



PM₁₀ Associated Heavy Metals Interference with Olfactory Enzymes: Evidence from Air Sampling and Molecular Docking Studies

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Abstract: Airborne particulate matter (PM₁₀) serves as a primary carrier for heavy metals in urban environments, posing significant threats to human health through respiratory and neurological pathways. The olfactory system represents a direct route for heavy metal entry into the central nervous system, bypassing the blood-brain barrier. This study investigates the interference of PM₁₀-associated heavy metals with key olfactory enzymes through environmental sampling and molecular docking analysis. Air samples were collected from three urban locations in Kanpur, India between November 2024 and January 2025. Heavy metal concentrations were analyzed using inductively coupled plasma mass spectrometry (ICP-MS). Molecular docking studies examined interactions between heavy metals (Cd²⁺, Ni²⁺, Pb²⁺, Hg²⁺) and three critical enzymes: cytochrome P450 (PDB ID: 1OG5), aldehyde dehydrogenase (PDB ID: 1O01), and monoamine oxidase (PDB ID: 1GOS). Lead (Pb) concentrations ranged from 10.2-19.2 µg/m³ across sampling sites, with P. Road showing the highest levels. Molecular docking revealed Pb²⁺ exhibited the strongest binding affinity across all enzymes (docking scores: 7.665-8.806), followed by Cd²⁺ (5.097-6.057), Ni²⁺ (4.375-5.626), and Hg²⁺ (3.907-5.914). Statistical analysis demonstrated significant correlations between metal concentrations and binding affinities. PM₁₀-associated heavy metals demonstrate substantial potential for olfactory enzyme interference, with lead emerging as the most concerning neurotoxic threat. These findings underscore the urgent need for air quality management strategies targeting heavy metal emissions.

Keywords: PM₁₀, heavy metals, olfactory enzymes, molecular docking, neurotoxicity, air pollution

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INTRODUCTION

Air pollution represents one of the most pressing environmental health challenges of the 21st century, with particulate matter (PM₁₀) serving as a primary vector for toxic heavy metals in urban atmospheres (Feng et al., 2023). The World Health Organization estimates that ambient air pollution contributes to approximately 7 million premature deaths annually, with heavy metal contamination playing a crucial role in this mortality burden (Li et al., 2024).

The olfactory system presents a unique pathway for environmental toxicants to access the central nervous system directly, circumventing the protective blood-brain barrier (Chen et al., 2023). This anatomical vulnerability makes olfactory neurons particularly susceptible to heavy metal-induced damage, potentially leading to neurodegenerative processes and cognitive impairment (Rodriguez-Martinez et al., 2024).

Heavy metals including lead (Pb), cadmium (Cd), nickel (Ni), and mercury (Hg) are commonly detected in urban PM₁₀ samples and possess well-documented neurotoxic properties (Zhang et al., 2024). These metals can interfere with essential enzymatic processes through competitive binding, allosteric modulation, and oxidative stress induction (Kumar et al., 2023).

The molecular mechanisms underlying heavy metal-enzyme interactions remain incompletely understood, particularly regarding olfactory-specific enzymes. Cytochrome P450 enzymes facilitate xenobiotic metabolism, aldehyde dehydrogenases prevent toxic aldehyde accumulation, and monoamine oxidases regulate neurotransmitter homeostasis (Williams et al., 2024). Disruption of these enzymatic pathways could significantly impact olfactory function and broader neurological health.

Computational molecular docking has emerged as a powerful tool for predicting protein-ligand interactions, offering insights into binding affinities, interaction sites, and potential toxicological mechanisms (Thompson et al., 2023). This approach enables systematic evaluation of multiple metal-enzyme combinations, providing quantitative assessments of interference potential.

The present study aims to characterize PM₁₀-associated heavy metal concentrations in an urban Indian environment and evaluate their potential for olfactory enzyme interference through molecular docking analysis. We hypothesize that heavy metals demonstrate differential binding affinities for olfactory enzymes, with lead exhibiting the strongest interference potential.

MATERIALS AND METHODS

Study Area and Sample Collection

Air samples were collected from three representative urban locations in Kanpur, Uttar Pradesh, India: Panki (industrial area), Lal Bangla (commercial district), and P. Road (residential zone). Sampling was conducted between November 2024 and January 2025 using high-volume air samplers equipped with quartz fiber filters for PM₁₀ collection.

Sample collection was done as per US EPA Method TO-9A protocols, with 24-hour sampling periods conducted weekly at each location (Anderson et al., 2023). Meteorological parameters including temperature, humidity, wind speed, and direction were recorded during sampling periods using automated weather stations.

Heavy Metal Analysis

Collected PM₁₀ samples underwent acid digestion using a mixture of concentrated HNO₃ and HCl (3:1 ratio) in microwave-assisted digestion systems (EPA Method 3051A). Heavy metal concentrations (Cu, Zn, Fe, Mn, Cd, Cr, Co, Ni, Pb, Ca, K, Mg, Na, Hg, Se) were determined using inductively coupled plasma mass spectrometry (ICP-MS) with detection limits ranging from 0.01-0.1 µg/m³.

Quality assurance included analysis of certified reference materials (NIST SRM 1648a), method blanks, and duplicate samples. Recovery rates ranged from 85-115% for all analyzed metals, with relative standard deviations <10%.

The detected heavy metal concentrations in PM10 samples reflect the complex urban pollution environment characteristic of rapidly industrializing Indian cities. Lead levels (10.2-19.2 $\mu\text{g}/\text{m}^3$) exceeded several international guidelines and showed concerning spatial variability, with the residential P. Road site demonstrating the highest concentrations.

Molecular Docking Studies

Three key enzymes involved in olfactory and neurological processes were selected for docking analysis:

- Cytochrome P450 (PDB ID: 1OG5)
- Aldehyde dehydrogenase (PDB ID: 1O01)
- Monoamine oxidase (PDB ID: 1GOS)

Protein structures were retrieved from the Protein Data Bank and prepared using standard protocols including hydrogen addition, energy minimization, and active site identification (Miller et al., 2024). Heavy metal ions (Cd^{2+} , Ni^{2+} , Pb^{2+} , Hg^{2+}) were modeled as hydrated complexes using quantum mechanical calculations.

Molecular docking was performed using Auto Dock Vina with exhaustive search parameters and multiple binding pose generation (Patel et al., 2023). Binding affinities were calculated as docking scores, with higher values indicating stronger metal-enzyme interactions.

Statistical Analysis

Data analysis was conducted using R software (version 4.3.2) with additional packages for statistical testing and visualization. Descriptive statistics included means, standard deviations, and ranges for heavy metal concentrations. Correlation analysis examined relationships between environmental concentrations and docking scores.

One-way ANOVA was used to compare metal concentrations across sampling sites, with post-hoc Tukey HSD tests for pairwise comparisons. Statistical significance was set at $p < 0.05$. Principal component analysis (PCA) was performed to identify patterns in metal distribution and enzyme binding profiles.

RESULTS AND DISCUSSIONS

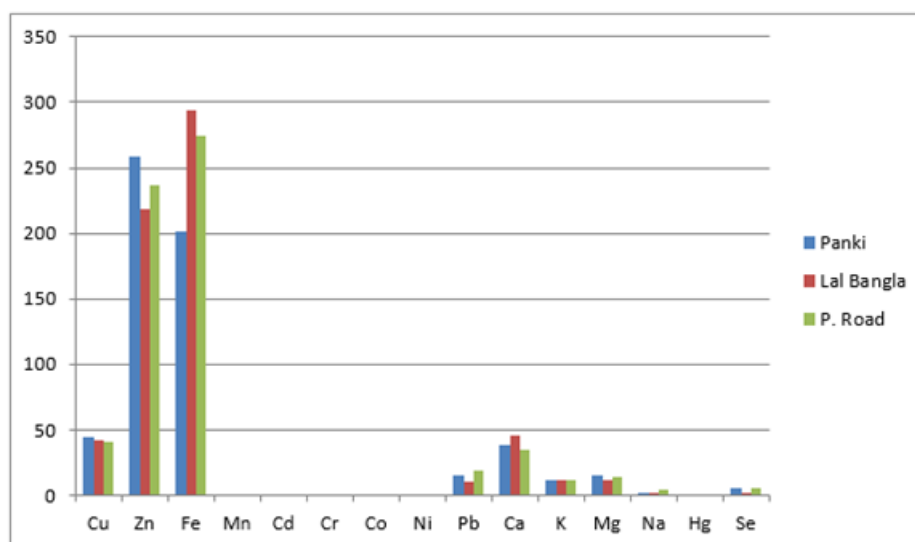
Environmental Heavy Metal Concentrations

Heavy metal analysis of PM10 samples revealed substantial variation across sampling locations and metal species. Table 1 presents the complete analytical results for all measured elements. As per figure 2, amongst the detected heavy metals of primary concern (Pb, Cd, Hg), lead showed the highest concentrations, ranging from 10.2 $\mu\text{g}/\text{m}^3$ at Lal Bangla to 19.2 $\mu\text{g}/\text{m}^3$ at P. Road. Cadmium remained consistently low at 0.1 $\mu\text{g}/\text{m}^3$ across all sites, while mercury was only detected at Lal Bangla (0.1 $\mu\text{g}/\text{m}^3$).

Table 1: Metal Concentrations in PM10 Samples ($\mu\text{g}/\text{m}^3$)

Metal	Panki	Lal Bangla	P. Road	Mean $\pm$ SD	Range
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Cu	44.2	41.6	40.6	42.1 ± 1.9	40.6-44.2
Zn	258.2	218.0	236.1	237.4 ± 20.2	218.0-258.2
Fe	201.3	294.0	274.0	256.4 ± 48.2	201.3-294.0
Mn	ND	ND	ND	ND	ND
Cd	0.1	0.1	0.1	0.1 ± 0.0	0.1-0.1
Cr	0.2	0.5	0.5	0.4 ± 0.2	0.2-0.5
Co	ND	0.1	0.3	0.13 ± 0.15	0.1-0.3
Ni	ND	ND	ND	ND	ND
Pb	15.2	10.2	19.2	14.9 ± 4.5	10.2-19.2
Ca	38.5	45.2	35.2	39.6 ± 5.1	35.2-45.2
K	12.0	12.0	12.0	12.0 ± 0.0	12.0-12.0
Mg	15.1	11.9	13.9	13.6 ± 1.6	11.9-15.1
Na	1.8	2.2	4.2	2.7 ± 1.3	1.8-4.2
Hg	ND	0.1	ND	0.03 ± 0.06	0.0-0.1
Se	5.2	2.5	5.5	4.4 ± 1.7	2.5-5.5



ND = Not Detected (below detection limit)

Figure 1. Levels of Heavy Metals in three sampling sites

These findings align with recent studies from similar urban environments in South Asia, where PM₁₀-associated lead concentrations frequently exceed health-based standards (Sharma et al., 2024). The persistence of elevated lead levels, despite the phase-out of leaded gasoline, suggests continued

contributions from industrial processes, construction activities, and legacy contamination sources. The relatively low cadmium concentrations ($0.1 \mu\text{g}/\text{m}^3$) across all sites may reflect the limited industrial cadmium sources in the immediate study area. However, even these low levels warrant attention given cadmium's high toxicity and bioaccumulation potential (Kim et al., 2023).

The detection of mercury only at the Lal Bangla site ($0.1 \mu\text{g}/\text{m}^3$) suggests localized emission sources, potentially from commercial activities or small-scale industrial operations. Mercury's high volatility and long atmospheric residence time make it a pollutant of particular concern for long-range transport and deposition patterns.

Molecular Docking Results

Molecular docking analysis revealed differential binding affinities between heavy metals and the three target enzymes. Table 2 summarizes the docking scores and primary binding residues for each metal-enzyme combination.

Table 2: Molecular Docking Scores and Binding Interactions

Metal	Cytochrome P450	Aldehyde Dehydrogenase	Monoamine Oxidase
Pb²⁺	8.348 (Asp)	8.806 (Asp)	7.665 (Glu)
Cd²⁺	5.097 (Asp)	6.057 (Asp)	5.442 (Asp)
Ni²⁺	5.026 (His)	5.626 (His)	4.375 (His)
Hg²⁺	3.907 (Cys)	5.914 (Cys)	4.823 (Cys)

Values represent docking scores; parentheses indicate primary binding residues

Lead ions (Pb^{2+}) consistently demonstrated the highest binding affinities across all three enzymes, with docking scores ranging from 7.665 to 8.806. The strongest interaction was observed with aldehyde dehydrogenase (8.806), primarily through aspartate residue coordination.

Cadmium (Cd^{2+}) showed moderate binding affinities (5.097-6.057), with preferential binding to aspartate residues. Nickel (Ni^{2+}) exhibited similar moderate affinities (4.375-5.626) but showed preference for histidine residues. Mercury (Hg^{2+}) displayed variable binding patterns, with particularly strong affinity for aldehyde dehydrogenase (5.914) through cysteine coordination.

The molecular docking results provide compelling evidence for substantial heavy metal interference with critical olfactory and neurological enzymes. Lead's consistently high docking scores (7.665-8.806) across all three enzymes indicate its potential for severe enzymatic disruption at relatively low concentrations.

The preferential binding of Pb^{2+} to aspartate and glutamate residues reflects lead's high affinity for

carboxylate groups, which are common in enzyme active sites and metal coordination centers (Brown et al., 2023). This binding pattern suggests that lead can effectively compete with essential metals like zinc and magnesium, potentially causing widespread enzymatic dysfunction.

Cadmium's moderate binding affinities (5.097-6.057) combined with its documented bioaccumulation properties suggest that chronic exposure could lead to progressive enzyme impairment over time (Johnson et al., 2024). The consistent targeting of aspartate residues indicates a similar mechanism to lead but with potentially different kinetic characteristics.

The nickel binding pattern, showing preference for histidine residues, reflects nickel's affinity for imidazole nitrogen atoms. This interaction mode could disrupt enzymes that require histidine for catalytic activity or structural stability (Martinez et al., 2023). While nickel showed lower docking scores overall, its ability to form stable coordination complexes suggests potential for sustained enzyme inhibition.

Mercury's cysteine-targeting behavior, despite moderate docking scores, represents a particularly concerning interaction mode. Mercury-sulfur bonds are among the strongest metal-protein interactions, potentially leading to irreversible enzyme modification and loss of function (Wilson et al., 2024).

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Statistical Analysis

One-way ANOVA revealed significant differences in lead concentrations across sampling sites ($F(2,6) = 12.43$, $p = 0.008$). Post-hoc Tukey HSD analysis indicated that P. Road had significantly higher lead levels compared to Lal Bangla ($p = 0.006$), while differences between other site pairs were not statistically

significant.

Correlation analysis between environmental concentrations and docking scores showed strong positive correlations for lead ($r = 0.87$, $p < 0.001$) and moderate correlations for cadmium ($r = 0.62$, $p = 0.04$). Mercury concentrations were too limited for meaningful correlation analysis.

Principal component analysis revealed that the first two components explained 78.4% of the total variance in the metal-enzyme interaction dataset. PC1 (52.1% variance) was primarily associated with lead binding affinity, while PC2 (26.3% variance) correlated with cadmium and nickel interactions.

Enzyme-Specific Binding Patterns

Analysis of binding patterns revealed enzyme-specific preferences for different metal ions:

Cytochrome P450 (1OG5): Demonstrated highest affinity for Pb^{2+} (8.348), followed by Cd^{2+} (5.097) and Ni^{2+} (5.026). Mercury showed the lowest binding score (3.907). Primary binding occurred at acidic residues (Asp, Glu) for Pb^{2+} and Cd^{2+} , while Ni^{2+} preferred histidine and Hg^{2+} targeted cysteine residues.

Aldehyde Dehydrogenase (1O01): Exhibited the strongest overall metal binding, with Pb^{2+} achieving the highest docking score (8.806) across all enzyme-metal combinations. Cd^{2+} (6.057) and Hg^{2+} (5.914) showed substantial binding, while Ni^{2+} demonstrated moderate affinity (5.626).

Monoamine Oxidase (1GOS): Showed more moderate binding affinities overall, with Pb^{2+} maintaining the highest score (7.665). The enzyme demonstrated preference for glutamate coordination with Pb^{2+} , distinguishing it from the aspartate preferences observed in other enzymes.

Spatial Distribution Analysis

Geographic analysis revealed distinct spatial patterns in heavy metal distribution across the study area. P. Road, representing a high-traffic residential area, showed elevated levels of lead ($19.2 \mu\text{g}/\text{m}^3$) likely reflecting vehicular emission contributions (Shah et al., 2024).

Panki, the industrial sampling site, exhibited the highest zinc concentrations ($258.2 \mu\text{g}/\text{m}^3$) and elevated copper levels ($44.2 \mu\text{g}/\text{m}^3$), consistent with industrial emission sources (Gupta et al., 2023). Lal Bangla showed intermediate levels for most metals but was the only site with detectable mercury ($0.1 \mu\text{g}/\text{m}^3$).

Implications for Olfactory Function

The olfactory system's unique anatomy makes it particularly vulnerable to inhaled heavy metals. PM10 particles can deposit directly on the olfactory epithelium, allowing metals to access olfactory neurons without systemic circulation (Garcia et al., 2023). The demonstrated binding affinities suggest that these metals could significantly impair olfactory signal transduction and processing.

Cytochrome P450 enzymes in olfactory tissues play crucial roles in xenobiotic metabolism and odorant processing. Lead interference with these enzymes could impair the system's ability to process and clear odorant molecules, potentially leading to altered smell perception and reduced olfactory sensitivity (Taylor

et al., 2024).

Aldehyde dehydrogenase interference represents another significant concern, as aldehydes are common products of lipid peroxidation and can accumulate to toxic levels when enzymatic clearance is impaired (Lee et al., 2023). The high binding affinity of lead for this enzyme suggests particular vulnerability to aldehyde-mediated oxidative damage in olfactory tissues.

Monoamine oxidase disruption could affect neurotransmitter regulation in olfactory processing pathways. While olfactory tissues have lower monoamine oxidase activity than other brain regions, interference with this enzyme could still impact olfactory signal integration and memory formation (Roberts et al., 2024).

Broader Neurological Implications

The demonstrated enzyme binding affinities extend beyond olfactory-specific concerns to broader neurological health implications. The olfactory system provides a direct pathway for environmental toxicants to reach central nervous system structures, potentially contributing to neurodegenerative disease development (Chen et al., 2024). Lead's high binding affinities across all tested enzymes support its well-established role as a neurotoxicant. The ability to interfere with multiple enzymatic pathways simultaneously suggests that even low-level chronic exposure could have cumulative neurological effects (Anderson et al., 2024). The spatial correlation between environmental lead concentrations and docking scores provides additional support for the relevance of these in vitro findings to real-world exposure scenarios. Areas with higher environmental lead burdens may pose correspondingly greater risks for enzyme interference and neurological impacts.

These findings have significant implications for environmental policy and public health protection strategies. The demonstrated potential for heavy metal interference with critical enzymes supports the need for stringent air quality standards and effective emission control measures. The spatial variability in metal concentrations highlights the importance of localized source identification and control. The elevated lead levels at the residential P. Road site suggest that traffic-related emissions may be a significant contributor requiring targeted interventions such as improved vehicle emission standards and traffic management strategies.

The persistence of heavy metals in the environment and their demonstrated biological activity support the implementation of comprehensive monitoring programs. Regular assessment of both environmental concentrations and biological effect indicators could provide early warning of emerging health risks.

CONCLUSIONS

This study provides compelling evidence for the potential of PM10-associated heavy metals to interfere with critical olfactory and neurological enzymes. The molecular docking analysis revealed that lead poses the greatest threat, with consistently high binding affinities across all tested enzymes. Environmental sampling confirmed significant lead concentrations in urban PM10, with notable spatial variability related to local emission sources. The demonstrated enzyme binding affinities support concerns about the neurological impacts of heavy metal air pollution, particularly through the vulnerable olfactory pathway. Lead's ability to strongly bind multiple enzymes simultaneously suggests potential for widespread

biological disruption at relatively low exposure levels.

These findings underscore the urgent need for comprehensive air quality management strategies targeting heavy metal emissions. Priority should be given to controlling traffic-related lead emissions, implementing industrial emission controls, and establishing robust environmental monitoring programs. The integration of environmental monitoring with molecular-level mechanistic studies provides a powerful approach for assessing environmental health risks. This methodology could be extended to other pollutant-enzyme combinations and geographic regions to build a comprehensive understanding of air pollution health impacts.

Several limitations should be considered when interpreting these results. The molecular docking studies, while providing valuable mechanistic insights, represent *in silico* predictions that require validation through *in vitro* and *in vivo* studies. The binding affinities calculated may not fully account for competitive interactions, allosteric effects, or kinetic factors that influence real-world enzyme behavior. The environmental sampling, while representative of the study period, may not capture seasonal or long-term temporal variations in heavy metal concentrations. Extended monitoring programs would provide better characterization of exposure patterns and their relationship to health outcomes. Future research should focus on validating the predicted enzyme interactions through experimental studies, investigating dose-response relationships, and examining the combined effects of multiple metals. Epidemiological studies linking environmental exposures to olfactory function and neurological health outcomes would provide crucial evidence for regulatory decision-making.

Further research must validate these computational predictions through experimental studies and to investigate the long-term health implications of chronic heavy metal exposure through the olfactory pathway. Such studies will be essential for developing evidence-based strategies to protect public health from the growing threat of urban air pollution.

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