African Journal of Pharmacy and Pharmacology Vol. 7(7), pp. 318-331, 22 February, 2013
Available online at http://www.academicjournals.org/AJPP
DOI: 10.5897/AJPPX12.005
ISSN 1996-0816 ©2013 Academic Journals

Review

Toxicity of exhaust nanoparticles

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Accepted 14 January, 2013

The environmental problems in India are growing rapidly. The increasing economic development and a rapidly growing population that has taken the country from 300 million people in 1947 to more than one billion people today, is putting a strain on the environment, infrastructure, and the country's natural resources. Industrial pollution, soil erosion, deforestation, rapid industrialization, urbanization, and land degradation are all worsening problems. Over-exploitation of the country's resources, be it land or water, and the industrialization process, has resulted in environmental degradation of resources. Environmental pollution is one of the most serious problems facing humanity and other life forms on our planet today. The rapid growth in motor vehicle activity and rapid industrialization is contributing to high levels of urban air pollution. The population is mainly exposed to high air pollution concentrations; where motor vehicle emissions constitute the main source of fine and ultrafine particles, having a serious impact on our urban air quality and public health. Studies showed that the composition of atmospheric particulate matter has a great impact on human health. In this study, we have reviewed the toxicity of vehicle exhaust, especially diesel exhaust nanoparticles and the associated health problems.

Key words: Pollution, diesel exhaust, toxicity, air pollutants, nanoparticles.

INTRODUCTION

The World Health Organization (WHO) estimates that about two million people die prematurely every year as a result of air pollution (Table 1), while many more suffer from breathing ailments, heart disease, lung infections and even cancer. Fine particles or microscopic dust from coal or wood fires and unfiltered diesel engines are rated as one of the most lethal forms or air pollution caused by industry, transport, household heating and cooking. The main four sources of air pollution are emissions from vehicles, thermal power plants, industries and refineries. The source of indoor air pollution is mainly due to kitchen stoves in rural areas. In the 2007, the Blacksmith Institute listed the top ten polluted areas in the world as Azerbaijan, China, India, Peru, Russia, Ukraine, and Zambia (Blacksmith Institute). Vehicle emissions are responsible for 70% of the country's air pollution. Air pollution from vehicle exhaust and industry is a worsening problem in India. Exhaust from vehicles has increased eight-folds over a period of twenty years; industrial pollution has risen four times over the same period.

The economy has grown two and a half times over the past two decades but pollution control and civic services have not kept pace. Air quality is worst in big cities like Kolkata, Delhi, Mumbai, Chennai, etc. Bangalore holds the title of being the asthma capital of the country. Studies estimate that 10% of Bangalore's 60 lakh population and over 50% of its children below 18 years suffer from air pollution- related ailments. In Chennai and Mumbai, exhaust from vehicles, dust from construction debris, industrial waste, and burning of municipal and garden waste are all on the rise; so are respiratory diseases, including asthma. At least six of the 10 top causes of death are related to respiratory diseases (The Times of India).Particulate matter (soot, PM) is the major air pollutant in the atmosphere. It is a complex mixture of organic and inorganic substances present in the atmosphere as both liquids and solids. Coarse particulates can be regarded as those with a diameter greater than 2.5 µm

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Table 1. Common air pollutants and their effects.

Pollutant source	Pollutant	Adverse effect	Reference
Smoke, dust	Particulate matter (PM)	Pulmonary problems, effect on immune system	Batsura et al. (1981), Mott et al. (2002) and Taylor (2002)
Chemical industries	Pesticides	Cancer, neurotoxicity	Antonini et al. (2006) and Gold et al. (2001)
Volcanos, rocks, water, soil	Radon, nano-sized particles	Pulmonary toxicity Podoconiosis, Kaposi's Sarcoma	Fuller (2005), Montella et al. (1997) and Mott et al. (2002)
Air conditioner, refrigerators, fire extinguishers	Chlorofluorocarbons, nanoparticles, particulate matter	Ozone effects	Buzea et al. (2007), Mott et al. (2002) and Sapkota et al. (2005)
Vehicle Exhaust	Sulphur dioxide (SO_2)	Pulmonary toxicity, affects vision	Donaldson (2004), Knox, (2005), Peters (2005), Risom et al. (2005) and Vermylen et al. (2005)
Motor emissions	Carbon dioxide (CO_2), particulate matter	Pulmonary toxicity, climatic changes, myocardial damage	Buseck et al. (1999), Peters et al. (2001), Pope et al. (2002)
Incomplete combustion from automobiles	Carbon monoxide (CO)	Neurotoxicity, affects visibility	Donaldson et al. (2005)
Burning Fuels	Nitrogen oxides (NOx)	Respiratory health	Hogan et al. (2004)
Coal mining, natural gas systems	Methane	Pulmonary toxicity, climatic changes	Antonini et al. (2006), Borm et al. (2002), Shah, (1998) and Weiss (2005)
Dust, soil, mining units	Lead, manganese	Organ toxicity, neurotoxicity	Borm et al. (2002) and Gustavsson et al. (1988)
Hazardous waste	Mercury	Neurotoxicity, immunotoxicity	Shah, (1998) and Gatti et al. (2004)
Paint, cosmetics	Propellants	Effects on ozone layer	Gatti et al. (2004), Lademann et al. (1999), Oberdorster et al. (2005), Takenaka et al. (2001) and Rehn et al. (2003)
Vehicle and industrial emissions	Ozone (O_3), lead, cadmium	Pulmonary toxicity	Kocbach et al. (2006) and Waalkes, (2003)
Old cosmetics, vehicle emissions	Aerosols	Organ toxicity	Donaldson et al. (2004), Kocbach et al. (2006), Peters et al. (2001) and Takenaka et al. (2001)
Building materials, building demolition	Asbestos fibres, lead, glass, wood, paper	Respiratory health	Fireman et al. (2004) and Stefani et al. (2005)
Agriculture	Ammonia	Cytotoxicity	Buzea et al. (2007)
Hydrocarbons	Diesel exhaust emissions	Pulmonary and organ toxicity	Donaldson et al. (2005), Hoet et al. (2004), Risom et al. (2004) and Vermylen et al. (2005)

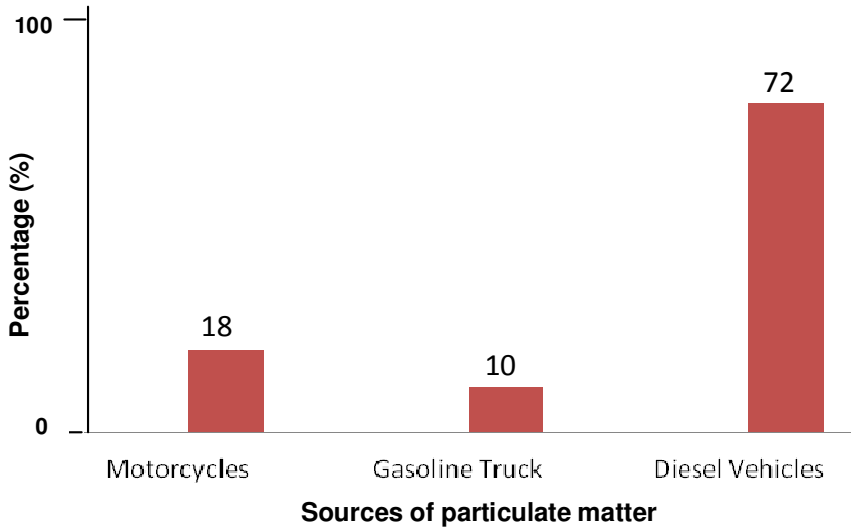

Figure 1. Different sources of particulate matter 2.5 µm (PM 2.5).

and fine particles less than 2.5 µm (Figure 1). The most significant primary sources of particulate matter are motor exhaust (25%), non-combustion processes (24%), industrial combustion plants and processes (17%), commercial and residential combustion (16%) and public power generation (15%) processes (Peters et al., 2006). Inhalable particles, particularly fine particles, have the greatest demonstrated impact on human health. Their small size allows them to get deep into the lungs and from there they can reach or trigger inflammation in the lung, blood vessels or the heart, and perhaps other organs. Studies have linked PM exposure to health problems and environmental issues. Studies showed that the composition of atmospheric particulate matter has a great impact on human health (Chan and Lippmann, 1980; Braunfahrlander et al., 1992; Dockery and Pope, 1994; Pope et al., 1995; Berico et al., 1997).

Motor exhaust emissions is a complex mixture of gases and particulate matter. The particles consist of a core of elemental carbon (EC) to which organic compounds formed during the combustion is adsorbed. Traces of metal compounds and sulphates are also present in the particulate fraction. At formation, the particles are very small, with an aerodynamic diameter of less than 0.1 µm, later they aggregate and form larger particles. Most of these are still smaller than 1 µm (IARC, 1989). These particles can penetrate deep into the respiratory system, and studies indicate that the smaller the particle, the larger the health impacts.

In Chennai (India), vehicles are the major source of air pollution. It is estimated that vehicular emissions contribute more than 300 tons/day of pollution load into the city atmosphere. As at 1st January, 2008, the vehicle population in the city was estimated as Car/jeep (3.0 lakhs); two wheeler (2.0 lakhs). According to the Comprehensive Transportation Study of the Chennai Metropolitan Development Authority (CMDA), levels of suspended particulate matter (SPM) in the city ranged from 274 to 1,470 mg/m^3, which is much higher than the World Health Organization's (WHO) prescribed limit of 200 mg/m^3 (Durga et al.,2012). It goes on to say that about 70% of the pollution load is vehicular. Studies by Bathmanabhan et al. (2010) measured average particulate matter PM10, PM2.5 and PM1 concentrations near an urban roadway in Chennai city, India. Results indicated that highest PM concentrations were observed during weekday's peak hour traffic and lowest PM concentrations were found during trickle traffic (afternoon and night-time).

Combustion Derived Nanoparticles (CDNPs) are defined as primary particles with at least one dimension < 100 nm, while ultrafine particles are defined as particles < 100 nm in all dimensions and are commonly produced by combustion processes (Avakian et al., 2002; Lighty et al., 2002). Nanoparticles have the ability to escape from the site of deposition in lungs and reach other organs through circulation, and are capable of causing inflammation (Donaldson et al., 2004). Diesel soot, welding fume, carbon black and coal fly ash are the major sources of CDNPs.

Diesel-powered vehicles contribute 72% and gasoline/petrol vehicles contribute 10% to particulate matter on roads. Diesel vehicles produce ~2 to 40 times more particles than petrol-powered vehicles, depending on the type of diesel fuel and the detailed construction of the engine (IARC, 1989). Combustion of petrol in modern vehicles produces less nitrogen oxides (NOx) and particulates than diesel but more than Liquid Petroleum Gas (LPG). LPG vehicles tend to produce lower levels of emissions across a range of air pollutants compared to

petrol, biodiesel and diesel fuelled vehicles. Toxicologists can more readily study the components of PM and there has been considerable amount of research demonstrating the toxicity of combustion-derived particles such as diesel soot (Dybdahl et al., 2004; Hirano et al., 2003), welding fume (McNeilly et al., 2004), carbon (Renwick et al., 2004). They mediate a range of adverse effects in the lungs and other organs, and warrant further research.

NANOTOXICOLOGY

Nanotoxicology is a branch of bio-nanoscience which deals with the study and application of toxicity of nanomaterials. Some nano-particles, depending on their composition and size, can produce irreversible damage to cells by oxidative stress and/or organelle injury. The toxicity of nanoparticles depends on various factors, including size, aggregation, composition, crystallinity, surface functionalization etc. In addition, the toxicity of any nanoparticle to an organism is determined by the individual's genetic complement (Buzea et al., 2007).

Nanotoxicology publication statistics

The total number of papers on toxicity is seen to increase in the graph (Figure 2) that has been published in the ISI web of knowledge database, but till the year 2005, only around 500 toxicological articles has been published. This clearly indicates that more studies are required in the area of nanotoxicology; especially, toxicology of environmental nanoparticles need more concern.

About 60% of nanoparticles in the environment are due to road transport, and a further 27% come from other combustion processes such as power stations. It is the air-borne nanoparticles that are of most concern to human health as it has been shown that increase in the levels of ultra-fine particulates in the air which are less than 10 micrometre in diameter can be considered as being responsible for the increased respiratory and cardiac diseases, and there is increasing evidence that nanoparticles within this fraction can penetrate the lung, causing inflammation and can spread to other organs within the body (http://www.nanoforum.org).

DIESEL AND PETROL ENGINES

Diesel fuel used in diesel engines such as compression-ignition diesel engine was invented by Rudolph Diesel in 1892 as an alternative to the spark-ignition gasoline engine (Gilman, 2002). Petrol engine also known as gasoline engine is a type of internal combustion engine designed to run on petrol (gasoline) and similar volatile fuels. It differs from a diesel engine in the method of mixing the fuel and air, and in the fact that it uses spark plugs to initiate the combustion process. In a diesel engine, only air is compressed (and therefore heated), and the fuel is injected into the now very hot air at the end of the compression stroke, and self-ignites. In a petrol engine, the fuel and air are usually pre-mixed before compression. Diesel fuel is a middle distillate of petroleum which contains paraffin's, alkenes and aromatics.

The engine's popularity expanded because it had excellent fuel economy and durability and it required less maintenance, and the fuel was used in mass transportation vehicles such as trucks, buses, and trains. Diesel fuel and the products of its combustion represent one of the most common toxins to which people living in both urban and rural areas of the world are exposed. Diesel engines are typically separated according to their service requirements, light-duty or heavy-duty. The total particulate emission concentration from light-duty diesel engines is much smaller than from heavy-duty diesel engines. However, the total particulate matter emitted from diesel engines is much higher than from petrol engines and LPG engines (IPCS, 1996).

Composition of diesel exhaust and petroleum exhaust

Our previous study demonstrated that the collected vehicle exhaust samples contained carbon aggregates consisting of tens to thousands of primary carbon particles and mineral particles. The Petrol Exhaust Particles (PEPs) contained slightly larger size particles (Figure 3) compared to the Diesel Exhaust Particles (DEPs) (Figure 4). Both samples contained particles of nano-size. The elemental analysis for the two samples, PEPs and DEPs, was performed using the Scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM-EDX) technique. Both the samples contained carbon as the major element. The percentage of carbon in PEPs was comparatively more than in DEPs. Besides carbon, the PEPs contained elements like aluminium, silica, lead, sulphur, calcium and iron in trace amounts compared to the DEPs, which contained only carbon, oxygen and sulphur (Durga et al., 2012).The inorganic fraction of the particulate phase of diesel fuel combustion emissions primarily consists of small elemental carbon particles. The organic and elemental carbon accounts for approximately 80% of the total particulate matter mass. The remaining 20% is composed of sulfate (mainly sulfuric acid) (Pierson et al., 1983) and some inorganic additives and components of fuel and motor oil. The organic compounds identified in diesel exhaust emissions contain hydrocarbons and hydrocarbon derivatives. Diesel exhaust particulates are capable of adsorbing relatively large amounts of organic material because of their high surface area.

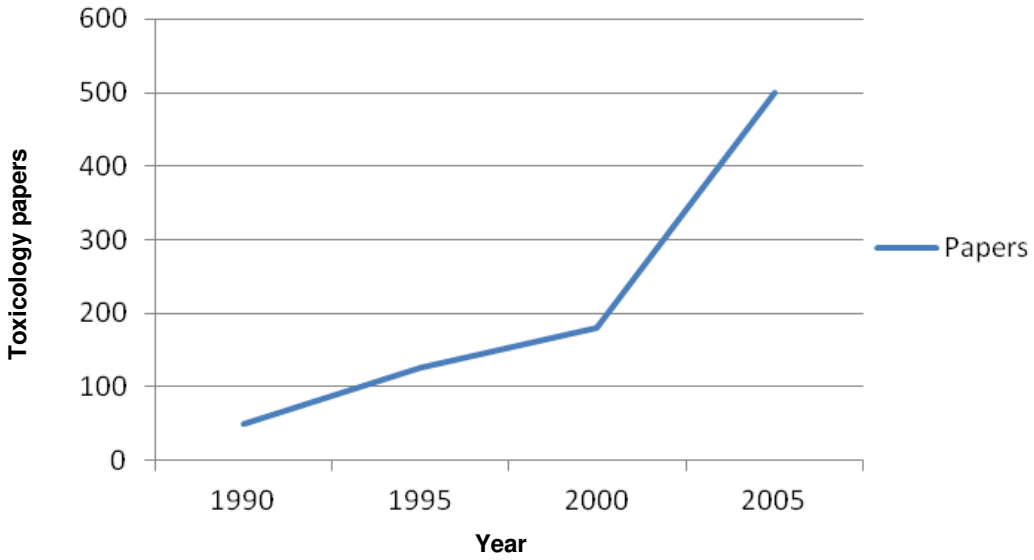

Figure 2. Publication statistics of toxicology papers.

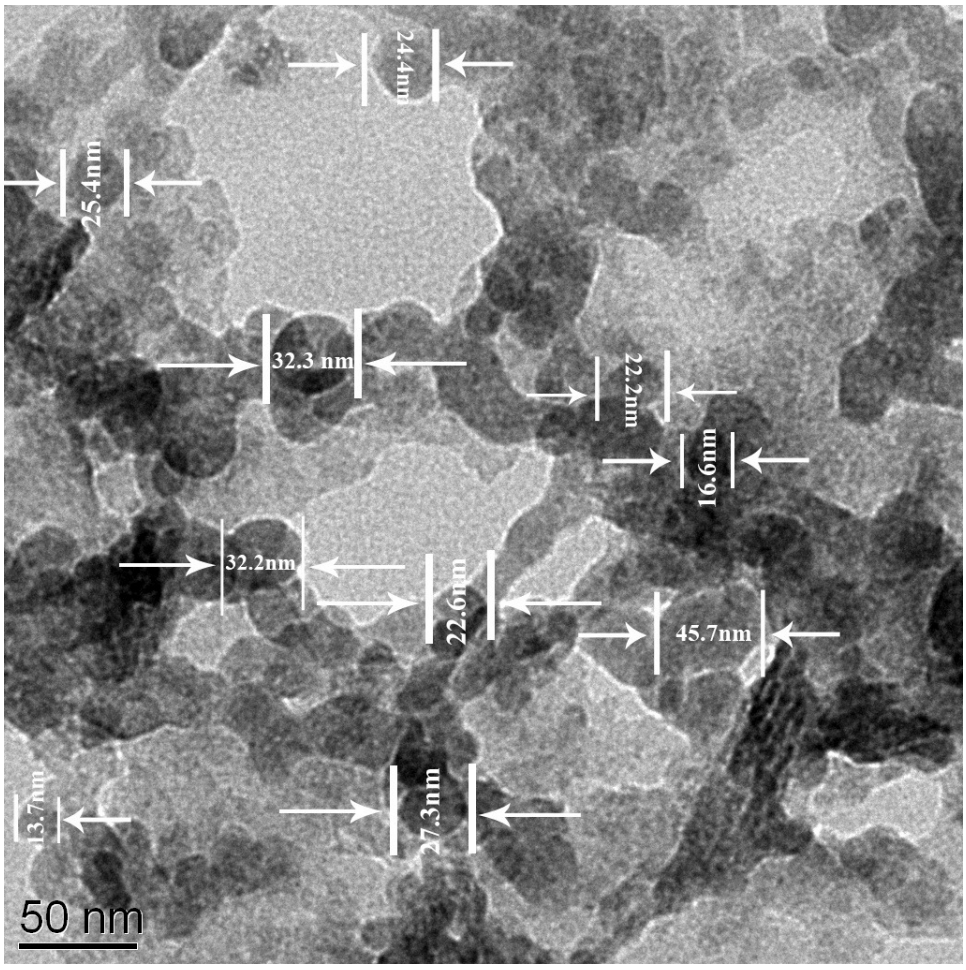

Figure 3. TEM micrograph of petrol sample showing carbon aggregates of various sizes.

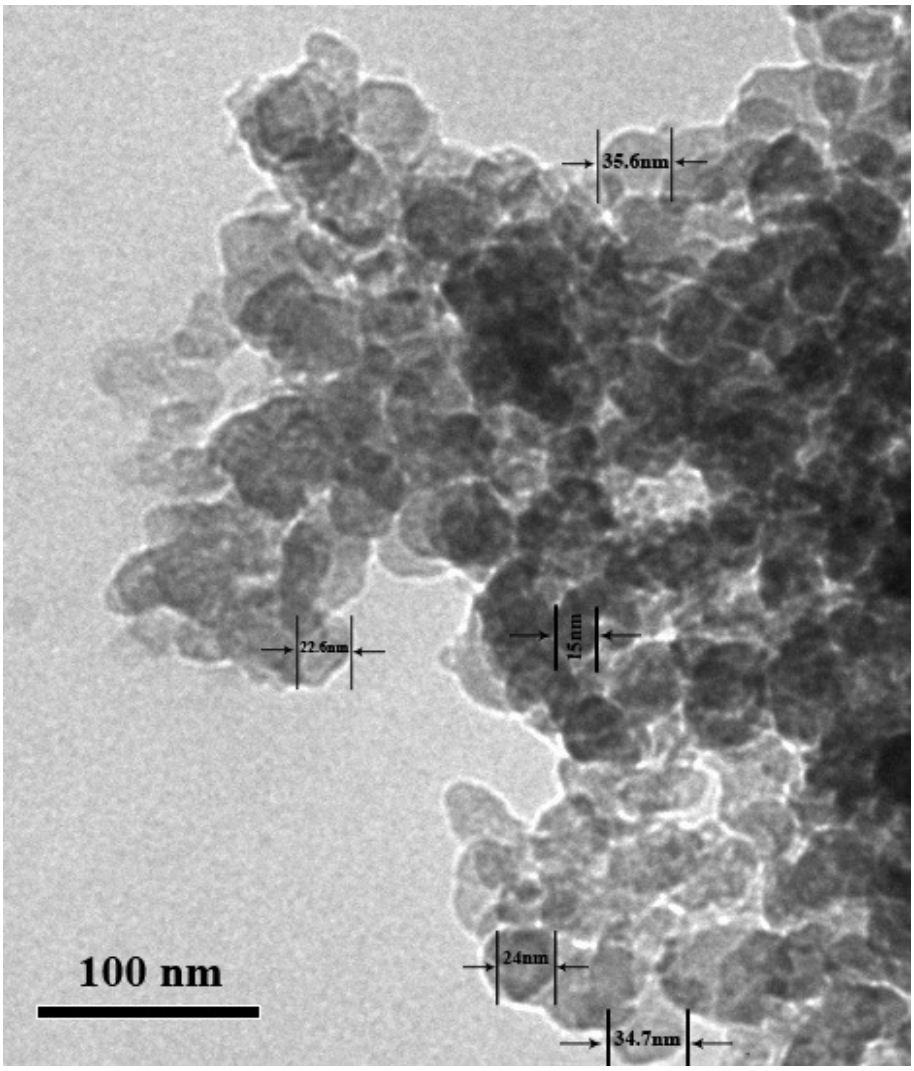

Figure 4. TEM micrograph of diesel sample showing carbon aggregates of various sizes.

Vehicle exhaust of clinical significance

The significant sources of vehicle exhaust include roads and highways, airports, railway stations, truck stops or distribution points, construction sites, tunnels, gas stations, vehicle repair and maintenance shops, bridges, parking lots, bus depots, fire stations, boat harbors and mines (Irina et al., 2008).

IN VITRO TOXICITY STUDIES OF DIESEL EXHAUST PARTICLES (DEPS)

DEP caused oxidative stress in a number of models *in vitro* such as oxidation of low density lipoprotein (LDL) (Ikeda et al., 1995) and in exposed epithelial cells (Li et al., 2000; Hirano et al., 2003). The component responsible for the oxidative stress and subsequent pro-inflammatory signaling is principally the organic fraction (Bonvallet et al., 2001), although transition metals may also be involved (Ball et al., 2000). Studies on broncho-epithelial cell lines have shown increase in levels of cytokines such as IL-8 and granulocyte macrophage stimulating factors (Doornaert et al., 2003).

Le Prieur et al. (2000) studied the toxicity of diesel engine exhausts in an *in vitro* model of lung slices in biphasic organotypic culture, and the results showed induction of a proinflammatory and apoptotic responses. Studies on toxicity of diesel exhaust particles were done in Human Eosinophilic cells; results indicated that DEPs induce monocyte chemoattractant protein-1 (MCP-1) and interleukin-8 (IL-8) production by up-regulating nuclear factor -kappa B (NF-κB) activity and also promotes eotaxin-induced chemotaxis. A possible association between chronic DEP exposure and Parkinson's disease has been explored because DEPs have been shown to

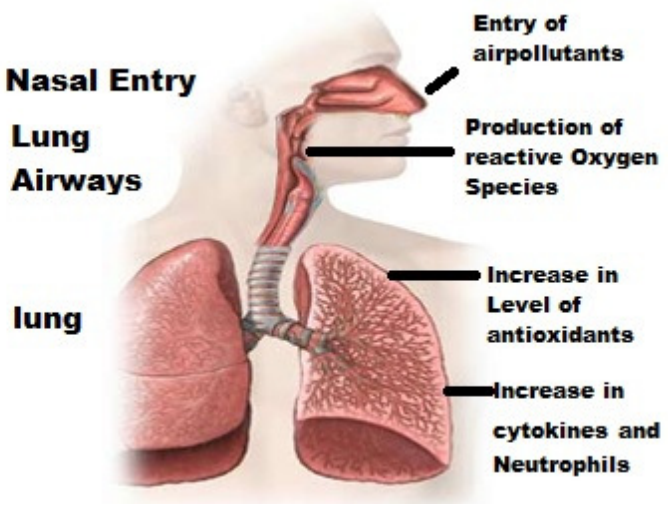

Figure 5. Effect of air pollutants on the lungs.

decrease the number of dopaminergic neurons in the brain tissue of mice (Block et al., 2004). Hartz et al. (2008) studied the *in vitro* effect of blood-brain barrier proteins on exposure to diesel exhaust particles in rat brain capillaries and as a result observed up-regulation in P-glycoprotein, Multi-drug resistance associated protein 1,2 and 4, presence of cytokines and reactive oxygen species in brain capillaries. In our previous study, the cytotoxicity of vehicle exhaust nanoparticles were investigated (Durga et al., 2012). The Petrol Exhaust Nanoparticles (PENPs) and the Diesel Exhaust Nanoparticles (DENPs) were screened for their cytotoxicity on HT29, A549, MDA MB 231, HEP 2 and VERO cell lines at various concentrations of up to 1,000 µg. The IC_{50} (Concentration at which growth of 50% of the cell lines is inhibited) values for DENPs and PENPs in monkey kidney cell lines (VERO) and colon cancer cell lines (HT29) were found to be 250 and 125 µg/ml, respectively. Both the nanoparticles exhibited the same level of effect on the above two cell lines. Whereas in contrast to this, in lung cancer cell lines (A549) and larynx cancer cell lines (HEP2), the PENPs were found to be toxic at low concentrations of 62.5 µg in comparison to the DENPs which were toxic to A549 only at 250 µg and HEP2 at 125 µg.

Studies on breast cancer cell lines (MDA MB231) indicated that DENPs were more toxic at low concentrations of 62.5 µg than PENPs, which were found to be toxic only at 125 µg. Hence, the studies indicate different levels of cytotoxicity of these two particles on five different cell lines. It was observed that the cell viability was significantly reduced in a dose-dependent manner after the cell lines were treated with the vehicle exhaust nanoparticles using the Tetrazolium dye (MTT) assay.

Accurately assessing the toxicity and safety of these vehicle exhaust nanoparticles to human health is of utmost importance. Toxicity data generated in this study will be potentially useful to assess human risk exposure to these nanoparticles. Future studies should be focused on investigating the potential risk of these nanoparticles to human health at the microscopic cellular level by implementing appropriate *in vivo* toxicity method to reveal the general mechanisms of organ toxicity. More studies will be carried out in detail for organs like the brain and kidneys. The results of the present study indicate that these nanoparticles can be toxic to normal cell lines and to the cancerous cell lines at varying levels. Thus, the *in vivo* studies should be carried out to study in detail the vehicle exhaust particle-mediated toxicity.

IN VIVO TOXICITY STUDIES OF DIESEL EXHAUST PARTICLES

The human skin, intestinal tract and lungs are constantly in contact with the environment. The lungs and the intestinal tract allow the transport of water, oxygen or nutrients by the method of active or passive diffusion, whereas the skin acts as a strong barrier. The lungs and the intestinal tract are more prone to the entry of nanoparticles inside the human body (Hoet et al., 2004). Once these particles enter the circulatory system, they can cross various organ barriers (Table 2) and affect other vital organs (Figure 5). Inflammation, oxidative stress and carcinogenicity are the major effects of nanoparticles.

Lung toxicity

The lungs being the main site of gas exchange have two important parts; airways for the transportation of air and the alveoli for gas exchange. Human lungs contain about 2,300 km of airways and 300 million alveoli. In human adults, the internal surface area of the lungs is 140 m^2. The large surface area of the alveoli makes the alveoli less protected against environmental damage when compared to the airways, hence the lung is the primary site of entry for the inhaled nanoparticles (Hoet et al., 2004; Buzea et al., 2007). The main mode of deposition of these nanoparticles is diffusion, due to displacement when they collide with air molecules. The lungs mainly receives nanoparticles of size between 10 to 20 µm, while the naso-pharyngeal region captures particles of size less than 10 µm as shown in the figure (Oberdorster et al., 2001). DEP causes inflammation in rat lungs (Miyabara et al., 1998; Tsurudome et al., 1999) and in human lungs (Nordenhall et al., 2000) following short-term, high level exposure.

Evidence of the oxidative properties of DEP *in vivo* is shown by increased level of 8 OH dG (8 hydroxy deoxyguanine), the oxidative adduct of hydroxyl radical in the lungs of rats following exposure, and in cells in culture treated with DEP (Ichinose et al., 1997; Arimoto et al., 1999). Studies have shown that DEP exposure may be

Table 2. Nanoparticles and related toxicity.

S/No.	Mode of entry of nanoparticle	Toxicity involved	Related diseases	References
1	Lung through inhalation	Pulmonary toxicity	Asthma, bronchitis, emphysema, lung cancer, and neurodegenerative diseases, such as Parkinson's and Alzheimer's diseases	Borm et al. (2004, 2006), Oberdorster et al. (2005) and Peters et al. (2006)
2	In circulation	Organ toxicity	Arteriosclerosis, blood clots, arrhythmia, heart diseases, and ultimately cardiac death	Brown et al. (2002), Chen et al. (2006), Geiser et al. (2005), Liu et al. (2006) and Vermylen et al. (2005)
3	In the gastrointestinal tract	Intestinal toxicity	Crohn's disease and colon cancer	Buzea et al. (2007), Gatti et al. (2004), Oberdorster (2004) and Takenaka et al. (2001)
4	Immune system	Immunotoxicity	Autoimmune diseases, such as systemic lupus erythematosus, scleroderma, and rheumatoid arthritis	Ng et al. (2004), Peters et al. (2006), Noonan et al. (2006) and Pfau et al. (2005)
5	Through skin	Dermal toxicity	Dermatitis	Borm et al. (2006), Oberdorster et al. (2005), Tinkle et al. (2003) and Toll et al. (2004)

be the cause of diseases such as asthma in patients (Proietti et al., 2003; Takizawa, 2004). The study subjects were exposed to DEP of concentration 300 pg/m^3, results indicated marked neutrophilic inflammatory response in the airways followed by increases in blood neutrophil and platelet counts (Holgate et al., 2003). Visits to the emergency department for pulmonary complaints have been shown to increase during periods of severe air pollution (Wilson et al., 2005).

Studies by Diaz-Sanchez et al. (2000) showed that diesel exhaust particles can cause degranulation of mast cells and release histamine which further can cause chronic cough, sinusitis, pharyngitis and laryngitis (Groneberg-Kloft et al., 2006). Many of the hydrocarbon molecules emitted by diesel engines are quite toxic to the lungs. Studies in Mexico City on humans by Churg et al. (2003), showed that ultrafine particles were embedded in the airway mucosa. Workers in enclosed spaces such as mines and ships are especially at risk from DEP-induced pulmonary disease (Jorgensen and Svensson, 1970).

TOXICITY OF THE HEART

Diesel exhaust particles also induce cardiac effects such as heart rate variability and ventricular arrhythmia. A significant decrease in left-ventricular systolic pressure and an increase in left-ventricular end-diastolic pressure were observed in animal models (Wold et al., 2006; Anselme et al., 2007). Myocardial damage due to superoxide radical induced by DEP was studied (Okayama et al., 2006). Cardiac effects due to diesel exhaust particles results in coronary vasoconstriction, transient thrombus formation, carbon monoxide exposure, and altered myocardial energetic (Mittleman, 2007).

A recent study of postmenopausal women concluded that there was an increased risk of cardiovascular disease with long-term exposure to air pollution containing diesel (Miller et al., 2007). Onset of myocardial infarction was seen associated with one hour exposure to vehicle traffic containing diesel exhaust particles (Peters et al., 2004). DEP exposure studies in guinea pig models proved them to be cardiotoxic (Minami et al., 1999). Effect of DEP on the synthesis of Immunoglobin E and on the release of histamine was studied (Mamessier et al., 2006). The relationship between atherosclerosis and air pollution has also been investigated. The study rabbits were exposed to particulate matter of size 10 microns for 4 days, followed by histological examination of bone marrow lesions (Suwa et al., 2002).

DEP AND HYPERTENSION

Several studies demonstrated the relationship between DEP exposure and hypertension. Short-term inhalation of fine particulate air pollution and ozone, at concentrations that occur in the urban environment, causes acute conduit artery vasoconstriction. 25 healthy adults underwent exposure to 2 h inhalation of ≈150 µg/m^3 of concentrated ambient fine particles along with ozone (Brook et al., 2002). At levels encountered in an urban environment, inhalation of dilute diesel exhaust impairs

two important and complementary aspects of vascular function in humans: the regulation of vascular tone and endogenous fibrinolysis. These important findings provide a potential mechanism that links air pollution to the pathogenesis of atherothrombosis and acute myocardial infarction (Mills et al., 2005).

RENAL TOXICITY

Acute renal failure (ARF) is increasingly becoming more frequent and is associated with high costs and adverse clinical outcomes, including excess mortality, increased length of hospital stay, and the requirement for chronic dialysis in survivors.

Studies showed the potentiating effect of diesel exhaust particles (DEP) in an animal model of ARF induced by a single ip injection of cisplatin (CP) in rats, followed by the intra-tracheal administration of DEP of concentration 0.5 or 1 mg/kg. The results indicated increased serum concentrations of urea and creatinine and the reduced glutathione (GSH) concentration and superoxide dismutase activity in renal cortex. Also, renal tubular necrosis; increased urine volume, protein concentrations, and N-acetyl-*b*-D-glucosaminidase (NAG) activity, followed by decreased urine osmolality was seen (Nemmar et al., 2010). The changes in the above parameters can be considered as evidences for renal toxicity.

BRAIN TOXICITY

Association between exposure to diesel exhaust and neuro-inflammation was investigated in study rats. Rats were exposed to DEP through a nose only exposure chamber for 6 h a day, 5 days a week, for 4 weeks. Pro-inflammatory markers such as cytokines were studied in different brain sections and compared.

Tumour necrosis factor alpha and Interleukin 1 were found to increase in the striatum region of the brain (Miriam et al., 2010).

Another study group demonstrated that brain inflamemation was induced by air pollution from different sources and as a result, histopathology changes similar to those seen in patients with Alzheimer's disease were observed (Garciduenas et al., 2004). Learning ability, coordination, memory, and judgment in both children and adults were affected due to chronic exposure to diesel exhaust particles (Margai and Henry, 2003). Studies demonstrated slowness of response, memory loss and disordered sleep which is suggestive of neurobehavioral impairment in workers whose occupations involved significant indoor diesel exhaust exposure (Kilburn et al., 2000).

DEP AND INFERTILITY

Many studies have shown a correlation between diesel exhaust exposure and premature births, low birth weight in infants and elevated infant mortality rates (Kim et al., 2004; Parker et al., 2005; Dolk at al., 2003). Another study group demonstrated decrease in adult sperm production and sperm motility in animal models (Watanabe, 2005) and aberration of sex hormone production in chronically exposed female rats. Exposure of DEP to pregnant rats demonstrated negative effects (Fredricsson et al., 1993). Isolation of 4-nitrophenaol (PNP) from DEP demonstrated that DEP has estrogenic and antiandrogenic activities *in vivo*, leading to sterility (Li et al., 2006). Investigations have also reported that the presence of PNP in the environment may be one of the factors responsible for the increasing incidence of sterility in humans and animals.

DEP AND CARCINOGENICITY

In 1989, the International Agency for Research on Cancer concluded that there is sufficient evidence for the carcinogenicity of diesel exhaust in experimental animals but limited evidence for carcinogenicity in humans. Animal studies showed direct DNA damage and carcinogenesis due to DEP exposure (Dybdahl et al., 2004) as a result of generation of reactive oxygen species. Mutation and DNA strand breakage were also observed due to formation of Poly Aromatic Hydrocarbon-DEP adducts (Li et al., 2006). Lung cancer has been reported by studies on railway workers, smokers as well as non-smokers (Parent et al., 2007). Gustavsson et al. (1993) reported that workers exposed to combustion products had a higher incidence of esophageal cancer. The possible relationship between exposure to DEP and multiple myeloma was investigated (Lee et al., 2003). In a study by Guo et al. (2002) human exposure to DEPs was associated with a higher risk of ovarian cancer but not with esophageal, testicular, or urinary tract cancers or leukemia.

DEP AND HEPATOTOXICITY

Diesel exhaust contain dozens of liver damaging poisons such as lead, sulfur and nitrogen oxides, acetaldehyde, cadmium, and peroxyacetylnitrile. The ability of liver microsomes to oxidize benzo alpha pyrene on chronic exposure to diesel exhaust particles was studied. Results showed that the microsomes were unable to generate polar metabolites from benzo alpha pyrene on exposure to highest concentration of DEP. Further studies with liver microsomes showed that after several months of exposure, there was no evidence for the induction of either cytochrome P-450 or cytochrome P-448 (Navarro et al., 1981). Studies indicated that DEP exposure and mortality due to atherosclerosis and cirrhosis of the liver are directly related. The main factor involved in atherosclerosis is Peroxisome Proliferator Activated Receptor (PPAR α). Studies were investigated whether nanoparticle-

rich diesel exhaust (NR-DE) affects the liver and how PPARα is involved in the NR-DE induced effects. The results indicated that NR-DE induced hepatic inflammation and dyslipidemia (Ito et al., 2011).

DEP AND PLACENTAL TOXICITY

Studies investigated the effects of DEP exposure on DNA adduct formation, and DNA deletions and levels of oxidative DNA damage during the embryonic development in mice. Oral exposure to various concentrations of DEP resulted in black pigmented spots in the retinal pigment in the epithelium of offspring mice. Results also revealed that transplacental exposure to DEP showed increase in frequency of DNA deletions and other genetic alterations in the mice offsprings (Reliene et al., 2005). Recent studies suggest that diesel exhaust possesses endocrine activity and therefore may affect reproductive outcome (Hougaard et al., 2008). Studies involving *In utero* exposure to DEP revealed decrease in weight gain of DEP exposed offspring compared to the control groups. This difference increased significantly during lactation. The other biomarkers of placental toxicity were found to be similar. mRNA levels of inflammatory cytokines IL-2, IL-5, IL-12 alpha, IL-12 beta increased in placentas exposed to DEP. IL-5 mRNA was markedly increased in DEP-exposed placentas, although levels were barely detectable in control placentas. IL-6 mRNA expression was increased approximately 10-fold in placentas exposed to DEP. It has been studied that expression of mRNA encoding proteins involved in immune function in the placenta is increased during fetal absorption in mice (Ayaha et al., 2005).

POTENTIAL TREATMENT FOR TOXICITY

The particle component of air pollutant called the particulate matter is responsible for deaths of more than 5 lakh people every year (US Environmental Protection Agency); the major composition being vehicle exhaust particles which mainly include DEP. The DEP contain dozens of organ damaging poisons. It consists of a carbon core onto which different compounds of organic nature are attached. The main mechanism involving the toxicity of diesel exhaust particle include the depletion of antioxidant enzymes.

Lung inflammation was induced in male mice using DEP for 20 days using the method of intranasal instillation. Ten days before instillation, animals were treated with different concentrations of natural treatment product *Annacardium occidentale* (cashew). The different enzymatic activities such as glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase (GST) and catalase (CAT) were evaluated. Results showed that the lungs were protected by the increasing antioxidant enzyme activity of *A. occidentale* (cashew) (Carvalho et al., 2011). Similar treatment studies were performed for other air pollutant induced toxicity like 1,2-dimethylhydrazine (DMH) using natural and synthetic treatment products (Durao et al., 2011).

Treatment studies were performed in Wistar rats using synthetic products like bisdemethoxycurcumin analog (BDMC-A) on 1,2-dimethylhydrazine (DMH)-induced oxidative stress during colon carcinogenesis. The animals were given sub-cutaneous injection weekly for 5 days of DMH, DMH+BDMC-A. The group administered with only DMH showed lower lipid peroxidation with higher activities of GSH-dependent enzymes. In the other group, no tumours were observed. The Lipid peroxidation and GSH-dependent enzyme levels were also similar to that of the control group. Hence, It shows that BDMC-A offers chemoprevention against colon carcinogenesis (Devasena et al., 2005). Thus, both natural and synthetic drugs can be used for the treatment of toxicity. Treatment studies for *in vitro* and *in vivo* toxicity are underway in our laboratory.

DISCUSSION

The atmosphere is a complex dynamic natural gaseous system that is essential to support life on planet Earth. The earth's lower atmosphere or troposphere extends from the ground to a height of 15 km and is filled with breathable gases. It also contains environmental aerosols that originate from anthropogenic and biogenic activities (man-made and natural). Indoor air pollution and urban air quality are listed as two of the world's worst pollution problems in the 2008 (Blacksmith Institute World's Worst Polluted Places report). Population in India is increasing day by day and in turn increasing the urban pollution levels through increase in mass transportation vehicles. The population is mainly exposed to high air pollution concentrations, where motor vehicle emissions constitute the main source of fine and ultrafine particles, having a serious impact on our urban air quality and public health. Motor exhaust emissions is a complex mixture of gases and particulate matter (PM).

PM emitted by motor vehicles consists of fine particles, and a large fraction of these particles has an aerodynamic diameter less than 1 µm. $PM_{2.5}$ of diameter 2.5 µm can also be formed in the atmosphere as aerosols from chemical reactions that involve gases such as sulphur dioxide and nitrogen oxides. Sulfates, which are commonly generated by conversion from primary sulfur emissions, make up the largest fraction of $PM_{2.5}$ by mass. $PM_{2.5}$ can also form as a result of solidification of volatile metals salts as crystals, following cooling of hot exhaust gases from vehicles in ambient air. Gasoline fueled vehicles have lower PM emission rates than diesel-fueled vehicles. PM emissions from gasoline fueled vehicles result from unburned lubricating oil and ash-forming fuel

and oil additives. PM emitted by diesel-fueled vehicles consists of soot. Diesel exhaust particles (DEPs) are globally relevant air pollutants that exert a detrimental human health impact. However, mechanisms of damage by DEP exposure to human respiratory health and human susceptibility factors are only partially known.

CONCLUSION

Until alternative energy are fully developed and implemented, reliance on diesel fuel will increase. Acute and chronic exposure to diesel exhaust will continue to be a problem in India. This will ultimately increase the number of patient to emergency departments with pulmonary, cardiopulmonary disease, neurological disorders, and adverse perinatal events. New regulations and technology to reduce DEP emissions in vehicles by the government should be fully implemented effectively. Also, treatment using both natural and synthetic drugs against *in vitro* and *in vivo* toxicity should be explored.

ACKNOWLEDGEMENT

We would like to acknowledge the financial support provided by DST, New Delhi under the INSPIRE FELLOWSHIP SCHEME Proc No. 8946/PD6/2010.

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