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Nicotine isn't the only hazard to be found in e-cigarettes



Flashy flavors have helped e-cigarettes, designed to vaporize a nicotine solution, grow into an industry with an estimated \$3.5 billion in annual U.S. sales. (Getty Images/iStockphoto)

By **Sara Shipley Hiles**

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Wander into a vape shop in the mall or online, and you can find a smorgasbord of flavors: cotton candy, vanilla custard, even Unicorn Milk or Katy Perry's Cherry.

Flashy flavors have helped e-cigarettes, designed to vaporize a nicotine solution, grow into an industry with an estimated \$3.5 billion in annual U.S. sales. Less than a decade after the battery-powered devices were introduced in the United States, an estimated 10 percent of American adults and 13 percent of high school students "vape," according to recent surveys. In Connecticut, 28 percent of the 3,847 teens in a new Yale School of Medicine survey said they use e-cigarettes and almost 19 percent said they have used e-cigarettes to vaporize hash oil, the resin from marijuana plants.

While many users perceive e-cigs as safer than traditional cigarettes, some of the flavorings that make them so enticing may have their own toxic consequences.

A growing number of studies find that some of the liquids used in e-cigarettes contain flavorings whose inhalation has been associated with lung problems, ranging from irritation to a rare but serious lung disease. For example, diacetyl, a butter-flavored chemical, has been linked to dozens of cases of bronchiolitis obliterans, a life-threatening obstructive lung disease.

E-cigarettes are unregulated, but that may change. The Food and Drug Administration is considering a rule to extend its cigarette-regulating authority to e-cig devices. More than 7,700 e-cig flavors are being sold under more than 450 brands, with no labeling or testing requirements.

Jessica Barrington-Trimis, an epidemiologist at the University of Southern California who studies tobacco's health effects, said that flavorings are particularly worrisome because they "have a history of being known respiratory toxins." Barrington-Trimis, who spoke at an FDA panel looking into e-cigs in March, said that because the devices produce an ultrafine aerosol that goes deep into the lungs, their flavorings "are a natural target" for further investigation. "We need to research this more to understand what chemicals are in these things and what these chemicals may be doing to the lungs of the user," she said.

One of the first people to highlight e-cig flavoring concerns was a physician who uses e-cigarettes himself. Konstantinos Farsalinos, a researcher at the Onassis Cardiac Surgery Center in Athens, tested 159 sweet e-cig liquids, such as toffee, chocolate and caramel flavorings, and found that 74

percent of the samples contained diacetyl the chemical associated with bronchiolitis obliterans or a chemically similar substitute, acetyl propionyl. Among the ones that tested positive, nearly half would expose users to levels that exceed recommended workplace limits for breathing the two chemicals, his 2014 study found.

Diacetyl is found naturally in butter, beer and other foods, and it is added to baked goods, candy and snack foods to impart a buttery or creamy taste. Although it is considered safe to eat, breathing it may not be.

In 2002, the National Institute for Occupational Safety and Health, reported that eight workers in a Missouri microwave popcorn plant had developed bronchiolitis obliterans after breathing diacetyl on the job. Half of them needed lung transplants, and five have died of respiratory causes, Kathleen Kreiss, a NIOSH expert in occupational respiratory disease, said in an e-mail. Dozens of cases of bronchiolitis obliterans known in some circles as "popcorn lung" have since been found at other food and flavorings plants.

Farsalinos, who has accepted some funding from the vaping industry, said he believes that e-cigarettes are safer than tobacco cigarettes. Acetyl propionyl and diacetyl are also naturally present in cigarette smoke, Farsalinos said, at levels higher than those he found in e-cigs.

Still, Farsalinos said, "these specific chemicals should be completely removed" from e-cigs. "Why? Because it's a 100 percent avoidable risk."

Some manufacturers avoid diacetyl. For example, Nicoventures, a division of British American Tobacco, does not use diacetyl in its nine e-cigarette flavorings, Sandra Costigan, a company toxicologist said in an e-mail.

The American Vaping Association, an advocacy group for the industry, believes that diacetyl and acetyl propionyl should not be added to e-cigarette flavorings, association president Gregory Conley said.

In 2012 the Flavor and Extract Manufacturers Association, which represents the U.S. flavorings industry, issued a list of 27 "high-priority" flavoring chemicals that, while safe in food, may pose a risk of respiratory injury and for which it recommends reducing inhalation exposure. The list includes chemicals found in e-cig liquids, such as diacetyl and benzaldehyde, which is used in almond and cherry flavors.

"When we saw flavors were being used in e-cigarettes, we wanted to put the word out right away that it's a possibility that flavors being inhaled through an e-cigarette could also be harmful," John Hallagan, the association's senior adviser and general counsel, said in an interview.

"Flavors are not made to be inhaled," he said. "In the absence of safety information, what we're saying is we really need to pay attention to this from a safety perspective."

A 2013 study found that several cinnamon-flavored e-cig liquids contained a chemical, cinnamaldehyde, that researchers said was highly toxic to human cells in lab tests. A co-author of that study, Prue Talbot, a professor of cell biology at the University of California at Riverside, said the results corroborated online reports by e-cig users of problems related to cinnamon flavors, including swollen throats and mouth sores.

Another study examined 30 e-cigarette liquids and found that many flavors including a cotton candy, a bubble gum and a French vanilla contained aldehydes, a class of chemicals that can cause respiratory irritation, airway constriction and other effects. The 2015 paper described two flavors, a dark chocolate and a wild cherry, that would expose vapers to more than twice the recommended workplace safety limit for the aldehydes vanillin and benzaldehyde. Different brands and even different batches of e-cig liquids can contain different amounts of flavoring chemicals.

"There's no going by the flavor names as to say what's in it," said James Pankow, a chemistry and engineering professor at Oregon's Portland State University, one of the co-authors of the study.

The FDA's proposed rule on e-cigarettes would restrict sales to young people and prohibit unsubstantiated health claims. If e-cigs are brought under the FDA's regulatory authority, the agency would have to go through additional rulemaking to set standards on flavorings, FDA spokesman Michael Felberbaum said in an e-mail. The FDA prohibits adding flavorings, other than menthol, in traditional tobacco cigarettes.

Some e-cig companies are doing their own research on flavorings. Nicoventures, the British company, recently proposed a screening process to avoid liquid flavorings that are classified as respiratory allergens, carcinogenic, mutagenic or toxic to reproduction, among other criteria. The company has rejected diacetyl and acetaldehyde as flavorings and avoided developing a flavor that uses cocoa shell extract because of concerns that it might be a respiratory sensitizer, Costigan said in an e-mail. "We wanted to demonstrate that they 1 / 8 flavorings 3 / 8 could be used responsibly even when there are limitations in data," she said.

The company says that flavorings benefit public health by helping smokers transition away from combustible tobacco. However, the science isn't settled yet on whether e-cigs help people quit tobacco cigarettes or get them hooked. A recent study, for instance, found that ninth-graders who used e-cigs were about 2 1 / 2 times as likely as their peers to start smoking traditional cigarettes.

Conley, of the American Vaping Association, says e-cigarettes flavored with watermelon helped him stop smoking five years ago, and he will fight to keep flavorings on the market.

"There's a reason why the gum, patch and lozenge have such pitiful success rates," he said, referring to some common approaches to smoking cessation. "We have to avoid medicinalizing these products 1 / 8e-cigarettes 3 / 8 and making them bland and boring," he said.

Even if e-cigarette users are exposed to diacetyl, he asserted, the risk of harm is only a fraction of that from smoking tobacco, which causes 480,000 deaths per year in the United States, according to federal data.

Talbot, who conducted the cinnamon flavoring study, said the problem is that people are now "inhaling a product into their lungs, and we don't currently know what the consequences or long-term health effects of that will be." While it is true, she said, that e-cigs contain fewer chemicals than the brew of 7,000-plus that are in traditional cigarette smoke, "it would only take one bad one."

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