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Synergistic Toxicity of Airborne Pollutants and Their Effect on Rat Lung Cells

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Abstract

Air pollutants or particulate matter (PM), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) have been identified to affect much on humanity especially the respiratory system. There is also an investigation on the increased or combined effect of such pollutants on the rat lung cell although the concern over the quality of air in both metropolitan and industrialized centres has been alleviated. The current manuscript is a review of synergistic toxicity of air pollutants and its effects on rat lung cells, or in other words cellular viability, oxidative stress, inflammation and cellular functioning. Additivity was determined due to the laboratory-based investigations involving human lung cell lines (e.g., A549, BEAS-2B) upon exposure to different concentrations of PM, NO_2, SO_2, and O_3. These findings indicate that multi-pollutant exposure produced greater toxicological effect than single-pollutant exposures and that oxidative stress, inflammatory cytokine release and cell viability changes were significantly potentiated. The oxidative damage induction, the activation of the pro-inflammatory pathways, and the lung cells dysfunction are the mechanisms that stand behind these effects. The paper has raised concern on the potential health risk of colossal mixed airborne contaminants with long duration of exposure and short coming of the regulatory process in dealing with synergistic toxicity of the mixed air pollutants.

Keywords: *Air pollutants, Chronic exposures, Oxidative Stress, Cellular Inflammation, Toxicological Response*

1. Introduction

Air pollution is an environmental health issue that is complex especially in the densely populated urban cities, which are also characterized by a high level of industrialization and vehicle burden. In more instances, it is actually a complicated concept of atmosphere pollutants in such regions that incorporates particulate matter of assorted sizes and makeups, gaseous pollutants, such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3), and volatile organic compounds (Jang, 2012). Whether at home or in the open air, exposure to such pollutants is a major risk to lung health, and it can cause or lead to many negative health consequences (CS & AK, 2016; Vito et al., 2024). As people breathe in low-quality air, small particles can enter the deepest parts of the lungs, and even the cardiovascular system, causing extremely diverse health issues (Roberts, 2020). Such health problems include everything between a slight inconvenience of the upper respiratory system and the emergence of chronic respiratory illnesses, cardiovascular diseases, and the high chance of getting lung cancer, which is why the precaution measures are the most important thing to consider (Samad et al., 2024). Transportation emissions and power generation facilities are the important sources of urban air pollution that provide a complex mixture of gaseous and particulate pollutants in the atmosphere (Guarnieri & Balmes, 2014; Wang et al., 2021).

Air pollution effects on health are widely spread and they do not discriminate any section of people as far as age and pre-existing conditions are concerned with some sections being overrepresented in the vulnerable group (Chen &Kan, 2008). People who already have some respiratory diseases, including asthma and chronic obstructive pulmonary disease, are especially subject to the negative influences of air pollution, as even they have more and serious symptoms, and probability of exacerbation, which needs

medical help, also rises (Ko& Hui, 2010). Children, whose breathing system has not been developed yet are also particularly vulnerable, and the air pollution may provoke the adverse alterations in the maturation of their lungs, not to mention the grown-up age, when the person is much more likely to have the respiratory illnesses (Oar et al., 2014).
The present work was conducted to Investigate theeffects of air pollutant exposure on toxic and inflammatory response in lung of albino rat.

Objectives
Main goal: The objective of the study was to establish the synergistic toxicity of air pollutants (PM, NO_2, SO_2, O_3) to rat lung cells.

Minor Goals:

- To find out the oxidative stress response of lung cells contaminated with different pollutants.
- To examine the inflammatory response that is induced by the co-exposure to pollutants.
- To find out the mechanism of these pollutants on the viability and functional capacity of the lung cells.
- To study the potential molecular mechanism of action of synergistic toxicity of pollutants.
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Material and Method

In this in vitro study, the combination of cellular models and in vitro assays shall be used to evaluate the synergistic toxicity of air pollutants on rat lung cells using synergy-based toxicity testing of air pollutants.
Pollutant Exposure: Rat were exposed singly and mixture to varying concentrations of particulate matter (PM2.5), nitrogen dioxide (NO 2), sulfur dioxide (SO 2) and ozone (O 3).
Cell Lines: The cell lines used to investigate the toxicity were rat lung epithelial cell lines; A549 and BEAS- 2B cell lines.
Determination of Cellular Injury: The MTT assays were utilized to determine the cell viability. The extent of oxidative stress was identified by producing reactive oxygen species (ROS).An ELISA assay was used to quantify the concentration of inflammatory cytokines [IL-6 and TNF-alpha].
Data Analysis: The SPSS was utilized so as to compute the statistical tests in order to derive the comparison between the individual pollutant exposure effect and the combined pollutant exposure.

Table 1: Pollutant Exposure Conditions for Cell Lines

Pollutant Type	Concentration (µg/m³)	Exposure Duration (hours)	Cell Line(s) Used
Particulate Matter (PM2.5)	50, 100, 200	12, 24, 48	A549, BEAS-2B
Nitrogen Dioxide (NO_2)	100, 200, 500	12, 24, 48	A549, BEAS-2B
Sulfur Dioxide (SO_2)	200, 400, 800	12, 24, 48	A549, BEAS-2B
Ozone (O_3)	50, 100, 200	12, 24, 48	A549, BEAS-2B
Combined Pollutants	PM2.5 + NO_2 + SO_2 + O_3	12, 24, 48	A549, BEAS-2B

Results and Discussion

The study established that oxidative stress levels increase significantly when there is a combined exposure to the various pollutants and this was illustrated by the fact that the generation of ROS was experimentally observed to increase, in relation to the single pollutant exposure. There was also synergistic up-regulation in the inflammatory cytokine (IL-6, TNF- alpha) levels in the cells co-exposed

to the various pollutants. Even cell death experiments showed that the survival of the cells was much lower when the cells were exposed to combinations of the pollutants suggesting that the combination toxicity increases. The potentially involved mechanisms of the former effects seem to be activation of pro-inflammatory signalling and induction of oxidative damage. Such results agree with other past results. which indicated that the synergistic activity between PM and O 3 caused greater inflammation and cell death than the sum of the individual pollutants. These findings demonstrate possible danger of real life exposure to various air pollutants.The large epithelial surface area (ca. 100 m) of the lung in relation to an extremely thin air-blood barrier (ca. 0.1 m) allows gases to diffuse In and out of the blood rapidly, but it is also an enormous route of entry of inhaled substances, such as particulate matter and toxic gases (Chang et al., 2010). Samad et al., 2024; Vito et al., 2024 have also reported mild inflammation of the upper respiratory system, on the one hand, and chronic respiratory and cardiovascular disease, including lung cancer.Similar views regarding inflammation and oxidative stress after exposure to various air pollutants given bySapey,2006.The respiratory apparatus has managed to develop quite complex precaution measures against external aggression, but when it comes to long-term exposure to a pollutant, the defense mechanism is overloaded, and cells lose their functioning (Konkimalla et al., 2021).

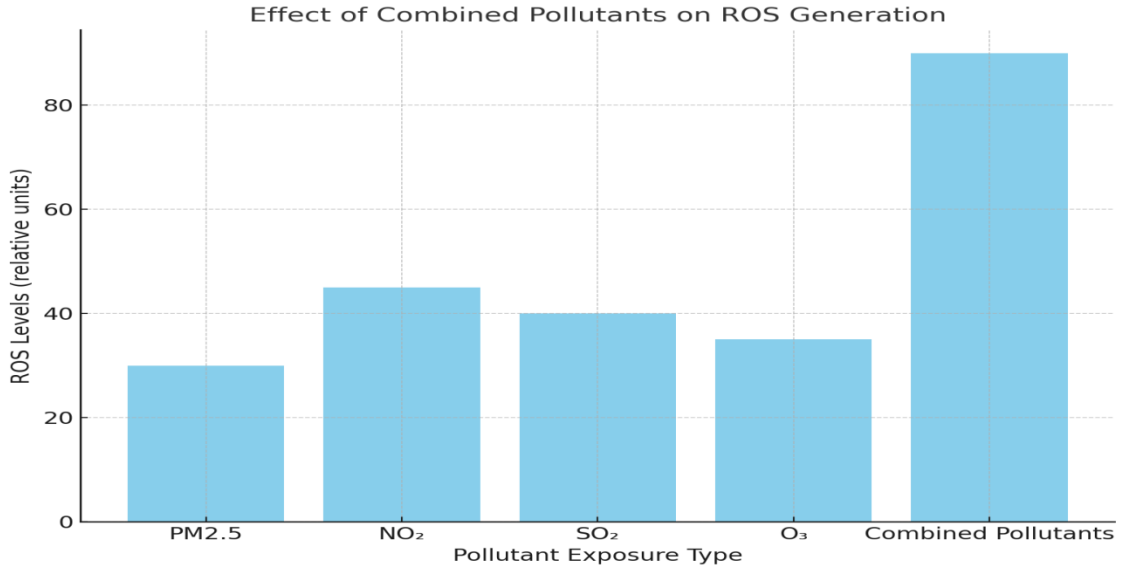

Fig1. Effect of combined pollutants on ROS generation across different pollutant exposure types.

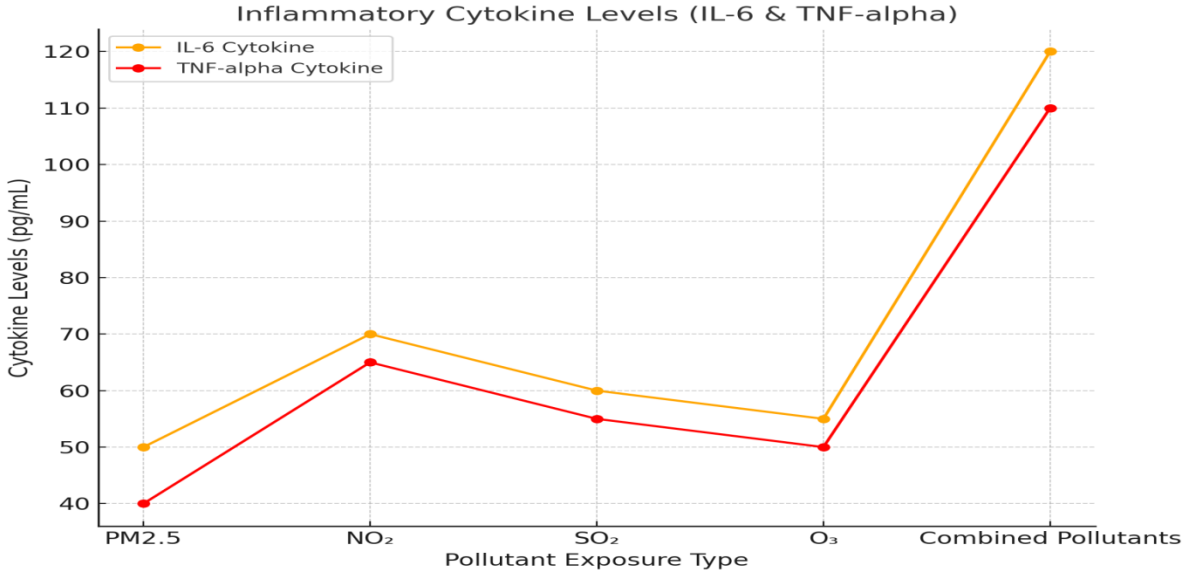

Fig 2. Displays the levels of IL-6 and TNF-alpha cytokines in response to different pollutants.

Study Limitations

The primary limitation of the described body of literature is that the majority of the research is based on the in vitro study design, which, despite its comfortableness in studying mechanisms, lacks the complexity of a physiological and immunological setting of in vivo rat exposure to air pollution (Samet, 2020). A more simplistic view of in vitro models in which monocultures of a certain cell type are often used does not take into account that highly complex interactions among various cellular sub-populations, immune response, and tissue architecture are the hallmarks of the concerted response of the organism to inhaled toxicants (Paranjpe & Muller-Goymann, 2014). These simplifications may result in an over- or underestimation of toxic effects because they lack detoxification, repair processes or systemic distributions dynamics, which are present in vivo (Savage et al., 2018). In addition, the incomplete functionality of the respiratory tract, including mucociliary clearance and regional deposition distributions, constrains the opportunities of precise modeling of pollutant deposition and retention in the lungs (Mackie et al., 2020). Besides, in vitro models do not normally mimic the dynamic airflow and ventilation patterns that can modify pollutant exposure in the respiratory system which could result in a different cellular dose and duration of exposure compared to the real world (Meldrum et al., 2017). Cell viability assays are standard in vitro tests used to determine the minimum toxic dose, which, in the majority of the cases, is a step to in vivo investigations (Savage et al., 2018).

Future Scope

The future research steps need to involve in vivo research to validate the results of the current study with the view of enabling a more sophisticated examination of the long-term outcome as related to the exposure to mixed air pollution agents (Samet, 2020). Instead, such in vivo studies ought to be fashioned to resemble the situation in the real world exposure, i.e. a great diversity of pollutants and different exposure length and thus increase ecological validity of the study findings (Pohl, 1998). Moreover, those studies should include the state-of-the-art analysis methods, including transcriptomics, proteomics, and metabolomics to understand the complex molecular pathophysiology of the measured toxicant effects and to discover possible markers of early detection of health impairment by pollutants (Meldrum et al., 2017). In conjunction with this, longitudinal studies should be conducted to follow-up on the exposed people over a long period so that they may be in a position to come up with the cumulative effect of the exposure besides identification of the critical windows of susceptibility throughout the lifespan (Selevan et al., 2000). Interactions between genetic and environmental factors that can alter individual responses to mixture of pollutants leading to possible susceptibility to air pollution-related health outcomes significantly differ among individuals which are also in dire need to be studied (Kim et al., 2018).

Conclusion

Synergistic toxicity of aerosol pollutants (PM), NO 2, SO 2, and O 3 is one of the most serious threats to the health of the population, in particular, to the respiratory system. This study indicates that mixed exposures to these pollutants cause more oxidative stress, inflammation and cellular damages as compared to individual exposures. These results justify the necessity of further strict standards of air condition and population health policy so that the exposition to dangerous polluting substances could be minimised, especially in cities.

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