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# Reactive Oxygen Species (ROS) Mediated Particulate Matter Toxicity in Progression of Disease: Toxicological Review

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## Abstract

Particle pollution is a complex mixture of extremely small particles and liquid droplets, and includes nitrates, sulfates, organic chemicals, metals, and soil or dust particles. Exposure to particles is a health concern because they can pass through the throat and nose and enter the lungs, where they are persistent within cells and tissues, which can lead to the induction of persistent inflammatory and/or oxidative responses can cause respiratory and circulatory and associated problems, through oxidative stress mediated toxic action of air pollutants. Air pollution PM is an important environmental health risk factor for several diseases morbidity and mortality. Oxidative stress can trigger redox-sensitive pathways that can lead to different biological changes such as inflammation, cell death as well as genotoxicity. Further, PM is inextricably linked with genotoxicity and mutations. In turn, this may result in alterations of gene-expression and cell-cycle regulation.

**Keywords:** Particulate matter, Oxidative stress, Cytotoxicity, Carcinogenicity, Genotoxicity

## I. Introduction

Particulate matter (PM) is highly associated with increased morbidity and mortality (Maier et al., 2008; Abbas et al., 2009). In current anthropogenic era, the problem of PM pollution is serious health concern for both developing and developed countries. PM refers to a suspension of solid, liquid or a combination of solid and liquid particles in the air (Hinds, 1999; Wilson et al., 2005). Air pollution originating from PM is generally characterized by its highly complex nature (Alfaro-Moreno et al., 2002; Abbas et al., 2009). PMs are complex mixture of particles and droplets in the air, consisting of a variety of components such as organic compounds, metals, acids, soil, and dust (Cienciewicki and Jaspers, 2007; Rai et al., 2014; Rai and Panda, 2014). PM is one of six 'criteria pollutants' designated by the US Clean Air Act of 1971 (Wilson et al., 2005). The PMs belong to the class of poorly soluble particles that also encompasses carbon black, coal mine dust, and titanium dioxide (Borm et al., 2005; Moller et al., 2008). Measurements of the PM in ambient air are usually reported as the mass of particles with an aerodynamic diameter that is less than 2.5  $\mu\text{m}$  (PM<sub>2.5</sub>) or 10  $\mu\text{m}$  (PM<sub>10</sub>) (Zhu et al., 2006). Particle sizes are important factor for their pertinent health impacts (Rai and Pana, 2014; Rai et al., 2014; Kim et al., 2015; Yang et al., 2015).

The environmental air quality is continually affected by emission from stationery and mobile combustion sources. Mobile sources contribute to the emission of major urban air pollutants including carbon dioxide (CO<sub>2</sub>), nitrogen oxides (NO<sub>x</sub>), sulphur oxides (SO<sub>x</sub>), particulate matter (PM), Lead (Pb), photo chemical oxidant, such as ozone (O<sub>3</sub>) and ozone precursors like hydrocarbons and volatile organic compounds (Costa, 2004). Among these pollutants, the concentration of PM<sub>10</sub> and PM<sub>2.5</sub> airborne aerosols are comparable with traffic released pollutant and other combustion process (Prajapati and Tripathi, 2007). PM has been widely studied in recent years and the United Nation estimated that over 600 million people in urban areas worldwide were exposed to dangerous levels of traffic generated air pollutants (Cacciola et al., 2002).

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## II. Sources of Particulate Matter

Sources of PM pollution may be natural as well as anthropogenic. Natural processes that emit PM into the atmosphere include volcanic eruption, geochemical sources, wind-blown dust, soil and spray from marine sources. Natural sources of PM e.g. volcanic eruptions may contain sulphurous particles and may have an adverse effect on cardio-respiratory health in adults (Longo et al., 2008). Anthropogenic sources include power plant, traffic, agriculture and various industrial activities such as mining and the metallurgical industries.

Diesel exhaust emissions are found to be major source of PM<sub>2.5</sub> in urban environment. Vehicular emissions consist of PMs and gaseous emissions, with biologically active carbonaceous components present in both phases. Black carbon, mainly from diesels, is found in ultrafine and fine size fractions, mainly less than 1 $\mu$ m in size and predominantly below 0.18 $\mu$ m (Mauderly and Chow, 2008). Such vehicular particulates are often coated with condensed organic and inorganic compounds (Mauderly, 2001; Health Effects Institute, 1995). Ambient concentrations of the platinum group elements (PGE) platinum (Pt), palladium (Pd) and rhodium (Rh) have been on the rise, largely due to the use of automobile catalytic converters which employ these metals as exhaust catalysts and these PGE may impose a considerable human health risk (Wiseman and Zereini, 2009).

## III. PM-induced Oxidative Stress

Ambient PM that consists of complex and various mixtures of particles suspended in the air varies from one microenvironment to the others. Many of the individual pollutants that make up this ambient mix are found to be free radical (such as nitrogen dioxide) or have ability to drive free radical reactions. As a consequence of exposure to a wide range of air pollutants gives rise to oxidative stress within the lungs and other organs. Various results have shown the oxidative potential of fine and ultrafine particles as a result of significant amounts of organic carbon compounds such as quinones and polyaromatic hydrocarbons (PAHs), (Squadrito et al., 2001; Finlayson-Pitts et al., 1997). The main pathways of metabolic activation of PAHs are generation of diol epoxides catalyzed by cytochrome P450 (CYP450) resulting into formation of DNA adduct and formation of redox active quinones (Bonvallot et al., 2001). Valavanidis et al., 2005 reported that redox-active transition metals, redox cycling quinoids and PAHs act synergically to produce reactive oxygen species (ROS).

Transition metals such as iron, lead mercury, cadmium, silver, nickel chromium, copper and vanadium adsorb on the surface of PM and exert ROS formation mediated through Fentons reaction (Sioutas et al., 2003). With the conjugation of PM, these transition metals have been found to be involved in a number of pathological condition of the respiratory system through free radical-mediated damage (Vidrio et al., 2008).

## IV. PM and associated disease

Diesel and gasoline vehicle exhaust in the urban area have dominantly contributed to environmental fine particles. Attributed to their small size and large surface area these fine particles have shown unique physicochemical properties such as increased ability to adsorb or absorb organic molecules and their excess into cellular targets in the human pulmonary and cardiovascular systems (Pope et al., 2006) where they can induce arrhythmias, reduce myocyte contractility and decreased coronary blood flow (Delfino et al., 2005). Approximately 75% of diesel PM<sub>2.5</sub> emissions consist of carbon (Health Effects Institute, 2003). In one of the study of Turkish restaurants indicated that cooking smoke is a significant source of indoor particulate matter that can cause adverse health effects and the lifetime cancer risk associated with As and Cr (VI) exposure which might of concern for restaurant workers (Taner et al., 2013). Of the multiple components of typical environmental air pollution, particulate matter is considered the most toxic of the high-volume pollutants and has been the most heavily researched (Taner et al., 2013).

Particulate pollution exacerbates virtually all pulmonary diseases and likely plays a causative role in reactive airways disease. It is associated with increased rates of hospitalization and death from respiratory diseases from neonates to the elderly (Taner et al., 2013). A strong correlation has been found between redox-active compound associated with PM with their adverse effects on damaging the macrophages and bronchial epithelial cells (Ferecatu et al., 2010; Baulig et al., 2003). Particulate pollution permanently inhibits lung growth in children, preventing them from achieving their full adult lung capacity. Brief exposure to either ozone or particulate matter reduces lung function even in young healthy adults and the reduction can last for a week after the pollution exposure is over (Taner et al., 2013). It has been reported that the oxidised species resulting from the complex reaction between the ozone and lung fluid can trigger the signalling cascade of inflammatory cells into the lung can cause acute bronchoconstriction and hypersensiveness in asthma on encounter of these pollutants (Song et al., 2011; Mudway et al., 2000).

Particulate pollution causes morphologic changes in the placenta, inhibiting blood transfer to the foetus. Pregnant women exposed to more air pollution have multiple adverse pregnancy outcomes including higher blood pressure, higher rates of pre-eclampsia, intrauterine growth retardation, premature births, low birth weight syndrome and neonates with smaller head circumference. Air pollution is associated with higher rates of birth defects, including neural tube and cardiac birth defects (Taner et al., 2013).

The systemic inflammation caused by particulate pollution also affects the brain. Air pollution components reach the brain not only through the vascular system, but translocate via the nasal mucosa, along axons of the olfactory and trigeminal nerves into the central nervous system (CNS), allowing deep penetration into the parenchyma and brain stem (Taner et al., 2013). Furthermore, many of the compounds adsorbed to particulate matter, like heavy metals, are neurotoxic. Through this mechanism, particulate pollution causes CNS oxidative stress, neuroinflammation, neuronal damage, cortical stress measured by EEG, enhancement of Alzheimer type-abnormal filamentous proteins, Blood Brain Barriers (BBB) changes, and cerebrovascular damage. Many of these changes can be found in children and young adults. Greater air pollution exposure is associated with lower intelligence, poorer motor function, attention deficits and behavioural problems in children, decreased cognition in adults, higher rates of strokes, multiple sclerosis, autism, Parkinson's and other neurodegenerative diseases (Taner et al., 2013).

## V. PM-induced Genotoxicity

By triggering the inflammatory cascade, particulate pollution causes systemic oxidative stress, cytotoxicity, and can penetrate cellular structures, including the cell nucleus, causing chemically mediated epigenetic changes to chromosomal function. Sorensen et al., 2005 in his one of the study has reported that Vanadium and chromium (VI) present in PM<sub>2.5</sub> exert an oxidative DNA damage in human lymphocytes after the reduction to chromium (III) in bodily reaction. This genotoxicity may represent air pollution's greatest impact on public health. Pregnant women are more prone to such exposure of air pollution give birth to babies with significantly more chromosomal aberrations and epigenetic changes which can be passed on to multiple subsequent generations (Taner et al., 2013).

When exposure even to brief episodes of pollution occurs at critical stages in the development of the human embryo, it can result in increased likelihood of multiple chronic diseases, including those of the heart, lungs, immune system and brain and even obesity, diabetes and cancer (Taner et al., 2013). Exposure to intermittent air pollution is associated with sperm DNA damage and consequent increase in the rates of male infertility, miscarriages and other adverse reproductive outcomes. Children living near petrochemical industries are exposed to high PAH levels which appear to be particularly capable of provoking DNA damage. Industrial pollution is even more genotoxic than traffic pollution. In of the very elegant studies (Somer et al., 2002, 2004) it has been reported that exposure to air pollution can induce DNA mutations that offspring inherit from parents concluding that exposure to polluted air due to the inhalation of airborne mutagens can induce inheritable germline mutations *in vivo*.

It has been reported that chemicals associated with the polluted air can cause DNA and protein adducts. Long term inflammation and oxidative stress as a result of exposure to PM in pollutants may result in to development of cancers (Vineis et al., 2005).

The American Heart Association published guidelines based on hundreds of epidemiologic studies offering a quantitative assessment of particulate pollution's mortality impact suggesting that the air pollution in a typical urban setting, where most Americans live, increases the mortality rate between 10 and 14%. Concomitantly, average life expectancy has improved by about five months from just 20years' worth of reduced particulate pollution (Taner et al., 2013).

## VI. Conclusion

Outdoor air pollution is a mixture of multiple pollutants generating from either form naturally or anthropogenic sources that may include transport, power generation, industrial activity, biomass burning and domestic activities. Various experimental and epidemiological studies have reported that exposure of air pollution to be an important factor for pulmonary, cardiovascular and other risk damage to vital organs through ROS production has been identified as one of most important underlying mechanism for toxic air pollutants effects. Oxidative stress can trigger redox sensitive mechanism that lead to different biological processes like inflammation, genotoxicity, carcinogenicity and eventually cell death. The findings regarding the carcinogenicity of outdoor air pollution as a mixture and particulate matter specifically are remarkably consistent in epidemiological research and progression of cancer. Effective management of air quality is mandatory tool to reduce health risk to a minimum by widening our research and understanding the mechanism of PM-induced health effects.

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