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Airborne Particulate Matter and Increased Risk of Lung Cancer- Mechanisms of Carcinogenesis by Reactive Oxygen Species and the Role of Oxidative Stress

Abstract

Urban air pollution has been one of the most important pollution problem for many decades. Airborne particulate matter (PM) from combustion sources is considered the most important air pollutants for adverse health effects to humans, especially for acute and chronic respiratory diseases and lung cancer. Airborne particles contain a number of toxic and carcinogenic substances as well as persistent free radicals entering the lung's alveoli. PM in the lungs can generate free radicals and reactive oxygen species (ROS), initiating mechanisms of oxidative stress, inflammation and mutagenic damage to cellular DNA. These conditions lead progressively to increased morbidity and mortality as well as to increased risk of lung cancer. In the last decades a number of studies investigated PM size focusing to PM with aerodynamic diameter below l0 μm (PM_{10} and $PM_{2.5}$), transition metals, polycyclic aromatic hydrocarbons (PAH), stable quinoids ɑnd carcinogenic nitropyrenes. ROS generated by PM are linked to the pathogenesis of pulmonary oxidative damage, lipid peroxidation, damages to enzymes and cellular DNA. In our experimental study we investigated ROS generation by airborne PM (exhaust soot diesel and gasoline) by Electron Paramagnetic Resonance (EPR) and persistent free radicals characteristic to a mixture of semiquinone radicals. Also, we examined by EPR the formation of oxidative damage to guanosine nucleobase. by PM in aqueous phosphate buffer (pH 7.4) and the formation of the cancer biomarker 8-hydroxy-2'-deoxyguanosine.

Keywords: Airborne particulates; Particulate matter; Reactive oxygen species; Free radicals; Lung cancer; Carcinogenic mechanisms; Cancer biomarker.

Introduction

In the last two decades numerous studies and epidemio-logical investigations have established an association between exposure to airborne particulate matter (PM) from various air pollution sources and adverse health effects [1]. Current day concentrations of ambient air pollution have been associated with premature mortality and morbidity due to cardiovascular and respiratory diseases and lung cancer [2]. Air pollution pollutants, especially inhalable particulate matter (PM) has been associated with increased risk to lung cancer for non-smokers inhabitants in urban cities [3-7].

Case-control studies in the last decade provided the evidence of a link between air pollution from traffic and lung cancer for non-smokers [8, 9]. Short-term studies in the USA investigated the 20 largest metropolitan areas (50 million inhabitants) during 1987-1994. All-cause mortality increased by 0.5% for each 10 μg/m^3 of PM_{10} [10]. These findings are very close to the European results from the APHEA Programme with studies covering 43 million people living in 29 European cities. The combined effect estimate showed that all-cause daily mortality increased by 0.6% for each 10 μg/m3 increase in PM_{10} [11, 12].

Although inhaled air PM and other air pollutants have been linked epidemiologically with increasing respiratory and cardiovascular morbidity and mortality, there is still a fundamental lack of understanding of the underlying biological mechanisms [13]. Suspended air particulates, O_3 and NO_x share the same properties as potent oxidants, oxidizing important cellular and other biological molecules, either through direct attack in the cellular compartments or indirectly through the activation of intracellular free radical pathways [14, 15]. Experimental observations in vivo and in vitro showed that particulate air pollutants cause pulmonary toxicity by retention and direct interaction in airways and alveoli, interference with either mucociliary or phagocytic clearance of inhalable particles. PM contain numerous toxic chemical adsorbed onto the porous surface of the particle and can easily be transported in the lungs. PM is known for the ability to generate reactive oxygen species (ROS) and other oxidants, which cause oxidative stress and subsequently initiate respiratory inflammatory responses [16-19].

Studies showed that lung cancer (LC) and cardiovascular disease (CVD) mortality risks increase with smoking and exposure to fine airborne particulate matter (PM) for aerodynamic diameter 10-2.5 μm (PM_{10}, $PM_{2.5}$). Prospective cohort data for 1.2 million adults were collected by the American Cancer Society as part of the Cancer Prevention Study II. For lung cancer mortality, excess risk rose nearly linearly, reaching maximum Relative Risks (RR) > 40 among long-term heavy smokers. Excess risks for CVD mortality increased steeply at low exposure levels and leveled off at higher exposures, reaching RRs of approximately 2–3 for cigarette smoking. The exposure–response relationship associated with PM2.5 is qualitatively different

for LC versus CVD mortality. At low exposure levels, CVD deaths are projected to account for most of the burden of disease, whereas at high levels of $PM_{2.5}$, LC becomes proportionately more important [20]

Epidemiological studies have reported associations between airborne fine particles in urban air pollution (aerodynamic diameter ≤ 2.5 μm; $PM_{2.5}$) and mortality. Researchers addressed epidemiological problems by using 11 additional years of follow-up of the Harvard Six Cities study, incorporating recent lower exposures. Each increase in $PM_{2.5}$ (by 10 μg/m3) was associated with an increased risk of all-cause mortality of 14%, 26% increase of CVD and 37% of lung cancer mortality [21].

Why inhalable PM cause lung toxicity and oxidative stress

The aerodynamic diameter of the airborne particles plays an important role for the penetration and retention into the lungs and their cytotoxicity. Particles penetrate into the lower respiratory system, the PM_{10} and $PM_{2.5}$ and into the gas-exchange region of the lungs. The ultrafine particles (smaller diameter than 0.1 μm), which are abundant in numbers with very large surface area can be absorbed into tissues and can enter the blood circulation [22, 23] The lung airways retain mostly $PM_{2.5}$ rather than PM_{10}, a finding supporting the observation, in some studies, that adverse health effects appear to correlate better with $PM_{2.5}$ than with PM_{10} concentrations Analytical electron microscopy measurements in never-smoking long-term residents of Vancouver (low air pollution) showed that 95% of the effectively retained particles in the lung parenchyma were $PM_{2.5}$ and only 5% were ultrafine particles [24-26].

Although the actual mechanisms by which the particles cause acute and chronic pulmonary damage remain more complicated than it was suggested at first, it is widely accepted that inhalable PM causes oxidative damage to the tissues of the lungs through the generation of ROS [27, 28] Experiments with metals and metal complexes associated with PM surfaces were found to cause acute lung injury (oxidative damage mainly, enzyme oxidation) in experimental animals. Also, Iron (Fe) released from airborne PM play a catalytic role in the generation of reactive oxygen species (ROS), especially hydroxyl radicals (HO•), causing extensive damage to cellular biological molecules [29-32].

Generation of ROS, reactive nitrogen species (RNS) and other oxidants [such as ozone (O_3) and nitrogen oxides (NO_x)] are considered very important mechanisms for pulmonary damage, oxidative stress leading to inflammation and subsequently to initiation of carcinogenic mechanisms [15, 33-35].

Research on inhalable PM from combustion sources (diesel, gasoline, wood burning, cigarette smoke tar, etc)) discovered that particles contain high concentrations of stable and persistent semiquinone radicals that have the ability to generate ROS (including highly reactive HO•) by quinoid redox cycling. The redox cycling of semiquinones has been proposed as a mechanism of toxicological importance in the lungs by diesel exhaust particles. Cigarette tar contains stable semiquinone [36] radicals that is considered as the most damaging component [34, 37] Persistent free radicals in PM and transition metals catalyse the generation of ROS causing increased oxidative damage and cellular cytotoxicity [38-41]. Airborne particulates in urban areas and their ability to generate ROS and oxidative damage in the lungs is considered as an important mechanism for the increased risk of lung cancer [35, 42].

In this study, we used a series of specimens of particulate matter from various pollution sources: a) Total Suspended Particulates (TSP), PM_{10} and $PM_{2.5}$ from a commercial area with heavy vehicle traffic (center of Athens, Greece), b) fresh soot produced from diesel and gasoline vehicles and soot of diesel and gasoline deposited in the exhaust pipes, c) soot deposited on chimney walls from wood combustion. Our aim was to explore the possible mechanisms, interactions and parameters influencing the formation of reactive oxygen species of toxicological and carcinogenic interest. We investigated the generation of stable free radicals by Electron Paramagnetic Resonance (EPR), the formation of superoxide anion ($O_2^{\bullet-}$) and hydroxyl radicals (HO•) through the involvement of the transition metals and stable radicals of quinoids, present in the airborne particulate matter. Also, we investigated the radical damage to nucleobases of DNA by hydroxyl radicals produced from PM in aqueous buffer solutions.

Materials and Methods

Samples of airborne suspended particulates

(a)Total suspended particulates (TSP) were collected in the period 2003–2004 (centre of Athens. Greece by technicians of Division of Atmospheric Pollution and Noise Control of the Ministry of Environment, Regional Planning and Public Works), by high volume pumps ($80m^3/h$ on a 24 h basis) using pre-weighed glass microfiber filters (Whatman GF/A 20.3 × 25.4 cm) with 99% collection efficiency for particles with 0.3 mm diameter, (b) Samples of soot from diesel vehicles were collected on annealed glass-fiber filters (Ø 5 cm), using a low volume air sampler, at a distance of 0.5m from the exhaust pipe of a diesel taxi. (c) Samples of gasoline exhaust particles were collected from a gasoline on annealed glass-fiber filters (Ø 5 cm), using a low volume air sampler, at a distance of 0.5m from a gasoline exhaust engine, (d) Samples of soot from wood combustion (pine, olive oil tree, beech) were collected on a glass microfiber filters from a domestic fireplace exhaust., (e) PM10 were collected in the same site as in the case of TSP with a high volume sampling system equipped with a six-stage slit cascade impactor (Andersen) with back-up filter, which effectively separated into seven fractions., (f) $PM_{2.4}$ were collected with the same high-volume cascade impactor (Andersen) system. We used the fraction with aerodynamic diameter 2.4 μm.

Electron Paramagnetic Resonance (EPR) characterization of particulate matter

The EPR spectra of all samples were measured using a Varian E-4 EPR spectrometer. The g-values of EPR spectra were calculated from the g-value (2.0036) of the stable free radical of 2,2-diphenyl-1-picrylhydrazyl (DPPH). Pre-weighed samples (mg) of soot were inserted in quartz EPR tubes and their spectrum was recorded. Comparison was achieved with the EPR spectrum of pre-weighed sample of DPPH (which is known to be 95% in a stable free radical state).

Extraction and separation of PM from filters-identification of radicals by EPR

Filters were cut into smaller pieces and added to a conical flask with 50 ml of deionised water. PM were extracted, first by vigorous shaking (20 min) and subsequently by sonication in a waterbath at 20°C for another 20 min. The suspension was centrifuged for 20 min and the precipitate was dried with a speed vacuum-dryer; under these conditions, 0.01-0.05 g of solid (TSP) was obtained

The EPR spectral characteristics of o- and p-semiquinone radical

anions were observed in aqueous extracts of PM following the method by Zang et al. [43]

Aqueous extracts of PM samples (sonication for 30 min) were incubated in air-saturated 50 mM carbonate-buffered solution (pH 10.0). The EPR spectral profile showed the presence of o- and p-semiquinone radical anions with g values of 2.0035–2.0040. To confirm the generation of o- and p-semiquinone radical anions, we compared the EPR spectra of freshly prepared, aerated buffered solutions (pH 10.0) of 1,2-and 1,4-naphthoquinone, 1,4-benzo-quinone, catechol and 1,4-dihydroxybenzene under similar alkaline conditions.

Spin trapping of superoxide anion and hydroxyl radicals

The first set of experiments concerned the generation of superoxide anion ($O_2^{\bullet-}$) spin-trapped by DMPO (5,5-dimethyl-pyrroline N-oxide), without addition of H_2O_2 of the final volume of the mixture. The positive standard for $O_2^{\bullet-}$ is based on the spin-trapping of DMPO-OOH generated by KO_2 in DMSO with the addition of 18-crown-6 ether to complex K^+. The generation of hydroxyl radicals from soot ($HO^{\bullet}$) was performed with the spin trap DMPO using well known techniques.

Spin-Trapping of $OH^{\bullet}$ and its adduct to guanosine-5'-phosphate nucleobase

One of the most important biomarker of oxidative attack by ROS in DNA is the 8-hydroxy-2'-deoxyguanine (8-OHdG). An extensive review on the subject of 8-OHdG and its valuable contribution as a biomarker of carcinogenesis was published by Valavanidis et al [44].

We experimented with the formation of 8-OHdG by suspended particulates at pH 7.4 solutions.

Samples of particulate matter (PM) from various pollution sources were extracted by dichloromethane then evaporated to dryness and re-suspended in phosphate buffer (pH 7.4). These samples were tested for their ability to produce oxidative damage to the nucleobase, 5'-guanosine monophosphate, sodium salt (G-5'-P) through the production of hydroxyl radicals ($HO^{\bullet}$). As a standard method of hydroxyl radicals it was used the Fe^{2+}/EDTA (sodium salt)-H_2O_2 couple in phosphate buffer (pH 7.4) and the produced radical of the nucleobase was spin-trapped by the MNP (2-methyl-2-nitroso-propane, dimmer, Me_3C-N=O). The MNP solution contained 10-15% acetonitrile (having been left to stir for 2-5 hours to bring about the dissolution of the spin-trap). The EPR spectra support the formation of a mixture of C5 and C4-hydroxyl adducts. To test the effect of chelators on the radical generating activity of PM samples, we used EDTA- Na_2 and desferrioxamine. Ferrous ions (Fe^{2+}) form complexes with EDTA, which increase the ability to produce hydroxyl radicals by lowering the redox potential of iron via chelation. Desferrioxamine blocks all available valences of iron thus reducing substantially its redox potential. Concentrations of the reactants in the final sample were typically 15-30 mg cm-3 (substrate, nucleobase), MNP 10-2 mol dm-3, 25-50 mg cm-3 sample of particulate matter, hydrogen peroxide, H_2O_2 , 1×10^{-2} mol dm^{-3}, phosphate buffer (pH 7.4). Before and during mixing, solutions for EPR experiments were purged with dry nitrogen for 2 min to expel oxygen and then transferred in a flat-type quartz cell EPR instrument.

Results of Experiments

EPR measurements of persistent quinoid radicals

The EPR spectra of solid samples of particulate matter from a series of air pollution sources: A. diesel, B. gasoline exhaust particulate matter, C. wood burning soot and D. TSP from the Athens area, are shown in traces A-D (Figure 1). For comparison, trace E depicts the

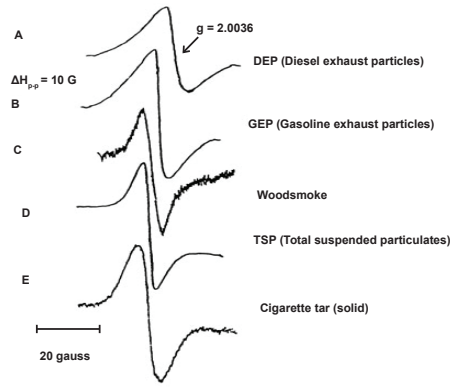

Figure 1: EPR spectra for the particulate matter samples from 5 different air pollution sources. Trace A, diesel exhaust soot (center of Athens); trace B, gasoline exhaust soot; trace C, wood burning soot; trace D, TSP; trace E, cigarette tar.

EPR spectrum of a sample of cigarette tar (in solid form) from smoking of 5 cigarettes retained on a Cambridge filter, extracted with benzene and evaporated to dryness. All samples have similar EPR spectra with a single broad unstructured signal with g-value in the range of 2.0035-2.0040, corresponding to a signal from semiquinone ($QH^{\bullet}$) radical. The broadness, (ΔHp-p = 9.5-10 G) of the EPR signal indicates that is the result of a group of semiquinone, but it may due to the non homogeneous samples and various interactions of the semiquinones with metal ions.

The radicals observed in solid particulate matter of all samples are persistent and are observed even in stored samples for several months. As in the case of cigarette tar, these semiquinone radicals is a dynamic mixture of hydroquinone (QH_2), semiquinone ($QH^{\bullet}$) and quinone (Q) [43]

Measurements of $O_2^{\bullet}$ and $HO^{\bullet}$ from PM extracts

The production of superoxide anion from DMSO solutions of organic solution extracts of PM is considered as a very important mechanism for the generation of hydrogen peroxide and then the damaging hydroxyl radicals ($HO^{\bullet}$). We experimented with whole suspensions of particulate matter (both soluble and insoluble) in DMSO with the spin trap DMPO (concentrated, 110 mM). The production of $O_2^{\bullet-}$ depends on the incubation time. The incubation time (at 37°C) plays an important role. Superoxide anion adducts [DMPO-OOH] were formed after 10 min incubation at room temperature and in subsequent EPR spectra were still present after 20 min (Figure 2).

Also, the EPR spectrum contains signals for another two radicals, namely adducts of hydroxyl radicals $HO^{\bullet}$[DMPO-OH] and CH_3 radicals [DMPO-CH_3], generated from the DMSO [$(CH_3)_2SO$] by the oxidative attack of the hydroxyl radical. The relative contribution of each of these spin adducts to the simulated spectrum was approximately 1:1:1. Fresh diesel exhaust particles (DEP) are the most active, compared to other PM samples, in the production of $O_2^{\bullet-}$. These results are similar to in vitro experiments with DEP in DMSO (DEP was extracted twice with CH_2Cl_2, evaporated to dryness and residues were dissolved in DMSO) by Sagai and co-workers [33,37]. In order to show that the production of $O_2^{\bullet-}$is the result of quinoid substances in PM, we washed DEP with methanol (removing most of the adsorbed compounds) and the remaining black soot (which is similar to Norit charcoal), after drying, produced under similar conditions very little $O_2^{\bullet-}$ (results not shown).

In another series of experiments, we used the supernatant solution

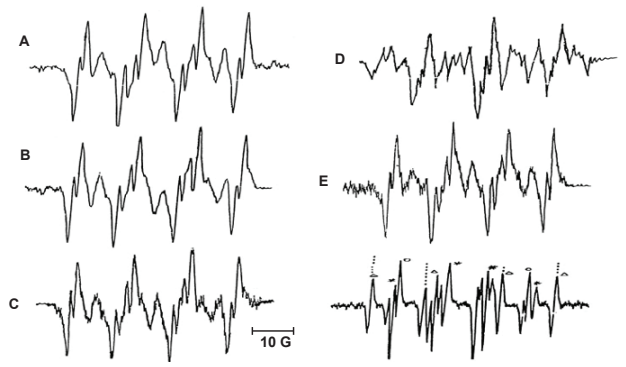

Figure 2: EPR spectra of particulate matter in DMSO. The multiple spectrum represents three spin adducts: DMPO-OH, DMPO-OOH and DMPO-CH_3 (produced from the attack of HO• radical to DMSO [(CH3)2SO]. A, DEP; B, GEP; C, TSP; D, woodsmoke soot; E, cigarette tar; F, simulation of three spin adducts with EPR parameters (hyperfine coupling constants):

(after centrifugation) and the whole suspensions of PM in phosphate buffer (pH 7.4) without H_2O_2 and in the presence of concentrated spin trap DMPO (100 mM) (Figure 3).

Superoxide anion was formed immediately in the suspension (EPR spectra of spin adduct DMPO-OOH, 2 min after final mixing), but it was replaced very quickly (7-8 min) by hydroxyl radical adducts [DMPO-OH] due to the spontaneous thermal decay of superoxide adduct. The supernatant solution (centrifuged and filtered, containing mainly soluble metal ions and inorganic salts) without H_2O_2 did not produce the spin adduct DMPO-OH (spectra not shown). However, when H_2O_2 was added to the supernatant solution, only a strong signal of DMPO-OH appeared (Figure 4). In another series of experiments, we used the supernatant solution (after centrifugation) and the whole suspensions of PM in phosphate buffer (pH 7.4) without H_2O_2 and in the presence of concentrated DMPO (100 mM) (Figure 3).

Generation of radical HO• by the addition of H2¬O¬2

Iron (Fe) is the most prominent transition metal present in PM suspensions, its role was assessed using the iron chelators EDTA and desferrioxamine. Ferrous ions in PM generate hydroxyl radicals. It was tested by the addition of EDTA-Na2 which increased the signal of DMPO-OH (Figure 4). The addition of desferrioxamine inhibited HO• formation totally. Under physiological conditions, iron is only slightly soluble, tending to form precipitates with anions and inorganic phosphate.

However, a variety of chelating agents (such as EDTA) greatly increase the solubility of iron. The addition of EDTA to a generating system of $O_2^{\bullet-}$ in the presence of Fe3+ markedly increased the formation of HO• by increasing the effective concentration of Fe^{3+} (the catalytic activity of iron requires at least one co-ordination site that is open or occupied by a readily dissociated ligand such as water) at neutral pH (Figure 4).

EPR measurements of adducts to guanosine nucleobase

Spin-trapping experiments confirm that hydroxyl radicals produced by various samples of PM in the presence of hydrogen peroxide induce damage in the form of hydroxy-adducts to guanosine 5'-monophosphate nucleobase in phosphate buffer solutions (pH 7.4). The EPR spectra observed are similar to the ones observed with the Fe^{2+}-EDTA/H_2O_2 couple, producing

hydroxyl radicals. The hyperfine splittings: α(α-N)=1.54 mT (or 15.4 G) is the dominant signal triplet of triplets (1:1:1), and α(b-N) = 0.3 mT is assigned to with the spin trapping of the C4-OH radical moiety [38, 45,46]

Results and Discussion

Size and composition of PM has been important in promoting mechanisms of ROS, oxidative stress and inflammation in the respiratory system. Active quinoid substances are chemisorbed to the porous surface of the particles, may not be easily leach out and constitute the persistent part of the semiquinones with toxic properties. Similar radicals have been found in PM2.5, remarkably persistent and can be observed by EPR techniques [22, 41]

Various mechanisms have been proposed for the generation of superoxide anion ($O_2^{\bullet-}$) by the dynamic mixture QH_2/QH•/Q of quinoids in cigarette tar and fine PM. Superoxide anion can be transformed easily into H_2O_2 and the biologically damaging HO• in a metal-dependent reaction.

$$QH^{\bullet} + O_2 \rightarrow Q + O_2^{\bullet-} + H^+ \quad (1)$$

$$O_2^{-} + 2H^+ \rightarrow H_2O_2 + O_2 \quad (2)$$

These reactions establish a redox cycle, where the dynamic quinoid mixture in the presence of oxygen produces cytotoxic hydroxyl radicals which are well known for damages to proteins, lipids and DNA. Transition metals (relatively abundant in PM) play the usual role for the generation of HO•.

Pryor et al. published their pioneering investigation (1983) into the presence of stable free radicals in cigarette tar [47] Pryor and co-workers formulated the underlying mechanisms concerning oxidative damage and carcinogenesis by tobacco tar substances through ROS generation and oxidative damage to important biomolecules [36].

Ambient suspended air particulate matter (PM), which is produced by combustion of fuels (especially from motor vehicle exhausts) contains acid aerosols, organic compounds (quinones, PAHs, nitroPAHs, etc.), hydrocarbons, metals, crustal material and secondary particles formed

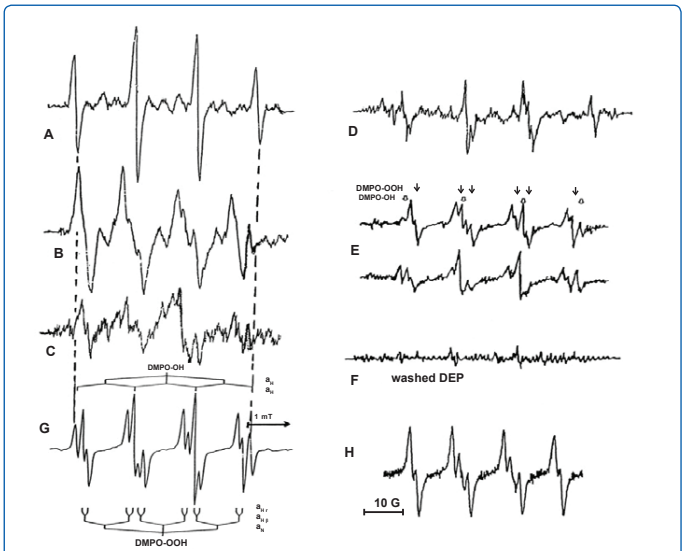

Figure 3: EPR measurements of $O_2^{\bullet-}$ and HO• generated from PM samples (suspensions) in phosphate buffer (pH 7.4): PM. A, TSP; B, DEP; C, GEP; D, wood smoke soot; E, cigarette tar; at two different time intervals, 2 min and 6 min; F, representative EPR spectra, DEP; G, simulation of spin adducts of DMPO-OH and DMPO-OOH; H, EPR spectrum of DMPO-OOH spin adduct.

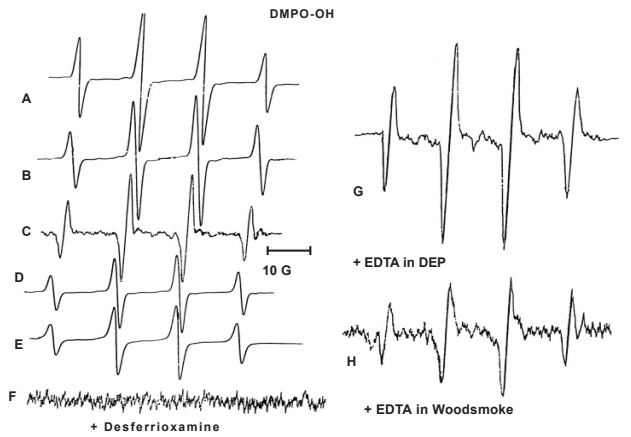

Figure 4: EPR spectra DMPO-OH. Generation of HO• by PM samples (addition of H2O2). Addition of EDTA increased the generation of HO•, whereas addition of desferrioxamine reduces substantially the production of HO• because it blocks effectively all co-ordination sites. A, DEP; B, GEP; C, TSP; D, wood smoke; E, cigarette tar; F, addition of desferrioxamine; G and H, addition of EDTA in DEP and wood smoke.

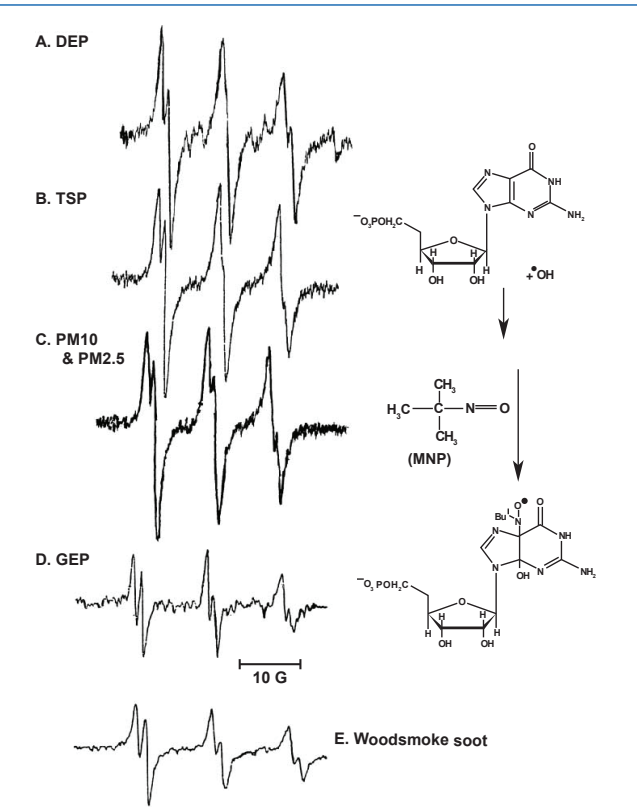

Figure 5: EPR spectra obtained from the reaction of HO• with 2' -deoxyguanosine at pH 7.4 in the presence of spin-trapping MNP. The hydroxyl radical was generated from various suspensions of airborne particulates with H_2O_2 in buffered solutions (pH 7.4). (A) diesel exhaust particles (DEP), (B) total suspended particulates (TSP), (C) PM_{10} and $PM_{2.5}$ (particulate matter), (D), gasoline exhaust particles (GEP), (E) woodsmoke.

by chemical reactions with gaseous air pollutants, adsorbed or attached to a typically carbonaceous core. The composition, size of particles and chemical characteristics of PM depend on combustion sources. Penetration and chemicals play an important role through mechanisms of ROS generation in promotinng oxidative stress, subsequently inflammation and finally initiate carcinogenic mechanisms in the lung environment [32, 35, 44, 46]

The presence of stable and persistent quinoid radicals in our opinion play a substancial part in PM toxicity in the respiraroty system. Samples of PM in our experiments showed the same broad EPR pattern of persistent free radicals for several months. The stabilization of the semiquinone radicals is probably the result of their adsorption into a polymeric carbonaceous core. Because of the carbonaceous core of the particles, we assumed that the main radicals are stable semiquinone radicals ($QH^{\bullet}$) or radical anions ($Q^{\bullet-}$) in a polymeric tarry matrix and carbon-centred radicals ($R^{\bullet}$). These radical have a potent ability to form continuously ROS.

The production of $HO^{\bullet}$ by suspended particulates in urban areas is an clear indication that transition metals, especially Fe^{2+}, or other metals with a redox potential, play an important role [47-49].

Although in cell-free experiments it was observed the production of ROS without the presence H_2O_2 , it is well known that H_2O_2 exists physiologically in various cell compartments, or is generated endogenously by certain cell types as a response to activation by specific cytokines or growth factors from inflammatory cells So this is another explanation why metals in PM play an important role for the generation of ROS.

The size of inhalable PM is also a very important factor for its cytotoxic potential. Fine particles can access subcellular compartments where they can deposit their toxic substances which are very difficult to clear by the mucociliary escalator. In these sites, they can effectively generate ROS near important biomolecules and cause oxidative damage. The $PM_{2.5}$ fraction is known to be retained in the lung parenchyma and in the respiratory bronchioles [23, 26, 50, 51]

Numerous experiments showed that suspended inhalable PM has the ability to cause oxidatively damaged to cellular DNA and the biomarker 8-hydroxy-2'-deoxyguanosine (8-OHdG) or its tautomer 8-Oxo-7,8-dihydroguanine (8-oxoGua) is an abundant mutagenic lesion which can give a clear indication for the carcinogenic process [44, 52].

Conclusions

Particulate matter from air pollution in urban areas, especially from fuel combustion, has the ability to generate ROS in the lungs, resulting in increased oxidative stress. Acute oxidative state can initiate inflammation in the respiratory system and mechanisms of carcinogenesis. The results of this study show that particulate matter from various pollution sources in urban areas, traffic-related diesel and gasoline exhaust particles and wood smoke, contains a mixture of stable semiquinone radical, metals and PAHs. The dynamic quinoid mixture in the presence of oxygen can produce superoxide anion and hydroxyl radicals without the presence of H_2O_2 in aqueous solution. It was found that the smaller of the aerodynamic diameter of the particles the higher the potential for the production of ROS, especially the damaging hydroxyl radical. Persistent free radicals, transition metals and other constituents of the respirable PM play an important role in mechanisms oxidative stress, leading to pulmonary tissue injuries and DNA damage. Thus, traffic-related particulate pollution can be very damaging to the respiratory system, causing acute and chronic respiratory diseases, inflammation, cytoxic processes that can initiate the multistep processes of lung cancer.

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