1. No.

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2. Title

   Elucidation of the Mechanism and Searching Protective Agents for Disruption of Epidermal Barrier Induced by Both Cigarette and Electrically-Heated Tobacco-Derived Thirdhand Smoke Compounds

3. Period

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4. Summary

Thirdhand smoke (THS) refers to a form of indirect passive smoking where nicotine and other tobacco constituents absorb onto fibers and surfaces, subsequently reacting with atmospheric compounds to form highly reactive nitrosamines that are then re-emitted into the environment. While this phenomenon is well-documented, its impact on skin barrier function remains largely unknown. In this study, we analyzed the effects of nicotine-derived THS compounds on the expression of CLDN1－a factor essential for the epidermal barrier－and their subsequent impact on intercellular barrier function.

The treatment of human epidermal-derived HaCaT cells with the nicotine-derived THS compounds 4-(methylnitrosamino)-4-(3-pyridyl) butanal (NNA) and N′-nitrosonornicotine (NNN) resulted in a significant reduction in CLDN1 protein expression through protein destabilization, leading to a decline in intercellular barrier function. Furthermore, we conducted a screening of food-derived compounds to identify those offering protective effects against NNA-induced reduction of CLDN1 levels. As a result, several candidate compounds were identified, including shikimic acid derivatives and flavonoids.This study demonstrates that the THS compound NNA potently reduces CLDN1 protein expression. Given that flavonoids proved effective against skin barrier impairment caused by nicotine-derived THS compounds, these findings suggest a promising future for the development of preventive agents and supplements to combat THS-induced degradation of epidermal barrier function.