

## **Chemical characterization and toxicological effects of emissions generated from new tobacco- and smoking-related products: comparison with conventional cigarette smoke**

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Cigarette smoke exposure is responsible for almost 30% of cancer deaths and the cause of nearly 90% of lung cancer. Smoking cessation is, at present, the only effective way to slow down the progression of cancer. Electronic cigarettes (e-cig) and more recently heated tobacco products (HTP) provide an alternative for smokers as they are generally perceived to be less harmful than conventional cigarettes. These new devices can quickly gain popularity, even before there is sufficient scientific evidence to determine their effects on the user.

This work was performed (i) to characterize the chemical composition (carbonyl compounds and polycyclic aromatic hydrocarbons) of these tobacco-related product emissions, (ii) to investigate their potential toxicity in human bronchial epithelial cells (BEAS-2B) cultured at the air-liquid interface, and (iii) to compare their emissions and their respective toxicities to those of cigarette smoke. Aerosols were generated by a smoking machine from different models of e-cig (low or high power) HTP or conventional cigarette (3R4F). The cytotoxicity of these aerosols was evaluated by measuring intracellular ATP levels thanks to CellTiter-Glo® Luminescent Cell Viability Assay (Promega). The numbers and concentrations of carbonyl compounds and PAHs emitted by HTP and e-cig are lower than with cigarette smoke. At the cellular level, HTP exposures induce a cytotoxicity higher than the different e-cig models tested, but lower than conventional cigarettes. Significant increases in IL-6, IL-8, IFN $\gamma$  and GM-CSF secretion are observed in BEAS-2B cells after HTP or 3R4F exposures, while only IL-6 is increased for e-cig.

Overall, these data evidence lower emissions of harmful chemicals and lesser *in vitro* toxicity of HTP compared to cigarette smoke. By contrast, HTP generate higher levels of hazardous compounds and result in greater cytotoxicity than e-cig. Moreover, effects observed with e-cig are more marked when they are used at high rather than low power. These first conclusions shall be further comforted by additional experiments conducted in animal models after long-term exposures.

The authors declare that they have no conflict of interest with tobacco, HTP or e-cig industries. This work benefited from grants from the INCa (Contract n°INCa\_11505) and from the INCa and IResP (Contract n°INCa\_13648).