NNN	ng/g	13	15	CRM-72	1
Nitrite	µg/g	1.0	-	*	2A
BaP	ng/g	0.18	0.15	CRM-82	1
Acetaldehyde	µg/g	0.09	0.1	CRM-86	2B
Crotonaldehyde	µg/g	0.04	0.05	CRM-86	2B
Formaldehyde	µg/g	0.09	0.1	CRM-86	1
Arsenic	ng/g	7.4	200	CRM-93	1
Beryllium	ng/g	3.7	200	CRM-93	1
Cadmium	ng/g	3.7	200	CRM-93	1
Chromium	ng/g	15	200	CRM-93	3
Cobalt	ng/g	3.7	200	CRM-93	2B
Lead	ng/g	3.7	200	CRM-93	2B
Nickel	ng/g	37	200	CRM-93	2B
Selenium	ng/g	15	200	CRM-93	3

*** Astoria Pacific Method A181**

Each of the assays used in this study has been fully validated in-house and, with the exception of BaP and Nitrite, is based upon a CORESTA Recommended Method. Our Nitrite method is based on Astoria Pacific Method A181 and our BaP method is a UPLC-Fluorescence method.

For pouched products, an integer number of whole pouches was extracted, so that the sample size was within an appropriate range for each test.

- TSNAs: 1.0 to 1.7 grams
- Nitrite: 1.5 to 2.2 grams
- BaP: 0.9 to 1.7 grams
- Carbonyls: 0.8 to 1.6 grams
- Metals: 0.5 to 1.7 grams

As seen in Table 2, the quantitation limits used for this study are similar to, or lower than, those reported in the CRMs.

Results and Discussion

Nitrite and TSNAs:

Nitrite is a precursor to TSNA formation and can be readily found in smokeless tobacco products. In most of the MONPs assessed, nitrite levels were found to be below LOQ. In products which contained measurable levels, they were at or below the levels found in the long cut tobacco, with the exception of one plant-based pouch product (G4), which contained an average of 7.8 µg/g.

Levels of the four TSNAs examined as part of this study, NAB, NAT, NNK, and NNN were either considered non-detect (ND) or below LOQ in all but two of the MONPs, which were found to contain very low levels of NAT, NNN and NNK. All levels observed in MONPs were significantly lower than the levels found in the tobacco products.

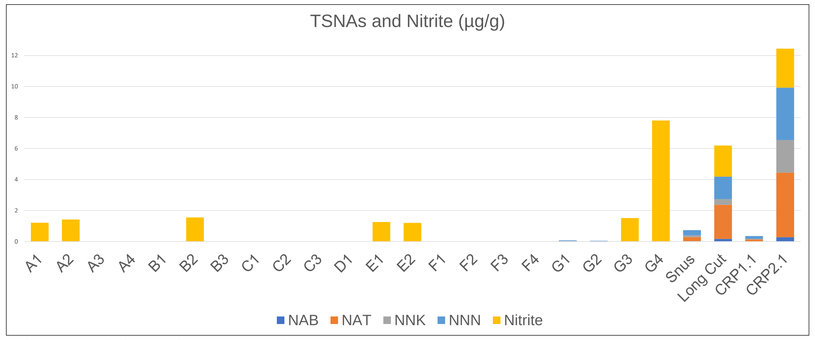

Figure 1. Nitrite and TSNA Results

Benzo[a]pyrene:

The levels of benzo[a]pyrene (BaP) were expected to be low for powder-based pouch products, as BaP is typically produced during combustion. However, depending on if the plant-based products undergo any type of curing or manufacturing process requiring heat, there is the possibility of producing BaP. Of all the MONPs examined, only one of the plant-based MONP (F4) resulted in detectable levels of BaP (1.27 ± 0.04 ng/g). Both of the smokeless tobacco long cut products examined displayed substantially higher levels of BaP (77.2 ± 2 ng/g and 151 ± 3 ng/g, respectively).

Carbonyls:

Generally, formaldehyde levels measured in the MONPs tested were comparable or lower than those seen in tobacco products. However, it appears formaldehyde levels were, on average, higher in the powder-based products than in the plant-based products. The levels were particularly high in products E1 and E2 which were measured at 13.4 ± 0.4 µg/g and 10.2 ± 0.7 µg/g, respectively, three to four time the levels observed in the CRP2.1.

The average acetaldehyde levels in powder-based MONP pouches were lower than those seen in all plant-based products. The levels of acetaldehyde in the plant-based MONPs ranged from below the levels found in the tobacco to significantly higher than the levels observed in the tobacco products. Some of the high values may be related to flavorings; for example, the two extremely high acetaldehyde values (F3 and G2) were in the two peach flavored products.

Crotonaldehyde was not observed in any measurable amount for any product tested as part of this assessment, including the reference products and traditional smokeless tobacco products.

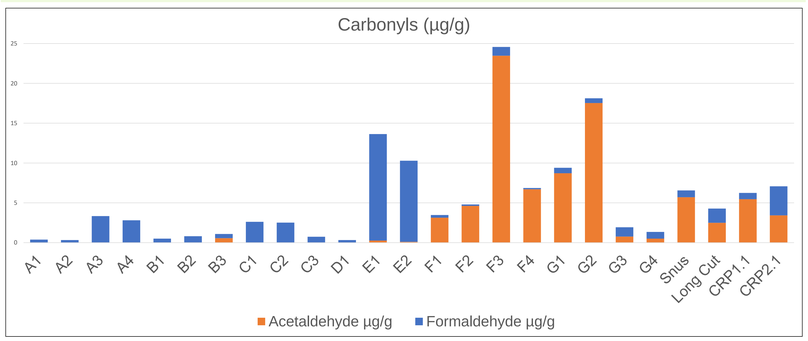

Figure 2. Formaldehyde and Acetaldehyde Results

Metals:

The metals of interest were observed in the products tested in general patterns based on the matrix type:

- Arsenic was observed in all plant-based products (MONP and Tobacco) at similar levels but was <LOQ or ND in all powder-based products.
- Beryllium was found in all plant-based products at levels <LOQ to ~ 10 ng/g but was <LOQ or ND in all powder-based products.
- Cadmium was found in all plant-based MONP, although at lower levels than in tobacco products, and was <LOQ or ND in all powder-based products.
- Chromium was found in all products, although the levels in the powder-based products were, on average, lower than in the plant-based products (MONP and Tobacco). There were a few exceptions, where levels in products C1 to C3 were close to or exceeded those seen in the tobacco products screened for this study. Chromium in the plant-based MONPs was found at or above levels seen in the tobacco products.
- Cobalt was found in most products, although the levels in the powder-based MONP were significantly lower than in the plant-based MONP, which, in turn, were dramatically lower than the levels found in the tobacco products.
- Lead and nickel were found in all products and in a similar pattern as for chromium, where the lowest values were in the powder-based MONP and the highest found in the plant-based MONP and tobacco products.
- Selenium was also found in all plant-based MONPs, and in some cases was close to the levels found in tobacco products. Additionally, two powder-based products were found to have selenium in them.

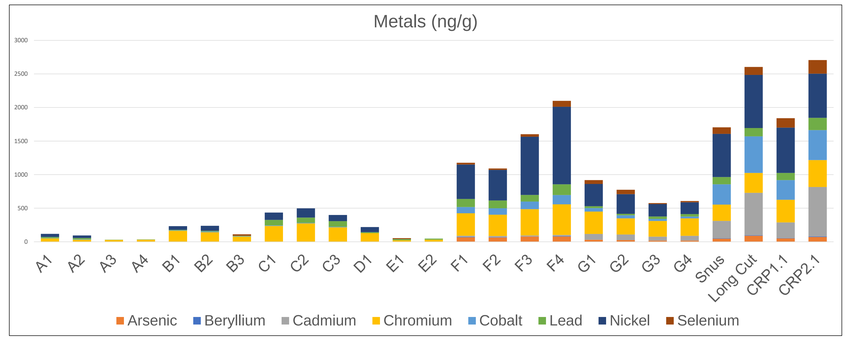

Figure 3. Metals Results

Conclusions

As expected, the average levels of most analytes measured in MONPs were lower than those measured in smokeless tobacco products (e.g. TSNAs, BaP, Nitrite). However, a few interesting differences were observed in the carbonyls and metals results between the powder-based and the plant-based products.

The powder-based MONPs had significantly higher levels of formaldehyde versus acetaldehyde and the plant-based MONPs had significantly higher acetaldehyde versus formaldehyde. In some cases, these acetaldehyde levels were even higher than those in the tobacco products.

All of the metals included in this study were more prevalent in the plant-based products than the powder-based products. The nickel and lead observed in the plant-based products were in a similar range as the tobacco products.

Although TSNAs would not be expected in tobacco-free products, very low levels of TSNAs were observed in two of the MONPs. The origin of the observed TSNAs may be related to the nicotine source used and/or any processing techniques used during production.

Based on these results, a number of compounds were successfully quantitated in the products tested, suggesting that the limits of quantitation were appropriate and the methods are likely to be suitable for the testing of MONPs.

References

1. David Azzopardi, Chuan Liu & James Murphy (2021): Chemical characterization of tobacco-free "modern" oral nicotine pouches and their position on the toxicant and risk continuums, Drug and Chemical Toxicology, DOI: 10.1080/01480545.2021.1925691
2. Karl A. Wagner et al. (2020): Characterization of on!® Nicotine Pouches – Part 1: HPHCs, SRNT 26th Annual Meeting, Poster #182