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E-cigarettes stress lungs, impair protein function

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Credit: AI-generated image (disclaimer)

E-cigarettes stress and inflame the lungs of rats, compromising important regulatory proteins through exposure, according to research recently published in the journal Redox Biology. The findings, made possible by a biomolecular technique developed by researchers at the U.S. Department of Energy's Pacific Northwest National Laboratory,

reveal that vaping induces subtle structural changes in proteins, marking the first time researchers have measured such damage. The results suggest that common compounds in the electronic alternative to conventional cigarettes are not without their own harms.

After exposing rats to e-cigarette vapor for three one-hour sessions for three days, researchers discovered signs of oxidative stress: an imbalance between the production of free radicals and the body's ability to mitigate their harmful effects. Free radicals are molecules with unpaired electrons, an inevitable byproduct of the body's many biochemical processes and, when in disproportionately large supply, a contributor to disease and dysfunction.

Previous research has shown that vaping can stress tissues, but the mechanisms and details behind that stress have remained murky. The new technique, said biochemist Charles Ansong, a coauthor of the study who led the research while at PNNL, identifies modifications made to proteins that shed light on how e-cigarettes lead to dysfunction.

"There have been a number of studies on this, and they generally have gross measures that say, 'OK, there's some oxidative stress going on here, but we don't really know what's going on,'" said Ansong, who has since become a program director in the Biochemistry and Bio-related Chemistry Branch of the National Institute of General Medical Sciences/National Institutes of Health. "But this technique identifies which proteins are being modified, which sites are modified, and it suggests how likely they are to impact protein function and molecular pathways. It gives us a lot of insight into the mechanism behind the injurious effects of e-cigarettes."

Bioanalytical chemist and coauthor Wei-Jun Qian, who developed and applied the technique to characterize protein changes at PNNL, said the results indicate that e-cigarettes certainly compromise cellular function,

though exactly how bad the damage is remains an area of future investigation.

Peering through the smoke

At the University of Rochester Medical Center in Rochester, N.Y., where the animal portion of this research was performed, rats inhaled a mixture of three compounds common in most e-cigarette liquids: propylene glycol (a synthetic liquid often found in cosmetics), vegetable glycerin and nicotine.

"I don't think many people think about how thick or viscous these liquids are," said Matthew McGraw, a physician scientist in pediatric pulmonary medicine at the University of Rochester Medical Center and coauthor of the study. "Vegetable glycerin is used in cooking oil. To heat that cooking oil and inhale it into your lungs—when you think about it, even just visually, that's quite a thing to do."

Looking at the lung tissue beneath the microscope revealed few changes after exposure. The researchers saw no significant shift in the number of white blood cells in lung fluid, nor did they observe any glaring differences in lung structure.

But Qian's protein analysis revealed thousands of oxidative changes, pinpointing subtle, reversible modifications that had previously evaded detection. Exposure altered a range of protein types, mainly those that regulate quality control in other proteins.

"Whatever biomolecular pathway that protein is a part of may be impaired, and that can lead to tissue dysfunction and disease" said Ansong, who compared abnormal proteins to biomolecular trash that can snowball into larger problems when regulatory pathways are compromised, leaving the body unable to keep its systems clean.

E-cigarette exposure modified multiple proteins associated with the body's inflammatory response, suggesting that frequent e-cigarette use could push the lungs into a state of chronic stress. Some of the detected changes promote clotting and systemic inflammation and were akin to those found in the lungs of traditional smokers, said McGraw, potentially implicating e-cigarettes as drivers of an inflammatory state. The greatest change in these pathways occurred when rats inhaled propylene glycol and vegetable glycerin alone; the addition of nicotine did not significantly change the lung's stress response.

The biochemical consequences of vaping

These protein alterations mark just one type of observed change, said Qian, leaving other potential alterations that could remain undetected.

"Oxidation is just one type of modification," said Qian. "It's not the only type. And we're only just beginning to understand this. I believe many other types of protein function can be monitored, too."

The group also plans to systematically explore other e-cigarette additives, like popular flavoring compounds, as well as varying doses and exposure levels. While the results stand as evidence of oxidative stress, the exact effect on human users is uncertain.

"Others have said that vegetable glycerin and propylene glycol are relatively safe," said McGraw. "While our results do not fully discredit that comment, we can say repeated inhalation exposure to e-cigarettes causes significant oxidative stress within the lung. This stress is an early sign that there could be potentially harmful, long-term changes if posed repetitively."

The findings arrived after the city of San Francisco enacted a ban on e-cigarettes in 2019, with the law taking effect in 2020. The District of

Columbia, Puerto Rico and 15 states passed laws in 2020 that restrict indoor smoking, including vapor produced by e-cigarettes, according to the Centers for Disease Control and Prevention.

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More information: Juan Wang et al, Protein thiol oxidation in the rat lung following e-cigarette exposure, *Redox Biology* (2020). DOI: 10.1016/j.redox.2020.101758

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