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Review Article

Toxicokinetics of Major Anthropogenic Indoor Air Pollutants and Their Effects on Human Health: A Review of Literature

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Abstract: Research studies have shown that about 90% of the time is spent in indoor environments (homes, hospitals, schools, offices, restaurants and subways). During the past decade, many studies have been conducted to assess indoor air quality in school environments. A large number of indoor air pollutants have been measured including volatile organic compounds, nitrogen oxides, sulphur dioxide, carbon dioxide, carbon monoxide, bioaerosols and particulate matters. In most low and medium-income countries, biomass fuel-based cooking and heating is considered to be a significant source of the household as well as ambient air pollution formaldehyde from clipboard and hydrocarbons from paints, cleaners and furnishings (anthropogenic sources). A wide range of acute and chronic diseases are now associated with exposure to air pollution, starting from diabetes mellitus, declining cognitive functions, and obstructive pulmonary diseases, haematopoietic diseases, to cardiovascular disease.

Keywords: Anthropogenic, pollutants, indoor air quality, health.

INTRODUCTION

Indoor air pollution is a serious health problem as it causes about 4.5 million annual deaths globally resulting from pneumonia (12%), stroke (34%), ischaemic heart diseases (26%), chronic obstructive pulmonary diseases (22%) and lung cancer (6%) [1 1, 2-4].

Research studies have shown that about 90% of time is spent in indoor environments (homes, hospitals, schools, offices, restaurants and subways) [5, 6-8].

During the past decade, many studies have been conducted to assess the indoor air quality in school environments. A large number of indoor air pollutants have been measured including volatile organic compounds, nitrogen oxides, sulphur dioxide, carbon dioxide, bioaerosols and particulate matters (PM) [9-12].

Pollutants occur in the form of gases and particulates from biological/natural and anthropogenic (human-made) processes released into the atmosphere. The greatest threat to indoor air pollution occurs in settlements (urban and rural), as many people continue to rely on traditional fuels for cooking and heating. Studies have also indicated that high air pollution levels have substantial effects on human health and infant mortality [13,14].

Previous studies estimated that residential biomass emissions make up more than 40% contribution to the PM2.5 (particulate matter less than 2.5um diameter) and 50% contribution to black carbon /particulate organic matter emissions in south Asia, East Asia, Eastern Europe and East Africa [15].

Globally, 91% of the total population is estimated to breathe polluted air while both household and ambient air pollution is responsible for 7 million deaths in 2016. The World Health Organization has also estimated that about 3 billion people are using polluting fuels, which are primary sources of household air pollution [1].

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In most low-and medium-income-countries (LMIC), biomass fuel-based cooking and heating is considered to be a significant source of household as well as ambient air pollution [16, 17].

Important indoor air pollutants include; carbon monoxide, carbon dioxide, radon, bacteria, (including legionella and fungi), PM [10], nitrogen dioxide, ozone, volatile organic compounds, formaldehyde and benzene [18, 19].

By-products of chemical reactions are discharged into the atmosphere, altering its chemical composition and spreading fine particulates; some of which, if inhaled, can attack the lung tissue, and may cause respiratory problems and/or death. Acute respiratory infections are among the leading causes of diseases worldwide and have been linked with exposure to pollutants from domestic biomass fuels in developing countries [20].

Justification of the study

Anthropogenic indoor air pollution has continued to constitute a major public health danger worldwide. Unfortunately, the current trend is likely to end anytime soon owing to the continuous global economic downturn which encourages the generation of indoor air contaminants. A large number of public health diseases are due to indoor air pollution and a lot of resources have been consumed in addressing these health challenges. Policies on the regulation of these activities that result in indoor air pollution are sadly weak.

This review aims to look at current literature on the toxicokinetics of major anthropogenic indoor air pollutants and their implications on public health globally.

Classification of air pollutants

The United States Environmental Protection Agency (EPA) categorizes air pollutants into three major classes.

1. Biological- these include bacteria, dust mites, dander, mold and pollen
2. Chemical – these are volatile organic compounds present in household products and building materials using during construction such as lead, radon.
3. Combustion-these include carbon monoxide (CO), nitrogen dioxide (NO2) polycyclic aromatic hydrocarbons (PAHs), and formaldehyde, benzene [21].

Anthropogenic sources of major air pollutants in indoor environment

The source of indoor air PM2.5 includes cooking, smoking of cigarettes, and resuspension during indoor activities [22].

The major sources of benzene in indoor setting are cigarette. Benzene is also used in the manufacturing of rubber, plastics, resins, pesticides and lubricants [23].

Heavy metals (lead, manganese, copper arsenic, chromium, cadmium are also absorbed by dust particles and can easily be inhaled, ingested or absorbed via dermal contact. Indoor dust also accumulates in the filters of air conditioning units with a lot of heavy metals [24, 25].

Building materials can release a wide range of pollutants such as formaldehyde from clipboard and hydrocarbons from paints, cleaners and furnishings [21].

Other indoor sources of pollutants include; heating systems, ventilation systems, air conditioning, environmental tobacco smoke, fossil fuels for home cooking, gas stoves, wood stoves.

The hazard of anthropogenic domestic sources originate from low quality of fuels (coal, biomass, or even refuse) used for heating during winter [9, 12, 26].

Dampness and high relative humidity indoors can be caused by high humidity outdoors, water leakage into buildings, leakage of pipes, flooding, water infiltration into building materials and moisture resulting from human activities such as cooking and bathing. Dampness can also occur as a result of water vapour condensation in building structure or on surfaces indoors. Dampness is also associated with mould exposures. Building dampness is associated with increased risk of respiratory symptoms such as cough, wheeze, asthma and respiratory infections [11].

Bond *et al*., 2004 reported that 20% of global black carbon emissions are due to cook stove emission world-wide. The known sources of indoor-generated particles are dependent on different factors, example – air exchange rate, building materials, building age, floor material and family and domestic characteristics [27].

The hazard of anthropogenic sources originate from low quality of fuels (coal, biomass, culm or even refuse) used for heating during winter [12, 28].

Environmental Tobacco Smoke (ETS) is considered one of the main sources of benzene. Benzene emissions from cigarette smoking range from 430 to 590ug per cigarette. Indoor benzene is also associated with human activities such as cleaning, painting, use of consumer products and mosquito expellants [29-31].

Carbon monoxide is produced by incomplete combustion of carbonaceous fuels such as wood, petrol, coal, natural gas, kerosene. Anthropogenic emissions are responsible for about two thirds of the carbon

monoxide in the atmosphere. Tobacco smoke, exhaust from motor vehicles operating in attached garages and incense burning are also major sources of carbon monoxide [32, 33].

Indoor sources of formaldehyde include furniture and wooden products containing formaldehyde-based resins such as particle board, plywood and medium-density fibreboard, insulting materials, textiles, paints, wall papers, detergents disinfectants, soaps, shampoos, nail vanishes and insecticides, candle, smoking, cooking or incense burning[34].

- Indoor sources of nitrogen dioxide include-fuel burning, stoves (wood, kerosene, natural gas, propane) tobacco use. The distance of building from roadways appears to have an impact on indoor nitrogen dioxide levels [35].
- Indoor air is contaminated by polycyclic aromatic hydrocarbons which come not only from infiltration or intrusion of outdoor air but also from indoor emission sources such as smoking, cooking, domestic heating and fuel stoves and open fireplaces as well as from incense and candle emissions [36].

Effect of some indoor air pollutants on human health

A wide range of acute and chronic disease are now associated with exposure to air pollution, starting from diabetes mellitus, declining cognitive functions, and obstructive pulmonary diseases as well as cardiovascular disease that lead to higher premature mortality and morbidity [37, 38].

Pollutants with strongest evidence of public health concern include particulate matter, ozone, nitrogen dioxide and sulphur dioxide [39]. Airborne particles are known to pose a major health risk to susceptible population groups such as patients with chronic respiratory or cardiovascular disease, asthmatics, the elderly and children [40, 41].

Microbes and non-infectious bioaerosols have been the best-studied contaminants of indoor air and they can evoke a large variety of adverse health effects such as respiratory infections, asthma and clusters of autoimmune disease [23, 42].

The degree of PM2.5-related toxicity mainly depends on its chemical components, including water-soluble organic ions such as sodium, potassium, calcium, ammonium, nitrate, chloride and sulphate. These were found to be the main components of PM2.5 and act as surface-active reagents, which increase toxicity of noxious organic substances [43]. The other main components that determine toxicity of PM2.5 are metallic elements, such a lead, manganese, copper, chromium, arsenic and cadmium. These can cause detrimental health impacts to human respiratory, cardiovascular and nervous system [38, 44, 45].

The greatest threat of indoor air pollution occurs in both rural and urban settlements, as many people continue to rely on traditional fuels for cooking and heating. Studies have also indicated that high air pollution levels have substantial effects on human health and infant mortality rates. As particulates (for instance dust, smoke, vehicular emissions and other small suspension) are released into air, they negatively impact air quality by polluting the air [13, 14].

Air pollutants and cytotoxic cell death

Apoptosis is one of the possible consequences of acute or chronic exposure to air pollutants and various toxicants such as particulate matters (PM), metals and pesticides are capable of targeting the mitochondria directly or indirectly [46,47].

The induce cytotoxicity by uncoupling ATP synthesis and the mitochondrial H+ gradient. Metals and water-soluble fractions of PM are also known to cause inflammation and cancer mostly due to DNA damage as a consequence of reactive oxygen species (ROS) generations. Indeed carcinogenic metals, namely As, Cd, Cr, Nc) promote apoptosis with DNA base modifications, strand breaks and rearrangement [48]. In addition, PM containing high levels of non-carcinogenic metals (i.e. cobalt, lead, iron and zinc) were often shown to provoke ROS production (e.g. H_20_2), leading to apoptosis through the mitochondrial pathway [49-52].

Toxicology of some indoor air pollutants

Benzene

Mechanism of action of benzene toxicity: At high exposure levels, benzene acts as a narcotic that depresses the central nervous system and causes cardiac sensitization [53]. Benzene acts mainly as a clastogenic agent, rather than causing point mutations. The phenolic metabolites formed in the liver can be transported in the blood to the bone marrow, a major site for toxic effects, and be oxidized to the highly reactive quinines by myeloperoxidases in the marrow. The reactive quinones can cause clastogenic damage to the DNA, such as mitotic recombinations, chromosome translocations and aneuploidies [54]. Benzene oxide and its adducts have been detected in the blood of workers exposed to benzene [23, 37]. Metabolites of benzene activate oxygenated radical species which can lead to DNA changes and the formation of hydroxylated bases such as 8-hydroxy-2- deoxyguanosine [56]. Death is often attributed to asphyxia, respiratory arrest or central nervous system depression [23].

Benzene is a genotoxic carcinogen in humans and no safe level of exposure can be recommended. It is present in both indoor and outdoor air. However, the

indoor concentrations are generally higher than their concentrations in outdoor air owing to the infiltration of benzene present in outdoor air and the existence of many other indoor sources [56].

Carbon monoxide

Kinetics and metabolism of carbon monoxide

It has been assumed that the effect of carbon monoxide exposure is due to hypoxic effects. Carbon monoxide enters the body via inhalation and is diffused across the alveolar membrane with nearly the same ease as oxygen. Carbon monoxide is first dissolved in blood, but is quickly bound to haemoglobin (Hb) to form COHb which is measured as the percentage of haemoglobin so bound, the binding of carbon monoxide to haemoglobin occurs with nearly the same speed and ease as with oxygen binds to haemoglobin, although the bond for carbon monoxide is about 45 times as strong as that for oxygen [21, 39].

This carbon monoxide competes with oxygen for haemoglobin binding sites but unlike oxygen, which is quickly and easily dissociated from the haemoglobin bond, carbon monoxide remains bound for a much longer time. In this way, COHb continues to increase with continued exposure, leaving progressively less haemoglobin available for carrying oxygen. The result is arterial hypoxaemia. Another effect of COHb is to increase the binding strength of oxygen to haemoglobin, thus making the release of oxygen into tissue more difficult [57]. This later effect is quantitatively described as a leftward shift in the oxyhaemoglobin dissociation curve, proportional to the COHb level [32, 58].

Formaldehyde

Kinetics and metabolism of Formaldehyde

Absorption: Owing to its solubility in water, formaldehyde is rapidly absorbed in the respiratory and gastrointestinal tracts and metabolized. More than 90% of inhaled formaldehyde gas is absorbed and rapidly metabolized to format in the upper respiratory tract [59].

It has been shown that when formaldehyde is mixed with particles, more of it is retained by the respiratory tract than when it is inhaled alone [58] **(10).** Formaldehyde and its metabolites in contact with human skin causes allergic and contract dermatitis. Ge et al demonstrated that exposure to formaldehyde can lead to haematopoietic toxicity by disrupting the haematopoietic [60]. Long-term exposure to formaldehyde at high doses can have toxic effect on the bone marrow, brain, lungs, nasopharynx and the skin [60].

Distribution

Following a 6-hour inhalation exposure of rats to formaldehyde, about 40% of the inhaled compound was eliminated as expired carbon dioxide over 70-hour period. 17% was excreted in the urine, 50% was excreted in the faeces and 35-39% remained in the tissues and carcass, indicating that absorbed formaldehyde and its metabolites are rapidly removed by the mucosal blood supply and distributed throughout the body [61].

Rodents excreted about 6.6% of the dermally applied dose in the urine over 72hours, while 21-28% was collected in air traps, likely due to the evaporation of formaldehyde from the skin [62].

Metabolism and elimination of formaldehyde

Formaldehyde reacts rapidly at the site of contact and is swiftly metabolized by humans by erythrocytes, which contain the enzymes formaldehyde dehydrogenase and aldehyde dehydrogenase [34,59,60,62].

Formaldehyde reacts virtually instantaneously with primary and secondary amines, thiols, hydroxyls and amides to form methylol derivatives. Formaldehyde acts as an electrophile and can react with macromolecules such as DNA, RNA and proteins to form reversible adducts of irreversible cross-links [34, 59].

Formate, the product of formaldehyde is incorporated in normal metabolic pathways or further oxidized to carbon dioxide.

The primary metabolism system for formaldehyde involves an initial spontaneous reaction with glutathione to form S-hydroxymethyl glutathione, followed by reaction facilitated by alcohol dehydrogenase to convert the intermediate to 5-formylglutathione. This intermediate is then further metabolized by 5-formylglutathione hydrolase to yield formate and reduced glutathione [52, 60].

Nitrogen dioxide

Kinetics and metabolism of nitrogen dioxide

Nitrogen dioxide is a free radical, it has the potential to deplete tissue antioxidant defences and as a consequence, cause injury and inflammatory conditions in humans.

Immunofluorescence studies show that nitrogen dioxide-exposed cells exhibited marked increases in the levels of nitrite (used as an index of nitric oxide), IL-8, IL-IB and TNF-α, thereby triggering inflammation [17, 18].

Polycyclic Aromatic Hydrocarbons

Toxicokinetics of Polycyclic Aromatic Hydrocarbons (PAHs)

Absorption: The major route of exposure to PAHs in the indoor environment is through the lungs

and the respiratory tract after the inhalation of PAH-containing aerosol and particles. PAH in particles follows biphasic absorption kinetics in the lungs. The absorption kinetics depends on the site of deposition in the respiratory tract. A fraction of PAHs in the diesel particles is quickly absorbed into circulation through Type1epithelial cells in the alveolar region and metabolized rapidly. In perfused rat lung, the absorption kinetics of PAHs is dose-dependent [17, 63].

Distribution: PAHs are rapidly and widely distributed in the body. Lipophilic compounds easily pass biologically membranes. Detectable levels of PAHs can be observed in most tissues in minutes to hours after exposure, irrespective of the exposure route PAHs undergo hepatobiliary clearance [17,18].

Excretion: The faeces are the main route of excretion of high molecular weight PAHs and their metabolites. Biliary and enterohepatic circulation are significant and increase the concentrations of metabolites and parent compounds in the GIT. Urine is the other main excretion route [18].

Metabolism: Metabolism is crucial for the toxicity of PAHs. Reactive intermediates and metabolites are formed that cause the toxicity and carcinogenicity. Three principal pathways activate PAHs for toxic intermediates and further metabolism:
i. Via dihydro diol-epoxide formation,
ii. Via radical cation formation and
iii. Via the O-quinone pathway [7, 17]

The key enzymes for PAH metabolism are Cyps (cytochrome P450) and epoxide hydrolase. Genetic polymorphism may contribute to the capacity to metabolize PAHs and affect toxicity [17].

CONCLUSION

Anthropogenic chemical pollution is of major concern as their sources are increasing in number and concentration with the increase in global human population and the consequent increase in energy demand. Pollutants occur in the form of gases and particulates from natural and anthropogenic (human-made) processes released into the air.

A growing body of evidence has indicated that air within homes and other buildings can be more seriously polluted than the outdoor air even in the largest and most industrialized cities.

It has been found that people spend approximately 90% of their time indoors. Thus, for many people, the risks to health from exposure to indoor air pollution may be greater than risks from outdoor pollution.

Various diseases like diabetes mellitus, chronic obstructive pulmonary diseases, cardiovascular disease, declining cognitive functions, haematopoietic diseases and bronchial asthma are associated with indoor air pollution from various anthropogenic sources.

Contribution of the authors

OCC conceptualized and designed the work and also drafted the manuscript. AGC, OED and ES critically reviewed the draft manuscript for intellectual content. The final draft of the manuscript was read and approved by all the authors before the submission.

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