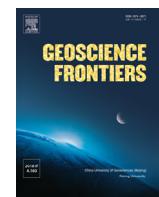




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## Research paper

# Sources, characteristics, toxicity, and control of ultrafine particles: An overview

Andrea L. Moreno-Ríos <sup>a,\*</sup>, Lesly P. Tejeda-Benítez <sup>b</sup>, Ciro F. Bustillo-Lecompte <sup>c</sup><sup>a</sup> Department of Civil and Environmental, Universidad de la Costa, CUC, Calle 58 # 55–66, Barranquilla, Atlántico, Colombia<sup>b</sup> Research Group in Biomedical, Toxicological and Environmental Sciences (Biotoxam), University of Cartagena, Campus of Zaragocilla, Cartagena, Colombia<sup>c</sup> School of Occupational and Public Health, Ryerson University, 350 Victoria Street, Toronto, ON M5B 2K3, Canada

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## ABSTRACT

Air pollution by particulate matter (PM) is one of the main threats to human health, particularly in large cities where pollution levels are continually exceeded. According to their source of emission, geography, and local meteorology, the pollutant particles vary in size and composition. These particles are conditioned to the aerodynamic diameter and thus classified as coarse (2.5–10 µm), fine (0.1–2.5 µm), and ultrafine (<0.1 µm), where the degree of toxicity becomes greater for smaller particles. These particles can get into the lungs and translocate into vital organs due to their size, causing significant human health consequences. Besides, PM pollutants have been linked to respiratory conditions, genotoxic, mutagenic, and carcinogenic activity in human beings. This paper presents an overview of emission sources, physicochemical characteristics, collection and measurement methodologies, toxicity, and existing control mechanisms for ultrafine particles (UFPs) in the last fifteen years.

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## 1. Introduction

Air pollution is one of the most studied environmental problems worldwide since it generates a continuous threat to people's health and quality of life. Particulate matter (PM) is among the primary air pollutants, and it is made up of a complex mixture of chemical and biological components (Garcia et al., 2014; Martinello et al., 2014; Schneider et al., 2015, 2016; Ramírez et al., 2019; Rojas et al., 2019; Silva et al., 2020a, 2020b; Zamberland et al., 2020). Depending on the aerodynamic diameter, particles are divided into coarse, fine, and ultrafine, ranging from nanometers (nm) to microns (µm), being the PM<sub>10</sub> particles with an aerodynamic diameter between 2500 nm and 10000 nm, PM<sub>2.5</sub> particles between 100 nm and 2500 nm, and PM<sub>0.1</sub> particles less than 100 nm (WHO, 2006; Jeong et al., 2017; Clifford et al., 2018; Rizza et al., 2019). More specifically, it has been recognized that particles with a size smaller than 300 nm are considered as atmospheric nanoparticles (Kumar et al., 2016), and even smaller particle sizes (<100 nm), i.e. PM<sub>0.1</sub>, are also considered as such (Dall'Osto et al., 2011; Da et al., 2019; de Jesus et al., 2019).

Ultrafine particles (UFPs) are produced by dynamic formation processes such as nucleation, condensation, and coagulation from compounds in the gas phase (León-Mejía et al., 2016, 2018; Ramírez et al., 2020). Nucleation frequently occurs in forested areas due to the emission of biogenic volatile organic compounds (VOCs) (Ehn et al., 2014). During condensation, gaseous molecules are transferred into nucleation mode particles or an existing particle (Seigneur, 2019). During coagulation, particle collisions can occur, leading to agglomeration into a single particle from two original particles. New nucleated UFPs coagulate readily with other particles, causing the deposition of UFPs (Zhao et al., 2015; Kwon et al., 2020). These UFPs processes are different from those in larger particles because changes in size, shape, surface area, volume, and number can occur at higher speeds than in larger particles (Kumar et al., 2016, 2018). After their formation, UFPs can remain suspended in the air for a longer time than larger particles (Abdel-Shafy and Mansour, 2016) and are later removed by dry and wet deposition (Kumar et al., 2011; Muñoz-Salazar et al., 2020).

Due to their size and large specific surface area, UFPs can be easily transported through the respiratory system penetrating the pulmonary alveoli (Clifford et al., 2018; Buzea and Pacheco, 2019). Thus, leading to pulmonary deposition (Guo et al., 2019) and systemic translocation (Allen et al., 2017; Bhargava et al., 2018; Clifford et al., 2018). Some hypotheses suggest that UFPs may have a higher health impact than larger particles (Da et al., 2019). However, there is still a short number of studies regarding long-term exposure to confirm such hypotheses and

\* Corresponding author.

E-mail addresses: [amoreno16@cuc.edu.co](mailto:amoreno16@cuc.edu.co) (A.L. Moreno-Ríos), [lptejedab@unicartagena.edu.co](mailto:lptejedab@unicartagena.edu.co) (L.P. Tejeda-Benítez), [ciro.lecompte@ryerson.ca](mailto:ciro.lecompte@ryerson.ca) (C.F. Bustillo-Lecompte).

explain the biological mechanism through which these particles affect human health.

When talking about number and surface, fine ( $PM_{2.5}$ ) and ultrafine ( $PM_{0.1}$ ) particles are the most toxic airborne particles (Xiao et al., 2016; Soppa et al., 2019). Several studies have documented the relationship between the exposure to these particles and the morbidity and mortality of respiratory (Gao and Sang, 2020; Nho, 2020) and cardiovascular diseases (Xiao et al., 2016; Bourdrel et al., 2017; Yang et al., 2017b; Liu et al., 2018; Møller et al., 2020).

Indeed, there is strong evidence that certain diseases such as asthma, chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, neurodegenerative diseases (Heusinkveld et al., 2016; Wei et al., 2017), cancer (Gao and Sang, 2020), and type 2 diabetes are related to the exposure of particles that are smaller than  $2.5\text{ }\mu\text{m}$  (Chen et al., 2016). Likewise, it is proposed that chemical compounds such as polycyclic aromatic hydrocarbons (PAHs), N-PAHs (Zhang et al., 2016, 2020; Agudelo-Castañeda et al., 2017), potentially toxic elements (colloquially named heavy metals) (Pourret and Hursthouse, 2019), sulphur and nitrogen oxides (Santibáñez-Andrade et al., 2017; Billet et al., 2018), commonly found in fine particles, can lead to genotoxic, mutagenic, and carcinogenic activity (Santibáñez-Andrade et al., 2017; Shukla et al., 2019).

Although there is plenty of information regarding PM's toxicological effects, few studies include UFPs in their toxicity analysis. This gap in the literature is attributable to technical difficulties in measuring the concentration of UFPs and estimating the exposure of the included population (Silva et al., 2012a; De Vallejuelo et al., 2017; Saikia et al., 2018). In this way, this paper presents an overview of the state of the art of research on atmospheric UFPs. Among the topics discussed are the primary emission sources, their main characteristics, collection and measurement methodologies, toxicity, and controlling mechanisms available to eliminate and prevent contamination.

### 1.1. Pollution sources of ultrafine particles

The pollutants that make up the particles vary in size and composition according to the sources of contamination. Fig. 1 shows the primary emission sources, which may be either natural or anthropogenic (Jones and Harrison, 2016; Mishra et al., 2016; Abramesko and Tartakovsky, 2017; de Oliveira Galvão et al., 2018). Indeed, PM is emitted directly into the atmosphere as primary particles or formed in the atmosphere from the transformation of gaseous precursors as secondary particles (Kumar et al., 2016) and photochemical generation of new particles (Ma and Birmili, 2015; Chu et al., 2019).

Natural sources of UFPs include forest fires, volcanic eruptions, marine aerosols, local minerals and runoff (Dalmora et al., 2016; Dias et al., 2014; Islam et al., 2019; Kronbauer et al., 2013). However, UFPs mainly originate from anthropogenic sources such as combustion of gas, coal or hydrocarbons, biomass burning (i.e. agricultural burning, forest fires and waste disposal), vehicular traffic (Abramesko and Tartakovsky, 2017) and industrial emissions (Keuken et al., 2015). Other sources are tire wear and tear from car brakes, air traffic (Keuken et al., 2015; Kecorius et al., 2016; Habre et al., 2018; Stacey, 2019; Møller et al., 2020), seaport, maritime transportation (Agudelo-Castañeda et al., 2019), construction, demolition, restoration and concrete processing (Azarmi and Kumar, 2016; Azarmi et al., 2016; Kumar et al., 2016), domestic wood stoves (Marabini et al., 2017), outdoor burning, kitchen (Chen et al., 2017), and cigarette smoke (Goel and Kumar, 2015).

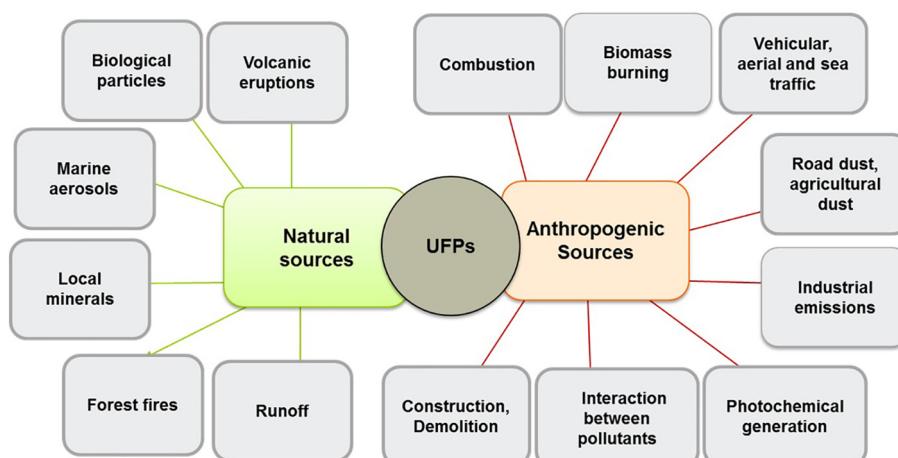
## 2. Characteristics of ultrafine atmospheric particles

### 2.1. Physicochemical properties of ultrafine particles

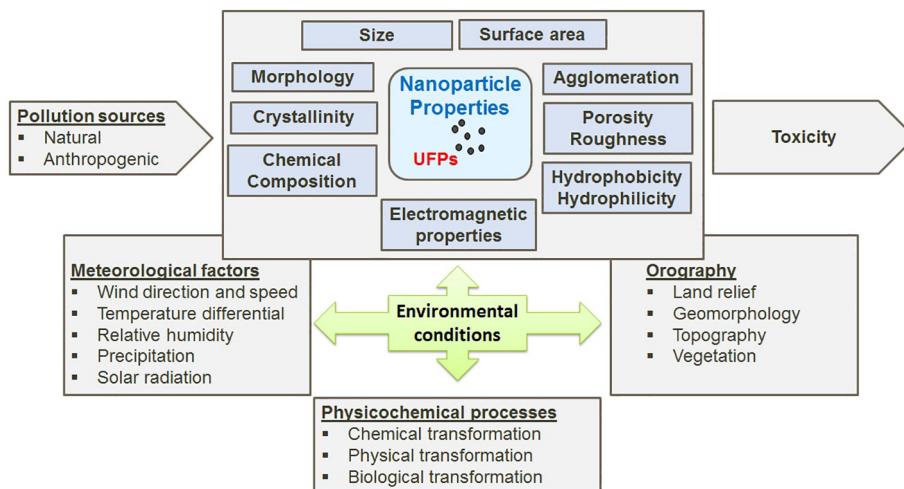
PMs are significant air pollutants as they undergo high variability in terms of their physicochemical and morphological properties, concentration levels, and composition, which vary with the season, climate, space and source; making it challenging to analyze its toxic components (Kelly and Fussell, 2012; Castro-Rodriguez et al., 2016; Lee et al., 2017; Saikia et al., 2018; Buzea and Pacheco, 2019). UFPs are PMs with an aerodynamic diameter of less than  $0.1\text{ }\mu\text{m}$ . UFPs are typically described in terms of surface area per particle, mass or particle number (PN), or concentration of either of those per volume (Kwon et al., 2020). Fig. 2 shows the main properties of UFPs and the factors that affect them.

Having a diameter of less than  $0.1\text{ }\mu\text{m}$  allows UFPs to remain suspended in the air for a more extended time than larger particles (Kelly and Fussell, 2012). It has been found that the residence time, dispersion, transport, and emission processes of UFPs in the air are affected by environmental conditions (Oliveira et al., 2017, 2019a, 2019b). These include the meteorological factors of the geographical area such as wind direction and speed, temperature variations, relative humidity, mixing height, precipitation and solar radiation, orography, and the physico-chemical processes that are carried out in the atmosphere, which also may vary depending on the location (Schneider et al., 2015; Kumar et al., 2016; Kumar et al., 2018).

UFPs are unstable and become larger particles through coagulation and condensation. These particles are mainly made up of sulphates, nitrates, trace metals, elemental and organic carbon, and adsorbed volatile and semivolatile organic compounds (Simkhovich et al., 2008).



**Fig. 1.** Ultrafine particle emission sources.



**Fig. 2.** Properties of UFPs and the factors that affect them.

However, the number of UFPs per unit volume is greater compared to the larger particles; this increases the available surface area increasing, in turn, the adsorption of other polluting elements such as organic gases, potentially toxic elements, forming larger coated or agglomerated particles, and with greater toxicity (Chen et al., 2016).

Following the above, the physicochemical properties of UFPs depend on the nature of the substances that form its nucleus and the different chemical components that make up their surfaces. For instance, the UFPs composition, when emitted by wood combustion, can be augmented or modified depending on the by-product combustion, such as PAHs, ions, potentially toxic elements, and other oxidizing components present in the air (Civeira et al., 2016; Oliveira et al., 2019a, 2019b). These particles may also undergo chemical modifications by exposure to UV-A and UV-B radiation (Marabini et al., 2017). It is shown that environmental UFPs are highly enriched in transition metals and easily oxidized organic chemicals, which harbour potent toxic properties and high oxidant power (Allen et al., 2017).

When combustion gases originate from motor vehicles, the emitted particles' characteristics hinge on the fuel's composition, the lubricants used, the thermodynamic conditions associated, ignition technology, and the number of vehicles running. For that reason, it is essential to perform emission inventories in big cities. For example, heavy vehicle emissions tend to be very high compared to smaller ones related to the type of fuel used (Sydbom et al., 2001). The particles emitted by diesel engine vehicles are mainly in the range of 20–130 nm, whereas gasoline is 40–80 nm (Agudelo-Castañeda et al., 2019).

## 2.2. Chemical composition of UFPs

The chemical composition of UFPs in different environments is not widely studied (AQEG, 2017). In the atmosphere, UFPs are derived from a considerable number of sources. To date, relatively little work has been devoted to breaking down the size distribution into source-related components due to the difficulty of changing size distributions from both particle evaporation and growth, as well as the influence of atmospheric nucleation processes that lead to the formation of new particles (Kumar et al., 2014). UFPs are mainly composed of organic compounds, elemental carbon, trace metal oxides, sulphates, and nitrate ions (Lü et al., 2012, 2016). Most of the mass of PM<sub>0.1</sub> is typically composed of carbonaceous material with small contributions of inorganic ions, thus confirming the dominant combustion sources (HEI, 2013). Table 1 shows the contaminants present in the particulate material according to their emission source.

**Table 1**

Emission source vs composition in ultrafine particles.

Emission source	Composition	References
Coal combustion	Al, As, Ba, C, Ca, Cd, Cr, Cu, Fe, K, Mg, Mn, Na, Ni, Pb, Rh, S, Se, Si, Ti, V, Zn, PAHs	Bzdek et al. (2012), Lü et al. (2016), Oliveira et al. (2017), Abbas et al. (2018), Saikia et al. (2018), Thurston et al. (2011)
Biomass burning	Organic Carbon, PAHs, Metals	Bzdek et al. (2012), Abbas et al. (2018), De Oliveira Galvão et al. (2018), Badran et al. (2020)
Fossil fuel combustion	BC, Organic Carbon, PAHs	Bzdek et al. (2012), Louis et al. (2016), Abbas et al. (2018), Paunescu et al. (2019)
Vehicular traffic	Ag, Al, As, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, K, Mg, Mn, Mo, Na, Ni, Pb, Pd, Pt, Rh, Rb, Sb, Se, Sr y Te, Ti, U, V, Zn, PAHs, BC	Srimuruganandam and Shiva Nagendra (2011), Hofman et al. (2018), Liati et al. (2018), Guo et al. (2019), Gao et al. (2020)
Industrial emissions	As, Cd, Cu, Co, Cr, Pb, Zn, Ni, Zn	Fernández-Camacho et al. (2012), González et al. (2017)

Metal sulphates and nitrates can exist as pure solid or aqueous particles or as a surface layer on other solids, such as ash or carbon particles (Cutroneo et al., 2014; Silva et al., 2020a, 2020b). Likewise, sulphate particles can be covered by toxic components such as transition metals or organic compounds (Kelly and Fussell, 2012). The elemental and organic carbon particles come mainly from combustion processes and contain up to 80% to 90% of UFPs, black carbon (BC), and organic carbon. These particles can serve as nuclei in which other chemical species are absorbed (Kelly and Fussell, 2012).

BC is a primary aerosol product of incomplete combustion of fossil fuels or biomass from anthropogenic activities such as transportation, industrialization, and burning solid waste (Silva et al., 2012a, 2012b, 2020a, 2020b; Ribeiro et al., 2013a, 2013b; Ribeiro and Flores, 2020; Gasparotto et al., 2018, 2019; Gasparotto and Da Boit, 2020). It is generally used as an indicator of the type of fuel used and the type of combustion because its physical properties and concentration levels change with fuel type (Jeong et al., 2017). Due to its physicochemical properties, BC can adsorb primary and secondary pollutants and serve as a substrate for various chemical processes, whereas at an environmental level, it can reduce visibility and hinder plant growth by adhering to its surface (Keukens et al., 2015; Kumar et al., 2018).

Among the organic constituents of PM, PAHs are of great interest. They are mainly introduced into the atmosphere during the combustion process and can give rise to atmospheric physicochemical reactions that

result in the formation of derivatives of PAHs such as N-PAHs and O-PAHs. The concentrations of these compounds in airborne particles can be very low, but their toxic effects are often considered higher than those of their parent compounds (Zhang et al., 2016; Abbas et al., 2018; Song et al., 2019).

The primary precursor gases for secondary UFPs are biogenic volatile organic compounds (VOCs) such as alpha-pinene, aromatic VOCs such as two to four-ring PAHs, NO<sub>x</sub>, and SO<sub>2</sub>. The formation of new particles is also favoured by photochemical processes mediated by solar radiation, the low concentration of pre-existing aerosols, and low relative humidity (Muñoz-Salazar et al., 2020).

On the other hand, there is a wide range of known sources that contribute to increased levels of metals such as Na, Ca, K, Al, Fe, Se, Ti, and potentially toxic elements (Hg, Pb, Cd, Cr, As) in the finer PM fractions (Sanderson et al., 2014). The concentrations of metals with a lower atomic mass (As, Cd, Zn) decrease with particle size, while those with higher atomic mass (Co, Cr, Fe, Sb, Sc, Sm, Th, Eu, Yb) increase their concentration in relation to the diameter of the particles. Most volatile compounds emitted in gaseous forms at high temperatures nucleate or condense during cooling (Sanderson et al., 2014), while the less volatile elements remain in their solid phase (Buonanno et al., 2011).

Among the sources of emission, heavy industries are considered one of the largest anthropogenic sources of trace metals (Fernández-Camacho et al., 2012; Zhou et al., 2014; González et al., 2017), even traffic emissions can be considered essential sources of PM and metals in urban atmospheres (Fernández-Camacho et al., 2012; Abramesko and Tartakovsky, 2017).

### 3. Toxicity of ultrafine atmospheric particles

Effects of particulate matter cover a wide range of problems. It is shown that in urban environments, PM can alter the climate, the biogeochemical cycles, the chemistry of the atmosphere, and adversely disturb public health (Koçak et al., 2007). Adverse biological effects associated with PM include oxidative damage (Miller et al., 2012; Wei et al., 2017; Bliss et al., 2018; Shukla et al., 2019; Gao et al., 2020), cytotoxicity (Buzea et al., 2007; Sharma et al., 2018), and mutagenicity followed by increased morbidity and mortality (Agudelo-Castañeda et al., 2017; Ohlwein et al., 2019). Likewise, this contaminant is highly related to diseases such as cancer (Gao and Sang, 2020) and cardiopulmonary mortality (Agudelo-Castañeda et al., 2017; Maji et al., 2017; Liu et al., 2018; Ohlwein et al., 2019).

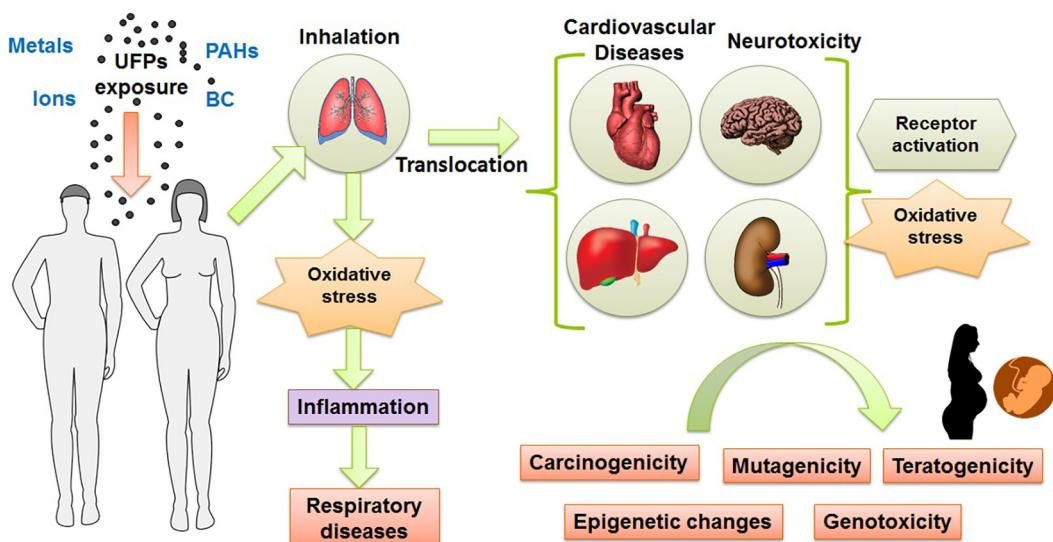


Fig. 3. Toxicological effects from exposure to UFPs.

Some authors have considered that the particles' toxicity depends mainly on their composition (Kelly and Fussell, 2012). However, as previously mentioned, both the chemical composition and the particles' size are highly dependent on geographic location, meteorological conditions, and emission sources, making the identification and prediction of their toxic effects complex.

**Fig. 3** summarizes the main effect and mechanisms of toxicity associated with exposure to UFPs. Between mechanisms associated with exposure to UFPs and their components (BC, metals, ions, organic compounds, among others), oxidative stress can lead to inflammatory processes and unchain cardiovascular diseases, carcinogenicity, epigenetics, genotoxicity, mutagenicity, neurotoxicity, and even teratogenicity (Miller et al., 2012; Wei et al., 2017; Bliss et al., 2018; Shukla et al., 2019; Cervellati et al., 2020; Gao et al., 2020). The toxicokinetics and mechanisms followed by UFPs and associated pollutants are presented below.

#### 3.1. Toxicokinetics of ultrafine particles

In order to get a better understanding of the toxicology of UFPs, the processes of absorption, distribution, metabolism and excretion, and the toxic consequences of the presence of UFPs in the human body are described below.

The inhalation pathway is the main route to UFPs exposure, and hence, causes the most significant effects on human health; whereas, dermal, ocular, and nasal mucosal contact constitute forms of lower exposure (Chen et al., 2016; Yang et al., 2017a, 2017b). The deposition sites in the respiratory tract are determined by the particles' characteristics, including size, shape, surface charge, chemical composition, morphological and physiological parameters of the exposed individual's respiratory tract system (Kelly and Fussell, 2012; Sharma et al., 2018; Martins et al., 2021). The latter can vary considerably according to various factors, such as age, physical activity, respiratory rate, and health status. The subject's age is essential because the respiratory system's morphology and dimensions change with age (Da et al., 2019).

Inhaled airborne UFPs initially enter the nasal cavity and then go deeper into the lower airways, including the trachea, bronchi, and pulmonary alveolus. A mucus layer constitutes the initial defence line in the respiratory tract's membranes, which retains the larger particles (Chen et al., 2016). The smaller the size of the particles, the deeper they can enter into the respiratory system. In this way, particles up to 100 μm will be deposited in the nasopharynx, those of 10 μm will be

deposited mainly in the primary bronchi, and those of sizes smaller than 2.5  $\mu\text{m}$  will penetrate the alveoli and terminal bronchioles (Kelly and Fussell, 2012). UFPs can penetrate deeper into the lung (Cheng et al., 2020; Nho, 2020) since the pulmonary alveoli and human cells have diameters of 200  $\mu\text{m}$  and 8  $\mu\text{m}$ , respectively, higher than those of the UFPs (Buzea and Pacheco, 2019).

The lungs of adult humans have about 480 million alveoli. These, in turn, are composed of type I and type II alveolar epithelial cells (pneumocytes) and thin blood capillaries. Non-ciliated bronchiolar epithelial cells and lung immune cells are also present, eliminating micro-organisms and inhaled particles (Nho, 2020). Macrophages are critical regulators in the immune response. When fine and ultrafine particles enter the respiratory system, macrophages are activated to eliminate them by phagocytosis. Simultaneously, they initiate the expression of various cytokines (IL-1 and TNF- $\alpha$ ) and chemotoxins that will promote the inflammatory response to neutralize the strange agent. These molecules can also stimulate epithelial and endothelial cells, producing pro-inflammatory mediators, and increasing the number of leukocytes, primarily neutrophils (Nho, 2020).

Some authors have suggested that episodes of high concentration of particles could affect the phagocytic capacity mediated by macrophages and mucociliary clearance, leading to inflammatory processes. UFPs can also damage airway epithelial cells and macrophages by producing reactive oxygen species (ROS) from redox reactions in the mitochondria (Habre et al., 2018). In this way, particles not eliminated by the alveolar macrophages can promote damage to the lungs and other organs (Donaldson et al., 2001; Lundborg et al., 2001; Oberdörster et al., 2002; Allen et al., 2017; Buzea and Pacheco, 2019; Da et al., 2019). These damages can be associated with the presence of chemical components in the particles, such as metals, BC, and PAHs that can contribute to the increase in ROS formation and consequently in the inflammatory processes (Klaassen, 2013; Zhang et al., 2016; Crobeddu et al., 2017; Sharma et al., 2018; Cervellati et al., 2020; Gao et al., 2020; Li et al., 2020).

The inhaled particles deposited in the respiratory tract can be translocated into the bloodstream and subsequently to the body's different organs (Buzea and Pacheco, 2019; Da et al., 2019). They can also be translocated through epithelial barriers and along the olfactory and sensory neuronal pathways to subsequently reach other organs, including the brain (Chen et al., 2016). This translocation may vary depending on the size, chemical composition, surface charge, and aggregation of the particles (Sharma et al., 2018; Martins et al., 2021). Once in the circulation, a part of these particles can be translocated through the blood-brain barrier to the brain parenchyma (Heusinkveld et al., 2016). The particles can pass through the blood-brain barrier intact in several ways, for instance, passive crossing by simple diffusion (passive lipophilic materials) or through a protein-mediated energy-dependent active transport carrier or receptors (Heusinkveld et al., 2016).

After the transport of the particles and their translocation to the different organs takes place, the pollutants present in the particles can accumulate selectively in adipose tissues of the body and/or interact with other substances, which can increase their toxicity (Timbrell, 2009; Klaassen, 2013; Zhang et al., 2019). This will depend on the chemical characteristics, reactivity, and affinity of the chemical substance. For instance, organic compounds are hydrophobic and tend to accumulate in the body's organs and lipid tissues, contributing to fatty liver diseases (Rengarajan et al., 2015; Abdel-Shafy and Mansour, 2016; Wahlang et al., 2019).

### 3.2. Mechanisms of UFPs toxicity

As previously mentioned, PM exposure effects depend on particle size, chemical composition, morphology, crystallinity, surface area, roughness, porosity, agglomeration, hydrophobicity, hydrophilicity, and electromagnetism. These characteristics depend on the place of

origin and source of contamination (Kelly and Fussell, 2012; Klaassen, 2013; Sharma et al., 2018; Buzea and Pacheco, 2019; Martins et al., 2021). In this way, contaminants found in UFPs include inorganic ions, trace metals, elemental carbon, carbonaceous organic matter, water, among others (Yadav et al., 2018; Song et al., 2019; Chen et al., 2020).

Many studies have confirmed that potentially toxic elements within PM were harmful to human health (de Kok et al., 2006; Saikia et al., 2018; Zhang et al., 2018; Briffa et al., 2020). Transition metals, such as Cr, As, Cd, and Ni, have been listed as carcinogenic to humans (Chen et al., 2019). Metals are known for their relationship with the generation of ROS, including hydroxyl radicals (Briffa et al., 2020; Gao et al., 2020), which can have unwanted effects, such as lipid peroxidation, proteins and DNA damage, cell death (apoptosis), and genotoxicity (Miller et al., 2012; Zhang et al., 2018b; Bhargava et al., 2019; Badran et al., 2020; Platel et al., 2020).

Oxidative stress and inflammation are associated with many disorders such as cardiovascular diseases (Simkovich et al., 2008; Jantzen et al., 2016; Bliss et al., 2018), neurological diseases (Wei et al., 2017), and cancer (Buzea and Pacheco, 2019; Gao and Sang, 2020). Both fine particles and UFPs contain higher concentrations of toxic metals, such as Pb, Cd, and Ni (Liu et al., 2018); this is partly because these particles have a higher surface area and volumetric ratio, which gives them a more significant potential to transport toxic compounds compared with coarse particles (Burtscher and Schüepp, 2012; Chen et al., 2016).

Concerning the cardiovascular effects generated by UFPs, Miller et al. (2012) proposed three hypotheses that explain how inhaled particles can cause cardiovascular effects: (i) particles induce an inflammatory response in the lungs, which leads to the release of cytokines and other third party particles in the systemic circulation, (ii) UFPs can be translocated through the alveolar wall and interact directly with the cardiovascular system, and (iii) particles can activate the autonomous nervous system through sensory receptors on the alveolar surface, altering the autonomic nervous system activity that leads to indirect alterations of cardiovascular function. Other pathways may also undergo some activities, such as the translocation and stimulation of sensory receptors in the upper airways and nasal epithelium, the translocation through the gastrointestinal tract after mucociliary clearance, the accumulation of constituents of PM, the amplification of the inflammatory pathways in adipose tissue, and the effects on the central nervous system (CNS) that can regulate the endocrine system (Miller et al., 2012).

On the other hand, the organic fraction of particles contains hundreds of different compounds, including VOCs, BC, PAHs, and N-PAHs (Kim et al., 2013; Badran et al., 2020). The latter have toxic, mutagenic, genotoxic, and carcinogenic properties (Kim et al., 2013; Topinka et al., 2013; Agudelo-Castañeda et al., 2017; Landkocz et al., 2017; Santibáñez-Andrade et al., 2017; Feng et al., 2019). Likewise, they are highly soluble in lipids, so they are easily absorbed in fatty tissues and lipophilic systems in the human body (Abdel-Shafy and Mansour, 2016; Abbas et al., 2018).

PM's genotoxic and carcinogenic effects have been found to be related to the organic fraction, including PAHs and their derivatives, which are part of the organic fraction. These compounds have been mainly related to the ultrafine fraction because they have a greater specific area than larger particulate material (Topinka et al., 2013). Despite the multiple effects related to the presence of PAHs in PM, there is still not enough evidence on the harmful effects of these substances; this is due in part to the fact that PAHs have a wide variety of physical and chemical properties that make their measurement difficult and expensive. In addition to the above, PAHs are usually present in small concentrations, making it difficult to carry out experimental exposure tests with biological models.

Something similar occurs with BC, a constituent of PM<sub>2.5</sub> and UFP, which has been related to respiratory alterations (Paunescu et al., 2019) and cardiovascular functions (Gao and Sang, 2020). As a fine particle, BC can be inhaled and consequently deposited in the lungs, becoming more harmful to people than other contaminants such as

**Table 2**  
Human toxicological studies related to UFPs exposure (<100 nm).

Age Group	Number of subjects	Study area	Country	UFPs quantification methodology	Biological test	Key findings	Reference
Adults	58	Indoor and outdoor environments	Copenhagen	Personal monitors for UFPs collection, CPC, Gravimetry for PM <sub>2.5</sub>	Endothelial progenitor cell levels by polychromatic flow cytometry; ROS production in leukocytes by flow cytometry with 2,7-dichlorofluorescein in blood.	Positive correlation between the levels of endothelial progenitor cells and the concentration of UFPs from external environments. No correlation with leukocyte-mediated oxidative stress.	Jantzen et al. (2016)
Children	655	Schools	Australia	CPC, TSI Model 3781 and TSI Model 3787. For particles larger than 6 nm and 5 nm, respectively.	Pulmonary function of children was assessed by interviewing their parents, spirometry, measurement of exhaled nitric oxide and serum C-reactive protein	UFPs did not affect the children's respiratory health, but they show systemic effects, detected in the form of a positive association with a biomarker for systemic inflammation.	Clifford et al. (2018)
Adults	22	Public parks at the LAX International Airport	USA	DiscMini diffusion charger (Testo AG), CPC 3007, TSI Inc, and an Aethalometer E51 to measure BC	Participants carried out a soft walking activity scheduled twice in public parks inside and outside the influence area. Spirometries were performed, exhaled nitric oxide, and circulating inflammatory cytokines before and after exposure were measured.	Existence of acute systemic inflation after exposure to UFPs related to the airport was demonstrated. The effects related to road traffic exposure were different.	Habre et al. (2018)
Newborns	158–743	Urban	Canada	Concentration of UFPs with software	Prenatal exposure (between the second and eighth week after conception, when the heart begins to form, risk of congenital heart defects) to UFPs	UFPs exposure was associated with an increased risk of the ventricular septal defect.	Lavigne et al. (2019)
Adults	50	Urban	Italy	Portable UFP monitors	Correlation between exposure to ultrafine particle concentrations and heart rate in a healthy population.	Short-term exposure to concentrations of UFPs is positively associated with heart rate for the evaluated people's different physical activities.	Rizza et al. (2019)
Children	305	Urban	France	Concentrations to BC and UFP with Portable monitors.	Forced expiratory volume in 1 s (FEV <sub>1</sub> ), forced vital capacity (FVC), and the fraction of exhaled nitric oxide (FeNO) was determined in children's exposure for 24 h.	Increase in 24-hour BC exposure concentrations were related to a statistically significant decrease in lung function parameters only among children with persistent respiratory symptoms	Paunescu et al. (2019)

PM<sub>10</sub>, PM<sub>2.5</sub> and inorganic particles (Kumar et al., 2018; Magalhaes et al., 2018; Zhang et al., 2019). BC particles are toxic through mechanisms of oxidative stress, cell signalling and activation, and the release of mediators initiating inflammatory processes in the respiratory tract (Nho, 2020) and the cardiovascular system (Paunescu et al., 2019). Besides, as a fine aerosol with a large specific surface area, BC can absorb carcinogenic contaminants, such as VOCs and PAHs, which can settle on the skin or even be inhaled, reaching the lungs; thus, affecting respiratory organ tissues. BC produces more harm to people than other contaminants, such as fine (2.5 µm) and coarse (10 µm) PM (Magalhaes et al., 2018; Zhang et al., 2019).

In addition to the toxicological effects mentioned previously, recent studies showed that UFPs have greater power to induce epigenetic modifications than larger particles (Wong et al., 2017; Bhargava et al., 2019). These modifications are mediated by an increase in the production of oxidizing species, which give rise to oxidative stress in the cells and activate inflammatory responses that then lead to epigenetic alterations of the miRNA. Hence, the epigenetic modifications (Wong et al., 2017). Likewise, UFPs lead to higher levels of DNA methyltransferase expression related to global changes in DNA methylation. Additionally, there may be changes in the histone code and mRNA transcription error, and protein translation levels in cells exposed to these particles (Bhargava et al., 2019). In addition to the above, Shukla et al. (2019) found that DNA modification may persist through downstream generations and result in the transgenerational epigenomic inheritance.

### 3.3. Human toxicity studies

Weak evidence of an association between daily UFPs and mortality has been found in epidemiological studies in several cities of Europe (Stafoggia et al., 2017). Similarly, in a regression study in cities in Germany and Eastern Europe, they observed positive but not statistically significant associations between prolonged exposures to UFPs and respiratory mortality (Lanzinger et al., 2016). However, in some time-series analyses and case-crossover studies performed in China, they identified sufficient information to support significant short-term mortality effects of various air pollutants, such as PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>.

Evidence from studies in different parts of the world relates high concentrations of UFPs with acute and chronic effects on human health, including systemic effects, neuronal deficiencies (Cory-Slechta et al., 2018) and neurological diseases, as well as cataracts, diabetes, health deficiencies in newborns, and behavioural alterations (Fleischer et al., 2014; Agudelo-Castañeda et al., 2017; Shukla et al., 2019). Likewise, it has been found that particles with an aerodynamic diameter less than 2.5 µm can exacerbate inflammatory diseases such as asthma and acute bronchitis; they can also cause acute heart attacks and contribute to chronic diseases such as diabetes or cardiovascular disease or they may have a role in lung cancer (Marabini et al., 2017). Tables 2 and 3 summarize some of the toxicological studies carried out in recent years in humans and human cells, respectively.

Some studies have found that children represent the most vulnerable group regarding exposure to fine particles and UFPs due to their state of growth and ways of exposure compared to adults (Da et al., 2019; Slezakova et al., 2019). Likewise, they lack a fully developed defence mechanism for detoxification, they inhale a more significant amount of air volume per body weight, and have a different metabolism (Burtscher and Schüepp, 2012; Da et al., 2019). It has also been found that adults of advanced ages and pregnant women are included in the population vulnerable to atmospheric particles. For the latter case, a recent study found an association between the increase in the concentration of UFPs in the air with adverse effects on blood pressure and systemic inflammation in healthy adults (Liu et al., 2018). Participants in this study were interviewed and examined periodically between 2014 and 2017; particle concentration was also monitored during this time.

**Table 3**  
Toxicological studies related to UFPs exposure (<100 nm) in human cells.

Type of cells	UFPs quantification methodology	Biological test	Key findings	Reference
A549	Three multi-stage impactors. Analysis of samples by gravimetric and identification of ions soluble in water, total carbon, PAHs and anhydrous sugar. UFPs monitoring (40 days) with a Hi-vol PTFE filter. Total organic carbon (TOC). Sievers analyzer. Metals: quantified by mass spectrometry de inductively coupled (SF-ICP-MS)	Genotoxicity in A549 cells (human lung carcinoma cells) exposed to UFPs from wood and firewood combustion was evaluated.	The presence of significant DNA damage was obtained after 24 h of treatment.	Marabini et al. (2017)
THP-1; Human monocytes from 8 non-smoker female donors	Exposure (24 h) to UFPs using aqueous suspensions. Cellular cytotoxicity: measured using lactate dehydrogenase (LDH) with an LDH colorimetric assay kit; ROS formation: measured through the 2,7-dichlorofluorescein diacetate and microplates to measure fluorescence. Cytokine levels were measured with an ELISA kit (human TNF- $\alpha$ )	Correlation between exposure to UFPs and oxidative inflammatory responses. Increased ROS formation in THP-1 cells	Cheng et al. (2020)	
Embryonic stem cells hESC	Ultrafine carbon nano-powder (Sigma -Aldrich) was used. Characterization of the particles by FE-SEM coupled with X-rays (EDS)	Cell viability assays, immunofluorescence staining tests, RNA extraction and RT-PCR analysis, were performed; protein extraction and quantification utilizing the BCA protein kit.	Exposure to carbon particles altered the differentiation of keratinocytes and genes related to inflammation and psoriasis	Gao and Sang (2020)
A549 human lung cancer cells	Four-stage cascade impactor sampling on quartz filters in a city in China. Characterization by AFM (atomic force microscopy)	Tumour endothelium adhesion assays, protein extraction after cell exposure following separation by sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE), Western blot assays, enzyme ligand and immunosortiment assay (ELISA), Immunofluorescence and immunoprecipitation assay.	The UFPs stimulated the release of HMGB1, induced the production of pro-inflammatory cytokines facilitated by NFkB through the interaction of HMGB1 with RAGE and resulted in the adhesion of cancer endothelial cells.	Platel et al. (2020)
Lung cells (BEAS-2B and NCI-H292) and human bronchial epithelial cells (NHBE)	The particles were collected in northern France with a High Volume Impactor. Trace metals: measured by ICP-MS. PAHs by high precision liquid chromatography.	Comet, micronutrients and erythrocyte-based Ptg-A gene mutation assays in vivo by flow cytometry	Fine particles and UFPs lack a genotoxic effect in vitro on primary NHBE cells. In contrast, positive results were obtained in the comet assay on BEAS-2B and NCI-H292 immortalized cell lines.	

Effects related to PM environmental exposure also include significant developmental neurotoxicity, a principal reason for developing diseases such as autism, Alzheimer's, and Parkinson's, where age adversely impacts neurotoxic damage, mainly due to PM's ability to generate ROS, induce oxidative stress, inflammatory response, mitochondrial deterioration, DNA damage, and other mutagenic activities (Shukla et al., 2019).

Recently, epidemiological studies have investigated the association of environmental exposure to UFPs with cardiopulmonary morbidity and mortality (Lanzinger et al., 2016; Liu et al., 2018). There is an association between increased UFPs levels and adverse effects on high blood pressure and systemic inflammation (Liu et al., 2018). Due to the size, UFPs have high alveolar deposition, a large surface area with adhered toxins, and can penetrate blood vessels, which may initiate oxidative stress and inflammation with subsequent atherosclerotic progression leading to thrombus formation (Møller et al., 2020).

Another determining factor in UFP's toxicity is the emission source, on which the concentration of pollutants on the surface of the particles depends. For instance, in a study conducted on people living less than 75 m away from a main road or highway, it was found that exposure to road traffic increases the risk of stroke with strong associations with ischemic stroke. Likewise, hourly or daily changes regarding pollutant concentrations were also related to an increased risk of stroke and stroke mortality, being this last risk linked to UFPs (Sade et al., 2015).

Concerning the above, Bourdrel et al. (2017) found that air pollution, particularly diesel exhaust, provokes a dramatic increase in ROS generation, which alters nitric oxide-mediated vasodilation and promotes vascular inflammation. These acute functional consequences of air pollution exposure have been demonstrated in regulating myocardial and pulmonary blood flow, and coagulation function. Combustion-derived particles have substantial adverse effects attributed to the small size of these UFPs and the PAHs and metals carried on their surface. Although UFPs have a substantial cardiovascular effect, their atmospheric concentrations are strongly underestimated according to standards (Bourdrel et al., 2017).

At the cellular level, effects such as inflammation (Habre et al., 2018; Xia et al., 2018), DNA damage, and genomic instability have been evidenced (Marabini et al., 2017). When having genomic instability, there is a high probability that the cell develops and accumulates genome alterations, which can lead to carcinogenic processes. These alterations' frequency is related to the loss of fidelity in mechanisms such as DNA replication, chromosomal segregation, DNA repair, and cell cycle progression (Santibáñez-Andrade et al., 2017).

An *in vitro* study with human embryonic stem cells revealed that ultrafine carbon particles could cause skin inflammation and psoriasis. Children are the most susceptible to such pollutants, mainly when they have not been born and are still in the womb. Premature skin aging, accompanied by high risks for skin inflammation diseases, such as atopic dermatitis and psoriasis, has been proved to increase in children exposed to air pollution (Cheng et al., 2020).

### 3.4. Biological models and toxicity studies

Laboratory bioassays that use organisms *in vivo* are essential tools to clarify the PM constituents' toxic action mode, identifying markers that discriminate the different potential toxins of atmospheric PM samples (Zhang et al., 2011). Several organisms have been used in *in vivo* studies regarding atmospheric particle toxicity, including rats (Sydbom et al., 2001; Zhang et al., 2011), mice (Morris-Schaffer et al., 2018), cats (Sydbom et al., 2001), birds (Cui et al., 2018), wild rodents (Gómez-Ugalde, 2003), snails (De Roma et al., 2017), fish (Gonzalez-Moragas et al., 2015), and nematodes (Zhao et al., 2014; Gonzalez-Moragas et al., 2015; Chung et al., 2019; Marimon-Bolívar et al., 2019; Sinis et al., 2019; Wu et al., 2019). For example, Zhang et al. (2011) used rats and found that the smaller the particle size, the greater the lungs' inflammatory effects, and consequently, the DNA damage. Other

**Table 4**  
Toxicological studies related to exposure to UFPs (<100nm) in biological models.

Study	UFPs quantification methodology	Biological test	Key findings	References
Mouse	CPC and SMPS for characterization of UFPs pups	Postnatal exposure (4–7 and 10–13) equivalent to the human third trimester at UFP concentrations similar to those of vehicular traffic in full-length exposure chambers.	Neurotoxicity, related to autism. Inflation and oxidative stress are associated as mechanisms	Allen et al. (2017)
Mouse	HUCAPS inhalation exposure chambers from a high volume UFP pups concentration were used to concentrate environmental particles generated on a nearby busy road. Aethalometer	The offspring were exposed for 4 h to concentrated UFPs (10–20 times) using a HUCAPS kit. Exposure was done on postnatal days 4–7 and 10–13. Behavioural tests were carried out. Maternal exposure to BC particles during pregnancy in female mice	Learning and memory deficits; memory, impulsive behaviours, behavioural problems.	Cory-Slechta et al. (2018)
Mice	Intranasal exposure of BALB/c mice to FP and UFPs. The particles were collected in northern France with a High Volume Impactor (HVIS, 400 L/min flow). Trace metals were measured by ICP-MS, PAHs, by high precision liquid chromatography.	Genotoxic effects were evaluated using (i) liver and lung in vivo comet assay, (ii) bone marrow in vivo micronucleus test, and (iii) in vivo test. Mutation test of the Ptg-A gene in peripheral blood, at doses of 10 and 100 µg per animal.	Neurotoxic effects on fetuses. Persistent pathological changes in the tissues of the cerebral cortex and impaired cerebrovascular function in offspring.	Zhang et al. (2019)
Mice	BC was measured using Transmission Electron Microscopy (TEM instrument and a field emission Scanning Electron Microscopy (SEM). SMPS dynamically monitored the diameter of BC particles	FP and UFP do not show genotoxic/mutagenic activity in vivo under the conditions analyzed.	Platel et al. (2020)	
Mice	Genotoxic effects were evaluated using (i) liver and lung in vivo comet assay, (ii) bone marrow in vivo micronucleus test, and (iii) in vivo test. Mutation test of the Ptg-A gene in peripheral blood, at doses of 10 and 100 µg per animal.	The reduction of antioxidant enzyme activities and the addition of ROS in BC exposure groups were observed, and the gene and apoptosis-related protein levels were increased in BC exposure mice. The BC-treated cells were consistent with those of mice, and the apoptosis rate was increased in BC treated cells.	Li et al. (2020)	

toxicological studies that were carried out in recent years on biological models are listed below (Table 4).

Wardoyo et al. (2018) conducted a study with mice where they found that the exposure to UFPs from motorcycle emissions have a significant effect since these particles can penetrate the pulmonary alveoli and subsequently deposit themselves in the kidney leading to renal cells deformation. The exposure to these type of particles results in alterations in glomerular and tubular epithelial cells; along these lines, the concentration of UFPs determines the deformation of such cells.

Besides, Wardoyo et al. (2018) found a positive correlation between total concentrations of UFPs in motorcycle exhaust emissions and physical damage in mice kidneys; this damage goes back to oxidative stress. Inhaled UFPs can deposit themselves in the lungs, coagulate, agglomerate, penetrate the pulmonary alveoli, enter the bloodstream, and subsequently reach vital organs, causing disorders like the case mentioned above. Similar results were previously reported by Sydbom et al. (2001). Other studies carried out with mice have found that UFPs can lead to neurological effects (Morris-Schaffer et al., 2018), such as memory loss (Cory-Slechta et al., 2018), behavioural problems, and changes in brain tissues (Zhang et al., 2019).

#### 4. Capturing, measuring and controlling UFPs

##### 4.1. Capture and measurement mechanisms

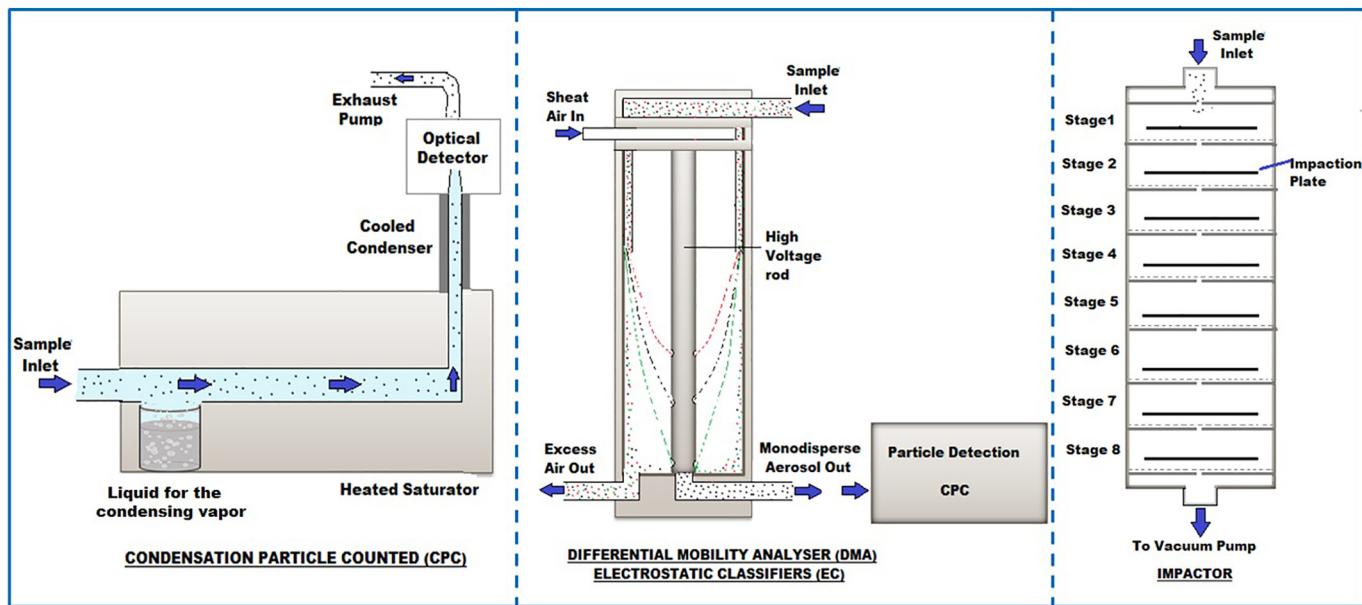
As mentioned earlier, the UFPs concentration in air is measured and expressed commonly in particle number (PN) per unit volume (Kwon et al., 2020). In most published studies where the particle number and size distribution are reported, researchers use condensation particle counters (CPCs) and electrostatic classifiers (ECs). Moreover, the measurement of particles up to 0.4 nm is made using ion mobility air spectrometers (Morawska et al., 2008; Kumar et al., 2014). Fig. 4 presents the general diagram of the operation of the typical methodologies used to measure UFPs.

In the CPC methodology, particles are initially enlarged by the vapour's condensation until a size is detectable, and then they are counted while passing through a laser beam (Da et al., 2019). Thus, the detection of the particles is done by optical methods. According to the instrument characteristics, this process will allow counting particles up to 3 nm in diameter (HEI, 2013). These instruments can be used in different combinations with other particle meters, such as differential mobility analyzers (DMAs), to separate the particles by size before condensation. Among the limitations presented by the CPCs are their high cost and their limited range regarding particle size.

One of the recently developed equipment is the portable optical particle counter (OPC) based on light scattering. However, these devices cannot accurately measure particles smaller than 300 nm, and thus, they are not considered adequate to determine UFPs (Kim et al., 2018). In a review published by Kumar et al. (2010), the equipment mentioned above's main commercial models were listed, and a classification of them is presented by particle size range.

There are also methods based on ECs that classify the particles according to size. In this methodology, electrically charged particles move and are separated by size when they are in contact with a high voltage electric field (Forti et al., 2005). These instruments work in combination with particle counters such as differential mobility/scanning particle classifiers, e.g. Differential mobility particle sizer (DMPS) or scanning mobility particle sizer (SMPS), and differential mobility spectrometers (DMS). The SMPS is a high-resolution nanoparticle meter that uses electrostatic classification (Agudelo-Castañeda et al., 2019).

Other types of equipment used are UFP monitors, laser aerosol spectrometer (LAS) with optical detection, and instruments manufactured by GRIMM Aerosol Technik Airlring GmbH & Co. KG that include combinations of SMPS, DMA, and CPC systems to measure particles (5–1110 nm) (Kumar et al., 2010). Low-pressure electric impactors (ELPI), aerodynamic particle sizer (APS) have also been used, but unfortunately, this



**Fig. 4.** Principles of operation of the main methodologies used to capture and measure UFPs.

equipment is mainly used for research purposes and, because of their high price, is not included in monitoring systems of air quality.

Unlike fine or coarse particles, which are unanimously agreed to be measured by mass-sensitive methods, there is still little consensus on whether UFPs should be better characterized by mass, volume, surface area/numerical concentrations or chemical properties. One of the latest methodologies developed to determine the size distribution of the number of UFPs is based on electrically charged particles, separated in an electric field, according to the particles' electric mobility. This family of instruments is called mobility particle size spectrometers (Kim et al., 2018). Within this family of instruments, we can mention the Testo DiSCmini, which is a miniature and portable handheld diffusion size classifier that obtains the concentration of the particles by measuring the electric current produced by the deposition of the charged particles in its two different stages (Luengo-Oroz and Reis, 2019).

PM<sub>0.1</sub> concentrations are typically less than 1 µg/m<sup>3</sup>, and commercial scales generally have detection limits of ± 1–5 µg for means of collection (e.g. filters). Mainly, for UFPs' collection, researchers use the cascading impactors, in which the particles can be separated into different fractions. Aerosol mass spectrometers and aerosol mass flight time spectrometers have also been developed; these last two can measure the chemical composition of UFPs for short periods. In these methods, the sampled particles are initially broken down into ions, following their main components, and then analyzed by mass spectrometry (HEI, 2013).

When sampling UFPs in a filter, different methods for their physico-chemical characterization can be used. Among the most common methods are transmission electron microscopy (TEM) along with energy-dispersive X-ray spectroscopy (TEM-EDS), scanning electron microscopy along with energy-dispersive X-ray spectroscopy (SEM-EDS), and X-ray fluorescence (XRF) spectrometry with synchrotron radiation. These methods are used to obtain morphological and chemical information about the particles. Nano aerosol mass spectrometry (NAMS) with TEM-EDS is used for size identification and elemental analysis; there are three nanoparticle sampling forms: (i) aerodynamic sampling, (ii) electrostatic sampling, and (iii) thermophoretic sampling. The aerodynamic sampling method involves the use of the impactors mentioned above. In the electrostatic sampling, particles with a unipolar or bipolar charge are deposited directly in the TEM network by

electrostatic forces via ultrafine aerosol time-of-flight mass spectrometry (UF-ATOFMS) (Bzdek et al., 2012).

In the case of BC, and since this pollutant has great variability due to both meteorological factors and pathways or distance from the generating sources, researchers use mobile monitoring with portable and fixed micro-aethalometers with aethalometers simultaneously with GPS to indicate the location (Van den Bossche et al., 2015; Tran et al., 2020). A challenge for monitoring UFPs, besides the detection limit, is measuring personal exposure to these particles due to the weak spatial correlation (Weichenthal et al., 2016), probably due to background concentrations in the fixed monitoring stations. Table 5 presents a summary of the main analytical methods used for sampling and the characterization of UFPs since 2008.

#### 4.2. Control mechanisms

Among the management mechanisms taken to ensure that the concentration of atmospheric particles does not exceed the authorized levels, affect human health, cause damage to flora, fauna or the environment in general, direct and indirect measures are developed. Indirect measures include all those actions aimed at preventing particle concentration from exceeding primary value limits; for instance, urban planning and territorial sanitation, air quality plans, information and awareness campaigns, sustainable mobility programs, control measures in different sectors, vehicle technology renewal, and fuel quality improvement (Morawska et al., 2008; Azarmi et al., 2014).

Direct measures are actions designed to reduce the particles' concentration through different control equipment; these are particle traps, which effectively control the solid fraction of the emitted exhaust particles, including elemental carbon (soot) and black smoke. Filters, wet particle scrubbers, electrostatic precipitators, and inertial impactors are also included. In electrostatic precipitators, particles of sizes between 0.1 µm and 1.0 µm are captured and operated at high gas temperatures (up to 1200 °F) (Morawska et al., 2008; Miller, 2011; Vallero, 2011; Pyo et al., 2017).

An alternative filtration method without filters is the use of water vapour condensation for UFPs. This method enables the growth of any type of UFPs in the form of a water droplet. Once UFPs have grown in diameter, these particles are easy to remove (Pyo et al., 2017).

**Table 5**  
Methodologies for the measurement and analysis of contaminants present in UFPs.

Country	Emission source type	Characterization and measurement methods	Contaminants identified	Mean UFPs concentration <sup>a</sup>	Reference
China	Urban zone	Sampling: 13-stage MOUDI Impactor. Characterization: SEM-EDX, SRXRF	Fine and ultrafine particles. Elements: Si, P, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, As, Se, Br, Rb, Sr and Pb Particle diameter: 5–10,000 nm	Coarse, fine and ultrafine particles: $9.38 \pm 2.18$ , $8.82 \pm 3.52$ and $2.02 \pm 0.41 \mu\text{g}/\text{m}^3$ , respectively. $(21.27 \pm 2.02) \times 10^3$ to $(732.27 \pm 442.51) \times 10^3 \text{ PN}/\text{cm}^3$	Lü et al. (2012)
United Kingdom	Particles from concrete mixing	Mass distribution of particles: GRIMM particle spectrometer and DMS			Azarmi et al. (2014)
Brazil	Urban area with high vehicular traffic	Measure concentration: NanoScan SMPS TSI	Particle diameter: 10–420 nm	$4.85 \times 10^4 \text{ PN}/\text{cm}^3$ to $1.80 \times 10^3 \text{ PN}/\text{cm}^3$	Schneider et al. (2015)
Italy	Urban transport	Measure concentration: CPC – TSI P-Trak	Particle diameter: 20–1000 nm.	Car: $5249$ – $48,428 \text{ PN}/\text{cm}^3$ ; Motorcycle $73,168 \text{ PN}/\text{cm}^3$ , bus $29,299 \text{ PN}/\text{cm}^3$	Grana et al. (2017)
China	Urban zone	Sampling: MOUDI Impactor	Particle diameter: 0.05–0.1 $\mu\text{m}$	UFPs ( $\mu\text{g}/\text{m}^3$ ): $1.47 \pm 0.88$ ; range between $0.14$ and $3.31$ .	Liu et al. (2018)
Greenland	Urban zone	Sampling: CPC – TSI P-Trak	Particle diameter: < $0.1 \mu\text{m}$ ( $\text{PM}_{0.1}$ ) in waste incineration plant (1), an area with high Vehicular traffic (2), a site close to buildings (3) and an airport (4).	(1) $478$ – $125,005 \text{ PN}/\text{cm}^3$ ; (2) $450$ – $77,009 \text{ PN}/\text{cm}^3$ ; (3) $5470$ – $43,422 \text{ PN}/\text{cm}^3$ and (4) $44,741 \text{ PN}/\text{cm}^3$	Pétursdóttir et al. (2018)
Belgium	Vehicular traffic	MicroAeth ethalometer for BC and a fixed aethalometer. UFPs concentrations: CPC – TSI P-Trak. Metals characterization: HR-ICP-MS	BC, UFPs and elements: Na, K, Rb, Mg, Ca, Sr, Ti, V, Cr, Mo, Mn, Fe, Co, Rh, Ni, Pd, Pt, Cu, Ag, Zn, Cd, Al, Pb, As, Sb, Se, U.	$3.3 \mu\text{g}/\text{m}^3$ to $13,391 \text{ PN}/\text{cm}^3$ for BC and UFPs, respectively.	Hofman et al. (2018)
Brazil	Urban area	Measure concentration: NanoScan SMPS TSI	Particle diameter: 2.5–250 nm, UFPs, $\text{PM}_{10}$ , NO, $\text{NO}_2$ , $\text{O}_3$ and $\text{SO}_2$	Particle levels in mornings: $20,245$ – $21,945 \text{ PN}/\text{cm}^3$ ; nights: $21,281$ – $21,071 \text{ PN}/\text{cm}^3$	Agudelo-Castañeda et al. (2019)
Mexico	Urban zone	Aethalometer for monitoring BC in real-time.	BC	$0.27$ – $0.75 \mu\text{g}/\text{m}^3$	Peralta et al. (2019)
Italy	Different workplaces	Three-stage DLPI (Dekati Low-Pressure Impactor) with polyurethane filters. Gravimetric analysis: Sartorius MC5 microbalance	Particle diameter: < $0.1 \mu\text{m}$ ( $\text{PM}_{0.1}$ )	$4.7$ – $19.8 \mu\text{g}/\text{m}^3$	Buiarelli et al. (2019)
Portugal	Air traffic	CPC - TSI P-Trak	UFPs	$2.3 \times 10^5$ to $3.4 \times 10^5 \text{ PN}/\text{cm}^3$	Lopes et al. (2019)
Global	Urban area	CPC TSI; DMPS / CPC; SMPS / CPC TSI; DMPS	UFPs y $\text{PM}_{2.5}$	Annual averages: $8.0 \times 10^3$ to $19.5 \times 10^3 \text{ PN}/\text{cm}^3$ for UFPs and $7.0$ – $65.8 \mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$ $7990$ and $19,310 \text{ PN}/\text{cm}^3$	de Jesus et al. (2019)
United Kingdom	Urban area	Testo DiSCmini nanoparticle counter	UFPs in $\text{PN}/\text{cm}^3$		Luengo-Oroz and Reis (2019)
Ghana	Elementary schools	Three Aerasense Nano Tracers	Particles: 10–300 nm; 20–120 nm	$1.83 \times 10^4$ to $8.93 \times 10^4 \text{ PN}/\text{cm}^3$	Nyarku et al. (2019)
United States	Urban area	UFPs concentration: CPC, SPMS, NAMS and BC monitor to measure particle size	Measurement of UFPs, $\text{PM}_{2.5}$ , CO and $\text{NO}_2$	$7500 \pm 1000 \text{ PN}/\text{cm}^3$ at bottom sites. For local roads $11,000 \pm 1200 \text{ PN}/\text{cm}^3$ . Close to restaurants $15,800 \pm 1300 \text{ PN}/\text{cm}^3$ ; High traffic roads: $15,000 \pm 2400 \text{ PN}/\text{cm}^3$	Saha et al. (2019)
United Kingdom	Air traffic	Particle number: CPC TSI. Particle classifiers: TSI with long DMA classifier and TSI DMA, both with SMPS technology	UFPs. Other pollutants: $\text{PM}_{10}$ , $\text{PM}_{2.5}$ , $\text{NO}_x$ and BC	UFPs: $2637$ – $10,046 \text{ PN}/\text{cm}^3$	Stacey et al. (2020)
Germany	Urban area	MPSS, CPC TSI and TSI electrometer	Particle size distribution and BC. Particles from 20 nm to 800 nm	Particles: $900 \text{ PN}/\text{cm}^3$ , BC: $0.1$ – $2.3 \mu\text{g}/\text{m}^3$	Sun et al. (2019)

<sup>a</sup> PN: particle number

## 5. Conclusions

According to the findings reported in the literature, the importance of continuing to carry out studies about UFPs is highlighted because they have been related to various conditions in people's health that contribute to the rise in morbidity and mortality rates worldwide. Among the main toxicological mechanisms associated with UFPs is the oxidative stress generated from reactive oxygen species associated with contaminants such as metals, PAHs, and BC. In this sense, the main effects found include respiratory problems such as asthma and chronic obstructive pulmonary disease, pulmonary fibrosis, neurodegenerative diseases, cardiovascular diseases, DNA changes generated from epigenetic changes, and genotoxic, mutagenic and carcinogenic activity.

Finally, despite the findings reported in this article and that there are multiple mechanisms for the measurement and control of atmospheric UFPs, it is necessary to continue in the study of the different effects of particulate material in order to obtain sufficient evidence that leads to the establishment of new public policies and measures for effective pollution prevention and control.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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