Can Laboratory Chambers Be Used to Create Complex Atmospheres for Use in Animal Exposure Studies?

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Science Question

How can smog chambers (or other laboratory devices to simulate sources or ambient air) be operated in a manner whereby biological assays can be exposed to atmospherically-relevant, controlled whole air mixtures to produce relevant health-effects information?

Research Goals

• Establish a set of simple and complex (including realistic source) whole air mixtures to test for relevant biological endpoints.

• Conduct measurements of both sources and photochemically transformed mixtures for evaluating responses in biological systems (e.g., lung-lining fluid, pulmonary cells) and potentially laboratory animals with linkage to cellular events.

• Conduct a comprehensive set of analytical measurements to physically and chemically characterize both the gas- and particle-phase constituents of the whole air mixture.

• Examine the biological response to whole air, the individual gas- and particle-phase components, and where possible individual chemical constituents.

• Characterizing the biological effects of unknown organic compounds in PM utilizing chromatographic separation techniques.

Methods/Approach

The methods and approach for this study are described through the use of several examples -

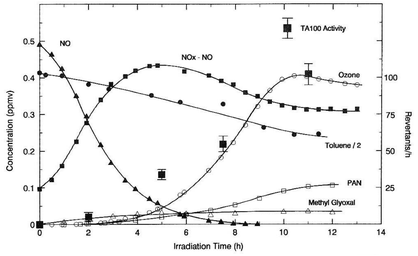
EXAMPLE 1. Past NERL-NHEERL Collaboration (1980s)

Focus of Study: Screen simple and complex air mixtures using in vitro genotoxic endpoints related to cancer.

Background and Description:
● 23 m^3 smog chamber operated in a flow-mode to produce constant air compositions for long period of time.
● Salmonella typhimurium, strains TA100 and TA98 were exposure to the gas and particle phase components of the air mixtures.
● Irradiated mixtures included simple hydrocarbons (toluene, propylene, allyl chloride) and complex sources (wood smoke, automobile exhaust), as well as individual photochemical oxidation products (e.g., PAN, HCHO, CH_3CHO).

Findings:
● Simple non-mutagenic hydrocarbons could be photochemically converted to products that showed strong activity.
● Mutagenic activity was detected in products of both the gas (TA100) and particle phases (TA98).

Mutagenic Activity (TA100) as a Function of the Extent of Photochemical Reaction for the Oxidation of Toluene



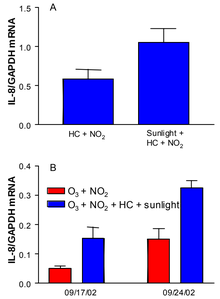
EXAMPLE 2. UNC-EPA Cooperative Agreement

Focus of Study: To determine whether products formed in photochemically transformed air mixtures show inflammatory responses using in-vitro assays.

Background and Description:
● Two 150 m^3 smog chambers operated in a static-mode to produce high volume pollutant mixtures from simulated complex emissions.
● Biological endpoint is enhanced IL-8 mRNA from A549 cells, an alveolor Type II-like cell line.
● Irradiated mixtures included isoprene, 1,3-butadiene, and a 55-component synthetic emissions mixture.

Findings:
● Independent of the presence or absence of O_3, secondary products generated by HC/NO_X reactions contribute to inflammatory responses induced by exposure to urban smog.
● Small structural differences in molecular form (e.g., $-CH_3$ group) were found to lead to toxicity difference.

Secondary Products Formed During Photochemical Transformation of VOCs Enhance IL-8 mRNA Levels in A549 Cells (w/, w/o O_3)



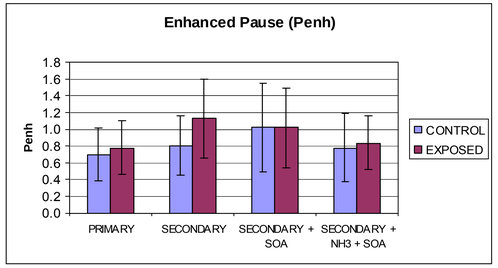
EXAMPLE 3. TERESA STUDY (A Collaboration between EPRI, the Harvard PM Center, the U.S. Department of Energy, and the State of Wisconsin)

Focus of Study: To evaluate the toxicity of secondary coal combustion emissions. To increase an understanding of the sources and components of air pollution responsible for health effects.

Background and Description:
● TERESA – Toxicological Evaluation of Realistic Emissions of Source Aerosols
● 200 L irradiation chamber operated in a dynamic-mode to produce photochemically-modified coal combustion emissions.
● Biological endpoints: pulmonary function, oxidative stress, blood cytology, bronchoalveolar lavage (BAL), pulmonary histopathology.
● Simulations of different atmospheric scenarios – oxidation of primary emissions, neutralization of acidic aerosols, oxidation in presence of hydrocarbons.

Preliminary Findings:
● No evidence of significant pulmonary functional change.
● No evidence of Inflammation or injury in BAL fluid.
● No evidence of in-vivo oxidant responses.

Measurement of Enhanced Pause (Indicator of Airway Restriction)



Results/Conclusions

In prior studies, laboratory chambers have successfully been interfaced with biological assays to produce indicators of activity.

Future Directions

NERL and NHEERL have developed an initiative to couple laboratory chambers to biological systems and test realistic atmospheric mixtures to contemporary bioassays to study effects of respiratory PM under oxidative conditions that better mimic atmospheric influences of ambient PM.

Impact and Outcomes

● Laboratory chambers can provide vital information on potential health outcomes of specified air mixtures.

● Controlled exposures provide a measure of feasibility for determining active agents in observed $PM_{2.5}$ health effects.

● Exposures linking biological effects to controlled air mixtures can provide the basis for a compound-based $PM_{2.5}$ regulation rather than a mass based regulation.

● In light of more recent data (near-road effects, organic composition of PM), specific scenarios can be reasonably tested.

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Source to Health Outcome