Impact of Air Pollution on Health: A Review

Pragya Sourabh, Vivek Singh & Bhutoo Ram

Faculty of Science
Mansarovar Global University, Sehore (Madhya Pradesh)

Abstract: Today's developed world is very concerned about air pollution because it represents a substantial toxicological risk to both human health and the environment. Through a variety of anthropogenic and natural processes, hazardous substances escape into the environment and endanger human health. The progressive transformation in the atmosphere's composition over the last century has been caused by more frequent usage of fossil fuels. Though many other industrial processes, emission sources, and motor vehicles were the two biggest contributors to air pollution. Air pollution has a negative influence on human health by both chronic and acute effect, having an impact on many organs and body systems. It increases the risk factor from acute upper respiratory irritation to chronic respiratory and heart disease, acute respiratory infections and lung cancer in children and chronic bronchitis in adults, threatening post heart and lung disease, or asthmatic attacks. A reduction in life expectancy and early death have also been associated to both long- and short-term interactions of particulate matter. The objective of this review is to focus on the causes and air pollution sources, and their devastating impacts on human health. The paper has a thorough description of air pollution and its sources and highlighting its worse impact of air pollution on health of every individual and wellbeing.

Keywords: Air pollutants, Human health, Infections, Respiratory disease, Toxicological.

Introduction:

For many years, air pollution has been a reason for concern. The first comprehensive scientific analysis on smoke mitigation was established by the Mellon Institute in Pittsburgh, Pennsylvania, USA, and led to regulations intended to reduce the harmful effects of smoky air (smoke) [1]. For illustration, in the United States, the Environmental Protection Agency suggested that activities to decrease diesel engine emissions could result in 15,000 less cases of heart attacks, decreasing death rate approximately 12,000, and 8,900 fewer hospital admissions every year [2]. The effects of air pollution on the pulmonary, cardiovascular systems, and among many other organs and systems. The community were very concerned about pollution from particulate matter (PM) and ozone (O3). High amounts of air pollution have a variety of negative health effects. It raises the risk of respiratory infections, heart problems, and lung cancer. Long-term and short-term exposure to air pollution has been associated to detrimental health impacts. Serious illness makes people more susceptible to negative consequences. The vulnerable include the young, the old, and those living in poverty. Tiny PM2.5 particles that penetrate deeply into your lungs and are directly connected to an increase in premature mortality are the most hazardous pollutants for your health.

The effects of air pollution on health have been the subject of extensive research in recent years. Exposure to pollutants like ozone and airborne particulate matter has been linked to an increase in mortality and hospital admissions from cardiovascular and respiratory diseases. Different human activities, such as power plants, residential fuel usage, vehicle traffic, industry, and all contribute to the emission of air pollutants. It becomes more widely recognized that implementing pollution reduction techniques may have significant positive effects on health.

Source of causing pollution:

There have been reports of a wide range of air pollutants, each of which has its own environmental persistence, emission traits, and capacity to spread over long or short distances, specific chemical qualities, reactive parameters, and possible health impacts on people or animals like in Table 1. They may be divided into four groups, although, since they share several characteristics:

- Persistent organic pollutants
- Gaseous pollutants
- Particulate Matter
- Heavy metals

Table 1. Sources of pollutants and their impact on human health

Types of pollution sources	Effects on the human body
Nitrogen oxides (NO, NO2)	hypoxia, a negative impact on the respiratory system
Carbon dioxide (CO2)	Headache, excessive breathing, difficulty in breathing, loss of vision, vomiting, increased pressure, and a faster heart rate
Volatile organic compounds (VOCs)	carcinogenic
Ozone	respiratory tract irritation, infection, and bronchial and lung damage
Particulate matters	Carcinogenic, irritating effects and allergic
Microorganisms	Pneumonia, bronchitis, and allergic reactions (runny nose, skin rashes, sneezing, and asthma)

Persistent organic pollutants (POPs):
POPs are essentially hydrophobic and lipophilic compounds. They effectively segregate to solids, particularly organic materials, in soils and aquatic systems, avoiding the aqueous phase. Importantantly, POPs tend to transform into gas at ambient temperatures. Hence, they are sensitive to breakdown mechanism in the air, they may volatilize from water bodies, soils and plants into the atmosphere and travel great distances before being re-deposited. Ingestion is the frequent main method of pollutant absorption since air pollution greatly adds to the contamination of water and food [3]. Pesticides, as well as dioxins, furans, and PCBs, are among them. Generally, PCDFs (polychlorinated dibenzo-furans) and PCDDs (polychlorinated dibenzo-dioxins) are referred to as "carcinogens," although PCBs (polychlorinated biphenyls) are referred to as "dioxin like compounds" and can act similarly in terms of dioxin-type toxicity [4]. Dioxins are formed whenever material containing chlorine (like plastics) are burnt and when combustion is incomplete. Dioxins are airborne pollutants that deposit on soil and water but do not pollute groundwater supplies because they are water insoluble. Due to their capacity to be securely connected to lipids, many dioxins in plants originate from air, dust, or pesticides and enter to the food chain.

Gaseous pollutants:
The principal cause of gaseous pollutants, significantly alter the composition of the atmosphere, and the burning of fossil fuels [5]. Nitrogen oxides are released as NO, which combines quickly with ozone or other airborne radicals to generate nitrogen dioxide. Portable and static combustion sources are the principal anthropogenic sources of pollution. Moreover, sunlight stimulates a sequence of process involving NO_2 and volatile organic molecules which results in the formation of ozone in the lower atmospheric layers.

On the other hand, incomplete combustion causes the production of Carbon. While mostly natural sources of Sulphur dioxide are volcanoes and seas, anthropogenic SO_2 is produced by the burning of sulfur-containing fossil fuels (mostly coal and heavy oils) and the smelting of sulfide-containing ores. The latter account for only 2 percent of all pollutants. Finally, VOCs (volatile organic compounds) are a major indication of compounds that fuel combustion, particularly processes for energy generation and road transportation, which are the main source of emissions. This classification of substances contains chemical species with an organic character, including benzene. Even while many gaseous pollutants are absorbed and primarily impact on the respiratory system, they may also cause cancer (CO, benzene) and hematological issues.

Particulate matter:
When gasoline, wood, coal, diesel fuel was burnt, a complex combination of solid and liquid particles suspended in air known as Particulate matter (PM). These pollutant particles were degraded into the environmental air. Moreover, it is developed when organic compounds and nitrogen oxides interact chemically in the atmosphere. Particulate matters may also come from cattle as soot, fly ash, and cement dust and from vegetation as pollen, spores, salt spray, and soil erosion. Cars, vehicles, and coal-fired power plants are seemed to contribute to the production of particulate matter in large cities.

Children and young adults are susceptible to allergy disorders including asthma and allergic rhinitis. Such individuals' exposure to certain aeroallergens, such pollens, causes a cascade of immunological alterations that eventually manifest as asthma symptoms. It is now well accepted that increasing air pollution has a detrimental influence on pollen generation, which has a negative impact on the prevalence and severity of allergic asthma. Allergic signs and symptoms can include a painful throat, heaviness in the chest, a persistent cough, and burning eyes. They may also cause asthma or cause early mortality, especially in senior people who already have a condition [6,7]. Furthermore, those who indulge in outdoor activity bear a greater risk since exercise increases the quantity of these matter that enters the airways. A person's risk is also higher if they have an illness (such as malnutrition or diabetes mellitus) [8-10]. Ristovski et al. provided a thorough analysis of diesel PM on Air pollution and lung illness and concluded that its exposure enhances the chance of higher risk [11].

Table 2. (EPA) Environmental Protection Agency terminology for particle sizes

EPA description	Particle size
Ultrafine	$d_{pa} < 0.1$ mm
Supercoarse	$d_{pa} > 10$mm
Fine	$0.1 < d_{pa} < 2.5$ mm
Coarse	$2.5 < d_{pa} < 10$mm

Heavy metals:
Mercury, lead, manganese, chromium, silver, nickel, vanadium, and cadmium are examples of fundamental metal elements. They can also be transported by air. They come from a variety of places, including industrial facilities, wastewater discharges, and combustion. They are necessary to sustain the regular metabolic processes and enter human bodies as trace elements. However, they may become poisonous at larger (albeit still quite low) doses [12]. Most of the heavy metals are harmful because of their propensity to bio-accumulate in living things. The process by which a chemical's concentration in a biological organism increases with time relative to that chemical's concentration in the environment is known as bioaccumulation. When substances are eaten, they quickly build up in organisms, accumulating faster than they can be eliminated or digested.

Impact of air pollutants on human health:
Every component of air pollution is harmful to human health, but ambient particulate matter (PM) has shown to have the worst effects because it contains and transmits a wide variety of toxic substances into the respiratory tract, and because the pollutants potential damage is inversely correlated with its diameter aerodynamically [13,14]. Although fine and micro-pollutants can enter to the alveoli in lung more deeply and maybe enter the blood vessels, granulated PM is maintained in the nasal cavities and upper airways after inhalation [15].

PM susceptibility is associated with an increase in mortality risk in now-a-days as well as in the future. According to several studies and meta-analyses. The effects of prolonged exposure have been evaluated in short-term studies have related death rates to daily changes in air pollution levels [16]. According to estimations, the absolute relative increase in risk for all-cause mortality is linked to short-term exposure range of PM from 0.4 percent to 1.5 percent per rise in coarser PM_{10} of 20 imperial gallon per meter cube and 0.6 to1.2 percent per increase in tiny $PM_{2.5}$ of 10 lg/m3 [17]. These increasements are even more pronounced in southeast Asian nations, notably China and India, where residents are subjected to very high levels of air pollution because of their quickly rising economies and dense populations [18,19].

According to a 2010 statement from the American Heart Association, 10 imperial gallon per meter cube increase in average $PM_{2.5}$ consumption results in an estimated 10 percent increase in all mortality rate occurrence [20]. Furthermore, the Harvard Six Cities Study's prolonged follow-up from 1974-2009 revealed a 14 percent of elevated risk of all-cause death [21].

Particulate matter ($PM_{2.5}$) effects on mortality are roughly two times greater than the previously found estimates in the European Study of Cohorts for Air Pollution Effects (ESCAPE) network of twenty-two European cohort studies (more than 300,000 subjects), and the association persists even among subjects exposed to annual mean $PM_{2.5}$ concentrations below 15 imperial gallon per meter cube [22]. In accordance with the Improving Knowledge and Communication for Decision-Making on Air Pollution and Health in Europe project, which was conducted in 25 European cities, living up to the highly ruled applicable, WHO Air Quality Guidelines for PM2.5 (annual mean no higher than 10 Imperial gallon per meter cube) resulted in an additional one year ten months (median 5.8 months) of life expectancy at the age of thirty [23].

Similarly, research done in the Italian Lombardy area by Baccini et al., that a 20 percent decrease in PM_{10} would alleviate the burden of short-term mortality by more than 30 percent [24]. In contrast to the correlation between outdoor air pollution and all-cause mortality, other studies distinctively demonstrated the relation between this and a variety of human disorders [25]. Increased mortality and hospital admission from respiratory and cardiovascular disorders are the most reliable connections.

Impacts of air pollution on various systems and organs:
Air pollution affect nearly every organ system through a complex interaction of increased oxidative stress, systemic inflammation, and immune dysregulation. Air pollution can affect almost every organ in the body. Some air pollutants can be absorbed through the lungs and circulate throughout the body due to its small size, which can cause carcinogenicity and systematic inflammation. Air pollution is a risk including all mortality and for any specific disease either acute or chronic disease. Chronic obstructive pulmonary disease, ischemic heart disease, lung cancer, stroke, cataract, pneumonia are the specific disease outcomes which are most strongly associated with exposure to air pollution.

The exposure to air pollution and a higher risk for adverse pregnancy outcomes, such as low birth weight and small for gestational age, as well as various malignancies, diabetes, cognitive decline, and neurological disorders. The children, elderly, and pregnant women are especially susceptible to diseases brought on by air pollution. A person's vulnerability to air pollution is also influenced by genetics, comorbidities, diet, and sociodemographic variables.

Cardiovascular System:
The binding of carbon monoxide changes the structure of hemoglobin and lowers its ability to transport oxygen [26]. This decreased oxygen availability have an impact on the functioning of several organs, particularly those with a high oxygen need, including the brain and heart, which may lead to disorientation, delayed reflexes, and a lack of attention. Particulate matter also causes systemic inflammatory responses that impact blood coagulation in contrast of pulmonary inflammation [27]. Angina or even myocardial infraction can result from obstruct (cardiac) blood arteries that are caused by air pollution's effects on the lungs and blood coagulation [28]. Due to the heavy metal contamination, specifically mercury, nickel, and arsenic, inhibits hematopoiesis, symptoms including tachycardia, elevated blood pressure, and anemia have been observed [29]. The increased mortality from ischemic heart disease has been related to dioxin exposure in epidemiologic studies, and heavy metals have been proven to raise triglyceride levels in mice [30].

Respiratory System:
Pollutants are absorbed through the airways, which may cause pulmonary diseases. For example, any of the three respiratory compartments—tracheobronchial, alveolar, and extra thoracic—can receive PM deposition [31]. Particles having a diameter more than 10 millimeter (coarse particulates) are deposited in the extra thoracic area, those between 5 and 10 millimeters are deposited in the tracheobronchial area, and those with a diameter less than 2.5 millimeter (fine particles) are deposited in the alveolar area (Fig. 1) [32].

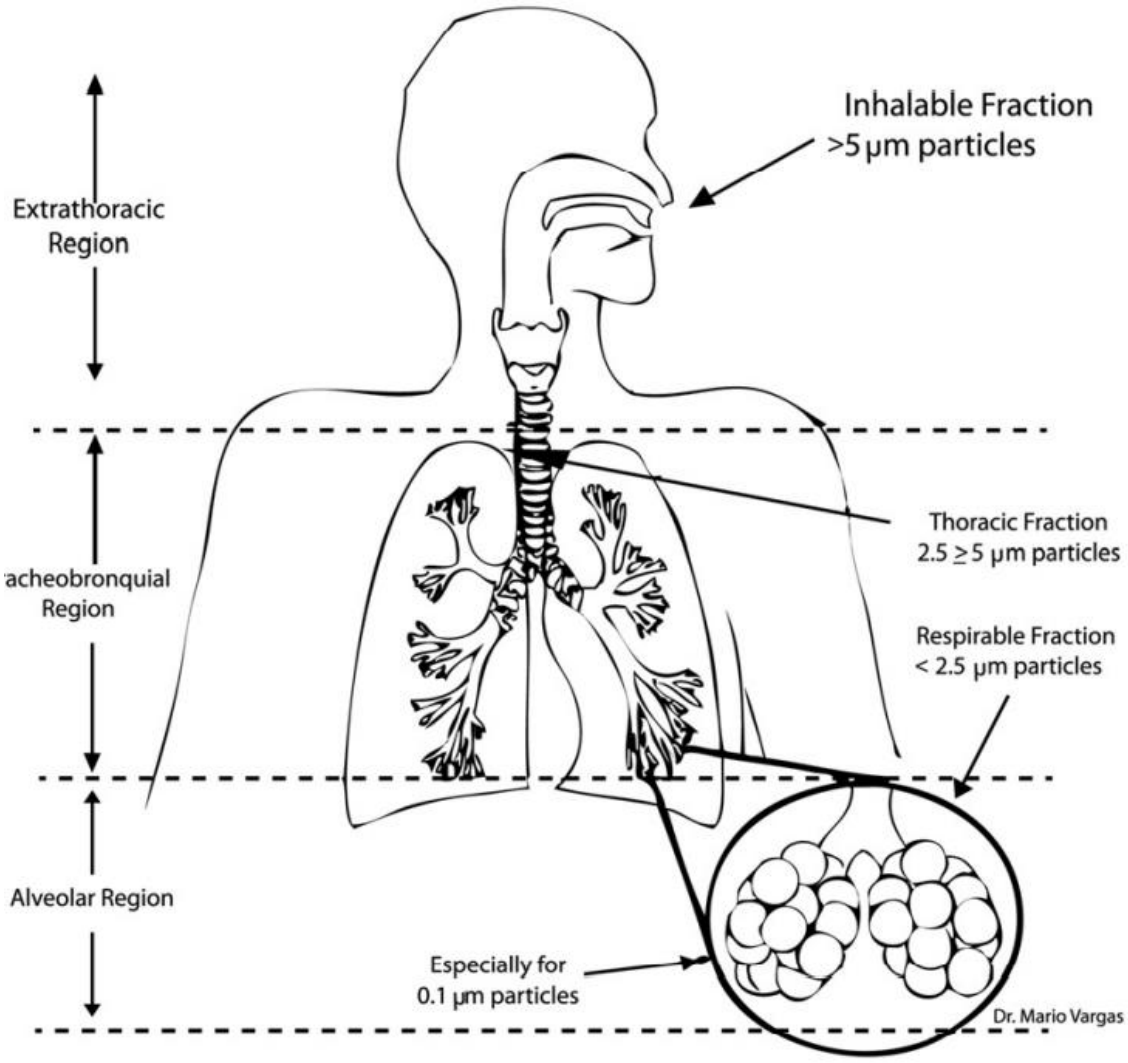

Figure 1. Particle spatial concentration in the human respiratory system.

The overall deposition percentage is higher for women than that for men between 3 to 5 millimeter in diameter [33]. Particles that enter the tracheobronchial and alveolar areas are those, whose potential health implications are most concerning [34]. When compared to healthy individuals, with recent or pre-existing respiratory diseases may also have higher deposition rates [35]. According to certain theories, micro particles (particles with a diameter of less than 0.1 millimeter) are more harmful than bigger particles because they could cover more of the alveolus. Phagocytosis of fine particulate matter by alveolar macrophages is one method of the host defense (Fig. 2). Ultrafine particles, on the other hand, overwhelm macrophage phagocytosis because of their tiny size, leading to enhanced penetration and harmful consequences in other organs (such as the brain, heart, bone marrow, etc.) [36, 37].

According to toxicological research, axon's transport particles from the nasal mucosa to the olfactory bulb in the brain [38, 39]. Cooking (in ovens, toasters, fryers, and barbecues), cleaning (vacuuming, dust, sweeping). According to Ozkaynak et al., cooking generated micrograms per minutes of particulate matter [2], with the fine fraction accounting for 40 percent of the total pollutants [40]. Once within the body, pollutant particles have an impact on several organ systems.

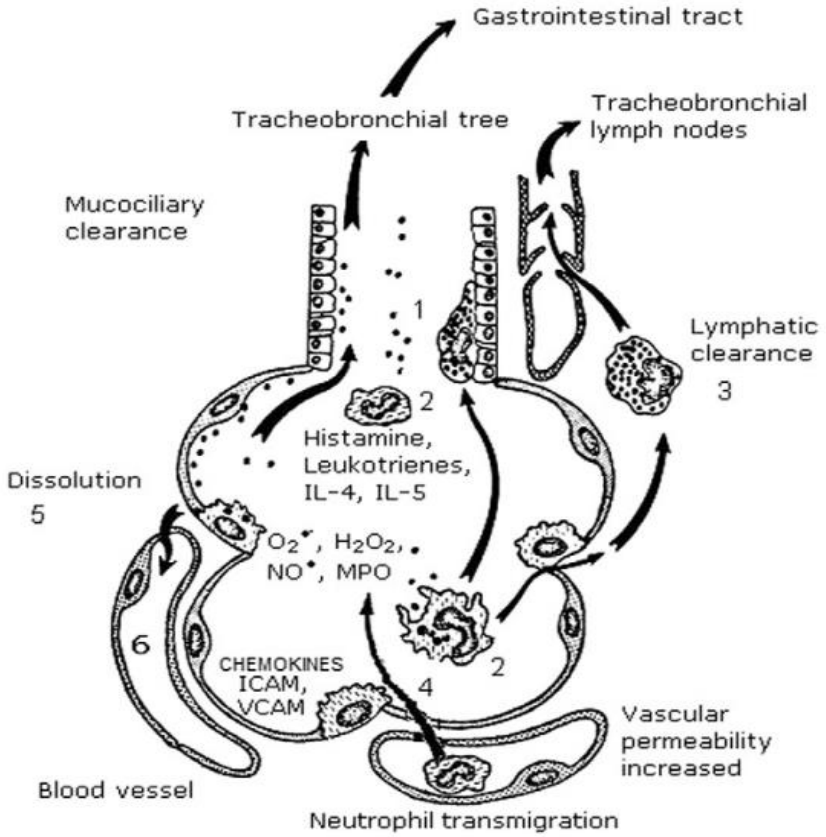

Figure 2: Particle accumulation in the alveoli and cell activation, the mucus layer has the potential to entangle and release particles that have collected in the tracheobronchial area (1); Alveolar macrophages phagocytose molecules throughout the lymphatic drainage system, may inhibit phagocytosis and cause inflammatory mediators to be released (2, 3); Additionally, neutrophil chemoattractant factors release reactive oxygen and nitrogen species as a result. (4); For instance, metals are soluble particle components that may cross the epithelial barrier and enter other organs, where they may cause harm (5); ICAM is also known as interleukin, myeloperoxidase, vascular cell adhesion molecule, and intercellular adhesion molecule (6).

Digestive System:

Increased blood levels of certain enzymes show that dioxins cause liver cell degradation, that also results in damaging gastrointestinal and liver cancer [41,42].

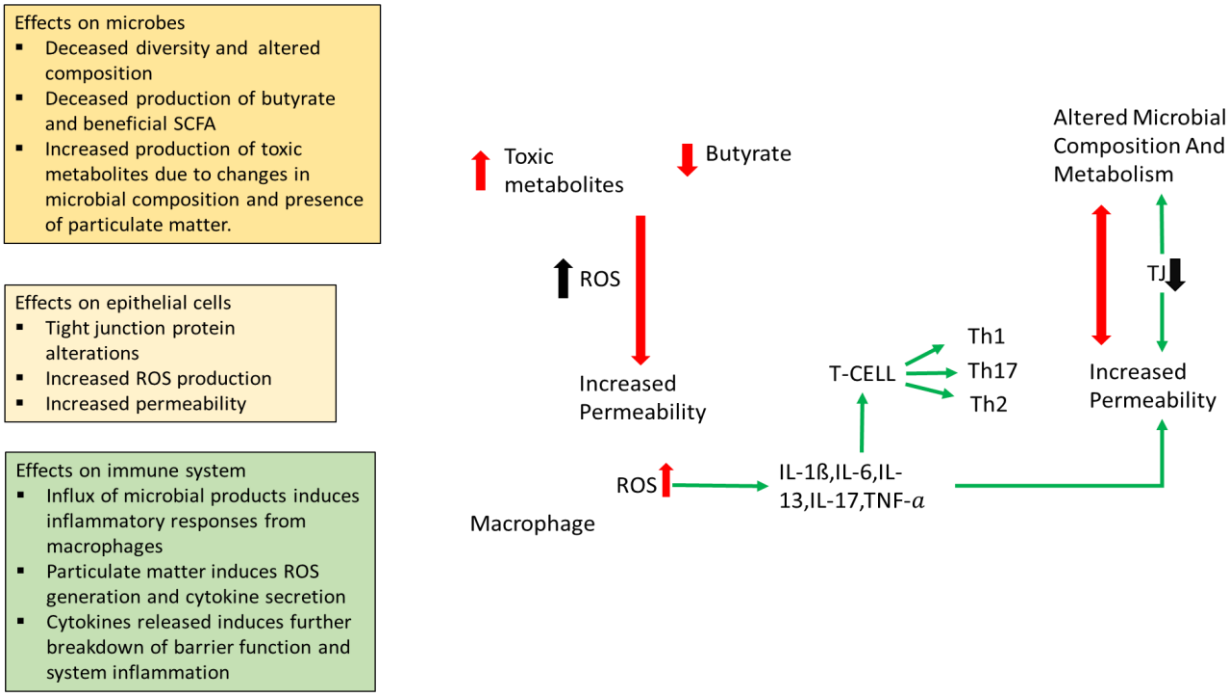

Figure 3. Induction of intestinal and systemic inflammation by particulate matter.

Micro particles directly affect the gut epithelial cells as well as be processed into hazardous compounds by the gut's resident microorganisms (fig. 3). Gut permeability is enhanced by particulate matter were induced abnormalities in ETJ (epithelial tight junctions) caused by reactive oxygen species generation, enabling more microbial products and particulate matter to enter the lamina propria and interact with immune cells. Due to the pro-inflammatory response of the body's immune cells because of this, the gut's permeability is further increased, and the luminal environment of the gut is altered to promote the development of bacterial strains that can survive in an inflammatory environment. The survival of certain bacteria and the function of the epithelium are directly impacted by the conversion of particulate matter into harmful byproducts. Short-chain fatty acid synthesis is decreased, and the production of toxic metabolites is increased because of the changed microbial community's effects on the host's metabolic processes.

Urinary System:
Because of their hemofiltration activity, the kidneys are exposed to air contaminants in the circulation due to their enormous blood supply. Increased risk of chronic kidney disease, end-stage of renal disease, and reduction in glomerular filtration rate have been linked to exposure to high levels of PM_{10}, NO_2, and CO [43]. By increasing the excretion of low molecular weight proteins, heavy metals may cause tubular dysfunction in the kidneys, which leads to a decline in GFR (glomerular filtration rate). In addition, they raise the risk of kidney cancer [44-46] and the development of stones or nephrocalcinosis [47,48].

Nervous System:
There is considerable evidence that air pollution has harmful consequences on the CNS (central nervous system). Increasing evidence from epidemiological research on humans shows that ambient air pollution may harm the CNS and lead to CNS disorders, and it is now thought to be a neurotoxicant [49]. Additionally, the nasal sensory mucosa allows for the direct absorption of fine PM into the lung and brain [50,51]. Also, it is identified that air pollution, particularly PM2.5 and NO (nitrogen oxides), has an adverse effect on the central nervous system, leading to (OS) oxidative stress, neuroinflammation, and systemic inflammation [52-54].

The main heavy metals and dioxins that affect the nervous system include Pb, Hg, and Ar. The symptoms of neurotoxicity leading to neuropathies after exposure to arsenic, lead, and mercury include memory loss, difficulty sleeping, anger, tiredness, hand tremors, blurred vision, and slurred speech [55,56]. Particularly harmed by lead exposure and essential for memory functions are the NMDA, glutamate, and dopamine receptor complexes [57,58]. Some incidences of neurological malignancy are also caused by mercury. Carcinogens slow down nerve transmission and diminish a child's ability to think clearly [59,60].

Exposure during pregnancy:
It is important to emphasize that a developing foetus may be affected by air pollution [61]. Lead exposure reduces foetal growth in pregnant women and increases the frequency of spontaneous abortion (preterm delivery, low birth weight). However, there is evidence connecting parental illnesses and injuries to congenital anomalies [62] and abnormalities of the developing neural system, which have a significant impact on a newborn's neurobehavioral development [63]. Dioxins were also shown to pass via the placenta from the mother to the foetus. They function as endocrine disruptors and influence the growth and development of the baby's central nervous system [64]. TCDD is considered as a developmental toxin in all the investigated species.

The role of air pollution in cellular mechanism:
Because of their propensity to interact directly with lipids, proteins, or free radicals, air pollutants often cause and the emergence of inflammatory responses [65,66]. Free radicals, ROS and N species, harm cellular lipids, proteins, and nuclear or m-DNA, impairing the cells' capacity to operate correctly. Additionally, they can interfere with mechanisms for cellular responses [67]. Humans are eukaryotic aerobic creatures that continuously create free radicals because of normal metabolism and in reaction to environmental exposures. When an organism's defenses are exhausted, an oxidative stress syndrome called free radical overconcentration occurs. Numerous degenerative conditions, including as cancer, atherosclerosis, heart attacks, strokes, chronic inflammatory conditions (like rheumatoid arthritis), cataracts, and conditions of the central nervous system (like Parkinson's and Alzheimer's disease), have been related to this oxidative state.

Organelles in cells collect metals through time and become dysfunctional. For instance, it has been shown that lead buildup in mitochondria causes several alterations, including a slow release of stored Ca2+ and an obstruction of Ca^{2+} absorption, a drop in transmembrane potential, and the oxidation of pyridine nucleotides [68]. Like proteins, metals attach to them and inhibit a variety of enzymes, including those found in the mitochondria [69,70].

Dioxin has a wide range of negative effects [71]. They alter metabolism by inducing several metabolic enzymes (such as estrogens, androgens, glucocorticoids, insulin, and thyroid hormones), growth and differentiation by interfering with growth factors, and several metabolic enzymes are some of the ways they affect homeostasis. After nuclear translocation, the basic helix-loop-helix transcription factor aryl hydrocarbon receptor binds with the dioxins [72], allowing interaction with DNA at the cellular level. The certain DNA regions binds with the receptor-ligand complex binds, changing the way that many genes are expressed, therefore. From the information above, it is evident that most contaminants have a significant impact on the development, spread, and progression of cancer cells (Fig. 4).

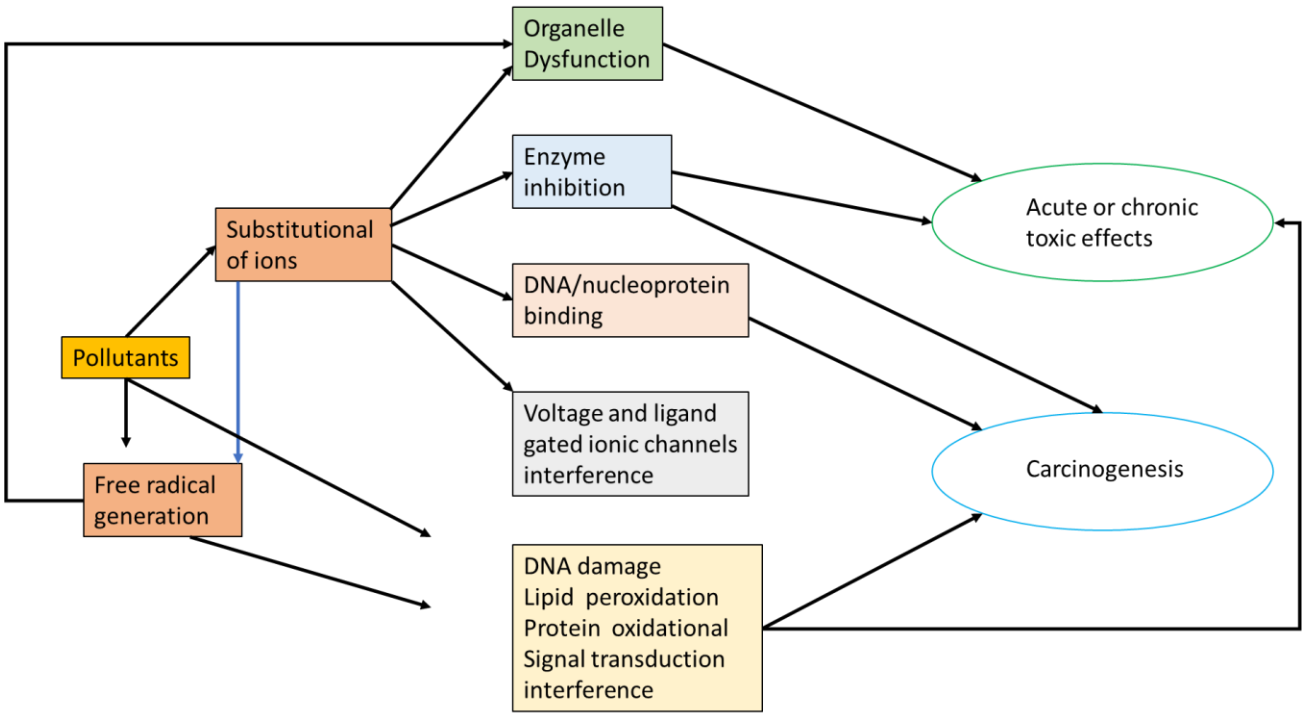

Figure 4. Basic mechanisms of carcinogenesis.

Managing air pollution with preventative measures:
The practice of reducing or eliminating the amount and toxicity of potentially harmful chemicals at their source, before they are created, processed, recycled off-site, or destroyed, is known as pollution prevention. Instead of emphasizing post-production pollution management, pollution reduction or prevention is emphasized. Since lowering pollution has a positive effect on health particularly that of individuals who are sensitive, it is well recognized that pollution has a substantial negative influence on health. Governments will contribute significantly to efforts to decrease air pollution via several different measures. For instance, the Chinese government was successful in reducing air pollution during the 2008 Olympic Games [73]. Consequently, compared to before the Olympics, there were 41.6 percent lower hospital visits for asthma on average during the Olympics.

As there are so many other ways that humans might contribute air pollution. There are various ways that people's health and the environment are adversely damaged. Only with a concerted effort from everyone can methods for preventing air pollution by implementing control measures of air pollution be minimized. The ten techniques mentioned below all help to lower air pollution.

Avoid Plastic Bags The environment is becoming devastated because of the use of plastic bags. Most plastic bags cannot be recycled or used again. It takes a very long time to break down and in decomposing. Moreover, burning plastic releases harmful pollutants into the atmosphere. Paper bags that degrade quickly may replace the plastic gas.

Avoid Burning of Plastics: Burning plastics and other similar items releases harmful gases into the atmosphere, which deteriorates the air quality. Using the government's waste disposal initiatives to get rid of plastics.

Product Recycling and Reuse: Some of the items that are discarded after usage may be recycled and used again to assist keep the atmosphere healthier. Recycling uses less energy than producing the same items, lowering the chemical emissions.

Using fans and instead of using air conditioners: The air conditioner absorbs more heat from the room than it releases into the environment. Global warming is caused by the increased heat discharged into the atmosphere. The ozone layer is destroyed by the usage of freon gas as a refrigerant, preventing dangerous UV radiation from reaching to the earth's surface.

Reduce Electricity Consumption: By turning off lights and appliances while not in use, households may consume less power. Burning fossil fuels may generate power in certain places. Therefore, reducing your energy use might greatly reduce air pollution.

Use Filters in Chimneys: Chimney smoke contains air pollutants that degrade the quality of the air. The quantity of air pollution that reaches the earth's atmosphere may be considerably decreased by placing filters in chimneys, however.

Public Transportation Usage: One of the major contributors to air pollution is the usage of fossil fuels. When more people use public transportation, there are lesser vehicles on the road, which reduces the requirement to burn fossil fuels. Less fuel burning results in lower emissions of greenhouse gases, which in turn slows the rate of global warming.

Avoid Crackers and Fireworks: Air pollution results from the lighting of crackers and fireworks. Large-scale usage of pyrotechnics and crackers during festivals degrades the air's quality and can affect eyesight.

Reduce the Use of Chemicals: Chemicals released into the atmosphere might be considered air pollutants. More swiftly contaminating body sprays and paints release the dangerous chemicals into the atmosphere.

Planting more Trees: By absorbing CO_2 and exhaling O_2 at the time of photosynthesis, plants help in purifying the air. This lowers the greenhouse effect, which again lowers air pollution. Additionally, tree planting contributes to reducing global warming.

Conclusion:

The introduction of air contaminants causes air pollution, which causes the poisoning in the air results in worse impact on human health. Both natural and man-made processes can result in air pollution. Human activity is the major cause of air pollution. This includes the usage of fossil fuels, the discharge of harmful chemicals, the emission of greenhouse gases, etc. Serious health issues including cancer, birth deformities, and respiratory conditions may all be brought on by air pollution. As a result, on the behalf of observation, there are several reasons and methods for the prevention of air pollution. The moment has arrived to take action and save the planet. The study should spur the key and state governments to provide enough long-term funding financing to stop the damaging effects of air pollution on health. The discovery of a pattern of respiratory illness that enhances vulnerability to air pollution, as well as future study on double or repeated exposures, are both in need of investigation.

References:

1. AG N. 1930; Pollution of the air. Can. Med. Assoc. J. 22:553-4.
2. US Environmental Protection Agency. Final regulatory analysis: Control of emissions from nonroad diesel engines
3. Thron RW. 1996; Direct and indirect exposure to air pollution. Otolaryngology--Head and Neck Surgery. 114(2):281-5.
4. Schecter A, Birnbaum L, Ryan JJ, Constable JD. 2006; Dioxins: an overview Environ Res 101 (3): 419–428.
5. Katsouyanni, K., 2003; ambient air pollution and health. Br. Med. Bull. 68, 143.
6. Ostro B, Tobias A, Querol X, Alastuey A, Amato F, Pey J, Pérez N, Sunyer J. 2011; the effects of particulate matter sources on daily mortality: a case-crossover study of Barcelona, Spain. Environmental health perspectives. 119(12):1781-7.
7. Künzli N, Tager IB. 2005; Air pollution: from lung to heart. Swiss Med Wkly. 10:697-702.
8. Carlisle AJ, Sharp NC. 2001; Exercise and outdoor ambient air pollution. British journal of sports medicine. 35(4):214-22.
9. Probst-Hensch N. 2010; Chronic age-related diseases share risk factors: do they share pathophysiological mechanisms and why does that matter? Swiss Medical Weekly.
10. Hinds WC, Zhu Y. 2022; Aerosol technology: properties, behavior, and measurement of airborne particles. John Wiley & Sons
11. Ristovski ZD, Miljevic B, Surawski NC, Morawska L, Fong KM, Goh F, Yang IA. 2012; Respiratory health effects of diesel particulate matter. Respirology. 17(2):201-12.
12. Järup L. 2003; Hazards of heavy metal contamination. British medical bulletin. 68(1):167-82.
13. Franchini M, Mannucci PM. 2015; Impact on human health of climate changes. European journal of internal medicine. 26(1):1-5.
14. Franck U, Odeh S, Wiedensohler A, Wehner B, Herbarth O. 2011; The effect of particle size on cardiovascular disorders—The smaller the worse. Science of the Total Environment.
15. Brown JS, Zeman KL, Bennett WD. 2002; ultrafine particle deposition and clearance in the healthy and obstructed lung. American journal of respiratory and critical care medicine. 166(9):1240-7.
16. Franchini M, Mannucci PM. 2011; Thrombogenicity and cardiovascular effects of ambient air pollution. Blood, the Journal of the American Society of Hematology. 9:2405-12.
17. Stieb DM, Judek S, Burnett RT. 2002; Meta-analysis of time-series studies of air pollution and mortality: effects of gases and particles and the influence of cause of death, age, and season. Journal of the Air & Waste Management Association. 52(4):470-84.
18. Gao H, Chen J, Wang B, Tan SC, Lee CM, Yao X, Yan H, Shi J. 2011; A study of air pollution of city clusters. Atmospheric Environment. 45(18):3069-77.
19. Shang Y, Sun Z, Cao J, Wang X, Zhong L, Bi X, Li H, Liu W, Zhu T, Huang W. 2013; Systematic review of Chinese studies of short-term exposure to air pollution and daily mortality. Environment international. 54:100-11.
20. Brook RD, Rajagopalan S, Pope III CA, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A. 2010; Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation. 121(21):2331-78.
21. Lepeule J, Laden F, Dockery D, Schwartz J. 2012; chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. Environmental health perspectives. 120(7):965-70.
22. Beelen R, Raaschou-Nielsen O, Stafoggia M, Andersen ZJ, Weinmayr G, Hoffmann B, Wolf K, Samoli E, Fischer P, Nieuwenhuijsen M, Vineis P. 2014; Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. The lancet. 383(9919):785-95.
23. Pascal M, Corso M, Chanel O, Declercq C, Badaloni C, Cesaroni G, Henschel S, Meister K, Haluza D, Martin-Olmedo P, Medina S. 2013; Assessing the public health impacts of urban air pollution in 25 European cities: results of the Aphekom project. Science of the Total Environment. 449:390-400.

24. Baccini M, Biggeri A, Grillo P, Consonni D, Bertazzi PA. 2011; Health impact assessment of fine particle pollution at the regional level. American journal of epidemiology. 174(12):1396-405.
25. Brunekreef B, Holgate ST. 2002; Air pollution and health. The lancet. 360(9341):1233-42.
26. Badman DG, Jaffé ER. 1996; Blood and air pollution; state of knowledge and research needs. Otolaryngology--Head and Neck Surgery. 114(2):205-8.
27. Riediker M, Cascio WE, Griggs TR, Herbst MC, Bromberg PA, Neas L, Williams RW, Devlin RB. 2004; Particulate matter exposure in cars is associated with cardiovascular effects in healthy young men. American journal of respiratory and critical care medicine. 169(8):934-40.
28. Riediker M, Cascio WE, Griggs TR, Herbst MC, Bromberg PA, Neas L, Williams RW, Devlin RB. 2004; Particulate matter exposure in cars is associated with cardiovascular effects in healthy young men. American journal of respiratory and critical care medicine. 169(8):934-40.
29. Huang YC, Ghio AJ. 2006; Vascular effects of ambient pollutant particles and metals. Current vascular pharmacology. 4(3):199-203.
30. Shang Y, Sun Z, Cao J, Wang X, Zhong L, Bi X, Li H, Liu W, Zhu T, Huang W. 2013; Systematic review of Chinese studies of short-term exposure to air pollution and daily mortality. Environment international. 54:100-11.
31. Dalton TP, Kerzee JK, Wang B, Miller M, Dieter MZ, Lorenz JN, Shertzer HG, Nebert DW, Puga A. 2001; Dioxin exposure is an environmental risk factor for ischemic heart disease. Cardiovascular toxicology. 1(4):285-98.
32. TASK I. 1966; Deposition and retention models for internal dosimetry of the human respiratory tract. Health Physics.12:173-207.
33. Lippmann MD, Yeates DB, Albert RE. 1980; Deposition, retention, and clearance of inhaled particles. Occupational and Environmental Medicine. 37(4):337-62.
34. Kim CS, Hu SC. 2006; Total respiratory tract deposition of fine micrometer-sized particles in healthy adults: empirical equations for sex and breathing pattern. Journal of Applied Physiology. 101(2):401-12.
35. Raabe OG. 1999; Respiratory exposure to air pollutants. Lung biology in health and disease.128:39-73.
36. Brown JS, Zeman KL, Bennett WD. 2002; ultrafine particle deposition and clearance in the healthy and obstructed lung. American journal of respiratory and critical care medicine. 166(9):1240-7.
37. Ferin J, Oberdorster G, Penney DP. 1992; Pulmonary retention of ultrafine and fine particles in rats. Am J Respir Cell Mol Biol. 6(5):535-42?
38. Moller W, Felten K, Sommerer K, Scheuch G, Meyer G, Meyer P, Haussinger K, Kreyling WG. 2008; Deposition, retention, and translocation of ultrafine particles from the central airways and lung periphery. American journal of respiratory and critical care medicine. 177(4):426-32.
39. Elder A, Gelein R, Silva V, Feikert T, Opanashuk L, Carter J, Potter R, Maynard A, Ito Y, Finkelstein J, Oberdörster G. 2006; Translocation of inhaled ultrafine manganese oxide particles to the central nervous system. Environmental health perspectives. 114(8):1172-8.
40. Oberdörster G, Sharp Z, Atudorei V, Elder A, Gelein R, Kreyling W, Cox C. 2004; Translocation of inhaled ultrafine particles to the brain. Inhalation toxicology. 16(6-7):437-45.
41. Jenkins P. 1996; Personal exposure to airborne particles and metals: results from the Particle TEAM study in Riverside, California. Journal of Exposure Anahsis and Environmental Epidemiolog. 6(1):57.
42. Kimbrough RD, Carter CD, Liddle JA, Cline RE, Phillips PE. 1977; Epidemiology and pathology of a tetrachlorodibenzodioxin poisoning episode. Archives of Environmental Health: An International Journal. 32(2):77-86.
43. Mandal PK. 2005; Dioxin: a review of its environmental effects and its aryl hydrocarbon receptor biology. Journal of Comparative Physiology B. 175(4):221-30.
44. Bowe B, Xie Y, Li T, Yan Y, Xian H, Al-Aly Z. 2017; Associations of ambient coarse particulate matter, nitrogen dioxide, and carbon monoxide with the risk of kidney disease: a cohort study. The Lancet Planetary Health. 1(7):e267-76.
45. Damek-Poprawa M, Sawicka-Kapusta K. 2003; Damage to the liver, kidney, and testis with reference to burden of heavy metals in yellow-necked mice from areas around steelworks and zinc smelters in Poland. Toxicology. 186(1-2):1-0.
46. Järup L. 2003; Hazards of heavy metal contamination. British medical bulletin. 68(1):167-82.
47. Loghman-Adham M. 1997; Renal effects of environmental and occupational lead exposure. Environmental health perspectives. 105(9):928-39.
48. Boffetta P, Merler E, Vainio H. 1993; Carcinogenicity of mercury and mercury compounds. Scandinavian Journal of Work, Environment & Health. 1:1-7.
49. Vamvakas S, Bittner D, Köster U. 1993; Enhanced expression of the protooncogenes c-myc and c-fos in normal and malignant renal growth. Toxicology letters. 67(1-3):161-72.
50. Calderón-Garcidueñas L, Calderón-Garcidueñas A, Torres-Jardón R, Avila-Ramírez J, Kulesza RJ, Angiulli AD. 2015; Air pollution and your brain: what do you need to know right now. Primary health care research & development. 16(4):329-45.
51. Ajmani GS, Suh HH, Pinto JM. Supplemental Material Effects of Ambient Air Pollution Exposure on Olfaction: A Review.
52. Costa LG, Cole TB, Coburn J, Chang YC, Dao K, Roqué PJ. 2017; Neurotoxicity of traffic-related air pollution. Neurotoxicology. 1; 59:133-9.
53. Andersen ZJ, Pedersen M, Weinmayr G, Stafoggia M, Galassi C, Jørgensen JT, Sommar JN, Forsberg B, Olsson D, Oftedal B, Aasvang GM. 2018; Long-term exposure to ambient air pollution and incidence of brain tumor: the European Study of Cohorts for Air Pollution Effects (ESCAPE). Neuro-oncology. 20(3):420-32.

54. Bergamaschi R, Cortese A, Pichiecchio A, Berzolari FG, Borrelli P, Mallucci G, Bollati V, Romani A, Nosari G, Villa S, Montomoli C. 2018; Air pollution is associated to the multiple sclerosis inflammatory activity as measured by brain MRI. Multiple Sclerosis Journal. 24(12):1578-84.
55. Braithwaite I, Zhang S, Kirkbride JB, Osborn DP, Hayes JF. 2019; Air pollution (particulate matter) exposure and associations with depression, anxiety, bipolar, psychosis and suicide risk: a systematic review and meta-analysis. Environmental health perspectives. 127(12):126002.
56. Ewan KB, Pamphlett R. 1996; increased inorganic mercury in spinal motor neurons following chelating agents. Neurotoxicology. 17(2):343-9.
57. Ratnaike RN. 2003; Acute and chronic arsenic toxicity. Postgraduate Medical Journal. 79(933):391-6.
58. Lasley SM, Gilbert ME. 2000; Glutamatergic components underlying lead-induced impairments in hippocampal synaptic plasticity. Neurotoxicology. 21(6):1057-68.
59. Lasley SM, Green MC, Gilbert ME. 2001; Rat hippocampal NMDA receptor binding as a function of chronic lead exposure level. Neurotoxicology and teratology. 23(2):185-9.
60. Thömke F, Jung D, Besser R, Röder R, Konietzko J, Hopf HC. 1999; Increased risk of sensory neuropathy in workers with chloracne after exposure to 2, 3, 7, 8-polychlorinated dioxins and furans. Acta neurologica scandinavica. 100(1):1-5.
61. Walkowiak J, Wiener JA, Fastabend A, Heinzow B, Krämer U, Schmidt E, Steingrüber HJ, Wundram S, Winneke G. 2001; Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. The Lancet. 10; 358(9293):1602-7.
62. Schell LM, Gallo MV, Denham M, Ravenscroft J. 2006; Effects of pollution on human growth and development: an introduction. Journal of physiological anthropology. 25(1):103-12.
63. Bellinger, D.C., 2005. Teratogen update: lead and pregnancy. Birth Defects Res. A Clin. Mol. Teratol 73, 409.
64. Garza A, Vega R, Soto E. 2006; Cellular mechanisms of lead neurotoxicity. Medical science monitor. 12(3): RA57.
65. Wang SL, Lin CY, Guo YL, Lin LY, Chou WL, Chang LW. 2004; Infant exposure to polychlorinated dibenzo-p-dioxins, dibenzofurans and biphenyls (PCDD/Fs, PCBs)—correlation between prenatal and postnatal exposure. Chemosphere. 54(10):1459-73.
66. Menzel DB. 1994; the toxicity of air pollution in experimental animals and humans: the role of oxidative stress. Toxicology letters. 2(1-3):269-77.
67. Rahman, I., MacNee, W., 2000. Oxidative stress and regulation of glutathione in lung inflammation. Eur. Respir. J. 16, 534.
68. Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. 2007; Free radicals and antioxidants in normal physiological functions and human disease. The international journal of biochemistry & cell biology. 39(1):44-84.
69. Chávez E, Jay D, Bravo C. 1987; the mechanism of lead-induced mitochondrial Ca2+ efflux. Journal of Bioenergetics and Biomembranes. 19(3):285-95.
70. GoERING PL. 1993; Lead-protein interactions as a basis for lead toxicity. Neurotoxicology. 14(2):45-60.
71. Rossi E, Taketani S, Garcia-Webb P. 1993; Lead and the terminal mitochondrial enzymes of haem biosynthesis. Biomedical Chromatography. 7(1):1-6.
72. Birnbaum LS. 1994; the mechanism of dioxin toxicity: relationship to risk assessment. Environmental health perspectives. 102(suppl 9):157-67.
73. Schwarz M, Buchmann A, Stinchcombe S, Kalkuhl A, Bock KW. 2000; Ah receptor ligands and tumor promotion: survival of neoplastic cells. Toxicology letters. 112:69-77.
74. Li Y, Wang W, Kan H, Xu X, Chen B. 2010; Air quality and outpatient visits for asthma in adults during the 2008 Summer Olympic Games in Beijing. Science of the Total Environment. 8(5):1226-7.