

Chondrocyte Viability and Function is Impaired by E-Cigarette Liquid Flavor Additives

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INTRODUCTION: With limited options for restoring lost tissue integrity, cartilage degeneration remains a major clinical challenge in orthopedic and respiratory health contexts. Environmental factors such as inhaled chemical agents may pose previously unrecognized risks to cartilage tissue. E-cigarettes, increasingly used among adolescents and young adults, deliver high concentrations of aerosolized chemical flavor additives directly to the cartilaginous structures of the airway. This study evaluated the cytotoxic and catabolic effects of common e-juice on chondrocyte health using the ATDC5 cell line as a chondrocyte model.

METHODS: ATDC5 cells were exposed to increasing concentrations of nicotine-free e-cigarette liquid flavor additives (ELFAs), followed by assessment of cell viability, extracellular matrix composition, and gene expression profiling.

RESULTS: Significant cytotoxicity was observed in Menthol- and Cinnamon-treated groups, with near-complete loss of cell viability at concentrations $\geq 4\%$ v/v. These additives also induced marked dysregulation of chondrocyte matrix metabolism and increased expression of inflammatory markers, notably displaying significant upregulation of MMP-13 and COX-2, two key proteins involved in cartilage matrix catabolism and inflammation, respectively. Additional shifts towards matrix catabolism were also induced by Tobacco and Flavorless additives.

DISCUSSION: These findings suggest that exposure to specific chemical flavorants present in common e-cigarette products acutely impairs chondrocyte viability and function, potentially inducing airway cartilage degradation. Avid e-cigarette use may also cause inflammation within these cartilage tissues, thereby contributing to structural weakening of the airway and long-term respiratory complications. While further *in vivo* studies are required to validate these effects, our results raise important concerns about the potential for e-cigarette flavorants to disrupt cartilage homeostasis and highlight the need for greater regulatory attention to inhaled chemical additives.

SIGNIFICANCE/CLINICAL RELEVANCE: (1-2 sentences): While further *in vivo* studies are required to validate these effects, our results raise concerns about the potential for nicotine-free e-cigarette flavorants to disrupt cartilage homeostasis. Given the widespread popularity of flavored vaping agents among youth in the United States, the present study highlights the need for greater regulatory attention to inhaled chemical additives. Additionally, recognition of environmental cartilage irritants may open new avenues for early intervention and prevention strategies.