

Cytotoxicity of water-soluble components of PM_{2.5} on human lung cells: oxidative stress, inflammation, immune defense, and viral infection

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PM_{2.5} can lead to various toxicities, and different chemical compositions result in different biological outcomes. Investigating the toxicity and identifying toxic components would be helpful for protecting public health more effectively. However, the PM_{2.5}-induced cellular toxicity remains inadequately understood. In this study, PM_{2.5} samples were collected in urban area of Guangzhou. The chemical characteristics and biological effects of water-soluble matters (WSM) were investigated by chemical analysis (soluble ions, metals, organic matters) and *in vitro* toxicity assays (reactive oxygen species (ROS) production, inflammatory and antiviral cytokines mRNA expression, and respiratory viral infection) of human alveolar epithelial cells (A549). The results demonstrated a significant increase in cellular ROS production, interleukin-8 (IL-8) expression and virus infection level in A549 after WSM exposure, with average fold increases of 2.9, 1.4, and 2.5, respectively. Additionally, WSM exposure downregulated the expression levels of the antiviral defense genes, including interferon beta (IFN- β), and surfactant protein D (SP-D), with notable reduction of 48% and 34%, respectively. An explainable machine learning was used to reveal the key components affecting these toxicities. The cellular ROS production positively correlated with Cu, Hg, and polycyclic aromatic hydrocarbons with high double bond equivalent ($\text{DBE} \geq 10$). The IL-8 levels were associated with Mn, Fe, and nitroaromatic compounds (DBE of 6–8, $2.5 \leq \text{aromaticity equivalent (Xc)} \leq 2.714$). While, the virus infection levels were positively related to Al, Cr, and protein like compounds with higher degrees of oxidation, especially CHON_2 species ($\text{DBE} \leq 4$, $0.9 \leq \text{OC} \leq 1.0$). Conversely, the IFN- β and SP-D levels were negatively correlated with Amino-sugar like and sulfur-containing compounds ($\text{DBE} \leq 5$, $0.6 \leq \text{OC} \leq 1.1$, $0 < \text{S/C} < 0.15$), respectively. These findings highlight the heterogeneity in the impact of chemical composition on cellular specific responses and provide new insights into the health risk of PM_{2.5} pollution.