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Abstract (in English)

The main objective of this research was to determine the exposure health effects of various types of atmospherically relevant submicron organic aerosol (OA) by using human lung cell lines. Airborne fine particulate matter of aerodynamic diameters < 2.5 μm ($PM_{2.5}$) contributes to poor air quality, climatic change and exhibits adverse health effects upon inhalation. $PM_{2.5}$ exposures trigger lung-associated pathologies, including asthma, allergy, chronic obstructive pulmonary disease (COPD), bronchitis, emphysema, decreased lung function, and increased instances of lung cancer. This research aimed to decipher changes in lung cells at the molecular, cellular, biochemical, and/or genomic levels, which were induced by submicron OA exposures originating from four different atmospheric sources, including from: (*i*) monoterpene-derived secondary organic aerosol (SOA) obtained through the ozonolysis of α-pinene, (*ii*) heterogeneously-aged isoprene-derived particulate 2-methyltetrol sulfates (2-MTSs), which are the most abundant particulate organosulfates (OS) detected in ambient $PM_{2.5}$ and contribute greatly to isoprene SOA, and (*iii*) atmospheric-relevant mono-nitrophenols (NPs), and (*iv*) other key components of biomass burning aerosol (BBA).

Two *in vitro* cell models, BEAS-2B (i.e., immortalized human bronchial epithelial cells) and A549 (i.e., adenocarcinoma human alveolar epithelial cells) were selected in the current thesis projects to determine acute exposure effects. In the first two sections of this thesis, an oxidation flow reactor (OFR) was used to produce SOA from α-pinene ozonolysis, and OS mixtures produced from the heterogeneous hydroxyl radical (•OH)-mediated oxidation of particulate 2-MTSs (equivalent to 0-22 days of atmospheric aging), respectively. The aerosol mixtures were analysed using liquid chromatography interfaced to high-resolution electrospray ionization tandem mass spectrometry (LC/ESI-HR-MS/MS) to detect organic acids and peroxides from α-pinene ozonolysis SOA, and multifunctional OSs from heterogeneously aged particulate 2-MTSs. Furthermore, qualitative chemical analyses of ambient $PM_{2.5}$ and SOA generated from the photooxidation of a series of monocyclic aromatic hydrocarbons in the United States (US) Environmental Protection Agency (EPA) smog chamber was conducted for atmospheric NPs.

The aerosol mixtures of known and characterized OA markers were then exposed to lung cells and assessed for the percentage of cellular proliferation using high throughput assays; subsequent time- and concentration-dependent viability values were used to determine the inhibitory concentration-50 (IC_{50}) of each atmospheric OA system. In addition, functional assays with fluorescent probes were used to detect cellular reactive oxygen species (ROS) and mitochondrial ROS (mtROS) post-exposure; these assays used flow cytometry and confocal microscopy, respectively. Changes in cellular viability were analysed through live/dead staining under a fluorescent microscope, whereas cells death mechanisms were determined through the Annexin V/Propidium Iodide assay using flow cytometry. Real-time quantitative polymerase chain reaction (RT-qPCR) was utilized to evaluate genomic changes that could result from exposures to heterogeneously aged particulate 2MTSs to determine the post-exposure responses via modulation of oxidative stress and inflammatory genes.

In the first part of this thesis, we quantified an increasing concentration response of three well-established α-pinene SOA tracers (pinic, pinonic, and 3-methyl-1,2,3-butanetricarboxylic acids) and a complete mixture of α-pinene ozonolysis SOA in A549 and BEAS-2B cell lines. The atmospheric ozonolysis of α-pinene ($C_{10}H_{16}$), an abundantly emitted monoterpene from terrestrial vegetation, contributes significantly to the global SOA budget; however, its impact on pulmonary pathophysiology remains uncertain. Cellular proliferation, cell viability, and oxidative stress were assessed as toxicological endpoints in this study. The three afore-mentioned tracers contributed ~57% of the α-pinene ozonolysis SOA mass; however, multifunctional hydroperoxides identified in the SOA could have contributed more than these individual SOA tracers to the toxicological changes observed.

The second part of this thesis focused on examining the inhalation toxicity associated with the isoprene-derived aerosol particles in the atmosphere. Isoprene (C_5H_8) is the most abundant reactive hydrocarbon released into Earth's atmosphere from vegetation. Once emitted to the atmosphere and exposed therein to $^{\bullet}OH$ under low-NO_x conditions, and in the presence of inorganic sulfates (generated from human activities), isoprene yields high quantities of gaseous epoxy diols (IEPOX). These reactive intermediates interact with acidic sulfate aerosol to afford a wide variety of low-volatility particle-bound reaction products, such as OSs. One of the most abundant atmospheric OSs is 2-MTSs. 2-MTSs can undergo further chemical changes in the atmosphere, which leads to the formation of photochemically-aged particles of far more complex chemical compositions. The goal of this portion of the thesis was to gain insights into how these changes might contribute to increased oxidative stress and inflammatory responses in BEAS-2B cells.

The third project of this thesis involved toxicological profiling of atmospherically relevant NPs using BEAS-2B and A549 cell lines. NPs are found as trace pollutants in various environmental matrices, including $PM_{2.5}$, agricultural residues, cloud water, rainwater, wildfires, and industrial wastes. First, an equimolar mixture of NPs was exposed to the eukaryotic lipid bilayer membrane to determine the exposure effects on the cell membrane surface. In addition, comparative toxicology of 2-nitrophenol (2NP), 3-nitrophenol (3NP), 4-nitrophenol (4NP), and their equimolar mixture was provided using several ROS, mtROS, cellular viability, and cellular death assays.

The last part of this thesis conducted a detailed toxicological analysis of four important BBA components in the A549 and BEAS-2B cell lines. BB is a major pollution source, particularly in urban, suburban, and rural areas, and was hypothesized to induce increased morbidity and mortality through long-term inhalation. The four BBA components included levoglucosan (LG), 3-nitrosalicylic acid (NS), 4-nitrocatechol (NC), and 4-nitroguaiacol (NG). The exposed cells were analysed for changes in general ROS and mtROS to predict altered biochemical pathways at different exposure concentrations and times. This study was concluded by proposing cellular death mechanisms upon exposure to these chemicals.

The profiling of atmospheric aerosol mixtures and their individual markers from four atmospherically relevant systems provide a comparative toxicology in lung cells. We predict the system with the highest adverse effects following inhalation using the IC_{50} values and the number of atmospherically relevant years required to achieve that effect. This thesis also determines the pathophysiological changes in lungs at the molecular and cellular level after exposure, which varied significantly with the chemical composition and chemical structure of

the markers, as well as time and concentration of exposure. The study further highlights the urgent need to develop regulations and control strategies to mitigate the emission rates of a few emission types due to their potential inhalation toxicity following acute exposure.