HPHC Analysis of Seven Flavors of a Temperature-Regulated Nicotine Salt Pod System

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Introduction

Combustible cigarettes reach temperatures in excess of 900 degrees Celsius[1] and consequently generate over seven thousand[1] thermal degradation products including chemicals and chemical compounds characterized as Harmful and Potentially Harmful Constituents (HPHCs) under the Food, Drug and Cosmetic Act (FD&C Act)[2]. The JUUL system is a temperature-regulated closed nicotine salt pod system (NSPS) possessing no user modifiable settings with the design intent of minimizing thermal degradation byproducts across a range of operating environments. The NSPS pods evaluated in these studies utilized a cotton wicking material to supply e-liquid for aerosolization. Seven different flavors, each at a nicotine concentration of 9 mg/mL, were analyzed for a select panel of analytes and HPHCs listed in the US FDA PMTA draft guidance document[2] for Electronic Nicotine Delivery Systems (ENDS) in comparison to a 3R4F Kentucky Reference Cigarette. The NSPS e-liquids contain 5 major ingredients: nicotine, benzoic acid, glycerol, propylene glycol, and flavorants. The assessed NSPS e-liquids, including 9 mg/mL nicotine concentration and flavors, are available in ex-US markets.

Materials and Methods

The aerosol HPHC profile generated by actuating NSPS pods with cotton wicking were evaluated by an accredited ISO 17025 3rd party laboratory (Enthalpy Analytical) using validated analytical methods. E-liquid flavors loaded into the tested pods spanned a combination of tobacco, mint/menthol, and fruit flavors (including Royal Creme, Apple Orchard, Mango Nectar, Glacier Mint, Alpine Berry, Golden Tobacco, Virginia Tobacco), all at nicotine concentrations of 9 mg/mL. Vaping topography was set at a 70 mL square wave volume puffed across a 3 second duration with a 30 second puff interval, a total of 10 technical replicates were analyzed with 50 puffs collected per replicate. Each analytical replicate was generated using a unique NSPS pod for each assay. 3R4F Kentucky Reference Cigarette replicates were smoked on a smoking machine under the Health Canada defined "intense puffing regime". A total of 30 puffs per replicate were collected with 10 puffs per cigarette and 3 cigarettes per replicate. A panel of 22 analytes was tested covering six categories of HPHCs - polyaromatic hydrocarbons (PAH), carbonyls, metals, tobacco specific nitrosamines (TSNAs), polyaromatic amines (PAA), and volatile organic compounds (VOC). Quantifiable means and standard deviations (±SD) for each analyte are represented visually by bars. Sample values below the limit of quantitation (LOQ) are visually represented by dashed bars set to the magnitude of the method LOQ divided by √2.

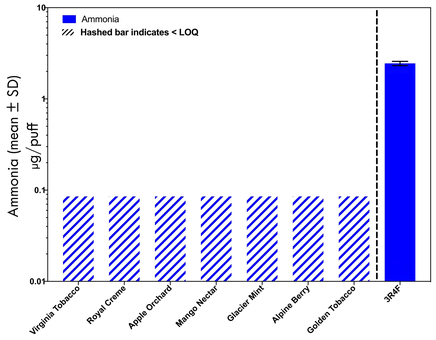
Results

Ethylene Glycol, Diethylene Gycol, and Anabasine were not detected in NSPS aerosol and were excluded from these figures due to a lack of comparable 3R4F data. Constituents expected in the NSPS aerosol such as nicotine, propylene glycol, glycerol, and menthol were identified analytically but excluded from subsequent representation. All formulations tested across the 22 panel analytes measured in these categories were evaluated against the Kentucky 3R4F reference combustible cigarette in order to generate a comparison of relative exposure. 95% of NSPS aerosol analytes were below the level of quantification. Notably, VOCs (acrylonitrile, benzene, 1,3-butadiene, isoprene, and toluene) and select carbonyls (diacetyl, acetyl propionyl, and crotonaldehyde) were uniformly below the level of detection in the aerosol generated by all seven flavors under these puffing machine conditions. NSPS aerosol composition for all seven flavors was also found to be markedly different from the mainstream smoke of the 3R4F reference combustible cigarettes, eliciting a 99% reduction in assessed HPHCs.

Table 1 : Limit of Quantitation (LOQ) Values Depicted in Figures

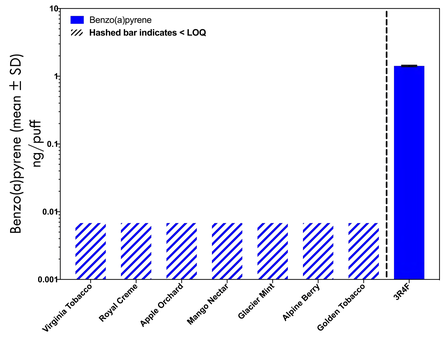
Analyte	NSPS LOQ	3R4F LOQ	Units
Ammonia	0.12	N/A	ug/puff
Cadmium	0.10	2.00	ng/puff
Lead	0.20	4.00	ng/puff
Chromium	1.00	8.50	ng/puff
Nickel	0.20	9.50	ng/puff
Benzo(a)pyrene	0.01	N/A	ng/puff
Isoprene	3.22	N/A	ug/puff
Acrylonitrile	0.32	N/A	ug/puff
Benzene	0.40	N/A	ug/puff
Toluene	0.40	N/A	ug/puff
1-aminonaphthalene	1.99	N/A	pg/puff
2-aminonaphthalene	1.97	N/A	pg/puff
4-aminobiphenyl	1.01	N/A	pg/puff
NNN	0.02	N/A	ng/puff
NNK	0.02	N/A	ng/puff
Formaldehyde	0.02	N/A	ug/puff
Acetaldehyde	0.02	N/A	ug/puff
Acrolein	0.02	N/A	ug/puff
Crotonaldehyde	0.02	N/A	ug/puff
Diacetyl	0.02	N/A	ug/puff
Acetyl Propionyl	0.02	N/A	ug/puff

Fig. 1 : Ammonia - Aerosol



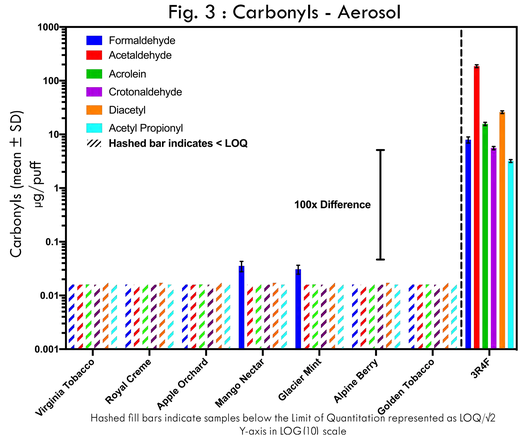
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 2 : Benzo(a)pyrene - Aerosol



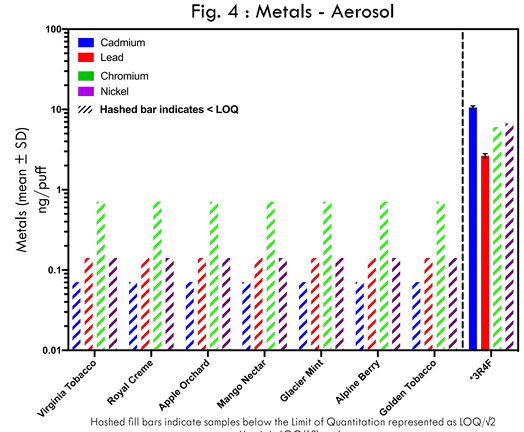
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 3 : Carbonyls - Aerosol



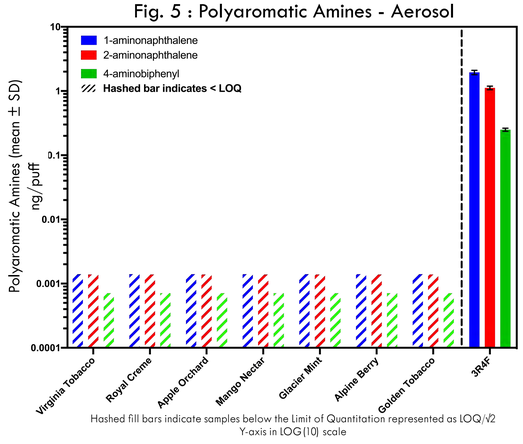
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 4 : Metals - Aerosol



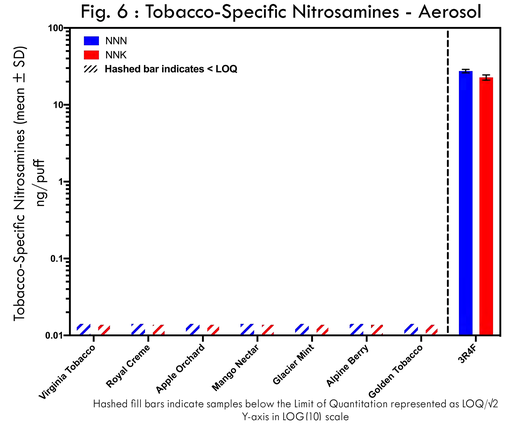
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 5 : Polyaromatic Amines - Aerosol



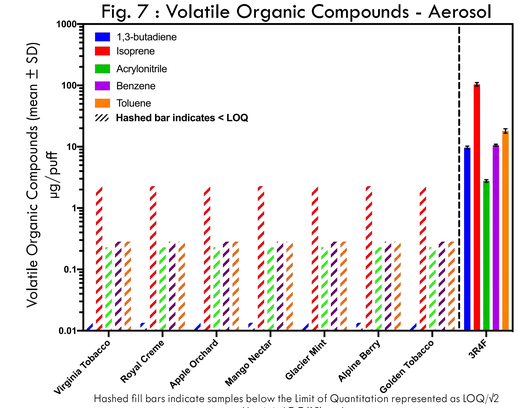
Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 6 : Tobacco-Specific Nitrosamines - Aerosol



Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Fig. 7 : Volatile Organic Compounds - Aerosol



Hashed fill bars indicate samples below the Limit of Quantitation represented as LOQ/√2
Y-axis in LOG(10) scale

Conclusion

Consistent with prior research, NSPS pods using a cotton wicking material demonstrated average reductions of > 99% in a standardized list of assessed HPHCs compared to reference combustible cigarettes.

Limitations

This was a preliminary assessment of ten replicates of each analytical method for each formulation using one puffing regime on a puffing machine under laboratory conditions. Comprehensive characterization of human HPHC exposure requires user topography data and biomarker analyses.

References

1. U.S. Department of Health and Human Services, "Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General", 2012.
2. FDA Draft Guidance, "Premarket Tobacco Applications for ENDS Products", May 2016.
3. G. Gilman, M. Johnson, A. Martin, M. Misra, "HPHC Analysis of Eight Flavors of a Temperature-Regulated Nicotine Salt-Based ENDS Product", Global Forum on Nicotine, Warsaw, Poland, Dec 2018.
4. I. G. Gillman, et al., "A Comparison of Quartz Filter Collection Versus Electrostatic Precipitation Collection in E-Cigarette Aerosol Samples", Tobacco Science Research Conference, Leesburg, Virginia, September 2019.

Note: Consistent with applicable laws and regulations, JUUL Labs does not, and cannot, promote its products as being less harmful than cigarettes.