Comparison of HPHCs in Aerosol Generated from a Novel Heated Tobacco Capsule (HTC) Prototype to HPHCs in Conventional Cigarette Smoke

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Abstract

Heated Tobacco Products (HTP) contain a tobacco substrate that is heated to low temperatures (below 350 °C), resulting in an inhalable nicotine containing aerosol. The objective of this work is to compare concentrations of select harmful and potentially harmful constituents (HPHCs) in the aerosols generated by a novel heated tobacco capsule (HTC) prototype to their corresponding concentrations in smoke generated from conventional cigarettes (University of Kentucky 1R6F Certified Reference Cigarette). The HTC prototype consists of a hand-held battery-operated device (BVR 3.2) and a disposable tobacco-containing capsule that is inserted into the device. The selection criteria employed to identify the 50+ HPHCs, compared across the HTC prototype and conventional cigarettes, will be discussed. Comparisons of the HPHC data will be presented on a per unit and normalized per nicotine basis. Data presented will demonstrate significant reductions (80-99 %) for most HPHC chemical classes such as carbonyls, volatile organic compounds, aromatic amines, carbon monoxide, and polycyclic aromatic hydrocarbons in the aerosols generated from the HTC prototype compared to cigarette smoke. The significant reduction in HPHCs substantiates that heating tobacco in the HTC prototype prevents high temperature pyrolysis and combustion reactions that occur when tobacco is burned in a conventional cigarette. The data indicates that Adults 21+ who smoke (AS) should significantly reduce their exposure to HPHCs by switching to use of the HTC prototype.

Introduction

HTPs contain a tobacco substrate that is heated to low temperatures (<350°C), as opposed to burning it in a conventional cigarette. Heating tobacco in an HTP prevents high-temperature pyrolysis and combustion reactions that occur in a burning cigarette and in turn, eliminates or reduces the generation of multiple HPHCs and other toxicants. HTC is an innovative HTP that does not have the visual cues of a cigarette. The HTC prototypes consist of a hand-held device that, unlike any other product in the HTP category, heats a disposable tobacco-containing capsule, rather than heating a tobacco stick (HTS). The device heats a capsule filled with ground tobacco to a precise temperature. Each capsule is single-use and lasts for one tobacco occasion. We demonstrate that aerosols generated from HTC prototypes are significantly different in composition compared to cigarette smoke. In the absence of guidance from the FDA on a specific list of HPHCs to be measured in HTPs, we assessed the HTC prototypes based on our internally developed Altria Client Services (ALCS) HTP HPHC list, which was developed using the 18 HPHCs identified for assessment in cigarette smoke in FDA's Guidance for Industry Abbreviated HPHC List (FDA, 2012), as a starting point. To make the ALCS HTP HPHC list more scientifically robust, we used the following four primary criteria to expand the list: [1] Analytes associated with multiple disease categories on FDA's Established HPHC List; [2] Alignment with other toxicant lists, primarily the WHO-38 Priority List; [3] Correspondence with established Clinical Biomarkers of Exposure (BoEs) with HPHCs to reflect the panel of BOEs which are well studied; and [4] Compounds that are specific to the HTP category (e.g., Humectants which are added to the tobacco to facilitate aerosol formation and their potential decomposition products). Two secondary criteria were also employed: [1] Availability of validated analytical methods; and [2] Analytes that support the demonstration of no combustion in HTPs.

Using the ISO 20778:2018 Intense puffing regime, HPHCs in the aerosols generated by the HTC prototype are compared to 1R6F on a per unit (i.e., 1 capsule vs. 1 stick) and on a normalized per nicotine basis. However, different HTPs have dissimilar defined session use lengths. Combining this with the fixed 30 secs puff interval for the Intense puffing regime leads to different numbers of puffs for which aerosol is collected during the assessment of the various HTPs. Though the per unit metric is a good standard for comparing HPHC yield in the HTC prototypes to their corresponding yields in cigarette smoke, it is not an appropriate metric for intra-category HPHC comparisons among HTPs. HPHC yields normalized to nicotine yield are more likely to reflect actual human exposure levels than HPHC yields expressed on a per unit basis. Therefore, HPHC data from aerosols of the HTC prototypes will be compared to corresponding HPHCs in 1R6F cigarette smoke, on both a per unit and normalized per nicotine basis. To further illustrate the reduced risk potential of the HTC prototypes, we demonstrate that the aerosols of the HTC prototype blends also show significant reductions compared to cigarette smoke (1R6F), when the HPHCs are categorized by the four disease outcome classifications listed in FDA's HPHC established List (FDA, 2012): [1] Carcinogens (CA), [2] Respiratory Toxicants (RT), [3] Cardiovascular Toxicants (CT), and [4] Reproductive or Developmental Toxicants (RDT).[1,2]

Methods

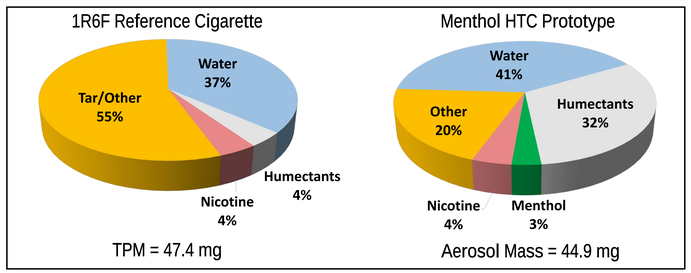
ISO 20778:2018 Intense puffing regime (2 sec puff duration, 55 cc puff volume, and 30 sec puff interval) was used for generations of aerosols from all products investigated in this study [4]. Analytical testing was performed by laboratories using methods included on their respective ISO 17025 scope of accreditation(s). The HTC prototypes were analyzed at:

- ALCS (Richmond, Virginia, USA) and onsite laboratory contractor, Eurofins Lancaster Laboratories Professional Scientific Services (ELL-PSS) (Richmond, Virginia, USA). The nine HPHC test methods performed included: Tobacco-specific Nitrosamines (TSNAs) (4), Carbonyls (7), Diacetyl, Aromatic Amines (AAs) (3), Phenols (7), Ammonia (NH_3), Nitrogen Oxides (NOx) (2), Carbon Monoxide (CO), and a combined method for Nicotine, Propylene Glycol, Glycerol, Menthol, and Water.
- Labstat International, Inc. (Kitchener, Ontario Canada). The six ISO 17025 accredited HPHC test methods performed at Labstat International, Inc. included: Volatile Organic Compounds (VOCs) (8), Polycyclic Aromatic Hydrocarbons (PAHs) (6). Metals (6), Mercury, Semi-Volatile Compounds (SVCs) (5), and Hydrogen Cyanide (HCN).
- Enthalpy Analytical (Richmond, Virginia, USA, and Durham, North Carolina, USA). Enthalpy performed the ISO 17025 accredited test method for Glycidol.

Glycidol data reported for University of Kentucky Certified Reference Cigarette (1R6F) smoke and aerosols of in-market HTP comparators were generated by Enthalpy Analytical. All other HPHC data reported for University of Kentucky Certified Reference Cigarette (1R6F) smoke and aerosols of in-market HTP comparators were generated by Labstat International, Inc.

Results

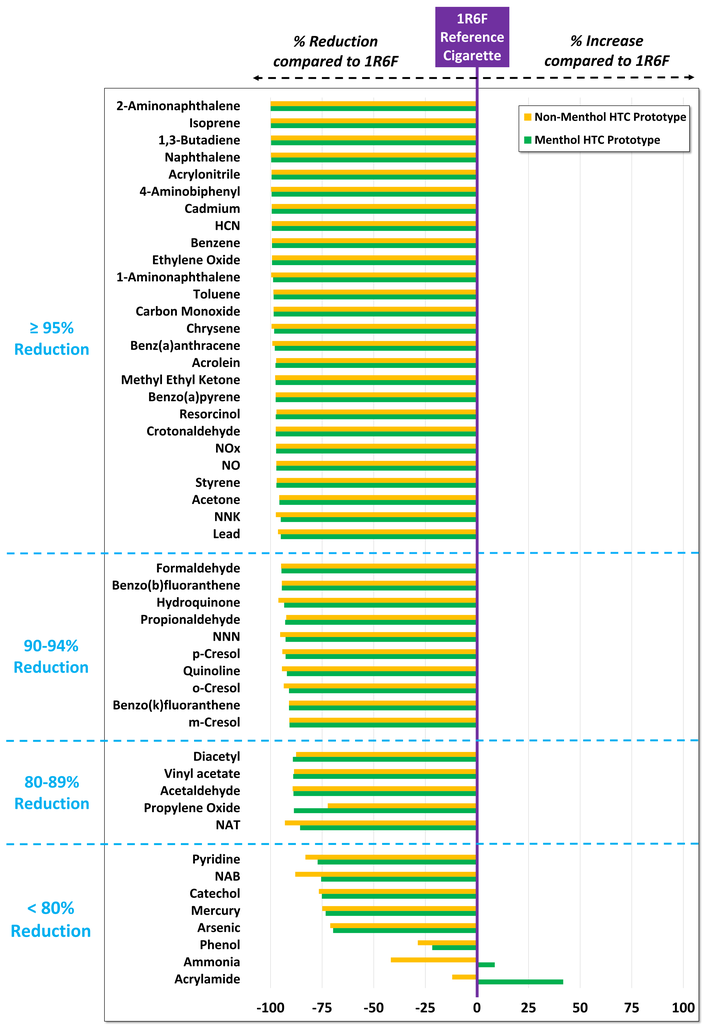
Aerosol Composition [Intense Puffing Regime]: HTC Prototype vs. Conventional Cigarette



HTC prototype aerosols have potential for nicotine delivery comparable to a cigarette, with substantial reduction in HPHCs and other toxicants (Water, Nicotine, Menthol and Humectants comprise ~80% of the prototype HTC aerosols).

We demonstrate a substantial HPHC exposure reduction potential for HTC Prototype aerosols compared to cigarette smoke

HPHCs: % Change Compared to 1R6F for HTC Prototypes (Per Unit Basis)*



***Per Unit** = 1 Cigarette for 1R6F and 1 Capsule for HTC Prototypes. Four HPHCs from the ALCS HTP HPHC List (Cr, Co, Ni & Nitrobenzene) are not included in the comparison, as both their 1R6F & HTC Prototype values were below LOQ.

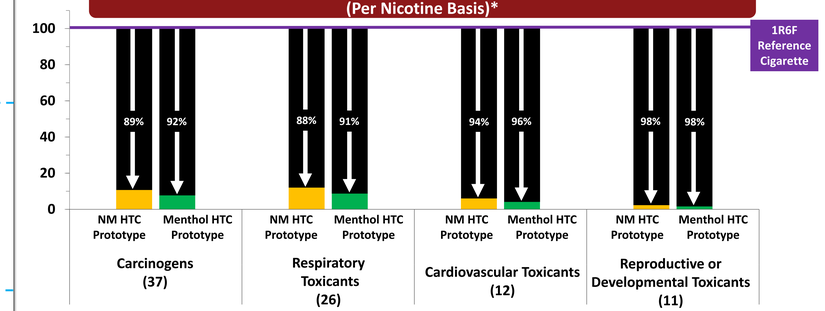
HPHCs: % Change Compared to 1R6F for HTC Prototypes and Comparator HTPs (Per Nicotine Basis)*

Chemical Class (Number of Constituents)	Non-Menthol HTC Prototype	Non-Menthol HTP Comparator 1^	Non-Menthol HTP Comparator 2^	Menthol HTC Prototype	Menthol HTP Comparator 1^	Menthol HTP Comparator 2^
TSNAs (4)	-91.4	-90.7	-74.3	-89.0	-90.6	-82.5
Carbonyls (8)	-87.0	-79.6	-80.9	-91.2	-73.9	-80.1
VOCs (8)	-99.4	-99.6	-99.8	-99.6	-99.4	-99.8
PAHs (6)	-99.4	-99.1	-98.7	-99.4	-98.9	-98.8
Aromatic Amines (3)	-99.7	-99.8	-99.6	-99.2	-99.7	-99.7
Metals (7)	-93.9	-94.0	-88.2	-95.4	-92.9	-88.3
Phenol	19.3	-90.8	-97.5	-11.1	-92.0	-98.3
Other Phenols (6)	-78.8	-89.6	-92.6	-83.3	-86.7	-93.8
Acrylamide	47.2	-29.4	-42.1	60.9	-43.5	-50.6
Other SVCs (4)	-78.1	-68.1	-79.2	-80.3	-66.0	-78.3
Ammonia	-2.54	-15.9	-43.4	23.2	-25.6	-61.4
HCN	-99.0	-98.9	-98.1	-99.3	-98.6	-98.3
NOx (2)	-95.4	-95.5	-90.8	-96.9	-94.3	-92.6
CO	-97.5	-98.0	-97.5	-98.3	-97.4	-97.7
Glycidol	251	63.3	-65.8	160	103	-85.6

** Negative values indicate that concentrations in HTP prototypes are reduced compared to those in 1R6F for that HPHC. Positive values indicate concentrations in HTPs are increased compared to 1R6F. ^ All HTP Comparator products tested use heated tobacco sticks (HTS).*

- Data demonstrate significant reductions (80% - 99%) for most HPHC chemical classes in the aerosols generated from the HTC prototypes compared to cigarette smoke, both on a per unit and per nicotine basis.
- Phenol, acrylamide, and ammonia are nominally reduced or increased in select HTC prototypes.
- Compared to cigarettes, concentrations of formulation-related humectants and their corresponding decomposition products (e.g., Glycidol) are higher in aerosols generated from the HTC prototypes.

HPHC Exposure Reduction by Disease Outcomes Classification[1,2] (Per Nicotine Basis)*



**Analysis does not account for potency of individual analytes and does not include Nicotine, Propylene Glycol, or Glycerol.*

Significant reductions in concentrations of measured carcinogens (89% - 92%) and other toxicants (88% - 98%) observed in aerosols generated from HTC prototypes compared to cigarette smoke.

Conclusion

The significant reduction in most HPHCs substantiates that heating tobacco in the HTC prototype prevents high-temperature pyrolysis and combustion reactions that occur when tobacco is burned in a conventional cigarette. The HPHC data indicates that Adults 21+ who smoke (AS) should significantly reduce their overall exposure to HPHCs by switching to use of the HTC prototypes.

References

1. FDA Draft Guidance 2012: Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act; 77 Fed. Reg. 20034 (April 2012).
2. FDA Draft Guidance 2012: Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke; Established List (April 2012)
3. Harmful and Potentially Harmful Constituents in Tobacco Products; Established List; Proposed Additions; Request for Comments (FDA, August 2019).
4. ISO 20778:2018: Cigarettes - Routine analytical cigarette smoking machine - Definitions and standard conditions with an intense smoking regime (Oct. 2018).

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