

Flavor Danger: Exploring Toxin Exposure During ENDS Use

Tabatha Reynolds, Morgan L. Fleming, Kristen D. Holtz, and Andrew Simkus

Background

Electronic nicotine delivery systems (ENDS) are the most popular tobacco product among adolescents,¹ and flavors contribute to their popularity. Indeed, among youth who report ENDS use, 88% report using a flavored product.² Research has well-established that flavors increase curiosity in ENDS initiation,³ facilitate easier use,⁴ and potentiate the addicting nature of ENDS.⁴⁻⁷ Youth are often attracted to using flavored vapes without knowing the severe health consequences.

There is no safe ENDS flavor, with or without nicotine. Both flavorings and nicotine are independently associated with serious potential health risks⁸ and addiction^{6,8}. To expand our nuanced understanding of ENDS use, however, this brief discusses additional factors that may relate to enhanced risk, including comparative toxicity of different ENDS flavorings and how device types, e-liquid composition, and usage behaviors can increase exposure to unsafe ENDS chemicals. A more detailed understanding of ENDS behaviors can contribute to specific research questions, regulatory statutes, and prevention messaging that target the “most dangerous” of this risky behavior.

Flavor danger

Science is still in the early stages of unveiling the exact chemicals and interactions between chemicals in ENDS vapor that are harmful. Such research is made more difficult by the fact that many ENDS companies ambiguously and

broadly label their e-liquid flavor ingredients as “natural and artificial flavors” without specificity. Nonetheless, a review conducted in 2021⁹ counted at least 65 unique ENDS flavor ingredients with known toxicity, among which cinnamaldehyde (often used in cinnamon flavoring) was most often reported as being toxic to human cells. Other ingredients that topped the toxicity list included vanillin and ethyl vanillin (often used in vanilla flavorings); menthol (often used in ice, mint, and menthol flavoring); ethyl maltol (often used in sweet/caramel/cotton candy flavorings); benzaldehyde (often used in cherry and almond flavors); and linalool (often used in fruit and lavender flavorings). The more complex the flavor is, the more ingredients it is likely to have, and the toxicity to the ENDS user increases in turn.¹⁰ Mixtures of flavorings have been found to damage human cells worse than individual flavorings.⁹ Researchers at University of North Carolina - Chapel Hill (UNC) have created a database of flavors that can be used to understand a wide range of flavors’ toxicity levels at www.eliquidinfo.org.¹⁰

Common flavoring chemicals have been found to induce toxicity in the respiratory tract, circulatory and cardiovascular systems, skeletal system, and skin.⁹ For example, a study of 36 flavors found that the following flavors were highly toxic to human lung cells: butterscotch, caramel, coffee, fruit, chocolate, menthol, tobacco, and cinnamon.^{9,11} Similarly, cinnamon and cookie flavors have demonstrated toxicity for the human cardiovascular and circulatory systems.^{9,12} Flavors such as Irish latte, mango blast, and sweet melon have demonstrated

negative impacts to the skeletal development through the flavors' chemicals effect on gene behavior.^{9,13} While the effects of ENDS flavors on the skin is still mostly unknown, one study found that skin exposure to e-liquid flavors such as balsamic lead to signs of tissue damage.^{9,14} While research is still unfolding, early signs indicate flavoring chemicals commonly used in ENDS have high and widespread impact on human cell function and health.

Device types and e-liquid composition

The type of ENDS device being used and its power output can all lead to differences in how ENDS e-liquids thermally degrade into toxic compounds.¹⁵ For example, dry puffs, or vape puffs when the e-liquid has run out, leads to exposure to toxic compounds called aldehydes.¹⁶ Specific aldehydes such as formaldehyde and acetaldehyde have been classified as a human carcinogen and probable human carcinogen respectively by the International Agency for Cancer Research.¹⁵ The taste of a dry puff is caustic, and ENDS users naturally avoid dry puffs for this reason. However, accidental dry puffs do happen. The type, power, or design of the ENDS device can affect the likelihood and intensity of dry puffs. The following sections describe the ways that the ENDS device specifics, such as construction and power intensity, effect the likelihood and intensity of dry puffs, which increase ENDS toxicity in turn.

ENDS devices can be sorted into two main categories depending on where the coil is found on the device: top coil, higher powered devices, which are more likely to induce a dry puff, and bottom coil, cotton wicked pod-based devices. Each device is associated with negative health consequences. Top coil devices tend to emit more toxins compared to pod-based devices that appear to emit substantially lower amounts of carbonyls.^{17,18} Carbonyls are chemical compounds that also include toxic chemical compounds such as aldehydes.^{16,17} Carbonyls emissions increase the risk of mortality and morbidity when using ENDS devices due to the emitted carbonyls being toxic and/or carcinogenic.¹⁷ While producing less carbonyls, pod-based devices tend to deliver more nicotine, the most addictive component of ENDS.¹⁸

In addition to coil placement, coil resistance impacts the level of carbonyls produced.¹⁹ Coil resistance describes how easily the electricity moves through and powers the ENDS coils, and can be categorized as either high resistance (high ohm) or low resistance (low ohm).¹⁹ Adolescents often seek a combination of low resistance ENDS coils and high wattage batteries to create thick clouds of vapor that leads to strong sensations and the ability to perform vapor tricks. However, such devices are linked to higher levels of carbonyls, which in turn are associated with rapid alterations

of gene expression in human epithelial cells. In addition, flavorings may thermally degrade differently with low resistance coils, increasing toxicity.²⁰

Aside from device characteristics, composition of the e-liquid aside from flavoring chemicals can influence toxicity. For example, higher concentrations of propylene glycol, the main e-liquid additive used to create vapor, have been also associated with higher levels of carbonyls that are associated with the risks described above.¹⁸

Usage behavior

Beyond device power and type, vape puff style and frequency of ENDS use may also impact a users' exposure to toxic chemicals. Longer puff durations by users have been linked to higher amounts of carbonyls and carbon monoxide.¹⁸ Dripping is a method of vaping where ENDS users drip the refillable ENDS e-liquid directly onto the heating coil, in attempts to create a thicker puff.¹⁷ This method of vaping causes the coil to burn much hotter, increasing the risk of toxicity and making accidental dry puffs and potential exposure to carcinogens more likely to occur.²¹⁻²³

Studies have shown that ENDS users who use ENDS e-liquids/devices with lower nicotine content tend to compensate by using their ENDS devices more frequently and with higher wattage compared to higher nicotine content users. These usage behaviors result in exposing lower nicotine users to higher rates of toxins, including nicotine, over time.^{24,25} While ENDS users with lower nicotine e-liquids/devices may be attempting to decrease their exposure to nicotine, it is important to limit usage frequency in tandem because more puffs equate to more toxic exposure.

Discussion

As we have explored, the toxicity of ENDS use relates to a variety of factors including the flavor, the type of ENDS device used, the device's power output settings, the composition of the ENDS e-liquids, and ENDS users' personal vaping behaviors. By informing current ENDS users about the risks associated with these factors, we may be able to help deter the most concerning types of toxicant exposure while simultaneously reminding ENDS users that no ENDS product or usage is safe.

More nuanced understanding of ENDS behaviors and the impacts of those behaviors paves the way for more specific research questions, regulatory statutes, and prevention messaging that targets the most dangerous

aspects of the addicting nature of ENDS products. Informative, trustworthy platforms such as UNC's flavor database allows health and public health professionals to gain that nuanced understanding needed to promote the safest ENDS options while warning against the most dangerous options. While not using any ENDS product is the only truly safe option, any potential increases in mindfulness about toxicant exposure among current health and public health professionals may be beneficial towards curbing the use of, or damage caused by ENDS products for current and future users.

References

- ¹ Walley, S. C., Wilson, K. M., Winickoff, J. P., & Groner, J. (2019). A Public Health Crisis: Electronic Cigarettes, Vape, and JUUL. *Pediatrics*, 143(6). <https://doi.org/10.1542/peds.2018-2741>
- ² Park-Lee, E., Jamal, A., Cowan, H., Sawdey, M. D., Cooper, M. R., Birdsey, J., West, A., & Cullen, K. A. (2024). Notes from the Field: E-Cigarette and Nicotine Pouch Use Among Middle and High School Students — United States, 2024. *MMWR. Morbidity and Mortality Weekly Report*, 73(35), 774–778. <https://doi.org/10.15585/mmwr.mm7335a3>
- ³ Chaffee, B. W., Couch, E. T., Wilkinson, M. L., Donaldson, C. D., Cheng, N. F., Ameli, N., Zhang, X., & Gansky, S. A. (2023). Flavors increase adolescents' willingness to try nicotine and cannabis vape products. *Drug and Alcohol Dependence*, 246, 109834. <https://doi.org/10.1016/j.drugalcdep.2023.109834>
- ⁴ Sidhu, N. K., Lechner, W. V., Cwalina, S. N., Whitted, L., Smiley, S. L., Barrington-Trimis, J. L., Cho, J., Wagener, T. L., Leventhal, A. M., & Tackett, A. P. (2022). Adolescent and Young Adult Response to Hypothetical E-Liquid Flavor Restrictions. *Journal of Studies on Alcohol and Drugs*. <https://doi.org/10.15288/jsad.21-00466>
- ⁵ Leventhal, A. M., Goldenson, N. I., Cho, J., Kirkpatrick, M. G., McConnell, R. S., Stone, M. D., Pang, R. D., Audrain-McGovern, J., & Barrington-Trimis, J. L. (2019). Flavored E-cigarette Use and Progression of Vaping in Adolescents. *Pediatrics*, 144(5). <https://doi.org/10.1542/peds.2019-0789>
- ⁶ Landry, R. L., Groom, A. L., Vu, T.-H. T., Stokes, A. C., Berry, K. M., Kesh, A., Hart, J. L., Walker, K. L., Giachello, A. L., Sears, C. G., McGlasson, K. L., Tompkins, L. K., Mattingly, D. T., Robertson, R. M., & Payne, T. J. (2019). The role of flavors in vaping initiation and satisfaction among U.S. adults. *Addictive Behaviors*, 99, 106077. <https://doi.org/10.1016/j.addbeh.2019.106077>
- ⁷ Notley, C., Gentry, S., Cox, S., Dockrell, M., Havill, M., Attwood, A. S., Smith, M., & Munafò, M. R. (2022). Youth use of e-liquid flavours—a systematic review exploring patterns of use of e-liquid flavours and associations with continued vaping, tobacco smoking uptake or cessation. *Addiction*, 117(5), 1258–1272. <https://doi.org/10.1111/add.15723>
- ⁸ Raloff, J. (2015). The Dangers of Vaping: Teens are falling for flavored e-cigs, but the vapors they inhale may be toxic. *Science News*, 188(1), 18–21. <https://doi.org/10.1002/scin.2015.188001019>
- ⁹ Stefaniak, A. B., LeBouf, R. F., Ranpara, A. C., & Leonard, S. S. (2021). Toxicology of flavoring- and cannabis-containing e-liquids used in electronic delivery systems. *Pharmacology & Therapeutics*, 224, 107838. <https://doi.org/10.1016/j.pharmthera.2021.107838>
- ¹⁰ Sassano, M. F., Davis, E. S., Keating, J. E., Zorn, B. T., Kochar, T. K., Wolfgang, M. C., Glish, G. L., & Tarran, R. (2018). Evaluation of e-liquid toxicity using an open-source high-throughput screening assay. *PLOS Biology*, 16(3), e2003904. <https://doi.org/10.1371/journal.pbio.2003904>
- ¹¹ Bahl, V., Lin, S., Xu, N., Davis, B., Wang, Y., & Talbot, P. (2012). Comparison of electronic cigarette refill fluid cytotoxicity using embryonic and adult models. *Reproductive Toxicology*, 34(4), 529–537. <https://doi.org/10.1016/j.reprotox.2012.08.001>
- ¹² Farsalinos, K., Romagna, G., Alliffranchini, E., Ripamonti, E., Bocchietto, E., Todeschi, S., Tsiapras, D., Kyrzopoulos, S., & Voudris, V. (2013). Comparison of the Cytotoxic Potential of Cigarette Smoke and Electronic Cigarette Vapour Extract on Cultured Myocardial Cells. *International Journal of Environmental Research and Public Health*, 10(10), 5146–5162. <https://doi.org/10.3390/ijerph10105146>
- ¹³ Otero, C. E., Noecker, J. A., Brown, M. M., Wavreil, F. D. M., Harvey, W. A., Mitchell, K. A., & Heggland, S. J. (2019). Electronic cigarette liquid exposure induces flavor-dependent osteotoxicity and increases expression of a key bone marker, collagen type I. *Journal of Applied Toxicology*, 39(6), 888–898. <https://doi.org/10.1002/jat.3777>
- ¹⁴ Cervellati, F., Muresan, X., Sticozzi, C., Gambari, R., Montagner, G., Forman, H., Torricelli, C., Maioli, E., & Valacchi, G. (2014). Comparative effects between electronic and cigarette smoke in human keratinocytes and epithelial lung cells. <https://doi.org/10.1016/j.tiv.2014.04.012>

- ¹⁵ Gillman, I. G., Pennington, A. S. C., Humphries, K. E., & Oldham, M. J. (2020). Determining the impact of flavored e-liquids on aldehyde production during Vaping. *Regulatory Toxicology and Pharmacology*, 112, 104588. <https://doi.org/10.1016/j.yrtph.2020.104588>
- ¹⁶ Farsalinos, K. E., Voudris, V., & Poulas, K. (2015). E-cigarettes generate high levels of aldehydes only in ‘dry puff’ conditions. *Addiction*, 110(8), 1352–1356. <https://doi.org/10.1111/add.12942>
- ¹⁷ Farsalinos, K. E., & Gillman, G. (2018). Carbonyl Emissions in E-cigarette Aerosol: A Systematic Review and Methodological Considerations. *Frontiers in Physiology*, 8. <https://doi.org/10.3389/fphys.2017.01119>
- ¹⁸ Son, Y., Bhattarai, C., Samburova, V., & Khlystov, A. (2020). Carbonyls and Carbon Monoxide Emissions from Electronic Cigarettes Affected by Device Type and Use Patterns. *International Journal of Environmental Research and Public Health*, 17(8), 2767. <https://doi.org/10.3390/ijerph17082767>
- ¹⁹ Cirillo, S., Urena, J. F., Lambert, J. D., Vivarelli, F., Canistro, D., Paolini, M., Cardenia, V., Rodriguez-Estrada, M. T., Richie, J. P., & Elias, R. J. (2019). Impact of electronic cigarette heating coil resistance on the production of reactive carbonyls, reactive oxygen species and induction of cytotoxicity in human lung cancer cells in vitro. *Regulatory Toxicology and Pharmacology*, 109, 104500. <https://doi.org/10.1016/j.yrtph.2019.104500>
- ²⁰ Noël, A., Hossain, E., Perveen, Z., Zaman, H., & Penn, A. L. (2020). Sub-ohm vaping increases the levels of carbonyls, is cytotoxic, and alters gene expression in human bronchial epithelial cells exposed at the air–liquid interface. *Respiratory Research*, 21(1), 305. <https://doi.org/10.1186/s12931-020-01571-1>
- ²¹ Talih, S., Balhas, Z., Salman, R., Karaoghlanian, N., & Shihadeh, A. (2016). “Direct Dripping”: A High-Temperature, High-Formaldehyde Emission Electronic Cigarette Use Method. *Nicotine & Tobacco Research*, 18(4), 453–459. <https://doi.org/10.1093/ntr/ntv080>
- ²² Kong, G., Morean, M. E., Bold, K. W., Wu, R., Bhatti, H., Simon, P., & Krishnan-Sarin, S. (2020). Dripping and vape tricks: Alternative e-cigarette use behaviors among adolescents. *Addictive Behaviors*, 107, 106394. <https://doi.org/10.1016/j.addbeh.2020.106394>
- ²³ Lerner, C. A., Sundar, I. K., Yao, H., Gerloff, J., Ossip, D. J., McIntosh, S., Robinson, R., & Rahman, I. (2015). Vapors Produced by Electronic Cigarettes and E-Juices with Flavorings Induce Toxicity, Oxidative Stress, and Inflammatory Response in Lung Epithelial Cells and in Mouse Lung. *PLOS ONE*, 10(2), e0116732. <https://doi.org/10.1371/journal.pone.0116732>
- ²⁴ Smets, J., Baeyens, F., Chaumont, M., Adriaens, K., & Van Gucht, D. (2019). When Less is More: Vaping Low-Nicotine vs. High-Nicotine E-Liquid is Compensated by Increased Wattage and Higher Liquid Consumption. *International Journal of Environmental Research and Public Health*, 16(5), 723. <https://doi.org/10.3390/ijerph16050723>
- ²⁵ Kośmider, L., Kimber, C. F., Kurek, J., Corcoran, O., & Dawkins, L. E. (2018). Compensatory Puffing With Lower Nicotine Concentration E-liquids Increases Carbonyl Exposure in E-cigarette Aerosols. *Nicotine & Tobacco Research*, 20(8), 998–1003. <https://doi.org/10.1093/ntr/ntx162>



KDH RESEARCH &
COMMUNICATION

145 15th Street NE,
Suite 831
Atlanta, GA 30309

www.kdhrc.com
publicaffairs@kdhrc.com



TABATHA REYNOLDS
is a Research Assistant at KDH Research & Communication.



MORGAN L. FLEMING
is an Account Associate at KDH Research & Communication.



KRISTEN D. HOLTZ
is the Founder and President at KDH Research & Communication.



ANDREW SIMKUS
was a Research Analyst at KDH Research & Communication.

KDH RESEARCH & COMMUNICATION is a non-partisan, public health, research and communications agency. The goal of the “Informing Public Health” brief series is to disseminate innovative, objective, and timely information to solve public health and other social issues. KDHRC actively contributes to a future when all people can find, understand, and act on information to safeguard the health of themselves, their families, and their communities.

The views expressed here are those of the authors and do not necessarily reflect those of KDH Research & Communication, its board, or funders. Permission is granted for reproduction of this document with attribution to KDH Research & Communication.
