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► To cite this version:

Valérie Forest, Jérémie Pourchez. Biological effects of brake wear particles in mammalian models: a systematic review. *Science of the Total Environment*, 2023, 905, pp.167266. 10.1016/j.scitotenv.2023.167266 . hal-04228704

HAL Id: hal-04228704

<https://hal.science/hal-04228704>

Submitted on 4 Oct 2023

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Biological effects of brake wear particles in mammalian models: a systematic review

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Abstract

Road traffic is a major contributor to air pollution through aerosols both from exhaust emissions (EE) and non-exhaust emissions (NEE). NEE result from mechanical abrasion of brakes and tires, erosion of road surfaces and resuspension of road dust into the atmosphere by passing traffic. EE have been thoroughly studied and have decreased over time due to a stricter control. On the other hand, NEE have not received such attention and there is currently no legislation to specifically reduce NEE particles. Consequently, NEE relative part has become prevalent, potentially making of these emissions a major human health concern. The aim of this systematic review was to provide an overview of the current state of knowledge on the biological effects of brake wear particles, a type of NEE. To this end, we conducted a bibliographic search of two databases (PubMed and Web of Science) on June 1, 2023, focusing on the toxicological effects of brake wear particles induced *in vitro* and *in vivo*. We excluded reviews (no original experimental data), papers not written in English, studies performed in non-mammalian models and papers where no toxicity data were reported. Of the 291 papers, 19 were found to be relevant and included in our analysis, confirming that the assessment of the brake wear particles toxicity in mammalian models is still limited. This review also reports that brake wear particles can induce oxidative stress, proinflammatory response and DNA damage. Finally, some perspectives for further research and measures to mitigate the risk of brake wear emissions are discussed.

Key-words: Brake Wear Particles; Human health; Toxicity; Air quality; Air pollution; Non-exhaust emissions

1. Introduction

1.1. Air pollution

Air pollution is estimated to be responsible for about 7 million premature deaths worldwide per year (WHO, 2022). Air pollutants include particulate matter (PM) which negative impact on human health has been clearly demonstrated. In particular, exposure to PM has been associated to cardiovascular and respiratory diseases, and cancers (WHO, 2022). Indeed, PM has been classified as a human carcinogen (group I) by the International Agency for Research on Cancer (IARC) (IARC, 2013).

Emissions from road traffic, including both gaseous pollutants and PM, contribute greatly to air pollution. Such emissions include exhaust emissions (EE), originating from fuel oxidation and lubricant volatilization during the combustion process, and non-exhaust emissions (NEE), resulting from the mechanical abrasion of brakes and tires, erosion of road surfaces and resuspension of road dust into the atmosphere by passing traffic (Amato et al., 2014; Fussell et al., 2022; Harrison et al., 2021; Lewis et al., 2019; Peikertova and Filip, 2015; Piscitello et al., 2021; Wahid, 2018).

EE have been thoroughly studied and their control has become stricter, resulting in their progressive decrease. On the other hand, NEE have not received such attention and there is currently no legislation to specifically reduce NEE particles. Consequently, the proportion of NEE has increased and now far exceeds that of EE in many countries (ADEME, 2022; Amato et al., 2014; Fussell et al., 2022; Grigoratos and Martini, 2015; Harrison et al., 2021; Lewis et al., 2019; Peikertova and Filip, 2015; Piscitello et al., 2021). NEE is a significant source of PM₁₀ and PM_{2.5} in urban environments, and the proportion of PM emissions from NEE sources are now estimated to be responsible for about 90% of all PM emissions from road traffic (OECD, 2020; Rexeis and Hausberger, 2009; Timmers and Achten, 2016). Furthermore, the part of NEE, a significant source of PM₁₀ and PM_{2.5} in urban environments, is destined to increase in the future, as vehicle traffic is expected to increase and due to the electrification of vehicles. Indeed, while the EE of electrical cars are reduced compared to that of traditional gasoline vehicles, NEE will increase because of the higher weight of electric vehicles, their increased power and torque capabilities (Amato et al., 2014; Harrison et al., 2021; Lewis et al., 2019;

OECD, 2020; Piscitello et al., 2021). The OECD estimates that NEE PM emissions from passenger cars will increase by 53.5 % globally, from 0.85 million tons in 2017 to 1.3 million tons in 2030, based on the projected growth in the global vehicle stock (Harrison et al., 2021; OECD, 2020). Regarding the sources of emission, it has been estimated that NEE traffic-related PM10 emissions are composed of 16-55 % brake emissions, 5-30 % tire road contact emissions and 28-59 % resuspended emissions (Joint Research Centre, 2018; OECD, 2020).

Many researches have reported data on NEE in terms of emission and physicochemical characterization (Amato et al., 2014; Harrison et al., 2021; Lewis et al., 2019; Piscitello et al., 2021), however, very few data are available on their potential impact on human health. We recently reviewed the biological effects of tire and road wear particles (TRWP) (Bouredji et al., 2023), and found that despite the limited availability of data, oxidative stress and inflammation were found to be the main mechanisms underlying the toxicity of TRWP both *in vitro* and *in vivo*. In the present paper, we chose to pay particular attention to brake wear particles, another important source of PM from NEE. Indeed, in urban environments, brake wear can contribute up to 55 % by mass to total non-exhaust traffic-related PM10 emissions and up to 21% by mass to total traffic-related PM10 emissions (Grigoratos and Martini, 2015).

1.2. Brake wear particles

The majority of car braking systems consist of a rotor (disc or drum), a pad (lining) and a caliper. During a braking event, the brake pads are forced against the disc to make the vehicle decelerate or even stop, in the meantime, the vehicle kinetic energy is transformed into thermal energy (Grigoratos and Martini, 2015; OECD, 2020; Wahid, 2018). The frictional contact between the disc and the pad generates wear particles (Grigoratos and Martini, 2015; OECD, 2020).

Particles worn from brake pads and discs contribute almost equally to total PM from braking systems. The physicochemical features and rate of the particles emitted vary depending on some parameters such as the chemical composition of the materials composing the brake disc and brake pads. While

disc brakes are typically made of grey cast iron (or in some cases steel, carbon-carbon, ceramic, or aluminum matrix composites), the composition of brake pads is very heterogeneous (OECD, 2020; Wahid, 2018). Indeed, brake pads generally consist of five main components (Grigoratos and Martini, 2015; Kumar and Ghosh, 2020; Stojanovic et al., 2022; Straffelini et al., 2015; Wahid, 2018):

- binders, which ensure the structural integrity under mechanical and thermal stress as they hold the components of the brake pad together. They are made of modified phenol-formaldehyde resins.
- Reinforcing fibers, which provide mechanical strength and ensure structure and stability to the brake pad. They mainly consist of copper, steel, brass, potassium titanate, glass, organic material and Kevlar.
- Fillers, which are used to improve thermal and noise pad properties and also reduce the manufacturing cost. They are usually made of inorganic compounds (barium and antimony sulphate, magnesium and chromium oxides), silicates, ground slag, stone and metal powders.
- Lubricants, which influence the wear characteristics of the lining. They can be inorganic, metallic or organic. Graphite is usually employed, but other common materials include ground rubber, metallic articles, carbon black, cashew nut dust and antimony trisulphide.
- Abrasives, which are used to control the frictional properties and ensure stability during the braking condition. Aluminum oxide, iron oxides, quartz and zircon are the most common abrasive constituents.

Depending on the proportion of these components, brake pads can be classified into three main groups, characterized by variable tribological performances (Grigoratos and Martini, 2015; Kumar and Ghosh, 2020; OECD, 2020; Stojanovic et al., 2022; Straffelini et al., 2015; Wahid, 2018):

- non-asbestos organic (NAO), mainly composed of organic compounds, mineral fibers and graphite. NAO pads are relatively soft and exhibit low brake noise compared to other types of pads, but they lose braking capacity at high temperature and create more dust than the other types. While for many years, brake pads contained asbestos fibers, they are now asbestos free.

- low metallic (LM), composed of a mixture of metal (10–30% by mass) and organic compounds; They exhibit high friction and good braking capacity at high temperatures.
- and semi-metallic (SM), including a metallic (mainly steel and iron) content typically between 30 and 60% by weight. SM brake pads are more durable and exhibit excellent heat transfer but tend to wear down rotors faster and be noisier.

It is noteworthy to mention that the chemical composition of wear particles may be different from the bulk composition of the brake pad due to the physicochemical transformations occurring during the friction process (*e.g.*, size fractionation, oxidation and volatilization). However, it has been reported that iron, copper, barium, antimony, zinc aluminum, chromium, potassium, titanium, and magnesium are the main components of brake wear particles and some of them have been commonly identified as possible tracers in literature (see below) (OECD, 2020; Peikertova and Filip, 2015).

Brake wear emission predominantly occurs in urban environments where it is necessary to slow down because of pedestrians or traffic lights. On the contrary, it is less important on highways where the driving speed is more constant, except at tolls or highway exits (Grigoratos and Martini, 2015; Stojanovic et al., 2022). It is estimated that approximately 50% of total brake wear is emitted as airborne PM₁₀. The rest may deposit on the road or nearby or maybe attracted by the vehicle (Grigoratos and Martini, 2015; OECD, 2020; Peikertova and Filip, 2015; Wahid, 2018). Average brake wear contributions to ambient PM₁₀ concentrations vary from negligible up to 4 µg/m³, or higher at specific traffic hotspots (Amato et al., 2014; Grigoratos and Martini, 2015). It was estimated that PM₁₀ from brake wear emissions represent 63-98% of the total suspended particles (OECD, 2020).

Brake wear emission can vary drastically depending on different factors such as the driving style (braking frequency), the brake characteristics (composition and age of pad and disc), and the vehicle weight. Thus, brake wear PM₁₀ emission factors ranging from 2.0 to 8.0 mg km⁻¹ veh⁻¹ have been reported for light duty vehicles, while those observed for heavy duty vehicles are approximately one order of magnitude higher (Grigoratos and Martini, 2015; OECD, 2020).

Brake wear particles exhibit various sizes and morphology: microsized particles present sharp edges, whereas particles in the nanoscale are rather spherical and often attached to the surface of larger particles (Grigoratos and Martini, 2015; Vouitsis et al., 2023).

Brake wear PM₁₀ mass distributions ranging between 2 and 6 µm have been reported (Grigoratos and Martini, 2015; Stojanovic et al., 2022; Vouitsis et al., 2023). This coarse size range is expected as brake wear particles are mainly produced by a mechanical process. However, finest fractions (< 100 nm), have also been observed and are explained as being the result of high temperatures at the brake/rotor interface which leads to the decomposition of brake lining materials (Fussell et al., 2022; Grigoratos and Martini, 2015; OECD, 2020; Stojanovic et al., 2022). It was generally found that the higher the temperature, the finer is the brake wear particles (Wahid, 2018). Thus, brake wear debris is a complex mixture containing particles with sizes ranging from several nanometers to millimeters (Kumar and Ghosh, 2020; OECD, 2020).

Despite the large variation in the chemical composition of commercial lining materials, most studies have reported Fe, Cu, Zn and Pb to be the most abundant metals in the brake lining. However, Pb content has decreased due to its replacement in modern linings. Other elements found in brake wear particles are Al, Sn, Mg, Si, Cr, Ti, K, W, Ni, Zr, Ba, S, C, P, F, Mn, Bi and Sb (Grigoratos and Martini, 2015; Vouitsis et al., 2023). Approximately 150 organic compounds have been identified including n-alkanes, n-alkenes, n-alkanols, glycerol compounds, phenolic compounds, and polycyclic aromatic hydrocarbons (PAHs) (Fussell et al., 2022). Chemical properties of the parent lining material are often modified due to high temperatures and pressures reached during the braking process. However, brake wear is characterized by a specific pattern of some heavy metals (Fe, Cu, Zn, Sn, Sb, Ba) in the airborne PM concentrations. These elements have been extensively used as specific tracers for brake wear, although these elements can also be emitted from other sources, mostly from industrial processes (Fussell et al., 2022; Grigoratos and Martini, 2015; OECD, 2020; Stojanovic et al., 2022; Wahid, 2018).

While brake wear particles have been thoroughly studied in terms of emissions and physicochemical characterization, their possible adverse health effects remain poorly documented. Indeed, many

studies have reported the negative impact of PM10 on human health, however, very few researches specifically investigate the contribution of brake wear particles. The aim of this paper is to present the current state of knowledge on the biological effects of brake wear particles through a systematic review.

2. Systematic review of the literature

Figure 1 schematically illustrates the method, the results and the analysis we performed, which is explained in more detail below.

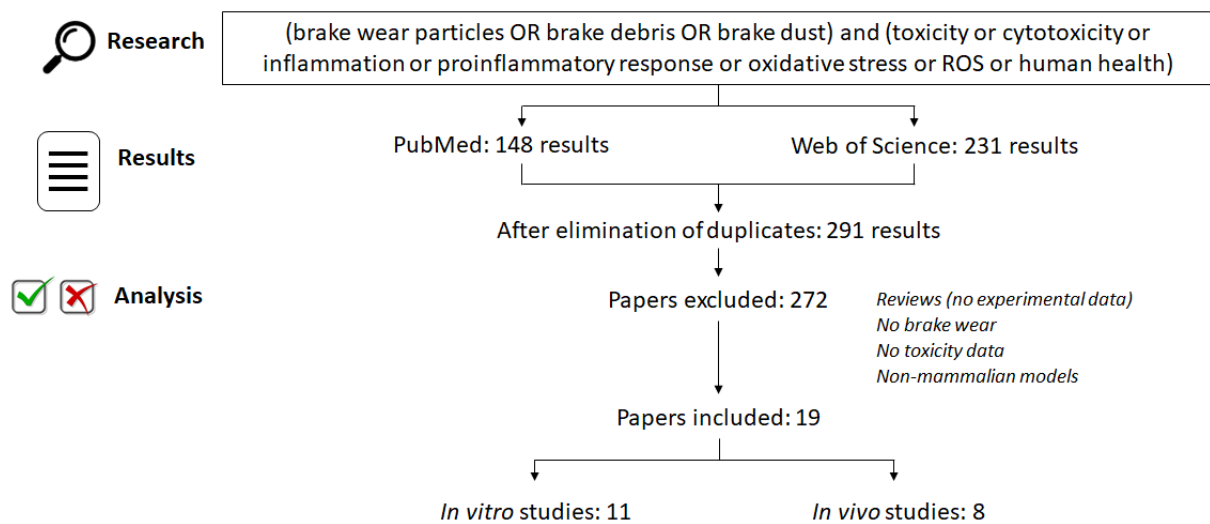


Figure 1 – Graphical summary of the research conducted and the results obtained.

2.1. Method

We selected the following keywords: (brake wear particles OR brake debris OR brake dust) and (toxicity or cytotoxicity or inflammation or proinflammatory response or oxidative stress or ROS or human health). We searched two databases: PubMed and Web of Science. We eliminated duplicates and analyzed the remaining papers. Papers were excluded from our selection based on 5 criteria: i) if they were reviews and thus did not contain original experimental data, ii) if the studies did not involve brake wear particles, iii) if no toxicity data were reported (*e.g.* if the studies focused only on the emission or

the physicochemical characterization of brake wear particles, iv) if studies were performed in non-mammalian models, and v) if papers were not written in English.

2.2. Results

As shown in Figure 1, the search (performed on June 1st, 2023) in PubMed yielded 148 papers, while the search in Web of Science yielded 231 references. After eliminating duplicates, 291 papers remained to be further analyzed. 272 papers were excluded and the remaining 19 papers were classified as *in vitro* studies or *in vivo* studies corresponding to 11 and 8 references, respectively.

2.3. Analysis of the results

Table 1 summarizes the studies carried out to assess the biological effects of brake wear particles in *in vitro* and *in vivo* in mammalian models.

Table 1 – Summary of the studies assessing the biological effects of brake wear particles.

Author	Year	Brake wear particle source	Biological model	Biological endpoints	Main results / conclusions	Reference
<i>In vitro</i> studies						
Alves et al.	2023	Brake wear particles (PM10) obtained from a dynamometer test chamber with different brake pads and different braking cycles.	Human epithelial alveolar cells (A549) exposed to 150-400 ng/mL of the particulate organic extracts for 24h.	Cell viability, cell cycle analysis, levels of intracellular reactive oxygen species.	Greater decrease in cell viability with low steel brake pads. No significant difference in cell cycle. No significant increase in ROS levels.	(Alves et al., 2023)
Figliuzzi et al.	2020	Particles emitted during braking bench tests performed with 4 different brake pad/disc combinations of variable Cu concentrations.	A549 cells exposed to 1-500 µg/mL brake wear particles for 48h.	Cell viability, oxidative stress, mitochondrial membrane potential, apoptosis, proinflammatory response and gene expression.	Positive correlation between Cu content in the brake wear particles and the effect on cell viability, mitochondrial membrane potential change, and cell apoptosis.	(Figliuzzi et al., 2020)
Barosova et al.	2018	Brake wear particles generated from low-metallic and non-asbestos organic (NAO) brake pads by a brake dynamometer test chamber.	Human 3D multicellular model: A549 cells and primary immune cells. Model exposed at a pseudo-air-liquid interface (ALI) to 2-0.5 mg/mL brake wear particles for 24h.	Cell viability, cell morphology, oxidative stress, and proinflammatory response.	No significant change in cell viability, no oxidative stress induced. No adverse biological effects induced by low-metallic brake wear debris. NAO brake wear particles induced a proinflammatory response.	(Barosova et al., 2018)
Gasser et al.	2009	Particles emitted from 2 braking behaviors.	A549 cells cultured at the ALI exposed to freshly generated brake wear particles for 24h.	Cytotoxicity, oxidative stress, proinflammatory effect, tight junctions.	No significant cytotoxicity, proinflammatory response or oxidative stress. The metals on brake wear particles damage tight junctions.	(Gasser et al., 2009)
Zhao et al.	2015	Brake wear dusts collected directly from brake drums of 7 small passenger vehicles.	A549 cells exposed to 2-100 µg/mL particles for 1h.	Acellular and cellular ROS production.	ROS were detected in the cell-free test, while exposed cells were not dramatically activated.	(Zhao et al., 2015)
Melzi et al.	2023	Brake dust collected from the brake linings of 3 different cars.	Bronchial cell line (BEAS-2B) exposed to 25-150 µg/mL brake wear particles for 24h.	Cytotoxicity, genotoxicity, oxidative, and inflammatory response.	Brake wear particles induced cytotoxic and genotoxic effects.	(Melzi et al., 2023)
Puisney et al.	2018	Brake wear particles obtained from a motor vehicle testing center and a test bench.	Human bronchial epithelial cells (Calu-3) exposed to 3-300 µg/mL brake wear particles for 24h.	Cell viability, oxidative stress, proinflammatory response.	Loss of cell viability, increased ROS production, limited proinflammatory effects.	(Puisney et al., 2018)

Puisney-Dakhli et al.	2023	Brake wear particles obtained from a motor vehicle testing center.	Calu-3 cell line exposed to 3-300 $\mu\text{g/mL}$ brake wear nanoparticles for 24h.	Particle translocation, mucus production, cytotoxicity and repair efficiency.	Brake wear nanoparticles able to cross the epithelial tissue in small amounts without affecting the barrier integrity. No cytotoxicity, no proinflammatory response, but increased production of the MU5AC mucin.	(Puisney-Dakhli et al., 2023)
Peikertova et al.	2016	Brake wear particles generated using an automotive brake dynamometer.	Human peripheral blood cells exposed to 0.12-75 $\mu\text{g/mL}$ particles for 48h.	Genotoxicity and immunotoxicity.	Brake wear debris particles could induce chromosomal damage, and change in immune response.	(Peikertova et al., 2016)
Selley et al.	2020	Brake abrasion dust extracted from a bag filter taken from the ventilation duct of a machinery testing plant.	U937 macrophages exposed to 4-25 mg/mL brake abrasion debris for 24h.	Mitochondrial function, proinflammatory response, bacterial phagocytosis ability.	Dose-dependent decrease in mitochondrial depolarisation, increased secretion of IL-8, IL-10 and TNF α and decreased phagocytosis of <i>S. aureus</i> .	(Selley et al., 2020)
Kazimirova et al.	2016	Brake wear debris generated by a brake dynamometer with various braking cycles.	Human lymphocytes exposed to 3-75 mg/cm^2 brake wear debris for 28 and 48h.	Genotoxicity.	Increase in frequencies of micronucleated binucleated cells. Brake wear debris could induce chromosomal damage.	(Kazimirova et al., 2016)
<i>In vivo studies</i>						
Bernstein et al.	2014 2015	Brake dust obtained by sanding of brake-drums.	Male Wistar rats exposed by inhalation (nose-only) 6 h/day for 5 days.	Deposition, translocation and pathological response.	No significant pathological response was observed.	(Bernstein et al., 2015, 2014)
Bernstein et al.	2018	Brake dust obtained by sanding of brake-drums.	Male Wistar rats exposed by inhalation (nose-only) 6 h/day for 5 days per week for 4 weeks. Animals were sacrificed immediately after the last exposure and following 1, 14 and 28 days.	Histopathology, broncho-alveolar lavage (BAL) analysis.	No significant pathological response observed.	(Bernstein et al., 2018)

Bernstein et al.	2020 2021	Brake dust obtained by sanding of brake-drums.	Male Wistar rats exposed by inhalation (nose-only) to 0.2-0.67 mg/m ³ of brake dust for 6 h per day 5 days per week for 13 weeks. Animals were sacrificed immediately after exposure, and following 45 and 89 days.	Histopathology, BAL analysis.	No significant pathological response was observed.	(Bernstein et al., 2021, 2020a, 2020b)
Gerlofs-Nijland et al.	2019	Brake debris (PM2.5) collected in an experimental setting under realistic simulated driving conditions. 4 types of brake pads.	Female BALB/c OlaHsd mice exposed by inhalation (nose-only) up to 9 mg/m ³ brake wear debris for 1.5, 3, or 6h.	Histopathology, BAL analysis.	Neither cytotoxicity nor oxidative stress was observed. Inflammation induced by exposure to wear emissions of the NAO and hybrid brake pads.	(Gerlofs-Nijland et al., 2019)
Kukutschova et al.	2009	Brake wear debris generated by a brake dynamometer. For comparison, identical brake lining samples were also ball milled.	Male rats (Wistar) intratracheally instilled with a single dose (0.5-3 mg) of ball milled particle suspensions in 1 mL of physiological solution and exposed for 1, 3, and 7 days.	Mutagenicity evaluated both for wear debris and ball milled particles (Ames test and SOS chromotest). Pulmonary inflammation and cytotoxicity and histopathological evaluation.	Potency of wear particles for interacting with DNA after metabolic activation. Strong inflammatory reaction in bronchial branch and strong cell reaction in alveolar tissue.	(Kukutschová et al., 2009)

First, it should be noted that studies on the toxicity of brake wear particles in mammalian models remain quite sparse. Then, we observe that results are heterogeneous: for a given biological endpoint, some *in vitro* studies report no effect after exposure of cells to brake wear particles, while others observe a significant change compared to control conditions. For example, some studies showed that cell viability was not affected after exposure to brake wear particles (Barosova et al., 2018; Gasser et al., 2009; Puisney-Dakhli et al., 2023), whereas other researches have clearly demonstrated cytotoxicity (Alves et al., 2023; Melzi et al., 2023; Puisney et al., 2018). Similarly, while Melzi *et al.* and Puisney *et al.* reported an increased ROS production (Melzi et al., 2023; Puisney et al., 2018), it was not observed in other studies (Alves et al., 2023; Barosova et al., 2018; Gasser et al., 2009; Zhao et al., 2015). Regarding a proinflammatory response, while this effect has been evidenced in several studies (Barosova et al., 2018; Puisney et al., 2018; Selley et al., 2020), it was not reported by Puisney-Dakhli *et al.* (Puisney-Dakhli et al., 2023).

In vivo, no significant pathological response, no cytotoxicity nor oxidative stress were observed after exposure of rats or mice to brake wear particles while inflammation could be induced (Bernstein et al., 2021, 2020a, 2020b, 2018, 2015, 2014; Gerlofs-Nijland et al., 2019; Kukutschová et al., 2009).

Overall, from the analysis of these papers, we can conclude that brake wear particles can cause significant adverse biological effects. The discrepancy in the observed effects can be related to the heterogeneity of experimental conditions (different types of samples, different biological models, different conditions of exposure of cells or animals to particles, etc., see the discussion on the limitations of these studies below).

Toxicity of brake wear particles is mainly related to their chemical nature. Indeed, their metallic compounds have already been shown to induce adverse effects. In particular, transition metals such as Fe, Cu, Ni and Cr can catalyze the formation of ROS which can lead to oxidative stress (Fussell et al., 2022; Grigoratos and Martini, 2015; Melzi et al., 2023). Moreover, metals such as Zn, Al and Pb, in

addition to their intrinsic toxicity, can also influence the toxic effects of transition metals either by enhancing or by lessening their activity (Grigoratos and Martini, 2015; Stojanovic et al., 2022).

In addition to oxidative stress, other mechanisms underlying the toxicity of brake wear particles have been shown to be proinflammatory response and DNA damage (Barosova et al., 2018; Gonet and Maher, 2019; Kazimirova et al., 2016; Kukutschová et al., 2009; Malachova et al., 2016; Puisney et al., 2018; Straffelini et al., 2015; Vouitsis et al., 2023).

The contribution of metals to brake wear particles toxicity has been underlined by Gasser *et al.* They showed that when cells were exposed to brake wear particles, tight junction protein occludin density decreased significantly with increasing concentrations of brake wear PM metal content (iron, copper, and manganese) (Gasser et al., 2009). Similarly, Barosova *et al.* compared the toxicity of brake wear particles with variable metal content. The low metal composite-derived PM elicited no toxicity, whereas the high metallic composite increased IL-8 (Barosova et al., 2018).

As brake wear emissions are particularly rich in Fe and Cu, the role of these metals should be paid particular attention (Grigoratos and Martini, 2015; Straffelini et al., 2015; Vouitsis et al., 2023). Fe-bearing nanoparticles in urban environments may be especially important because of their pathogenicity and possible association with neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases (Gonet and Maher, 2019; Maher, 2019). Focusing on the role of Cu in brake wear particles toxicity, Figliuzzi *et al.* reported a positive correlation between Cu content in the brake wear particles and the effect on cell viability, mitochondrial membrane potential change, and cell apoptosis (Figliuzzi et al., 2020).

Finally, brake wear emissions have been cited as a potentially important source of Sb. It originates from stibnite (Sb_2S_3), a lubricant included in brake pads. Stibnite can be oxidized during the braking process to Sb_2O_3 , which has been categorized as a potentially carcinogenic substance (Grigoratos and Martini, 2015).

3. Discussion

As previously mentioned, this systematic review reports studies showing very heterogeneous results, making it challenging to draw firm conclusions on the toxicity of brake wear particles. To better understand the observed discrepancies, we should consider the limitations of the cited studies.

First, there is no standardized procedure for the generation, characterization and toxicity assessment of brake wear emissions. This often leads in different experimental approaches by researchers and therefore in non-comparable results and conclusions (Feo et al., 2023; Grigoratos and Martini, 2015; OECD, 2020; Peikertova and Filip, 2015).

Regarding the origin of brake wear samples, three main sources can be distinguished: i) collection of particles in the laboratory using brake dynamometer tests, ii) collection of particles performed in ambient air and then brake wear emissions are identified by means of specific brake wear tracers, and iii) brake wear particles are directly sampled on-road under “real-world” driving conditions by means of mobile units (Grigoratos and Martini, 2015; Peikertova and Filip, 2015).

Generation of brake wear particles using a dynamometer may have limited applications, such as it cannot replicate wear behavior of real brake systems as it does not take into account the vehicle characteristics, the driving style (*e.g.*, variable speed, frequency and severity of braking) or weather conditions (Fussell et al., 2022; OECD, 2020; Wahid, 2018). All these parameters however can deeply influence the brake wear particles’ chemical composition and emission rates, and consequently their toxicological profile (Grigoratos and Martini, 2015; Peikertova and Filip, 2015).

Using particles sampled from ambient air involves the use of tracers for the identification of brake wear particles. Although some metals have been used as specific tracers for brake wear, their use can be inaccurate because they can originate from other sources in the environment. For instance, Cu can be found not only in brake wear, but also in tire wear, engine related pollutants, fertilizers, herbicides, and numerous other designs, requiring further analysis to confirm the source of the particles (Peikertova and Filip, 2015).

Using on-road collected samples seems to be the most representative of real-world conditions but first it is impossible to simulate all braking scenarios, and second, we have to face another challenge, which is the identification and separation of particles that originate from other sources of particles that originate from brakes (OECD, 2020; Stojanovic et al., 2022; Wahid, 2018). Indeed, brake dust particles may mix up with tire or road dust (Wahid, 2018).

Beside the lack of standardized sampling and testing methods, another factor hampering quantitative comparisons among different studies, is the heterogeneity of existing brake materials (OECD, 2020). Indeed, manufacturers use many components (usually more than 10 for one brake pad formulation), with very little information about the exact formulation of the brake pads. Also, due to the high temperatures and pressures reached during braking, new compounds different from the initial components are being created (Peikertova and Filip, 2015).

4. Perspectives

Two strategies can be proposed to limit the impact of brake wear particles on human health consisting of reducing i) the quantity or ii) the hazard of the emitted brake wear particles. Of course, these two strategies can be combined.

To reduce the amount of emission of brake wear particles, different measures can be proposed. They include the reduction in traffic volumes, vehicle speed/velocity, and aggressive driving styles (Fussell et al., 2022). Technologies to catch brake wear particles at the source through filtering devices mounted on the brake disc are also under development (Fussell et al., 2022). On the other hand, brake pad composition is a key factor as it affects the wear rate of a brake pad system (Kumar and Ghosh, 2020). For instance, it has been reported that low-metallic pads result in higher wear rates of the rotor material than NAO pads and thus in higher concentrations of airborne wear particles (Grigoratos and Martini, 2015; Stojanovic et al., 2022). Similarly, specific brake materials such as titanium, aluminum, ceramic, or carbide coatings have been proposed, they have been shown to have lower wear

properties and reduced brake wear emissions (Straffelini et al., 2015). Finally, legislation can play a critical role in the mitigation of such source of air pollution. In this regard, in November 2022, the European Commission has proposed new Euro 7 standards to reduce pollutant emissions from vehicles and improve air quality (European Commission - European Commission, 2022). The Euro 7 standards will be the first worldwide emission standards to move beyond regulating exhaust pipe emissions and set additional limits for particulate emissions from brakes and tires. These rules will apply to all vehicles, including electric ones.

Regarding the approaches proposed to reduce the toxicity of the emitted brake wear particles, pad composition is here again of paramount importance and it is evolving over time for that purpose. For instance, while asbestos has been used for many years in the composition of brake pads, it is now banned in most regions of the world (Fussell et al., 2022). Similarly, because copper can cause adverse effects on the environment and human health, its usage in brake pad formulations has been questioned and its replacement has led to new brake pad formulations known as “Cu-free brakes” or “eco-friendly brake pads” (Figliuzzi et al., 2020; Straffelini et al., 2015). However, we should keep in mind that the replacement of just one component in the brake pad formulation may not be not sufficient and the effects should be considered with regard to the brake performances. For example, in the absence of copper, the formation of a friction layer is less efficient, resulting in an increase in the wear rate and a larger production and emission of airborne wear debris (OECD, 2020; Straffelini et al., 2015). Also, we have to consider that even if harmful components are removed from brake pad formulation, brake wear products can exhibit another toxicological profile due to physicochemical modifications of bulk materials occurring during the braking process (Straffelini et al., 2015). Anyway, studies on the health effects of new or replacement materials are still needed (Vallabani et al., 2023).

Regarding the assessment of brake wear particles toxicity, some research directions could lie in the consideration of standardization for comparison purposes. Indeed, as mentioned before, there are currently no standardized methods for assessing the toxicity of brake wear particles, resulting in the

use of various types of samples and heterogeneous experimental conditions, making it difficult to make inter-studies comparisons and draw firm conclusions. Using samples and experimental conditions more representative of real-life exposure is also another important recommendation we can make. Indeed, many parameters can impact the brake wear particles' chemical composition and emission rates, and consequently their toxicological profile (*e.g.*, the vehicle characteristics, the driving style, the weather conditions...). Such parameters should be taken into account to further enhance the relevance of the tested samples (Beji et al., 2023; Feo et al., 2023; Lopez et al., 2023; Maricq, 2023; Men et al., 2022; Vojtišek-Lom et al., 2021). Another research avenue is the consideration of more relevant cell models and exposure scenarios. For instance, *in vitro* studies often use cell monocultures which are very convenient for screening purposes, but it has been suggested that more sophisticated cell models (advanced 3D models, models using dynamic conditions, etc.) are more predictive of *in vivo* biological responses. In addition, the exposure pathway should also be as realistic as possible. For example, air-liquid interface (ALI) systems should be recommended when assessing the respiratory effects of airborne particles (Forest and Pourchez, 2023). Finally, we could recommend considering repeated or chronic exposure, as we are constantly exposed to inhaled particles which accumulation in tissues and organs could lead to long-term effects. While most studies report particles toxicity following acute exposure, chronic exposure better recapitulates real-life conditions.

5. Conclusion

The publications analyzed in this systematic review have confirmed that the assessment of the toxicity of brake wear particles in mammalian models is still limited. *In vivo* and *in vitro* studies have nevertheless shown that brake wear particles can induce oxidative stress, proinflammatory response and DNA damage and that the toxicity of brake wear particles is mainly related to their chemical nature (Figure 2). However, it is challenging to extrapolate animal and *in vitro* studies to humans, pointing out the lack of comprehensive study linking brake wear emission with the adverse effects in human health.

Further experiments are thus required to better understand the specific hazard of brake wear particles and separate their contribution from that of other air pollutants. It also seems necessary to develop standardized approaches to allow comparison between studies.

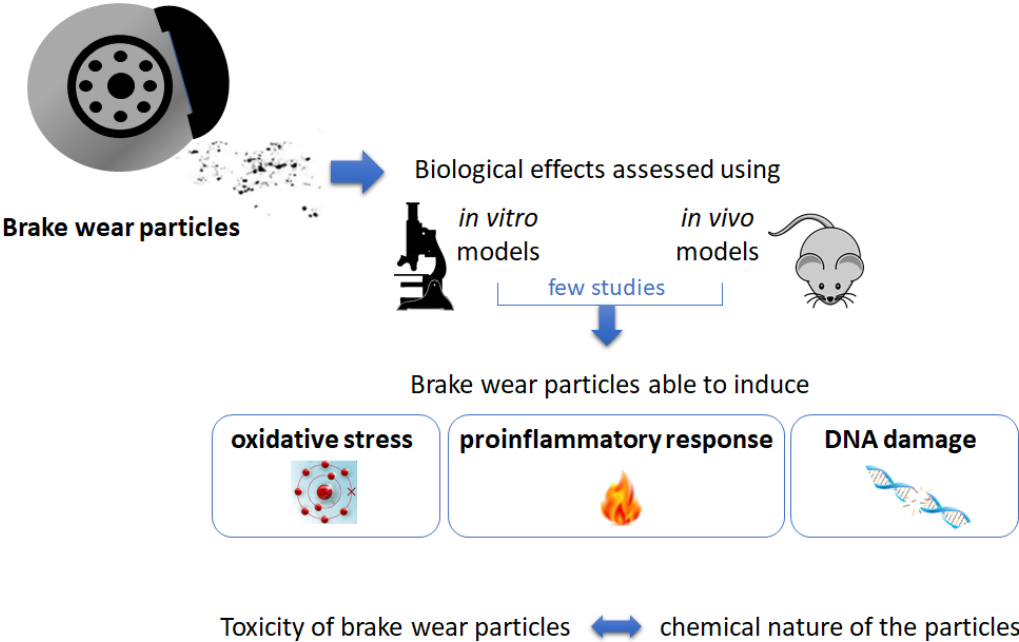


Figure 2 – Graphical summary of the main findings of this review.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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