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Rapid Report

Effects of E-Cigarette Flavor Enhancing Capsules on Inhalable Aerosols

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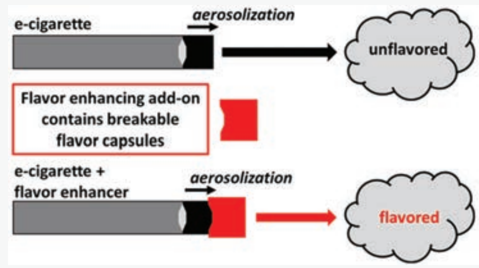
ABSTRACT: The flavor of inhaled e-cigarette aerosols may be augmented using crushable flavor capsules added to e-cigarettes. For example, Puff Krush contains breakable flavor capsules in a sorbent material. The capsules are crushed, and then, aerosol passes through the saturated sorbent material before inhalation. Herein, we used NMR and GC−MS to identify the capsule medium chain triglyceride (MCT) solvent and flavorants in selected Puff Krush flavor capsules and then determined which molecules from the capsule transfer into aerosols. MCTs from the Puff Krush were not found in the aerosols, and ~50% of Puff Krush flavorants transferred into the aerosol upon vaping.



Flavors in cigarettes mask the unpleasant taste of smoke, facilitate inhalation, and promote smoking initiation among adolescents.[1] The Food and Drug Administration (FDA) banned cigarettes containing most flavors other than menthol or tobacco in 2009. Flavors in other tobacco products (e.g., e-cigarettes, cigarillos, hookah, nicotine pouches) are mostly unregulated. For example, the sale of flavored cartridges for e-cigarettes (i.e., JUUL) were prohibited by the FDA in 2020, but this excluded menthol and tobacco flavored cartridges, flavored disposable e-cigarettes, and flavored e-liquids for open-tank systems. The FDA proposed a ban on menthol in cigarettes and cigars in 2022, but not in e-cigarettes despite their increasing popularity.[2]

Some cigarettes contain crushable flavor capsules (limited to menthol in the US and Canada) in the filter to give the consumer a choice between unflavored (uncrushed capsule) and flavored (crushed capsule) inhalable smoke.[3] Consumers of popular pod and disposable e-cigarettes (JUUL and Puff Bar, respectively) can enhance the flavor of their aerosols with products including Puff Krush. Puff Krush is a secondary silicone rubber mouthpiece containing two flavor capsules in sorbent material that fits over the mouthpiece on the e-cigarette (Figure S1).[4] Gaiha et al.[5] found that ~25% and ~30% of underage (<21) pod and disposable e-cigarette ever-users have used a flavor-enhancer (e.g., Puff Krush), respectively. Consumers are advised to attach the Puff Krush to their e-cigarette and then crush the flavor capsules. The aerosolized e-liquid passes through the flavor and capsule solvent-saturated sorbent material as the consumer inhales.

The compositions of the Puff Krush flavor capsule's shell, carrier fluid, and flavorant composition have not been reported in the literature to our knowledge. Patents for cigarette flavor capsules from Dube et al. (R.J. Reynolds),[6] Deal (R. J. Reynolds),[7] and Hartmann et al.[8] (V. Mane FILS) and an internal tobacco document from Dube[9] claim that the capsule shells are gelatin and that the carrier fluids are medium chain triglycerides (MCTs). Kim et al. analyzed the physical properties of flavor capsules in 31 Korean capsule cigarettes (i.e., number of capsules, mass, diameter, location in filter, color) and determined the menthol levels and flavorant profiles in the capsules by gas chromatography−mass spectrometry (GC−MS).[10] The capsule masses and diameters ranged from ~11 to ~48 mg and ~2.6 to ~4.3 mm, respectively. The number of capsules (1 or 2), location in filter (cigarette side, middle, mouth side), and color varied depending on the cigarette brand. The ranges for the menthol level in the capsules and whole cigarette (sum of menthol in the capsule, filler, filter, filler paper, and filter paper) were ~2100 to ~12 000 μg/capsule and ~2600 to ~23 000 μg/cigarette, respectively. The menthol levels in capsule cigarettes were greater than or equal to those in menthol cigarettes without capsules.

Herein, we report the weight of the individual Puff Krush flavor capsule components (i.e., shell, carrier fluid, and total flavorant mass), composition of the carrier fluid by GC−MS and NMR spectroscopy, and flavorant levels in the selected flavor capsules by GC−MS. Additionally, we collected aerosol samples from JUUL with and without a Puff Krush attached to determine what flavor capsule components were transferred into the aerosol using GC−MS and NMR spectroscopy.

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We have established a variety of methods for determining the flavorant and toxicological profiles of e-liquids before and after aerosolization using GC−MS and NMR spectroscopy.[11−13] GC−MS has higher sensitivity in analyzing volatile compounds compared to NMR and is typically used to determine the flavorant profile. However, NMR can identify and quantify some species not detectable by GC−MS. For example, Salamanca et al. have shown that total formaldehyde levels (formaldehyde + formaldehyde hemiacetals) in aerosols are underestimated when using methods other than NMR.[14] We selected four of the highest rated (based on online reviews) Puff Krush flavors for this study. Puff Krush capsules (2 capsules per Puff Krush) were individually crushed inside 40 mL amber VOA vials (1 per vial), and 0.5 mL of DMSO-d_6 or 10 mL of HPLC grade isopropyl alcohol (IPA) was added to the vial for NMR or GC−MS analysis, respectively. We transferred 0.5 mL of DMSO-d_6 into an NMR tube and 1 mL of the IPA solution into a GC autosampler vial for analysis. The plastic shell was removed from the vial and rinsed with methanol. The weights of the flavor capsule and dried shell of the capsule were recorded (Table 1). Experimental details regarding the GC−MS and NMR parameters are in the Supporting Information.

Table 1. Average ± Standard Deviation (n = 4) Weight of Individual Puff Krush Flavor Capsule Components

Puff Krush	capsule shell (mg)	carrier fluid (mg)	total flavorant mass[b] (mg/capsule)
KS[a] (blue capsule)	1.2 ± 0.2	18.8 ± 0.7	2.2 ± 0.2
KS[a] (green capsule)	1.3 ± 0.1	20.1 ± 0.8	0.5 ± 0.1
Peach Ice	1.1 ± 0.1	18.1 ± 0.3	5.6 ± 0.5
Mango	1.2 ± 0.2	16.1 ± 0.7	1.2 ± 0.1
Sour Apple	1.2 ± 0.1	14.5 ± 0.9	2.8 ± 0.1

[a]KS = Kiwi-Strawberry. [b]Determined by GC−MS.

We determined the carrier fluid mass by subtracting the capsule shell mass and target flavorant mass (determined by GC−MS) from the capsule mass (Figure 1 and Table 1). The mass of each Puff Krush capsule shell in this study was consistently ∼1.2 mg, but the mass of the carrier fluid and flavorant in each capsule varied per Puff Krush flavor (Table 1). The carrier fluid made up the majority of the capsule's weight. There were nontarget compounds in the Puff Krush, but they had small peak sizes compared to the target compounds. Therefore, not including them does not significantly affect the determined carrier mass accuracy.

The GC−MS and ^{1}H NMR analyses of MCT oil were identical with matching major compounds to the Puff Krush carrier fluid (Figure S2). The carrier fluid could also contain mixtures of food grade oils (e.g., vegetable, olive, mineral oils) that contain triglycerides.[8] MCT oil also acts as a cutting agent in cannabinoid (CBD)-containing fluids to decrease the viscosity of tetrahydrocannabinol (THC) oils. Duffy et al.[15] and Murthumalage et al.[16] identified MCT oil as a prevalent cutting agent in illicit CBD-containing fluids. MCT oil in capsules delivers a payload of flavorants to the cigarette filter or e-cigarette sorbent material in the mouthpiece that the smoke or aerosol can pass through before inhalation.

Flavor Capsule Analysis. We identified and quantified 74 of the 180 target flavorants selected in this study in the Puff Krush (Tables S1 and S2). The flavorants on the y-axis of the heatmap are categorized by their safety classification (toxic, harmful, irritant, no data; Figure 1).[17,18] The total mass and number of flavorants in each Puff Krush capsule are listed under the heatmap on the x-axis, and the individual flavorant levels ranged from 0.3 to 3383.7 μg/capsule (Figure 1). Peach Ice and Kiwi-Strawberry (KS; green) capsules contained the highest and lowest total mass (5672.4 and 532.5 μg/capsule) and number of flavorants (43 and 25), respectively. The mass of menthol made up ∼60% of the total flavorants in the Peach Ice capsules.

The mass of menthol was >1000 μg/capsule for Peach Ice and Sour Apple, but <10 μg/capsule for KS (blue), KS (green), and Mango (Figure 1). The percentages of flavorants ≥100 μg/capsule were 21% in KS (blue), 8% in KS (green), 14% in Peach Ice, 13% in Sour Apple, and 14% in Mango capsules. The majority of individual flavorants (between 79% and 92%) in the Puff Krush capsules were <10 μg/capsule. Most of the flavorants identified in the selected Puff Krush were chemically classified as esters, followed by alcohols, ketones, and terpenes, which are similar to chemical classifications of popular flavorants in refill e-liquids.[13,19]

Pankow et al. analyzed the menthol, triacetin, and flavorant content in "concept" descriptor (i.e., names that suggest a sensation) cigarettes from the U.S., Mexico, and Canada. They separated the filter from the tobacco portion of the cigarette and then crushed the flavor capsule in the filter for GC−MS analysis.[20] They found that the capsules in "Menthol-Plus" cigarettes from Mexico contained high levels of menthol (ranging from 320 to 3400 μg/cigarette) and varying levels of fruity flavorants. High levels of triacetin were observed in each cigarette due to its role as a plasticizer in cigarette filters. We analyzed the sorbent material in the Puff Krush (before crushing the capsules) and did not detect any of the target analytes—including triacetin (Figure S1).

We compared the flavorant profiles in flavor capsules from Puff Krush and cigarettes using the data from this study and Pankow et al.'s study in Figure 1, respectively.[20] The Camel Crush Menthol (CCM; from the U.S.), Marlboro Capsula Fresca (MCF; from Mexico), Pall Mall XL Black Edition Maui Crepuscule (PMXL; from Mexico), and Lucky Strike Convertibles Purple (LSCP; from Mexico) capsule cigarettes contained 1 capsule each. The selected cigarette flavor capsules contained 16 flavorants that were not detected in the selected Puff Krush. Menthol was the highest concentration compound in the cigarette, Peach Ice, and Sour Apple capsules. However, hexyl acetate, 3Z-hexenol acetate, and γ-decalactone were the highest concentration flavorants in KS (blue), KS (green), and Mango, respectively.

Transfer Efficiency of Puff Krush Components. We aerosolized a simulated JUUL pod containing 30:70 propylene glycol/glycerol (PG/GL) by mol with a Puff Krush attached to or crushed inside a pod to compare the transfer efficiency of the flavor capsule components (i.e., flavorants and MCTs) into the aerosol. The aerosol samples (3 puffs/sample) were collected using the protocol in the Supporting Information and analyzed using ^{1}H NMR spectroscopy. A simulated 30:70 PG/GL by mol e-liquid was used to match commercial JUUL e-liquids. The % aerosol collected was determined by dividing the mass of the collected aerosol by the mass of e-liquid consumed. Spectra associated with aerosol samples in Figures S3 and S4 were normalized to the PG methyl peak. Integrals in the ^{1}H NMR spectra from the selected flavorants in aerosolized

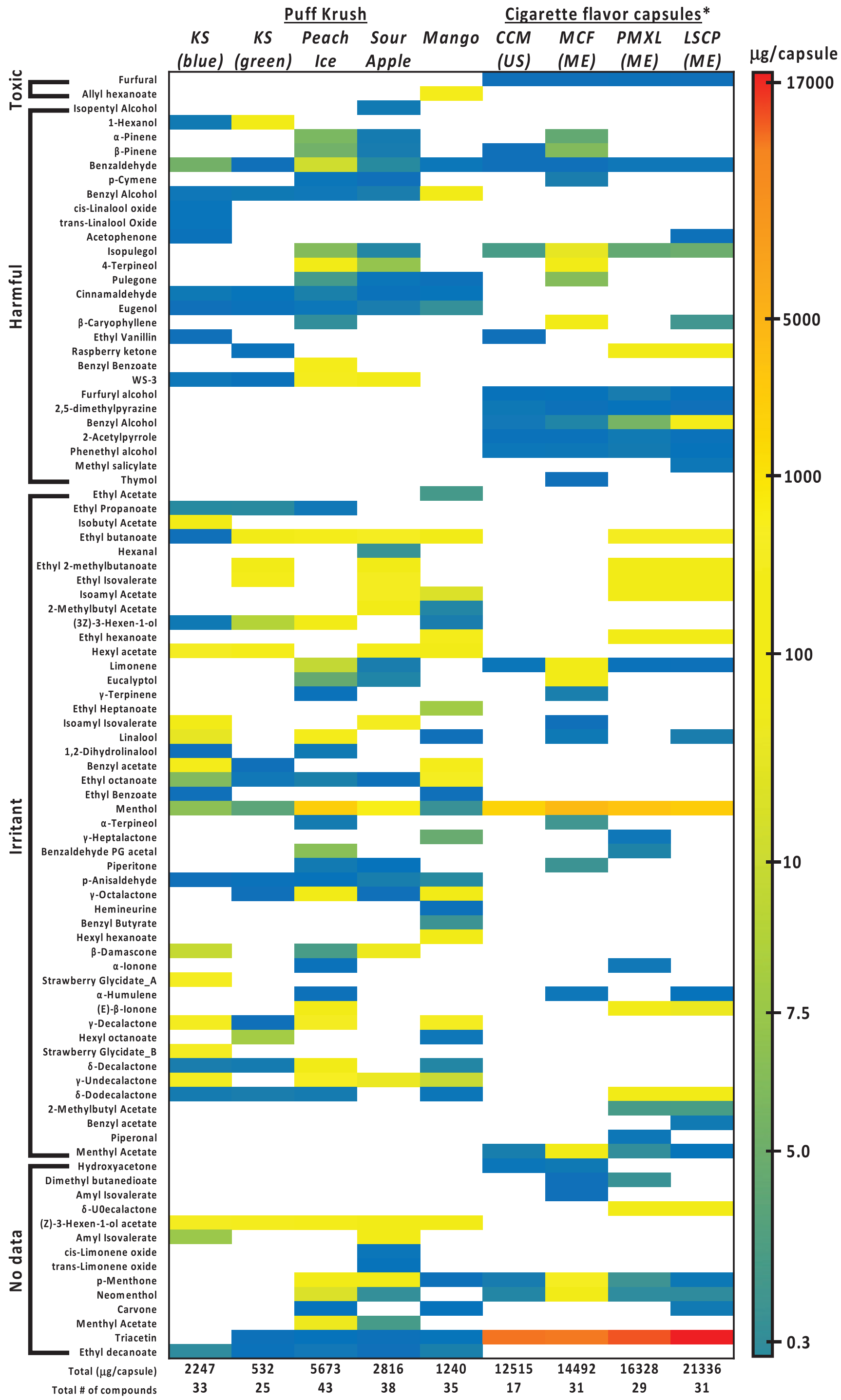

Figure 1. Heatmap showing the average mass of flavorants (μg/capsule) identified in individual Kiwi-Strawberry (KS; blue; n = 2), KS (green; n = 2), Peach Ice (n = 4), Sour Apple (n = 4), and Mango (n = 4) Puff Krush capsules. The cigarette flavor capsule data for Camel Crush Menthol (CCM; from the U.S.; n = 2), Marlboro Capsula Fresca (MCF; from Mexico = ME; n = 2), Pall Mall XL Black Edition Maui Crepuscule (PMXL; from Mexico; n = 3), and Lucky Strike Convertibles Purple (LSCP; from Mexico; n = 2) from Pankow et al. (labeled with ∗) were compared to the Puff Krush capsule composition.[20] Blank cells (white) indicate the flavorant was not identified in the sample. Pankow et al. crushed the flavor capsule (1 per cigarette) in the filter, and then analyzed the composition of the filter by GC−MS. There are 2 capsules in each Puff Krush, so the total flavorant amounts can be found by multiplying by 2, except for KS which had two different capsules, so they should be added. The flavorants are categorized by their hazard levels.[17,18] The total mass and amount of individual flavorants in each flavor capsule are at the bottom of each column. The limit of quantitation (LOQ) was 1.0 μg/capsule for the Puff Krush, and anything under the LOQ was an estimate.

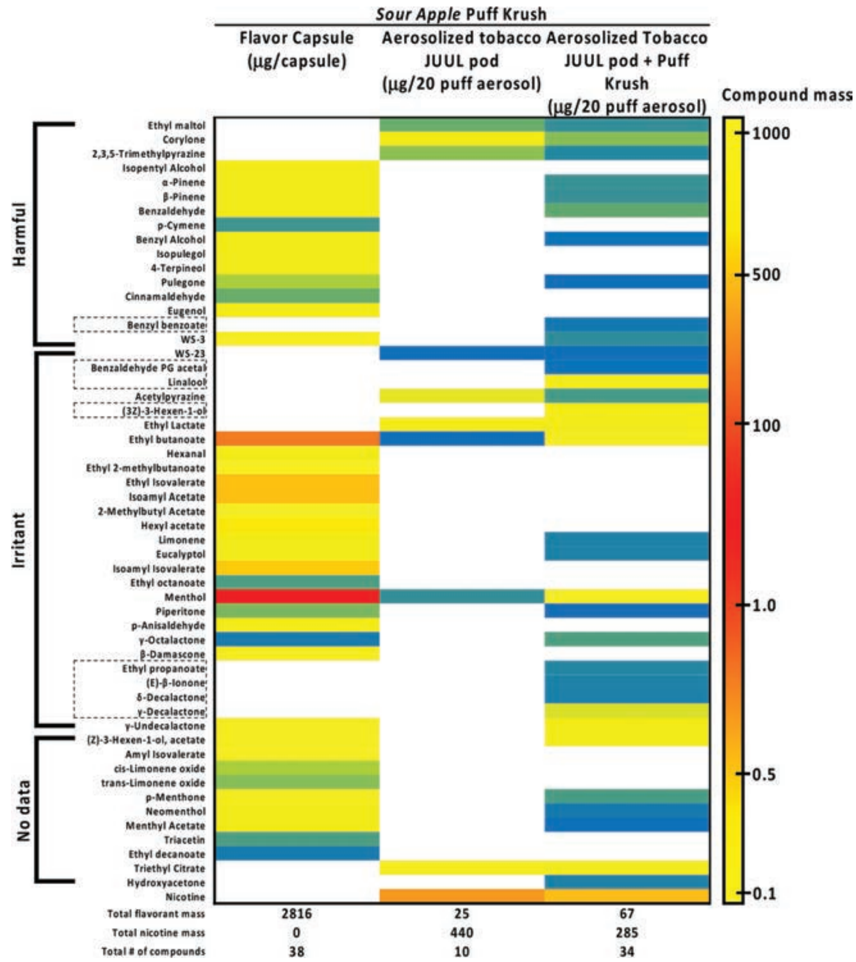

Figure 2. Heatmap comparing the average mass of flavorants and nicotine identified in Sour Apple Puff Krush flavor capsules (n = 4; μg/capsule), an aerosolized tobacco JUUL pod (3% nicotine; n = 1; μg/20 puff aerosol; average aerosol mass was 34.0 mg), and an aerosolized tobacco JUUL pod (3% nicotine) with a Sour Apple Puff Krush attached (n = 4; μg/20 puff aerosol; average aerosol mass was 34.0 mg). Data for the Sour Apple flavor capsules were from Figure 1, but the scale is restricted to 1000 instead of 17 000 for the mass. An aerosol sample from a tobacco JUUL pod (3% nicotine) was collected, followed by four more aerosol samples from a tobacco JUUL pod (3% nicotine) with a Sour Apple Puff Krush attached. Aerosol samples (20 puffs each) were collected using a coldfinger. The flavorants are categorized by their hazard levels.[17,18] The total mass (of flavorants and nicotine) and number of individual compounds in each sample are listed at the bottom of each column. Blank cells (white) indicate the flavorant was not identified in the sample. The eight flavorants that have a dashed border around them were only present in the aerosolized tobacco JUUL pod with a Puff Krush attached. The limit of quantitation (LOQ) was 1.0 μg/capsule and 0.5 μg/20 puff aerosol, and anything under the LOQs was an estimate. See Table 1 for the total mass of capsule flavorants.

e-liquids with a Puff Krush attached to versus crushed inside were compared, and the average values were reported.

The aerosolized PG/GL e-liquid passed through the flavorant-saturated sorbent material in the secondary mouthpiece when the Puff Krush was attached to the JUUL pod, whereas the e-liquid and flavorants were aerosolized when the two flavor capsules were crushed into the JUUL pod. The % aerosol collected for experiments with the Peach Ice attached was 22.9 ± 6.3%, Peach Ice inside was 9.6 ± 3.5%, KS attached was 24.4 ± 10.1%, and KS inside was 22.4 ± 8.1%. We primarily observed the same ^{1}H NMR peaks associated with the PG/GL and Puff Krush components for this experiment by the two collection methods (Figures S3 and S4). The only decomposition product observed when the capsule had been dissolved into the PG/GL was acetic acid. MCTs were absent in the aerosol samples based on this puff protocol and NMR analysis. However, we found that ∼5.2- and ∼1.9-fold more flavorants transferred into the aerosol when the Peach Ice and KS flavor capsules were crushed into the e-liquid versus attached to the JUUL pod, respectively. Flavorants are more volatile than MCTs and thus more likely to transfer into the aerosol inhaled by the consumer.[21]

Aerosol Composition Analyzed with GC−MS. Aerosol samples (20 puffs/sample) from a tobacco JUUL pod (3% nicotine) without and with a Sour Apple Puff Krush attached were collected using a coldfinger (Figure S5). The puff protocol and coldfinger setup are described in the Supporting Information. We compared the flavorant mass detected in the Sour Apple Puff Krush (μg/capsule; from Figure 1), aerosolized tobacco JUUL pod (3% nicotine; μg/20 puff aerosol), and aerosolized tobacco JUUL pod with a Sour Apple Puff Krush attached (μg/20 puff aerosol). Most of the flavorants detected in the tobacco JUUL pod were not present in the Sour Apple Puff Krush.

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Chem. Res. Toxicol. 2023, 36, 8−13

The average % aerosol collected was 36.6 ± 12.1% for this experiment and was calculated using the average mass of e-liquid consumed. The average % aerosol collected was ∼14% higher using the coldfinger compared to collecting the aerosol samples in vials with DMSO-d_6. 20 instead of 3 puffs per sample were collected to ensure the concentration of Puff Krush components was high enough for GC−MS analysis. The coldfinger is also better at capturing volatile compounds in the aerosol due to the low temperature compared to collecting the aerosol in vials at room temperature. Ideally the % aerosol collected would be 100% for any method, but each method has limitations based on the types of compounds they can collect. The classes of molecules collected by coldfinger and impinger methods have been found to be much the same, including the small molecule formaldehyde to larger molecules such as aldehyde hemiacetals, as detected by NMR spectroscopy.[14,22] More differences between the collection methods might be found by the more sensitive MS detection methods, and this is a limitation of the study.

The flavorants and nicotine on the *y*-axis are organized based on their safety classifications (harmful, irritant, no data; Figure 2).[17,18] The total mass (of flavorants or nicotine) and number of compounds are listed under the heatmap on the *x*-axis for each sample. The ranges for flavorant masses in the capsule and two aerosol samples were 0.1−1101.1 μg/capsule and 0.1−26.6 μg/20 puff aerosol, respectively (excluding nicotine). The highest flavorant mass in the capsule was menthol (1101.1 μg/capsule), in the aerosolized tobacco JUUL pod triethyl citrate (16.8 μg/20 puff aerosol), and in the aerosolized tobacco JUUL pod + Puff Krush menthol (26.6 μg/20 puff aerosol).

About half of the flavorants associated with the Sour Apple Puff Krush capsules were identified in the aerosolized tobacco JUUL pod with a Puff Krush attached (Figure 2). The total flavorant levels were greater in the capsule compared to the aerosolized JUUL pod with a Puff Krush. Some volatile flavorants at high levels (e.g., isoamyl acetate, ethyl isovalerate, amyl isovalerate; mostly esters) in the capsule were not detected in the aerosolized JUUL pod with a Puff Krush. The Puff Krush flavorants ability to bind to MCT-saturated sorbent material and aerosol composition that passes through the saturated sorbent material could alter which flavorants transfer into the aerosol inhaled by the consumer.

The total mass of flavorants and number of compounds were significantly greater for the aerosolized JUUL pod with a Puff Krush attached versus without (Figure 2). However, the masses of some flavorants (e.g., corylone, acetylpyrazine) and nicotine from the JUUL pod were higher in the aerosolized JUUL pod without, compared to with Puff Krush attached. The nicotine level was significantly higher than any flavorant in the aerosol samples. Eight flavorants (highlighted with a dashed border in Figure 2) were only identified in the aerosolized tobacco JUUL pod with a Puff Krush attached. The Sour Apple capsules used to determine their flavorant composition in Figure 1 were from a different package than the capsules used for the vaping experiments in Figure 2. There may have been small differences in flavorant profiles in different batches of Sour Apple Puff Krush. For example, we identified 4.5 μg/capsule of ethyl acetate in 1 of 4 Mango capsules which were all colored blue (Figure 1 and Figure S1).

MCT oil was not identified in the aerosol obtained from the tobacco JUUL pod with a Puff Krush attached using our aerosol collection method (see the Supporting Information) and GC−MS analysis. As aerosol passed through the Puff Krush, the MCT-saturated sorbent material absorbed and retained most of the aerosol components and Puff Krush flavorants. Consumers would receive less nicotine with a Puff Krush attached based on these results, yet could compensate by vaping more.[23,24] Future studies could compare flavorant levels in the first aerosol sample that passes through a Puff Krush to those following, since the saturated sorbent material composition changes throughout the experiment as it is exposed to more aerosol. Aerosolizing e-liquids with and without a Puff Krush attached could also affect the toxicant levels in the aerosol inhaled by the consumer. Lim et al. reported that the volatile organic compound (VOC) concentrations were enhanced in smoke collected from flavor capsule cigarettes with the capsule crushed compared to uncrushed.[25]

NMR spectroscopy and GC−MS were used to identify the chemical constituents in Puff Krush flavor capsules and aerosolized e-liquids with a Puff Krush. Puff Krush uses MCTs as a carrier solvent to deliver flavorants to a sorbent material in a secondary mouthpiece upon breaking the capsules. The inhaled aerosol passes through the sorbent material before reaching the consumer's oral cavity. The unregulated flavor enhancers can modify the aerosol inhaled by the consumer and expose them to additional irritating, harmful, or toxic compounds. Using these device add-ons does not, however, appear to give more degradation of the flavorants than normal e-cigarette use, nor do they deliver the high-molecular-weight carrier solvents.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.chemrestox.2c00273.

Materials & Methods, lists of target analytes, images of the Puff Krush, as well as additional NMR data and information (PDF)

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CRediT: **Paul J. Kerber** data curation, formal analysis, investigation, visualization, writing-original draft; **Wentai Luo** data curation, formal analysis, investigation, methodology, validation, visualization, writing-review & editing; **Kevin J. McWhirter** investigation, writing-review & editing; **Marley Powers** investigation, writing-review & editing; **David H. Peyton** conceptualization, formal analysis, funding acquisition, project administration, supervision, writing-review & editing.

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Notes

The authors declare no competing financial interest.

■ ABBREVIATIONS

e-cigarette, electronic cigarette
e-liquid, electronic cigarette liquid
FDA, Food and Drug Administration
MCT, medium chain triglyceride
GC−MS, gas chromatography−mass spectrometry
NMR, nuclear magnetic resonance
KS, Kiwi-Strawberry
PG, propylene glycol
GL, glycerol
CBD, cannabinoid
THC, tetrahydrocannabinol
CCM, Camel Crush Menthol
MCF, Marlboro Capsula Fresca
PMXL, Pall Mall XL Black Edition Maui Crepuscule
LSCP, Lucky Strike Convertibles Purple
VOC, volatile organic compound
IPA, isopropyl alcohol.

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