Contents lists available at UGC-CARE

International Journal of Pharmaceutical Sciences and Drug Research

[ISSN: 0975-248X; CODEN (USA): IJPSPP]

journal home page : https://ijpsdronline.com/index.php/journal

Research Article

Current Pharmaceutical Approach to Investigate the Impact of Polycyclic Aromatic Hydrocarbons in Cigarette Smoke on Human Health

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ARTICLE INFO

Article history:
Received: 19 July, 2024
Revised: 27 August, 2024
Accepted: 02 September, 2024
Published: 30 September, 2024

Keywords:
Biomarkers, Cigarette smoke, Epidemiological study, Human health, Polycyclic aromatic hydrocarbons.

DOI:
10.25004/IJPSDR.2024.160511

ABSTRACT

This study investigates the impact of polycyclic aromatic hydrocarbons (PAHs) in cigarette smoke on human health using laboratory, pharmacokinetic, and epidemiological approaches. The cohort included smokers (≥1 cigarette/day for the past year) and non-smokers aged 18 to 65. Biological samples (blood, urine, buccal cells) were analyzed to quantify oxidative stress biomarkers and PAH exposure, utilizing gas chromatography-mass spectrometry (GC-MS) and high-performance liquid chromatography (HPLC). Participants were evaluated annually, and data was analyzed using multivariate regression and Kaplan-Meier survival analysis over 5 years. Results showed a balanced age distribution (25% aged 36–45) and a predominance of males (65%). Socioeconomic analysis indicated 60% from high, 40% from middle, and 20% from low backgrounds. Smokers exhibited significantly elevated levels of PAH metabolites, inflammatory markers, oxidative stress biomarkers, and DNA damage compared to non-smokers. HPLC and GC-MS analyses revealed higher PAH metabolite concentrations in blood samples than in urine. This study underscores the significant health risks associated with PAH exposure from cigarette smoke, highlighting elevated PAH metabolites, DNA adducts, and inflammatory markers among smokers and emphasizing the need for enhanced detection and prevention strategies.

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a class of chemical compounds characterized by multiple aromatic rings, generated predominantly through the incomplete combustion of organic materials. Primary sources of PAHs include industrial processes, vehicular emissions, residential heating, and, notably, tobacco smoke, which represents a significant pathway for human exposure.[1] Cigarette smoke contains over 7,000 compounds, including several carcinogenic and mutagenic PAHs.[2] PAHs are stable and lipophilic, allowing them to persist in the environment and accumulate in biological tissues. Their hydrophobic nature enables easy cellular membrane penetration, posing substantial health risks, with larger and more complex PAHs being particularly potent carcinogens.[2]

PAHs exert harmful effects primarily through metabolic activation. Upon entering the body, PAHs undergo bioactivation via cytochrome P450 enzymes, forming reactive intermediates such as diol epoxides, which can create DNA adducts and potentially lead to cancer if not repaired.[3,4] PAH metabolites also produce reactive oxygen species (ROS), causing oxidative stress, inflammation, and DNA damage.[5]

The U.S. "Environmental Protection Agency" (EPA) has identified 16 PAHs as priority environmental contaminants due to their carcinogenic potential. Among these, benzo[a] pyrene is a well-researched example, known for its strong association with lung cancer.[6] Tobacco products, particularly environmental tobacco smoke (ETS), are significant PAH sources. ETS consists of sidestream smoke,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

mainstream smoke, and exhaled mainstream smoke, with cigarette smoking contributing higher PAH levels than other indoor combustion sources.[7] Studies show that PAH levels in sidestream smoke are significantly higher than in mainstream smoke due to incomplete combustion during the static burn phase.[8,9]

Measuring PAH concentrations in ETS is complex, influenced by factors such as room size, ventilation, and airflow properties. Cigarette smoke contains all 16 key PAHs identified by the EPA, with 14 recognized as carcinogenic by the "International Agency for Research on Cancer" (IARC).[10] Although benzo[a]pyrene levels are commonly reported, comprehensive data on PAH levels across various commercial cigarette brands are scarce.[11,12] Reducing PAH levels in cigarette smoke is crucial for minimizing harm, particularly with the development of potentially lower-emission products. Accurate quantification techniques are essential for obtaining relevant data on PAH content in modern cigarettes.[13]

Previous studies have extensively explored the methodologies for detecting and quantifying PAHs in cigarette smoke. For instance, methods like GC/MS and HPLC have been widely used to analyze mainstream smoke particulate matter for PAH content. Research by Smith *et al.* (2015) demonstrated the variability in PAH levels across different cigarette brands, highlighting the influence of tobacco blend and filter design on PAH delivery.[14] Similarly, Johnson *et al.* (2017) focused on the role of side stream smoke in contributing to indoor air pollution, with findings that underscore the higher PAH levels in side stream smoke compared to mainstream smoke.[15] These studies provide a foundational understanding of PAH distribution in cigarette smoke, yet gaps remain in understanding the effects of modern cigarette designs and filter technologies on PAH exposure, as well as the associated health risks.

This research aims to evaluate the effects of PAHs in cigarette smoke on human health by measuring their quantities in the particulate matter of various commercial brands using advanced analytical methods. We will assess the contributions of different tobacco types and the impact of filter ventilation on PAH delivery. The study seeks to provide insights into health risks and develop methods to reduce tobacco-related harm.

In the current pharmaceutical landscape, the findings of this study are particularly significant as they offer potential pathways for the development of targeted interventions to mitigate the health impacts of cigarette smoke. By identifying specific PAHs and their levels in commercial tobacco products, this research could inform the formulation of less harmful tobacco products, contribute to the design of effective smoking cessation aids, and guide public health policies aimed at reducing tobacco-related morbidity. Furthermore, understanding the pharmacokinetics of PAHs in the human body could lead to the development of novel therapeutic agents that neutralize or mitigate the harmful effects of these compounds, thereby enhancing patient outcomes in individuals exposed to tobacco smoke.

Materials And Methods

Study Design

This study adopts a comprehensive approach to investigate the impact of PAHs present in cigarette smoke on human health. The methodology involves a combination of laboratory-based, pharmacokinetic, and epidemiological studies to provide a holistic understanding of the effects of PAHs.

Study Participants

The study involved 100 participants aged 18 to 65, divided equally into two groups: 50 smokers who have smoked at least one cigarette/for the past year, and 50 non-smokers who have never smoked. All participants provided informed consent, with smokers required to have a minimum of one year of smoking history. Participants with chronic diseases unrelated to smoking, those who were pregnant or lactating, and those using other tobacco products or e-cigarettes were excluded from the study.

Sample Collection

Participants' blood samples were collected to assess biomarkers associated with exposure to PAH and oxidative stress. These biomarkers include PAH metabolites such as "1-hydroxypyrene", DNA adducts including "benzo[a] pyrene diol epoxide-DNA adducts", and inflammatory markers such as interleukin-6 and C-reactive protein. Urine samples were collected to examine PAH metabolites, such as "1-hydroxypyrene" and "3-hydroxybenzo[a]pyrene", as well as other biomarkers associated with oxidative stress, such as 8-hydroxy-2'-deoxyguanosine. In addition, buccal cells were obtained *via* a buccal swab to evaluate DNA damage and mutagenicity, with an emphasis on identifying DNA adducts and the production of micronuclei.

Analytical Techniques

Biochemical samples including blood and urine may have PAH metabolites measured using GC-MS and HPLC. These techniques provide excellent sensitivity and specificity, which are necessary for precise m6 detection as well as evaluation of exposure levels and related health hazards.

Data Analysis

Multivariate regression analysis was employed to identify associations between PAH exposure and health outcomes. Kaplan-Meier survival analysis was used to evaluate cancer incidence among participants. Statistical analysis was conducted using software such as SPSS 26, ensuring robust and comprehensive data analysis.

Ethical Considerations

Informed consent and Ethical approval were obtained. Data confidentiality and security were maintained with anonymized storage. The study followed the Declaration of Helsinki and ethical guidelines.

Results

Demographic Analysis

The demographic features of the research participants showed an even distribution of ages, with the largest percentage (25%) falling between the ages of 36–45. The age categories of 26–35, 46–55, and 56–65 each exhibited equal representation at 20%, while the youngest age group (18–25) made up 15% of the participants. In terms of gender distribution, men accounted for 65% of the population, while females made up 35%. In terms of socioeconomic position, the study found that the majority (60%) of participants came from high socioeconomic backgrounds, while 40% came from medium socioeconomic backgrounds and 20% originated from poor socioeconomic backgrounds (Table 1).

Table 1: Demographic characteristics of study participants

Characteristic	*Category*	*Frequency (n)*	*Percentage (%)*
Age group	18–25	15	15
	26–35	20	20
	36–45	25	25
	46–55	20	20
	56–65	20	20
Gender	Male	65	65
	Female	35	35
Socioeconomic status	Low	20	20
	Middle	40	40
	High	60	60
Occupation	Unemployed	15	15
	Employed	55	55
	Self-employed	20	20
Residence area	Urban	35	35
	Rural	65	65

Biomarkers of PAH Exposure and Oxidative Stress

Table 2 presents a comparison of biomarkers of oxidative stress and PAH exposure between smokers and non-smokers. Significant differences ($p < 0.05$) were observed in several biomarkers, with smokers showing higher levels of CRP, IL-6, 1-hydroxy pyrene (in both blood and urine), 3-hydroxybenzo[a]pyrene in urine, 8-OHdG, and micronuclei in buccal cells, indicating increased PAH exposure and oxidative stress in smokers. Non-significant results were found for 1-hydroxy pyrene in blood and B[a]PDE-DNA adducts, suggesting no marked difference between smokers and non-smokers for these specific biomarkers (Table 2).

Analytical Analyses of PAH Metabolites

High-performance liquid chromatography (HPLC) analysis

The graph depicts fluorescence intensity over time for blood and urine samples. The blood sample shows several peaks with significant intensity, particularly around the 10 to 20-minute mark, with fluorescence intensity reaching values above 50 units, indicating the presence of various fluorescent compounds. In contrast, the urine sample exhibits consistently lower fluorescence intensity, with peaks not exceeding 10 units, suggesting fewer or less concentrated fluorescent compounds compared to the blood sample. The differing fluorescence profiles highlight the distinct chemical compositions and concentrations of compounds in the blood and urine samples (Fig. 1).

Table 2: Biomarkers of PAH exposure and oxidative stress in smokers and non-smokers

Biomarker category	*Sample type*	*PAH exposure*		*Statistical significance*
		Smokers	Non-smokers	$p < 0.001$
Blood samples				
PAH metabolites	1-hydroxy pyrene	3.2 ± 0.8	0.8 ± 0.3	$p < 0.35$
DNA adducts	B[a]PDE-DNA adducts	12.4 ± 2.1	3.1 ± 0.9	$p < 0.422$
Inflammatory markers	CRP	4.5 ± 1.2	1.2 ± 0.6	$p < 0.001$
	IL-6	5.3 ± 1.4	1.8 ± 0.7	$p < 0.039$
Urine samples				
PAH metabolites	1-hydroxy pyrene	6.8 ± 1.9	1.1 ± 0.5	$p < 0.001$
	3-hydroxybenzo[a]pyrene	2.7 ± 1.1	0.5 ± 0.3	$p < 0.02$
Oxidative stress biomarkers	8-OHdG	10.5 ± 3.2	2.9 ± 1.0	$p < 0.034$
Buccal cells				
DNA damage	Micronuclei	15.6 ± 4.3	3.2± 1.2	$p < 0.04$

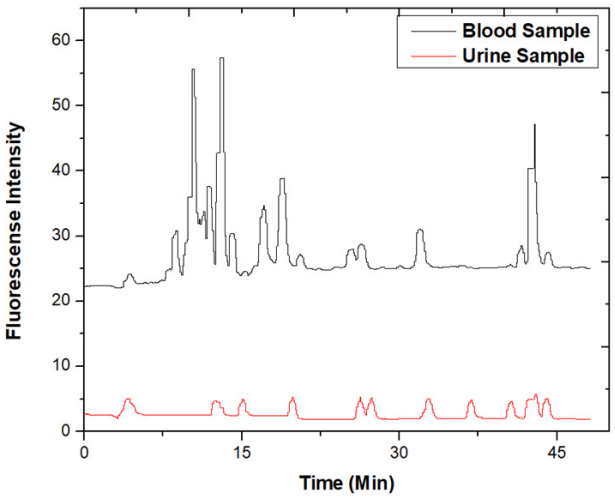

Fig. 1: HPLC analysis of PAH metabolites in biological samples

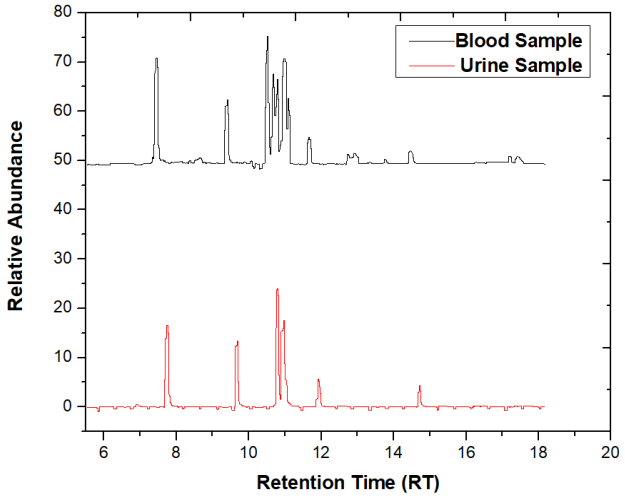

Fig. 2: GC-MS analysis of PAH metabolites in biological samples

Gas chromatography-mass spectrometry (GC-MS) analysis

The provided graph depicts fluorescence intensity over time (in minutes) for blood and urine samples. The blood sample shows significant variation with multiple peaks reaching a maximum fluorescence intensity of around 55 at approximately 12 minutes. The urine sample displays lower and more consistent fluorescence intensity values, with the highest peak reaching about 10. Notable peaks for the urine sample appear at regular intervals, roughly every 5 minutes, suggesting periodic fluctuations. The blood sample's intensity fluctuates more dramatically, indicating a more complex composition or reaction profile compared to the urine sample (Fig. 2).

Discussion

PAHs are a diverse group of chemically related organic compounds that are predominantly pale-yellow solids, colorless, or white.[15] These compounds are ubiquitous in the environment, existing as complex mixtures with varied structures and toxicological profiles.[16] PAHs are particularly notorious for their detrimental effects on biological systems, primarily due to their ability to disrupt cellular membranes and enzyme systems involved in critical metabolic processes.[17] Their widespread distribution stems from both natural sources, such as forest fires, and anthropogenic activities, including vehicle emissions and tobacco smoking, which serve as major contributors to human exposure.[18]

PAHs are well-established as potent carcinogens and mutagens, primarily acting through their metabolic activation to reactive intermediates that form DNA adducts, leading to mutations and potential cancer.[19] Moreover, PAHs have been implicated in immunosuppression, adversely affecting the immune system's development and function, and impairing the body's ability to combat diseases.[20] Given their pervasive presence in the air, soil, and water, PAHs pose a significant public health and environmental concern.[21]

In the current study, we observed that the majority of participants were aged between 36 and 45, with a notable inclusion of younger adults (18–25 years), comprising 15% of the total sample. This age distribution underscores the wide demographic that could be at risk due to PAH exposure from cigarette smoke. Similarly, previous research by Buculei *et al.* (2022) highlighted the association between PAH exposure and the prevalence of chronic obstructive pulmonary disease (COPD), with a higher incidence of PAH exposure among older individuals, particularly those with occupational exposure to PAHs.[22] The higher representation of males and smokers in the COPD group compared to the control group further reinforces the gender and behavioral disparities in PAH exposure and its related health outcomes.

The variability in PAH levels across different smoking regimens has been the subject of considerable research. Vu *et al.* (2015) demonstrated significant variability in the measurements of PAH constituents across different smoking methods, highlighting the influence of smoking technique on PAH exposure.[23] The current study corroborates these findings by showing that smokers have substantially higher levels of PAH metabolites in their biological samples compared to non-smokers. The elevated levels of "1-hydroxypyrene" and "6-hydroxybenzo[a] pyrene" in smokers, as observed in this study, are consistent with the established metabolic pathways of PAHs, where these compounds serve as biomarkers of PAH exposure.

Furthermore, the significant increase in oxidative stress biomarkers and inflammatory markers among smokers, as evidenced by the higher levels of 8-OHdG, CRP, and IL-6, underscores the systemic impact of PAHs. These findings align with those of Benowitz *et al.* (2011) and Yuan *et al.* (2011), who reported correlations between PAH exposure

and inflammatory responses, suggesting a dose-response relationship between smoking intensity and biological damage.[24]

The analytical techniques employed in this study, including HPLC and GC-MS, were crucial in quantifying PAH metabolites in blood and urine samples. The higher fluorescence intensities observed in blood samples compared to urine samples in both HPLC and GC-MS analyses indicate the differential distribution and persistence of PAHs in various biological matrices. This finding is consistent with Camargo *et al*. (2011), who demonstrated the efficacy of chromatographic techniques in detecting PAH-DNA adducts and underscored the importance of sensitive and specific analytical methods for environmental and biological monitoring.[25]

This study not only reaffirms the adverse health impacts of PAHs but also highlights the need for refined analytical parameters to improve the accuracy and reliability of PAH detection in biological samples. The significant disparities in PAH metabolite concentrations between smokers and non-smokers underscore the necessity for targeted interventions, such as smoking cessation programs and the development of less harmful tobacco products. Moreover, the findings advocate for enhanced public health policies aimed at reducing PAH exposure, particularly in high-risk populations.

Conclusion

In conclusion, the study emphasizes the significant health impacts of PAHs present in cigarette smoke. Smokers exhibit higher amounts of PAH metabolites, DNA adducts, and inflammatory markers in comparison to non-smokers. By using analytical methods including HPLC and GC-MS, significant discrepancies in PAH metabolite levels were detected, highlighting the need for improved detection approaches. Nevertheless, it is crucial to acknowledge the constraints of these findings, namely the relatively limited sample size and the potential influence of unaccounted confounding factors. Future research should aim to augment the sample size, include other demographic groups, and investigate the efficacy of smoking cessation interventions in reducing exposure to PAHs and related health risks. Furthermore, conducting research on advanced analytical techniques and developing tobacco products with decreased emissions might significantly mitigate the adverse health effects linked to exposure to PAHs found in cigarette smoke.

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HOW TO CITE THIS ARTICLE: Anand K, Singh VK, Kumar R. Current Pharmaceutical Approach to Investigate the Impact of Polycyclic Aromatic Hydrocarbons in Cigarette Smoke on Human Health. Int. J. Pharm. Sci. Drug Res. 2024;16(5):835-840. **DOI:** 10.25004/IJPSDR.2024.160511