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REVIEW ARTICLE

Hazardous components and health effects of atmospheric aerosol particles: reactive oxygen species, soot, polycyclic aromatic compounds and allergenic proteins

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Abstract

This review outlines recent advances in the investigation of the chemical properties, molecular interactions and health effects of hazardous compounds in atmospheric aerosols, in particular reactive oxygen species (ROS), soot, polycyclic aromatic compounds (PACs) and allergenic proteins. Epidemiological studies show correlations between air particulate matter and adverse health effects of air pollution including allergy, asthma, cardiovascular and respiratory diseases, but the causative relations and mechanisms of interaction on the molecular level are still unclear. ROS generated by photochemical and heterogeneous reactions in the atmosphere seem to play a key role in aerosol health effects and provide a direct link between atmospheric and physiological multiphase processes. Soot and PACs can trigger formation of ROS *in vivo*, leading to inflammation and cellular damage. PACs as well as allergenic proteins are efficiently oxygenated and nitrated upon exposure to ozone and nitrogen dioxide, which leads to an enhancement of their toxicity and allergenicity.

Keywords: *ozone, nitrogen dioxide, tyrosine nitration, pollen allergy, air pollution*

Introduction

Aerosols consist of small particles that are suspended in a gas. They are ubiquitous in the atmosphere and play a central role in the Earth system, climate and public health. Aerosol particles serve as nuclei for cloud droplets and ice crystals involved in the formation of clouds and precipitation, they can scatter or absorb radiation affecting the Earth's energy balance, and they participate in heterogeneous and multiphase chemical reactions affecting the abundance and distribution of trace gases [1]. Bioaerosol particles like airborne bacteria, fungal spores, pollen and viruses play an important role in the spread and propagation of biological organisms and ecosystems. Moreover, the inhalation of pathogenic or toxic particles can cause diseases and oxidative stress posing a threat to public health [2–4].

Primary aerosol particles are emitted from a wide range of natural and anthropogenic sources, including wind-driven suspension of bioparticles, dust and sea spray, volcanic eruptions, wildfires and fossil fuel or biofuel combustion [5]. Secondary particle formation in the atmosphere proceeds through gas-to-particle conversion by chemical transformation, nucleation and condensation of gaseous precursors like volatile organic compounds (VOC) and sulphur gases [6]. As shown in Figure 1, fine particles with diameters in the range from about 1 nm–1 μm consist predominantly of sulphate, secondary organic aerosol and soot with typical number concentrations of the order of 10^3 cm^{-3} in urban air [5]. Coarse particles with diameters larger than 1 μm are mostly dust, sea salt, and bioparticles, with typical number concentrations < 1 cm^{-3}. Note that technically there are different cut-off diameters of 1, 2.5 and 10 μm between fine and coarse particles. Cloud and fog droplets are in the same size range as coarse aerosol particles, but in atmospheric science, they are treated separately as they consist

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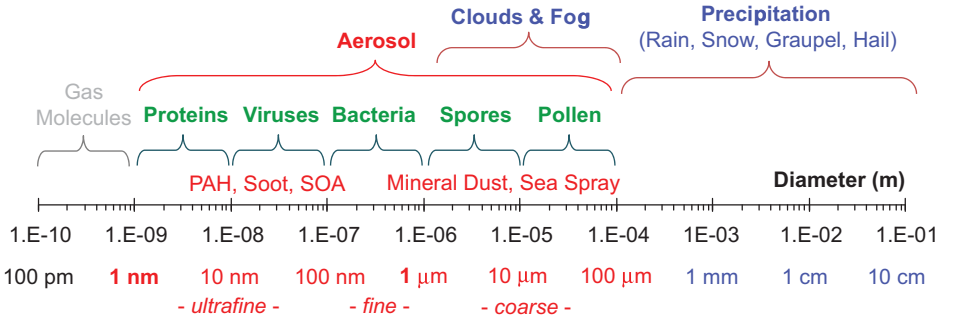

Figure 1. Size range of atmospheric aerosols and hydrometeors.

mostly of water [2]. Particles larger than about 100 µm are usually not regarded as aerosols, because they are rapidly lost by sedimentation [2].

In the atmosphere, aerosol particles undergo physical and chemical transformation (aging) such as coagulation, condensation and chemical reactions leading to changes of particle size, morphology, phase states and chemical composition. Cloud and fog processing are efficient ways of particle aging that occur when water vapour condenses on aerosol particles that serve as nuclei for cloud or fog droplets and ice crystals [2]. If the clouds or fogs evaporate rather than precipitate, the transformed particles are again released to the atmosphere. Key processes of chemical aging are reactions with atmospheric oxidants such as ozone, nitrogen dioxide, hydroxyl, nitrate and halogen radicals [7]. The reactants are partitioned between gas and particle phase depending on the volatility, and heterogeneous or multi-phase chemical reactions can occur at the interface and in the bulk of gas, liquid and solid phases. These processes can significantly alter the chemical composition and properties of aerosols such as hygroscopicity, volatility, toxicity and allergenicity [8]. Therefore, it is essential to understand and quantify the chemical aging of aerosols for reliable assessment of the effects of air pollution on public health.

Ozone is one of the most abundant atmospheric photo-oxidants, and it is central to the formation of reactive oxygen species (ROS) in atmospheric aerosols as discussed below (Section on ROS). In the lower atmosphere, ozone is mostly produced through photochemical reactions involving nitrogen oxides (NO_x) and VOC, including methane and non-methane hydrocarbons (NMHCs) [9,10]. Motor vehicles and the combustion of fossil fuels are major sources of NO_x and anthropogenic NMHCs including alkenes and aromatic hydrocarbons. Biogenic NMHCs such as isoprene and terpenes are emitted from the vegetation [11,12]. The typical surface concentration of ozone is ~30 ppb (parts per billion, 10^{-9}) in rural areas, and it can be as high as 100–400 ppb in polluted urban air [5]. Near-surface ozone concentrations have increased over the past decades globally and, especially, in densely populated areas of Europe and East Asia [13], which can be explained by enhanced anthropogenic emissions and atmospheric photochemistry [14–17]. This is not just a local but indeed a regional and global phenomenon. In Tokyo, for example, an increase of ozone is observed and likely due to the outflow of polluted air from continental Asia [18–20], although local emissions of NO_x and NMHCs are decreasing due to air quality control regulations [21].

Epidemiological studies show clear correlations between fine particulate matter (PM) in the polluted air and adverse health effects including cardiovascular, respiratory and allergic diseases [22–25]. Exposure to high concentration of aerosol particles including soot, sulphate, organics and dust can lead to inflammation and damage to cellular proteins and DNA [3,26–31]. Moreover, inhalation of transition metals such as copper and iron, or organic compounds such as soot and polycyclic aromatic compounds (PACs) can trigger the formation of free radicals and ROS *in vivo*, which can cause oxidative stress, cell death, biological aging and diseases [32].

Asthma and allergies are major health problems in most modern societies, and numerous studies indicate that allergic diseases have been increasing during the past decades [33–36]. The reasons for the increase in allergic diseases are still unclear. There are several hypotheses such as increased awareness and improved diagnostics, genetic susceptibility, psycho-social influences, nutrition, hygiene hypothesis, underlying disease and environmental pollution, which are discussed by several authors in more detail [35,37–41]. Immune responses can be affected by air pollutants including atmospheric particles, semi-volatile hydrocarbons and exhaust gases, which drive pro-allergic inflammation through the generation of oxidative stress [42]. Traffic-related air pollution with ozone, nitrogen dioxide, sulphur dioxide and PM appears to link cellular inflammation, allergic diseases and childhood respiratory health [25,42–45]. However, the effects of air pollution on the occurrence of allergic diseases are complex and poorly understood [35].

In the following sections, we review the important hazardous atmospheric aerosol components: ROS, soot and polycyclic aromatic hydrocarbons (PAHs)

and allergenic proteins. Especially, we focus on formation and chemical transformation of such hazardous compounds.

Reactive oxygen species

ROS play an important role in atmospheric chemistry as well as in physiological processes; ozone photochemistry, oxidative self-cleaning of the atmosphere, biological aging, metabolism and oxidative stress [2,46,47]. The narrow definition of ROS includes singlet oxygen ($^1O_2$), superoxide radical (O_2^-), hydrogen peroxide (H_2O_2), hydroperoxyl (HO_2) and hydroxyl radical ($^{\cdot}OH$). In physiology and biochemistry, the umbrella term ROS has been broadly defined to comprise a wide range of oxygen-centred and related free radicals, ions and molecules, including organic hydroperoxide (ROOH), organic peroxy radical ($RO_2^{\cdot}$), phenoxy radical ($RO^{\cdot}$), ozonide (OZ) and hypochlorite ion (OCl^-) [46–48]. The biomedical definition of ROS also includes reactive nitrogen species (RNS) like NO, NO_2 and ONO_2^- [47]. In atmospheric science; however, RNS are usually treated separately from oxy-, hydroxy- and peroxy radicals [5,8]. Reactive oxygen intermediates (ROIs) is the subset of ROS potentially involved in the reaction of ozone with surfaces, including organic and inorganic species with reactive oxygen atoms or groups (O, RO, RO_2, etc.) [49].

As shown in Figure 2, the physiological sources of ROS are intracellular metabolism and cytosolic enzymes. Toxins and therapeutics can also stimulate/trigger the formation of ROS *in vivo*. Once they are formed in the human body, they can cause oxidative stress, cell death, biological aging and various diseases [47]. The atmospheric sources are photochemistry and gas phase and multiphase reactions. ROS in the atmosphere may affect the chemical transformation of hazardous aerosol particles and formation and growth of secondary organic aerosol [49]. Moreover, different types of ROS are closely coupled by radical reactions and cyclic transformation [2,8]. The coupling and exchange of atmospheric and physiological ROS can proceed through various interfaces like plant surfaces and the human respiratory tract (emission and deposition of trace gases and particle deposition). For example, the ROS in the atmosphere can eventually deposit to the lungs or skin and cause physiological effects such as oxidative stress.

In the atmosphere, ROS are present both in the gas phase and particle phase. The sources of gas phase, ROS are photolysis of ozone and subsequent radical and multiphase reactions. Gas phase $^{\cdot}OH$ are one of the most important oxidants in the atmosphere, and they play a major role in atmospheric cleaning capacity. However, due to their low concentration levels of ppt (parts per trillion, 10^{-12}) and short lifetime of seconds [8], they may not cause adverse health effects directly. H_2O_2 and ROOH are also ubiquitous in the atmosphere with concentration levels of ppb [8]. They are water soluble, hence partition between the gas phase and cloud droplets and fogs [50–52]. Several studies have measured the concentration of H_2O_2 in the particle phase with a fluorogenic probe. They reported the mass loadings of about 10 ng m^{-3} and the concentration is higher for smaller particles [50,53–55]. ROOH and organic peroxide (ROOR) are found to be major constituents of biogenic secondary organic aerosol (SOA) and aged organic aerosol [56–61]. Moreover, substantial amounts of particle-bound ROS are found on biogenic SOA produced from α-pinene, linalool and limonene in a laboratory chamber [62–64].

Freshly fractured silica dust and welding fumes contain high concentration of free radicals [65–67].

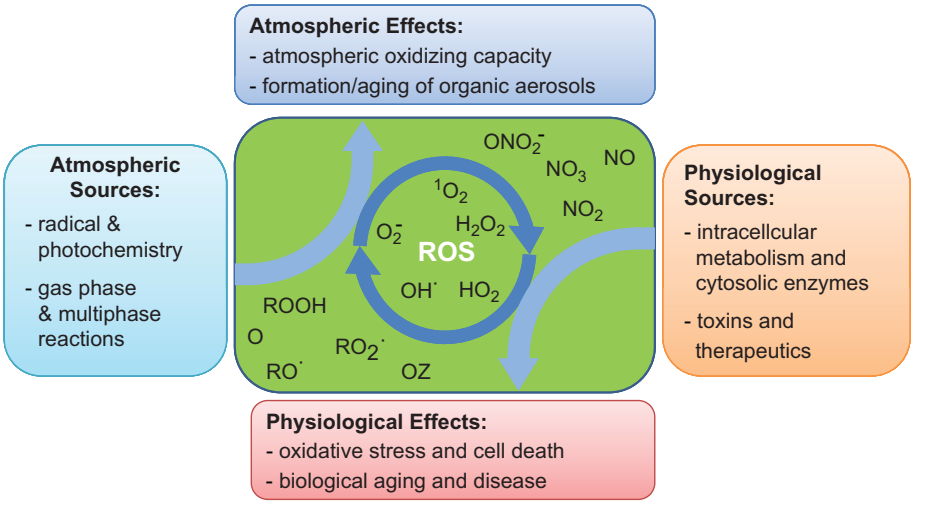

Figure 2. Illustration of the atmospheric and physiological sources, coupling and effects of reactive oxygen species (ROS) [adapted from Shiraiwa et al. 2011 [49].

The cigarette smoke, wood smoke and the smoke from plastics contain high concentration of free radicals and ROS [68,69]. The cigarette tar contains a semiquinone radical that is long-lived and stable enough to be directly observable by electron spin resonance (ESR) method [70]. Indeed large quantities of semiquinone radicals and other free radicals were found in ambient PM2.5 samples [71,72]. As shown in Figure 3, if atmospheric ROS is inhaled to human lung, they can directly cause oxidative stress. Moreover, the semiquinone radical reacts readily with molecular oxygen to generate O_2, which is further converted into H_2O_2 through chemical disproportionation reaction. The generated H_2O_2 interacts with metals such as Fe^{3+} (Fenton reaction) leading to the formation of $^{\cdot}OH$, which is very reactive and can cause damage to DNA, proteins, tissues and lipids [73].

Aerosol particles contain chemical species that are capable of generating ROS upon deposition in the lung. For example, they contain transition metals such as iron, copper, chromium mercury, nickel and lead, whose natural sources are soil, crusts and sea, and whose anthropogenic sources are combustion, smelting and corrosion [74]. The most abundant transition metal in atmospheric aerosol is iron with mass concentration of ~1 μg m^{-3} [74]. When particles with transition metals are inhaled, they can undergo Fenton-like reaction, resulting in the production of ROS *in vivo* [75]. Indeed transition metal-enriched particles were found to exhibit strong cytotoxic effect [76]. Asbestos and other synthetic fibres can also induce ROS and free radicals generation by catalysing the electron transfer reactions [77]. A class of organic molecules extracted from atmospheric aerosol particles and isolated from fog and cloud water is termed humic-like substances (HULIS) due to a certain resemblance to terrestrial and aquatic humic and fulvic acids [78,79]. HULIS represents up to 10% of total organic carbon in urban dust [78,79]. HULIS was found to be the major redox active constituent of the water-extractable organic fraction in PM and could be an active PM component in generating ROS [80–83].

The atmospheric gas phase ozone is also known to induce synergistic harmful health effects to humans, animals and vegetation [84–87]. Biosurfaces are naturally protected against ozone by fluid films containing antioxidants such as ascorbic acid, reduced glutathione, uric acid and α-tocopherol, which scavenge ozone and ROS before they reach the underlying tissues [88–91]. However, the oxidative aggression of ozone and ROS could be still transduced across epithelial-lining fluids (ELF) [92–94] by secondary oxidants such as secondary ozonide, epoxide and ROOR, generated in the ozonolysis of antioxidants and surfactant protein [95–100]. These secondary oxidants are stable enough to diffuse through ELF layers toward the biomembranes in a few microseconds which can trigger inflammatory responses [92,101,102]. The formation of such persistent secondary oxidants is enhanced especially in acidic conditions (pH≈5) [95,97]. Therefore, antioxidants, otherwise efficient ozone scavenger under normal physiological conditions, may gradually lose its reactivity in ELF layers that become locally acidified by simultaneous inhalation of acidic airborne particles or by pre-existent pathologies such as asthma [95,103,104].

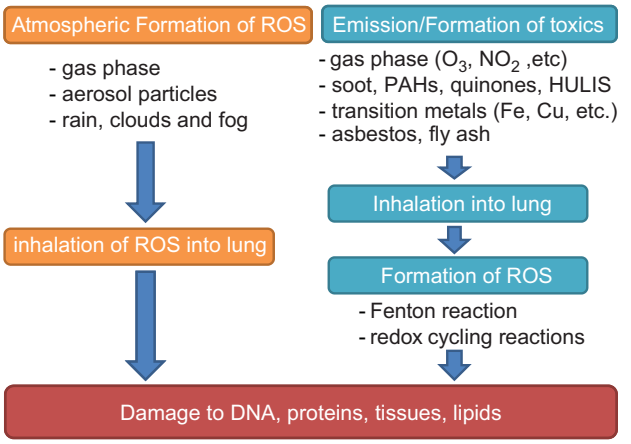

Figure 3. Two pathways for the formation of reactive oxygen species (ROS) in the lung: direct inhalation of ROS from the atmosphere and *in vivo* formation of ROS triggered by inhaled aerosol particles.

Soot and polycyclic aromatic compounds

Soot and PACs are one of the most prominent groups of toxic air pollutants related to health effects. Soot is the black solid product of incomplete combustion or pyrolysis of organic hydrocarbons, and it contains various amounts of organics including PACs, alkenes and carboxylic acids [105–107]. Soot and PACs are known to have high carcinogenic, mutagenic and allergenic potentials [8,31]. They are emitted from diesel exhaust, smoke and incomplete combustion and are in the submicron size range that can penetrate deep into human lungs [8].

Many epidemiological, human and animal model studies have shown that diesel exhaust particles including soot and PACs can trigger the formation of ROS *in vivo* and increase airway inflammation and exacerbate and initiate asthmas and allergy [25,108]. It is suggested that redox-cycling activity and toxicity of particles may be enhanced as they chemically age by oxidants like ozone [109]. Moreover, chemical transformation of PACs leads to the formation of oxygenated or nitrated derivatives (quinones, phenols, epoxides, lactones, etc.) which have enhanced toxicity [8,110–114]. Therefore, it is important to understand and quantify the chemical transformation of PACs in the atmosphere.

Many laboratory studies have investigated the heterogeneous reaction of ozone with PAHs adsorbed on soot and other substrates [115–119]. Figure 4 shows the schematics of the gas-particle interaction between benzo[a]pyrene (BaP) on soot surface and ozone, nitrogen dioxide and water vapour. BaP is one of the most powerful carcinogens among PAHs, and it consists of five aromatic rings. The adsorption of ozone can be measured by analysing the gas phase ozone concentration, and the surface reaction rate can be obtained by the particle analysis. The results show a non-linear dependence of the first-order PAH decay rate coefficient on gas phase ozone concentration. This observation is consistent with a Langmuir–Hinshelwood (LH) reaction mechanism, in which first ozone adsorbs to the surface and then reacts with PAH [120].

The ozone surface residence time (desorption lifetime) inferred from kinetic data, assuming a simple LH reaction between adsorbed ozone and surface PAH, are in the range of milliseconds to 10 seconds. However, according to quantum mechanical calculations based on density functional theory (DFT), the desorption lifetime of ozone on PAH should be only nanoseconds [121], which is more than six orders of magnitude less than the experimental values. Shiraiwa et al. (2011) [49] has resolved this discrepancy using the kinetic surface model [122] showing that adsorbed ozone decomposed to a long-lived reactive oxygen intermediate (ROI), which is a chemisorbed oxygen atom bound to the delocalized π electrons of an aromatic surface. The chemical lifetime of ROI exceeds 100 seconds, and ROI can react with PAH to form stable products, for example, quinones and phenols.

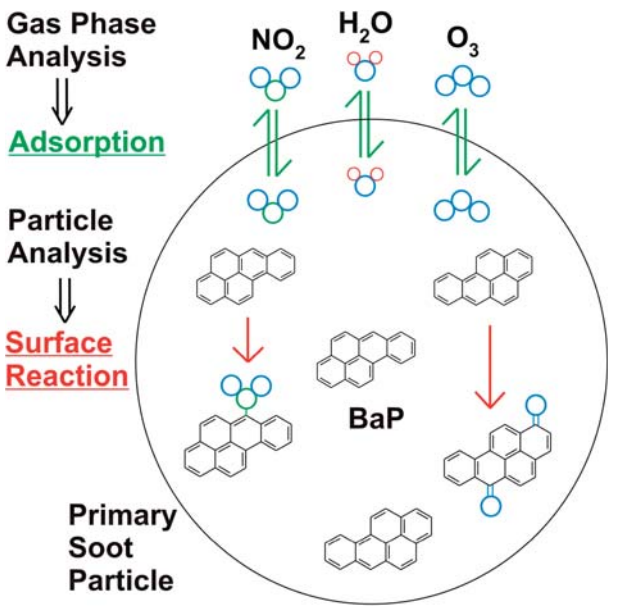

Figure 4. Schematic illustration of the chemical transformation of benzo[a]pyrene (BaP) on soot by gas phase ozone, nitrogen dioxide and water vapour: reversible and competitive adsorption of gas species followed by surface reactions [adapted from Pöschl 2002 [111]].

ROIs can be directly inhaled by human beings as they are long-lived, and they can directly cause oxidative stress because they are reactive. The quinones, primary products of heterogeneous reactions, are highly reactive organic chemical species that interact with biological systems by reducing oxygen to ROS, which promotes inflammatory, anti-inflammatory and anticancer actions to induce toxicities [112]. The mass loadings of quinones in suspended aerosol particle are typically 0.01–1 ng m^{-3} [123]. The quinones can be directly emitted into the atmosphere from incomplete combustion sources [124]. Some studies reported a correlation between concentration of quinones and NO_x and O_3, confirming the secondary formation of quinones via heterogeneous reactions in the atmosphere [125,126]. The modelling studies suggest that the timescale of turnover of PAHs via ozone, nitrogen dioxide, hydroxyl and nitrate radicals range from a few minutes on the surface of soot [122,127,128] to multiple hours on organic and inorganic solid particles and days on liquid particles [122].

Allergenic proteins

Primary biological aerosol particles (PBAPs) such as pollen, fungal spores, bacteria, biogenic polymers and debris from larger organisms are known to influence atmospheric chemistry and physics, the biosphere and public health. PBAPs account for up to ~30% of fine and up to ~70% of coarse particulate matter in urban, rural and pristine environment [129]. Proteins account for up to ~5% of urban air particulate matter and can be found in coarse biological particles such as pollen grains (diameter >10 μm) as well as in the fine fraction of air particulate matter with fine fragments of pollen, microorganisms or plant debris and mixing of proteins in rain water with fine soil and road dust particles [45,130–132]. Some of these bioaerosols are known to be allergenic and their important sources are wind-dispersed pollen grains from trees, grasses, and weeds, followed by excretions of house dust mites and cockroaches, fungal spores, animal dender and insect venoms. Type 1 hypersensitivity such as allergic rhinitis and allergic asthma are mediated by the production of IgE antibodies against, in principle, harmless proteins (allergens) [133].

Pollen allergy has become a global problem and the rapid prevalence of respiratory allergenic reactions induced by pollens has been on increase over the past decades [134–136]. Many studies have demonstrated that urbanization with high levels of air pollution are correlated with the increasing frequency of pollen-induced respiratory allergy and people living in urban areas tend to be more affected by pollen allergy than

people living in rural areas [137–141]. Air pollution associated with ozone, nitrogen dioxide, sulphur dioxide, and particulate matter can interact with pollen grains, leading to increased release of antigens characterized by modified allergenicity [134,142]. Moreover, the interaction between pollens and particular diesel exhaust particles or dust can cause an adjuvant immunological effect on IgE synthesis in atopic subjects [134,143]. Additionally, the bioavailability of pollen allergens is influenced by environmental factors such as light intensity, temperature and humidity [25,144–146].

Recent laboratory experiments have shown that ozone and nitrogen dioxide can promote the nitration of protein molecules in polluted urban air [49,131,147]. Indeed, nitrated proteins were detected in dust samples from various urban environments [131]. The nitration reaction leads to the addition of nitro-groups on the aromatic rings of tyrosine residues in the polypeptide chain. This post-translational modification can enhance the allergenic potential of proteins like the birch pollen allergen Bet v 1 [148], and it has also been shown that food allergens like the egg allergen ovalbumin (OVA) showed enhanced allergenicity after nitration [149]. Inhalation and deposition of these nitrated proteins in the human respiratory tract may lead to the adverse health effects. Accumulating data suggest a strong link between protein 3-nitrotyrosine and the mechanism involved in disease development [150]. This post-translational modification provides a molecular rationale for the enhancement of allergic diseases by traffic-related air pollution in urban and rural environments, which has been observed in epidemiological studies but remains to be elucidated on a molecular level [131,133,148].

Nitration of proteins naturally occurs during inflammation, oxidative stress and aging. Nitration may serve to optimize immune responses and has been reported in association with at least 50 diseases such as asthma, Alzheimer's disease or diabetes [151]. Under physiological conditions the reaction between free nitrogen oxide radicals (NO) and superoxide anion (O_2^-) can form strong oxidizing and nitrating intermediates such as peroxynitrite (ONO_2^-) which can nitrate tyrosine residues in proteins [152–154]. The biological precursors NO and O_2^- are produced by the nitric oxide synthase or NO-synthase [155]. 3-nitrotyrosine has become generally accepted as a biomarker in several pathologies like for example asthma [156], cardiovascular disease [157], Alzheimer's disease [158], Parkinson's disease [159], kidney diseases [160] and diabetes [161].

However, the kinetics of protein nitration and the dose-response relationship for nitrated proteins and allergies are not well known, and their investigation requires the development and application of suitable analytical methods. Nitration of tyrosine residues is a stable modification that can be suitably analysed by different specific techniques [162] like immunochemical techniques [163,164], HPLC coupled to ultra-visible (UV-vis) photometry [165] or fluorescence [166], gas chromatography (GC) coupled to thermal energy analyser or mass spectrometer [167], immunochemical enrichment methods [168], chemical labelling [169–171] or electrochemical methods [172] coupled to mass spectrometry or methods combining LC-MS and LC-MS/MS approaches [173,174].

Recently, a method was developed for the quantification of nitrotyrosine residues in protein molecules by HPLC coupled to a diode array detector of UV-visible light absorption (DAD) [147]. This method enables efficient determination of average nitration degrees in kinetic investigations of protein nitration, but additional site-specific information is required to elucidate reaction mechanisms and structure information. For site-specific quantification of nitration degrees of individual tyrosine residues a microfluidic chip system with electrospray ionization and tandem mass spectrometry (HPLC-MS/MS) can be used after tryptic digestion of nitrated proteins [174]. The nitration degrees determined for individual tyrosine residues provide information about site selectivity of the nitration reaction. Determining nitration sites of allergenic proteins may lead to a better understanding of the interactions between the immune system and the modified allergen. The schematics of these analytical methods are presented in Figure 5 [175].

Using these analytical approach, the site selectivity of nitration and its dependence on the nitrating agent and protein structure for bovine serum albumin (BSA) and OVA were investigated [174]. The proteins were nitrated either by tetranitro-methane (TNM) in liquid phase (Figure 6a) or by gaseous mixture of O_3 and NO_2 under atmospheric relevant conditions. The sum of nitration degrees of each tyrosine residue (ND_Y) determined by HPLC-MS/MS exhibited 1:1 correlations with the total protein nitration degree (ND) determined by HPLC-DAD, confirming the applicability and robustness of both techniques. The ratio of ND_Y versus ND can be interpreted as a proxy for the relative rate or reaction probability of individual tyrosine residues [174].

Recent kinetic experiments showed that the nitration reaction of proteins with O_3 and NO_2 proceeds through long-lived ROIs [49]. The protein first reacts with ozone to form ROI – most likely phenoxy radical derivatives of tyrosine, then ROIs can persist over extended periods of time and react with NO_2 to form nitrotyrosine residues (Figure 6b). The reaction between protein particles and oxidants are kinetically limited by diffusion of oxidants into the protein bulk, confirmed by numerical simulations using a kinetic model [176,177]. The reaction rate exhibits a pronounced increase with relative humidity [176], which can be explained by an increase of bulk diffusivity of

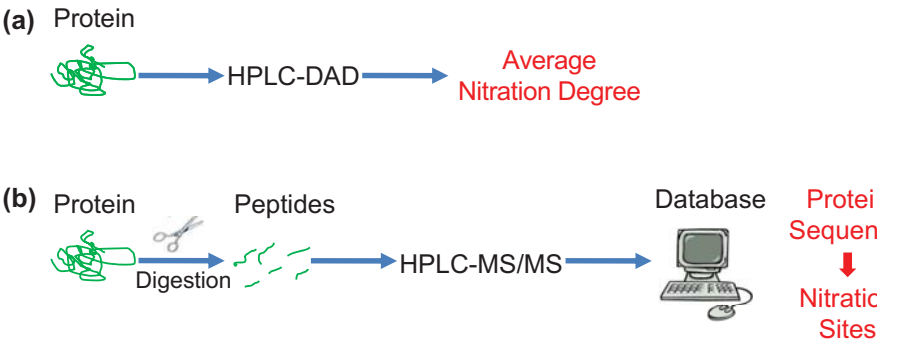

Figure 5. Quantification of nitrotyrosine residues in protein molecules. Determination of (a) average nitration degrees with HPLC-DAD and of (b) individual nitration degrees of different tyrosine residues with HPLC-MS/MS [175].

oxidant due to hygroscopic water uptake transforming the amorphous protein from a glassy solid to a liquid state (moisture-induced phase transition) [176,178,179]. These experiments suggest that proteins on the surface of aerosol particles are nitrated efficiently within minutes under photochemical smog conditions with high concentrations of O_3 and NO_2, but the nitration of protein in the bulk of aerosol particles proceeds slowly depending on ambient relative humidity and temperature.

The following mechanisms may be also essential for altered allergenic potential: conformational changes within the protein or the formation of higher order assemblies like dimers or multimers due to the modification as well as direct nitration of B and T cell epitopes. Concerning direct epitope modification, Untersmayr et al. showed that the most efficiently nitrated tyrosine residue of nitrated egg allergen OVA is part of human as well as murine IgE epitopes and is found in OVA T-cell epitopes as well, which might explain the enhanced allergenic potential of nitrated OVA [149]. Changes in the quaternary structure due to nitration like dimerization or oligomerisation also might have a strong influence on immunogenicity. The cross-linking of IgE antibodies by allergens is a key event in the sensitization process, and it needs at least two allergen epitopes, which certainly are provided by an allergen dimer. The capacity of protein aggregates to enhance immune responses to the monomeric form is already known [180,181], and the dimerization is a common and essential feature for allergens like Bet v 1 [182].

Summary and outlook

Over the past decades, epidemiological studies have provided accumulating evidence of the effects of air pollution on public health. Even though these studies can provide statistical associations between adverse health effects such as asthma and allergy and exposure dose of pollutants such as ozone and particulate matter, they cannot provide a causative relations and mechanism in the molecular level. Their elucidation, however, is critical for the policymaking of effective air quality control and for the medical treatment and new drug development of the related diseases.

The lifecycle of hazardous aerosol components in the atmosphere is still not fully understood. The identification of their emission sources and deposition sinks is essential for charactering their spatial distributions. Particularly, little is known about the physical and chemical transformation processes of aerosol particles in the atmosphere. The physical transformation

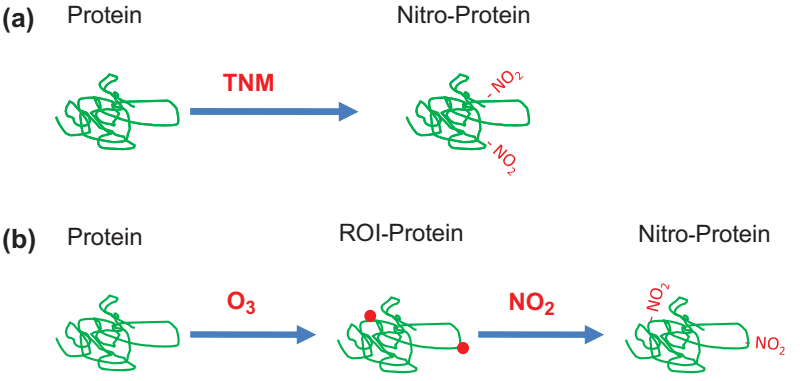

Figure 6. Nitration (a) with tetranitro-methane (TNM) in the liquid phase and (b) with NO_2 and O_3 in the gas phase. In (b) the reactive oxygen intermediate-protein (ROI-protein) consists most likely of phenoxy radical derivatives of tyrosine [175].

(size and morphology change) may change the deposition efficiency of particles into human lung and on plant surfaces. The chemical transformation can lead to the formation and decomposition of hazardous compounds, hence change the toxicity and allergenicity of particulate matters such as soot, PACs and allergenic proteins.

ROS is one of the most important constituents with regard to aerosol health effects. There are quite a few measurements of ROS in the gas phase (e.g. OH, H_2O_2), and their distribution and concentration is relatively well-understood, whereas the measurements of ROS in aerosol particles, rain, clouds and fog are still very limited due to the lack of established measurement methods and also lack of awareness of their importance for health effects. The detection of free radicals in the condensed phase can be easily subject to misidentification when traditional extraction and chemical analysis methods are employed because free radicals are often not stable and reacted away in the course of analysis [72]. Electron resonance spectroscopy is a powerful tool for identification and quantification of free radicals and ROS in the condensed phase [68,71,72,108].

The formation and decomposition kinetics of condensed phase ROS and hazardous chemical components are poorly understood. More field measurements on characterization and identification of ROS are needed and their temporal variations (annual, seasonal and diurnal cycles) should be investigated. Recently, ROIs were discovered in the reaction of ozone with aerosol particles, which play a key role in the formation of toxic organic aerosols [49]. More laboratory experiments and modelling are required to elucidate kinetics and mechanism of their formation and transformation.

The effects of diesel exhausted particles, ozone, nitrogen dioxide and allergenic pollen proteins on asthma and allergy are well established by a number of epidemiological studies, but the specific chemical reactions and molecular processes responsible for their effects have not yet been clearly identified [2]. Recent investigations suggest that allergenic proteins can be nitrated by ozone and nitrogen dioxide in the polluted air masses, which may enhance allergic reactions and influence inflammatory processes upon inhalation to human body [49,131,147,148,174]. Further investigations on formation kinetics of nitrated protein, their abundance in ambient air and their immunological effects are required.

The research on aerosol health effects is highly interdisciplinary. We need to 1) understand emission, formation, transport, sink and abundance of toxic and allergenic compounds (atmospheric science, meteorology), 2) develop analytical methods for quantification and identification of these compounds (analytical chemistry), 3) quantify their toxicity and allergenicity (immunology, toxicology), 4) investigate health-characteristic or health-determinant patterns in a population (epidemiology) and 5) elucidate mechanism and processes of health effects on a molecular level (biochemistry). For better understanding and assessments of aerosol health effects, knowledge of these research fields should be integrated that eventually allows optimized air quality control and improved medical treatments.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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