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Polycyclic Aromatic Hydrocarbons (PAHs) in the Atmospheric Air: Determination using Instrument, Air Pollution and Cognitive Impairment - A Review

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Air pollution is a global problem that has long and short-term consequences for human health. Newer scientific research have shown that particulate and gaseous pollutants (such as PM_{10}, $PM_{2.5}$, O_3, CO, SO_2, and NO_2) are damaging to public health and welfare even at very low levels and that they have an impact on economies and people's quality of life. PAHs are polycyclic aromatic hydrocarbons (PAHs) that bind to particulate matter (PM) and can penetrate deep into the respiratory systems of humans. Because of its qualities that resist environmental degradation, this problem has gotten worse for human health. Air pollution has been linked to detrimental effects on the central nervous system (CNS), inflammatory response and cardiovascular system. The relationships between PAH levels in atmospheric air exposure and cognitive impairment, on the other hand, are inadequately documented. PAHs may be linked to cognitive impairment (CI) and Alzheimer's disease (AD). Because there is no cure for Alzheimer's disease, identifying risk factors has become a priority in order to reduce the individual, social and economic burden. In recent years, scientists have become increasingly interested in the association between exposure to atmospheric PAHs and cognitive performance. This review focuses on the principles of analytical instrumentation in order to determine the optimal instrument for use in PAHs laboratory analysis as well as the results of important air pollutants linked to cognitive impairment among elderly.

Keywords: polycyclic aromatic hydrocarbons, air pollution, cognitive impairment

INTRODUCTION

Airborne PM is a complex combination with numerous sizes and structures in the formed of coarse particulate matter (PM_{10}), fine particulate matter ($PM_{2.5}$) and ultra-fine particulate matter (UFP). Each of various PM has different characteristics; less than 10 µm, 2.5 µm and 0.1 µm in diameters which is known as PM_{10}, $PM_{2.5}$ and

UFP respectively (Reche et al., 2014). Yet, $PM_{2.5}$ has gained more attention in recent years due to their role in various atmospheric processes, human health effects and environmental deterioration impact (Murillo et al., 2017). Recommended Malaysian Air Quality Guideline (RMAQG) have been upgraded the major air pollutants from five pollutants into six which is involved of fine particulate matter ($PM_{2.5}$) since 2018 till now and it is even being included in the calculation of Malaysian Air Quality Index (MAQI) to be measured. As $PM_{2.5}$ has inhalable properties deep into human respiratory systems, the impacts on human health have been extensively studied in relation to human respiratory diseases (Tellez-Rojo et al., 2020; Xing et al., 2016; Zainal-Abidin et al.,2014), health risks and health impact assessments (Ali-Taleshi et al., 2021; Jamhari et al., 2014; Othman et al., 2021; Sulong et al., 2017), mortality and morbidity (Kloog et al., 2013; Tellez-Rojo et al., 2020; Mahiyuddin et al., 2013), DNA damage (Sørensen et al., 2003) and toxicity (Sulong et al., 2019). Previous study was reported on $PM_{2.5}$ concentrations showed an association with brain Aβ plaques formation which a biomarker of Alzheimer disease (Iaccarino et al., 2021). Other studies also supported that PM exposure promotes pathological brain aging (Cacciottolo et al., 2017; Rhew et al., 2021) with the association in cognitive decline (Best et al., 2016; Grant, 2012). On top of that, different backgrounds settings such as urban, semi-urban, industrial, rural, power plant areas and different temporal seasons has been studied in relation to PM distribution (Amil et al., 2016; Ee-Ling et al., 2015; Fang et al., 2015; Jamhari et al., 2014; Ramírez et al., 2018). However, very few studies have been done since $PM_{2.5}$ shows highly potential or significant changes towards cognitive function that need to be explored in future.

Polycyclic aromatic hydrocarbons (PAHs) are a class of persistent organic pollutants (POPs) that bind to PM and can penetrate deep into human respiratory systems (Sarigiannis et al., 2015). One of the chemical features of PAHs is their resistance to biological, chemical and photolytic breakdown in the environment (Mohamad Firdaus et al., 2019). According to the United States Environmental Protection Agency (USEPA), 16 PAHs have been classified as priority pollutants due to their known toxicity. PAHs are more common in fine particles than coarse particles (Murillo et al., 2017). Both man-made combustion sources (automobile emissions and cigarette smoke) and natural processes such as forest fires (Mohamad Firdaus et al., 2019; See et al., 2007) contribute to the increased concentration of PAHs in the environment. The ratios between distinct PAH molecules are employed as diagnostic tools to establish their possible sources, making PAHs excellent markers for resolving PM source contributions (Jamhari et al., 2014; Khan et al., 2016; Liu et al., 2019; Xing et al., 2020). PAHs attached to particles have been shown to be carcinogenic and mutagenic (Hanedar et al., 2014; Murillo et al., 2017; Othman et al., 2021). PAHs have been identified as potential contributors to PM toxicity in a number of studies (Liu et al., 2019; Sulong et al., 2019). Because of its carcinogenic consequences, benzo[a]pyrene (B[a]P) is the most studied and determined (Hanedar et al., 2014; Liu et al., 2019). PAHs can also be acquired through ingestion and cutaneous contact, in addition to inhalation of ambient air. Another conclusion indicated that school students in Northern Thailand were exposed to $PM_{2.5}$ bound PAHs by nondietary intake during a haze episode. It was recommended that the ingestion route of exposure is significant and should not be overlooked (Pongpiachan et al., 2015). As a result, determining the amounts and compositions of PAHs in $PM_{2.5}$ is critical and should be investigated further.

There is new evidence that particulate matter (PM) air pollution can harm people' neurological systems as they age (Bandyopadhyay, 2016; Block et al., 2012; Costa et al., 2014; Lee et al., 2017; Liu & Lewis, 2014). The relationship between the effect of polycyclic aromatic hydrocarbon (PAH) linked to fine PM and cognitive functioning, on the other hand, is mainly unknown (Chen & Schwartz, 2009; Peters et al., 2015; Shehab & Pope, 2019; Suglia, et al., 2008; Xing et al., 2020). As a result, such exposure could be a risk factor for cognitive impairment (Best et al., 2016; Grant, 2012; Peters et al., 2015). Other investigations using urine PAH metabolites found a link between cognitive impairment and PAH metabolites (Chen et al., 2019; Cho et al., 2020). Controlling some of the sources of $PM_{2.5}$, according to a previous study (Bell et al., 2014), could safeguard public health more effectively than regulating particle concentration. As a result, as part of the mitigation approach, a possible reduction in health hazards from the most common sources of $PM_{2.5}$ is desired. Furthermore, this research interacts and strategizes policymaking that is environmentally friendly. A reliable extraction and detection analytical approach is required to understand the level of PAHs in relation to human exposure. This review discussed conventional and new extraction methods as well as several analytical techniques for detecting PAHs in the air.

EXTRACTION AND THE PRINCIPLES OF INSTRUMENTATION

The extraction, purification and detection techniques used to determine PAHs are all dependent on each other. These air contaminants can be sampled using a variety of approaches. The particles are collected using a variety of filters composed of PTFE, quartz/glass (Bates et al., 2008; Hisamuddin et al., 2022; Kim & Kim, 2015), PTFE-coated polystyrene, and polycarbonate (Bates et al., 2008; Hisamuddin et al., 2022).

Clean-up, detection and quantification measures come after the sample and extraction stages. However, because this conventional process is time intensive and requires significant volumes of chemicals as well as a sophisticated technique, it has limitations. The success of other stages and analytical techniques has a significant impact on the extraction strategy chosen (Bates et al., 2008). As a result, a conventional procedure known as pre-concentration and clean-up stage (such as solid phase extraction (SPE) and liquid–liquid extraction (LLE)) would be another option for removing interference and improving PAH detection, as PAHs are normally found in extremely small amounts in nature. Another drawback of the conventional approach is the extensive sample preparation required, which involves numerous manual processes. In short, conventional extraction processes are expensive, labor-intensive, take longer to complete, are easily contaminated and are harmful to the environment. Furthermore, more contemporary hyphenated procedures, while exact and precise, necessitate expensive equipment and an expert operator (Bates et al., 2008).

To improve on the conventional extraction procedure, advanced extraction methods have been developed. Microextraction and miniaturization (Manousi & Zachariadis, 2020) are examples of advanced techniques, with microextraction methods including various solid-phase microextraction (SPME) (flow injection and syringe SPME) and liquid-phase microextraction (LPME) (single-drop and hollow-fiber LPME, dispersive liquid–liquid microextraction, ultrasound/vortex-assisted LPME). Dispersive solid-phase extraction, stir bar/rod/plate sorptive extraction, magnetic solid-phase extraction, fabric-phase sorptive extraction, and pipette tip solid-phase extraction are examples of miniature extraction technologies (Patel et al., 2020). In comparison to conventional techniques, these improvised extraction methods are simple, less time consumption, minimize cost and require less labour during the handling phase (Manousi & Zachariadis, 2020; Patel et al., 2020; Piryaei, 2019). As shown in Table 1, the differences between two extraction approaches, conventional and advanced extraction methods, are summarized.

Table 1. Comparison of conventional and advanced extraction methods

	Conventional extraction method	Advanced extraction method
Level of difficulties	complex	simple
Duration of time	more time consuming	less time consuming
Number of solvent requirements	more	less
Amount of volume samples	higher	lower
Handling procedure	difficult	easy

One of the factors in PAH measurement is the detection technique. Using a range of chromatographic technologies, such as gas chromatography mass spectrometry (GC-MS) and high-performance liquid chromatography (HPLC), several methods for quantifying PAHs in air have been described (Bates et al., 2008; Manousi & Zachariadis, 2020; Patel et al., 2020).

The principle of gas chromatography mass spectrometry (GC-MS)

Chemical mixtures can be separated and the components identified at a molecular level using GC-MS instruments. It is one of the most recommended technologies for analyzing environmental materials due to its precision. The premise of gas chromatography is that when a mixture is heated, it separates into different components. Then, an inert gas, such as helium, acts as a carrier, allowing hot gases to travel through a column. The mixture flows into the mass spectrometry after being separated from the column opening (MS). As thousands of substances are maintained on a computer, MS is a definitive analytical detector (Sparkman et al., 2011). In order to get into the GC, a heated injector is used. Components are separated on a column based on molecular mass and polarity, and then entered the MS source via a heated transfer area in that order. Total ion chromatograms (TIC) and mass spectra of the separated components make up the analytical data.

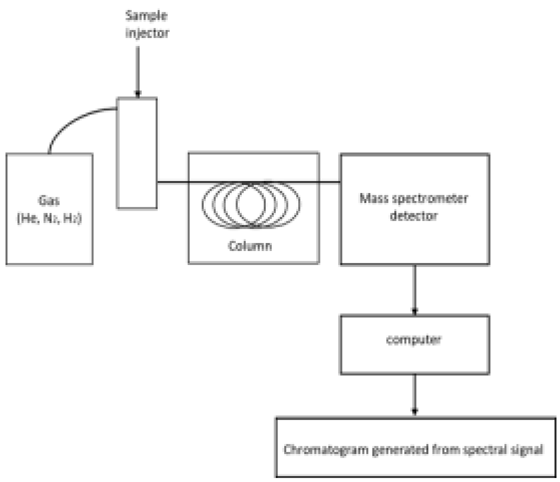

Figure 1. Principle of Gas Chromatography-Mass Spectrometry (GC-MS)

The principle of high-performance liquid chromatography (HPLC)

The HPLC principle is based on the dispersion of analytes between the mobile and stationary phases. The different constituents of the sample will elute at different times in order to achieve sample ingredient separation.

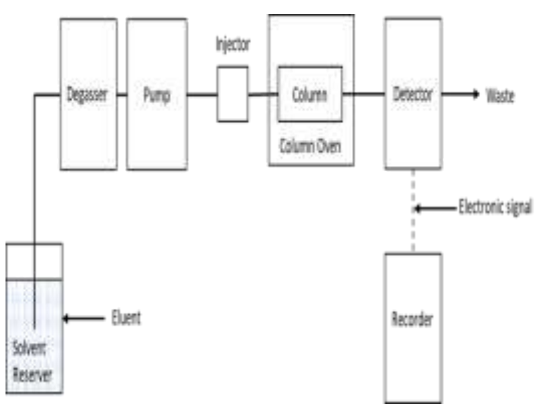

Figure 2. Principle of high-performance liquid chromatography (HPLC)

Comparison between analysis by GC-MS and HPLC

Gas chromatography (GC) is frequently used with mass spectrometry (MS) to generate very powerful GC-MS coupled techniques for the detection of PAHs in air. This GC-MS approach, rather than GC, can increase selectivity by producing yield with lower detection limits (LODs)(Wang et al., 2019).

Both GC-MS and HPLC produced excellent separation of PAHs, allowing for the quantification of each component individually. The GC-MS approach, on the other hand, has been claimed to reduce analysis time by at least two times (Díaz-Moroles et al., 2007). For the measurement of PAHs in food samples, GC-MS is a frequently used analytical equipment, and researchers have used it extensively in their research. This is due to the fact that GC has a higher resolution efficiency than HPLC, and MS has a high selectivity and sensitivity, as well as structural information on PAHs (Lawal, 2017). Because it detects analytes not only by retention time but also by mass spectrum, GC-MS is the most widely used technology for the analytical determination of various organic chemicals, including PAHs. The most common methods for determining PAHs in environmental media are GC-MS and HPLC with UV/fluorescence detectors, out of all the methods discussed. The two were chosen because of their key benefits of great sensitivity and selectivity (Adeniji et al., 2018).

AIR POLLUTION AND COGNITIVE IMPAIRMENTS

Air pollution has been a problem in both developing and developed countries for many years. Due to socioeconomic and anthropogenic activities, air pollution contributes to environmental toxicity among persons living in industrial and urban areas. Because of fewer and looser emission controls, rapid urbanization and industrialization in most developing countries has been reported to cause more severe air pollution than in developed countries (Manisalidis et al., 2020). More than half of the world's population now lives in cities, which are densely populated and have modern infrastructure. According to the World Health Organization (2020), this share, together with the world's aging demographic, is predicted to expand to two-thirds of the global population by 2050. Unfortunately, this urbanization population interacts with the environment, which usually results in air pollution.

In such circumstances, it seems logical to have an impact on human health and quality of life. Individual health has been shown to be significantly impacted by urbanization, particularly in densely populated locations near industrial facilities and transportation infrastructure, according to research. This condition frequently results in poverty and a lack of environmental management (Clifford et al., 2016; Power et al., 2016). Poor air quality is one of the most serious environmental threats to human health and it is quickly becoming the primary indication of whether a city is healthy or not. Not only urbanization is associated with increased pollution but it also has an impact on older people's daily behaviors (Michel, 2020).

According to a previous study, the increased cognitive deterioration observed in the urban group could be attributable to the impact of air pollution on cognitive performance (Shehab & Pope, 2019). More than 80 % of all cities in the globe surpass the WHO's air quality standards. Air pollution has been linked to central nervous system diseases (Block et al., 2012; Calderon-Garciduenas et al., 2011), as well as cardiovascular and pulmonary disease (Calderon-Garciduenas et al., 2011). In children, impaired cognitive function has been associated with low and bad air quality, as well as an increased risk of autism (Volk et al., 2013), however there have been few investigations in the elderly. Other studies have found that persons who live in cities are less likely to get CI than those who live in rural areas (Robbins et al., 2019). They suggested that increasing healthcare services and facilities in cities will promote healthy aging (Beard et al., 2016).

Air quality in Malaysia became a major issue a few years ago, particularly when it came to transboundary air pollution (Azid et al., 2014). The Air Pollution Index (API) is a produced index that closely resembles the USEPA's Pollution Standards Index in terms of delivering clearly understandable information on air pollution levels (DOE, 2020). This estimate is based on the internationally recognized Pollution Standard Index (PSI). Since the year 2017, Malaysia has improved the calculation of the Air Pollution Index (API) by employing six pollution criteria instead of five. As illustrated in Table 2, coarse particulate matter (PM_{10}), fine particulate matter ($PM_{2.5}$), carbon monoxide (CO), ozone (O_3), sulphur dioxide (SO_2), and nitrogen oxide (NO_2) are the six air pollutants that influence the air quality status.

According to API values, air quality is classified into five categories: good, moderate, unhealthy, very unhealthy, and hazardous, with values ranging from 0 to 50, 51 to 100, 101 to 200, 201 to 300, and greater than 300, respectively (DOE, 2020). If the API value, which determines the severity of the atmospheric pollution, is high, it raises health concerns. API readings will allow the public to quickly analyze the state of the air quality in order to take health measures and stay informed about the cleanliness of the environment. API values are usually determined by the concentration of PM, which is the most prevalent pollutant most of the time, particularly during haze in Malaysia.

Table 2. New Malaysia Ambient Air Quality Standard (DOE, 2020)

	Ambient Air Quality Standards		
Pollutants (μgm^{-3})	Averaging time	Interim-2 (2018)	Standard (2020)
PM_{10}	1 Year	45	40
	24Hour	120	100
$PM_{2.5}$	1Year	25	15
	24Hour	50	35
SO_2	1 Year	300	250
	24Hour	90	80
NO_2	1 Year	300	280
	24Hour	75	70
O_3	1 Year	200	180

Previous studies claimed that dirty atmospheric air appears to be a risk factor for cognitive impairment (Cabral-Pinto et al., 2018; Liu et al., 2019). In human and animal research, air pollutants were found to cause CNS illnesses, behavioral impairments, neuroinflammation and neuropathology (Block & Calderón-Garcidueñas, 2009; Lucchini et al., 2012). Few investigations have been done on pre-existing disease conditions, age and crucial times of development that may affect CNS effects in previous research on air pollution (Block et al., 2012). However, there is a gap in understanding of the mechanism of neurotoxicity and the sequences associated with exposure to air pollution in particular. Previous research has consistently focused on PM and O_3 when compared to other air contaminants (Cabral-Pinto et al., 2018; Liu & Lewis, 2014). PM exposure has been shown to cause diffuse deposition of cerebral beta amyloid plaque, hyperphosphorylated tau pre-tangles and peripheral systemic inflammation, which lead to the activation of microglia and astrocytes in the CNS, according to studies (Jankowska-Kieltyka, Roman, & Nalepa, 2021). Other air pollutants, such as CO, SO_2, NO, NO_2 and NOx, have been the subject of limited research (Chang et al., 2014; Clifford et al., 2016). However, the causes underlying cognitive deterioration remain unknown. A previous study found that exposure to various air pollutants might cause general cognitive decline as well as impairment in specific cognitive areas, with O_3 acting as a protective factor (Chen et al., 2021).

O_3 is a potent oxidative pollutant that has a negative impact on human health. In general, O_3 induces neurological harm by inducing the release of free radicals, activating the production of inflammatory cytokines and jeopardizing the blood-brain barrier's integrity. When compared to other airborne pollutants like NO_2 and SO_2, these pollutants are more spatially homogeneous as PM. Precursors to the creation of atomic oxygen, such as nitrogen oxides (NOx) and volatile organic compounds (VOC), contribute to the formation of O_3 (O). The creation of O_3 is the result of the reaction of this atomic oxygen with molecular oxygen (O_2). Because O_3 is a colorless gas with no unpleasant odor, there is likely less awareness of the severity of O_3 pollution, which this review should underline. The majority of data indicating that O_3 has a negative relationship with cognition is backed up by the lack of amyloid plaque growth associated with high O_3 concentrations (Iaccarino et al., 2021). Despite the majority of data pointing to a deleterious impact on cognition, a few epidemiological research (Martínez-Lazcano et al., 2013) found protective effects at low levels of O_3 exposure. Previous research, on the other hand, found a link between higher levels of O_3 and a higher rate of cognitive deterioration (Cerza et al., 2019; Cleary et al., 2018). Furthermore, the findings of connections between various air contaminants and global cognitive function, as well as different cognitive trajectories, have been inconclusive (Kilian & Kitazawa, 2018). Table 3 lists the numerous research, along with a brief explanation of the findings for each one. This review explains how important contaminants in atmospheric air can be used to identify the factors that should be investigated further.

Table 3. Details of studies investigating the relationship between exposure to air pollutants and cognitive functioning

Pollutant agents	Target population	Effects on cognitive function	References
O_3, $PM_{2.5}$	Older adults with MCI or dementia	Higher $PM_{2.5}$ concentrations showed an association with biomarkers of dementia. Yet, higher level of O_3 exposure is not associated with MCI or dementia.	(Iaccarino et al., 2021)
$PM_{2.5}$	Older adults aged more than 65-year-old in North Carolina	$PM_{2.5}$ showed an association with neurodegenerative diseases risks.	(Rhew et al., 2021)
PM	US cohort of older women	PM exposure promotes pathological brain aging.	(Cacciottolo et al., 2017)
PM bound PAHs	Older adults in the United States	Cognitive decline.	(Best et al., 2016)
$PM_{2.5}$ bound PAHs	48 states in US	Cognitive decline.	(Grant, 2012)
PAHs metabolites	US older adults aged more than 65-year-old	PAH exposure is closely associated with increased risk of total disability.	(Chen et al., 2019)
PAHs metabolites	Adult aged more than 50-year-old in the Republic of Korea	Trigger neurodegeneration.	(Cho et al., 2020)
All air pollutants	Taiwanese adults	Specific domains of cognitive functioning affected by all air pollutants. On the contrary, O_3 may be a protective factor.	(Chen et al., 2021)
O_3 $PM_{2.5}$	US older adults	Low O_3 with cognitive decline. Yet no correlation between $PM_{2.5}$ and cognitive function.	(Cleary et al., 2018)
NOx, NO_2, $PM_{2.5}$, PM_{10} and O_3	Rome hospitalized dementia older adults	NOx and O_3 showed positive association with dementia; NO_2 showed negative association with dementia.	(Cerza et al., 2019)

Nitrogen oxide (NO) levels	Older adults Northern Sweden	Showed positive association with vascular dementia and Alzheimer's disease.	(Oudin et al., 2016)
PAHs metabolites	Adults were recruited from a coke oven plant.	No association effects on cognitive function.	(Du et al., 2020)

CONCLUSION

The application of various analytical techniques for determining the presence of PAH in air was examined in this review in order to determine which is the best. This review adds to our understanding of the key air pollution agents that contribute to the development of cognitive impairment, particularly in the elderly. These findings suggest that airborne hazardous contaminants linked to cognition should be considered in public health policy decisions, as well as updating individual lifetime risk of getting MCI. This review will be able to address people's desires for senior folks to live healthy lifestyles. Regulatory steps for decreasing air pollution exposure would support major health advantages in advance if the data supporting this is further shown.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

AA: Suggested the work protocol, analyzed & interpreted the data, revised the manuscript. AM, ASO and SNS: Conceived & designed the framework, contributed materials, analysis tools or data, analyzed & interpreted the data. NAA: Performed the data gathering, analyzed, wrote the paper. All authors read and approved the final version.

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