

## **IN VITRO STUDY OF APOPTOTIC AND PROINFLAMMATORY EFFECT OF COMBUSTION-GENERATED ORGANIC NANOPARTICLES**

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Two decades of nanotoxicology research has shown that the interactions between for combustion generated nanoparticles (NPs) and cells, animals, humans and the environment are remarkably complex; complexity arises from NPs' ability to bind and interact with biological matter and change their surface characteristics.

There have been numerous studies demonstrating that NPs have biological effects on cardiopulmonary, neurological, gastrointestinal and skin system. Compared to larger particles, NPs have a higher deposition rate in the peripheral lung, they can cross the pulmonary epithelium and reach the interstitium, and may thus be systemically distributed in the bloodstream, raising the possibility to render larger degree of inflammation NPs have an enhanced capacity to produce reactive oxygen species (ROS) and, consequently, have a widespread toxicity since ROS generation by particles can exert protein, lipid, and membrane damage

Flame-generated particles provides interesting model nanoparticles composed mainly of organic carbon that simulate fresh combustion emissions near roadways or combustion sources. NPs with controlled chemical and morphological properties can be produced by controlling flame operating conditions and used to test possible toxicological mechanisms responsible for the observed health effects related to particulate matter.

In this study, flame generated organic carbon NPs have been used to investigate their possible effect on endothelial cell (EC) and keratinocytes (HaCaT) growth and production of proinflammatory lipid mediators. Results indicate a dose and time-dependent reduction in cell viability following incubation of EC and HaCaT with NPs for 24 and 48 hours ( $p < 0.05$ ). Fluorescence-activated cell sorting (FACS) revealed that cells treated with NPs showed a cell proliferation index significantly lower than that of control cells and an increased apoptotic cell death ( $p < 0.05$ ). The annexin assay confirmed the increased apoptotic cell death. Moreover, NPs also induced a time-dependent increase of proinflammatory lysophospholipid production with a peak within 2 min ( $p < 0.05$ ). These results, establishing that NPs induce EC proinflammatory lysophospholipid production and apoptotic cell death, provide the first evidence of the detrimental effect of combustion generated NPs on health.