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Review article

Children environmental exposure to particulate matter and polycyclic aromatic hydrocarbons and biomonitoring in school environments: A review on indoor and outdoor exposure levels, major sources and health impacts

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ABSTRACT

Children, an important vulnerable group, spend most of their time at schools (up to 10 h per day, mostly indoors) and the respective air quality may significantly impact on children health. Thus, this work reviews the published studies on children biomonitoring and environmental exposure to particulate matter (PM) and polycyclic aromatic hydrocarbons (PAHs) at school microenvironments (indoors and outdoors), major sources and potential health risks. A total of 28, 35, and 31% of the studies reported levels that exceeded the international outdoor ambient air guidelines for PM_{10}, $PM_{2.5}$, and benzo(a)pyrene, respectively. Indoor and outdoor concentrations of PM_{10} at European schools, the most characterized continent, ranged between 7.5 and 229 μg/m^3 and 21–166 μg/m^3, respectively; levels of $PM_{2.5}$ varied between 4 and 100 μg/m^3 indoors and 6.1–115 μg/m^3 outdoors. Despite scarce information in some geographical regions (America, Oceania and Africa), the collected data clearly show that Asian children are exposed to the highest concentrations of PM and PAHs at school environments, which were associated with increased carcinogenic risks and with the highest values of urinary total monohydroxyl PAH metabolites (PAH biomarkers of exposure). Additionally, children attending schools in polluted urban and industrial areas are exposed to higher levels of PM and PAHs with increased concentrations of urinary PAH metabolites in comparison with children from rural areas. Strong evidences demonstrated associations between environmental exposure to PM and PAHs with several health outcomes, including increased risk of asthma, pulmonary infections, skin diseases, and allergies. Nevertheless, there is a scientific gap on studies that include the characterization of PM fine fraction and the levels of PAHs in the total air (particulate and gas phases) of indoor and outdoor air of school environments and the associated risks for the health of children. There is a clear need to improve indoor air quality in schools and to establish international guidelines for exposure limits in these environments.

1. Introduction

Air pollution, indoors and outdoors, is a worldwide recognized threat to the health of humans, even at low doses, since it has been, beyond any doubt, associated with many effects on human health, including increased mortality and morbidity rates but also with ecosystems damage, impacts on the built environment and the climate (EEA, 2017; Landrigan et al., 2017). The World Health Organization (WHO) estimated a total of 12.6 million deaths in the world due to unhealthy environments, i.e., all polluted environments that present physical, chemical, and/or biological risk factors external to a person that can affect the health of people (excluding all the risks in natural environments that cannot reasonably be modified), representing 23% of total global mortality and 26% of deaths in young children (Landrigan et al., 2017; Prüss-Ustün et al., 2016). Some air pollutants can persist for long periods of time and accumulate in the environment and food chain, thus affecting humans and animals via multi-route of exposure (inhalation, dermal, ingestion). According to the European Environment Agency (EEA), transports, industries, energy, power plants, agriculture, households and waste management are the economic sectors that contribute the most to air pollution (EEA, 2017).

Particulate matter (PM) and polycyclic aromatic hydrocarbons

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(PAHs) are among the most health-relevant air pollutants. PM is a widespread complex mixture of solid and liquid particles suspended in air and varying in size, shape, origin, and composition (WHO, 2013; Zhang et al., 2015). PM is an air pollutant that is known as human carcinogen (group I, IARC, 2013) and its chemical composition comprises inorganic ions (e.g. sulfates, nitrates, ammonium, and soluble metals), insoluble metals, elemental carbon, organic compounds including PAHs and polychlorinated biphenyls, biological components (allergens), microbial agents, and water (EEA, 2017; Kim et al., 2015; WHO, 2013; Zhang et al., 2015). PM represents a serious health threat because it can penetrate into human respiratory system; the smallest fractions (PM ≤ 2.5 μm) may behave similar to gas molecules that can reach gas exchange regions of lungs and even translocate lungs and reach the circulatory system (Kim et al., 2015). Despite the mechanisms of adverse health effects are not fully understood, epidemiological studies have consistently shown an association between exposure to atmospheric PM, decreased lung function and a higher incidence of respiratory diseases including shortness of breath, asthma, rhinitis, sinusitis, and chronic obstructive pulmonary disease; long term exposure has been associated with the development of lung cancer (Hamra et al., 2014; Kim et al., 2015). Exposure to PM has been also linked with an increased risk of cardiovascular pathologies, including stroke, myocardial infarction and the exacerbation of congestive heart failure (Giorgini et al., 2016; Kim et al., 2015). Long exposition to PM, principally the lowest fractions (PM ≤ 2.5 μm), has been associated with the worsening of mental health which reflects in an increased risk of onset of depressive symptoms, and in a greater number of hospitalizations and emergency department visits (Buoli et al., 2018).

PAHs are a class of organic compounds widely known for their toxicity, mutagenicity, and carcinogenicity (ACGIH, 2005; IARC, 2002, 2010) that are portioned between the airborne gaseous and particulate phases. Some PAHs are referred in the European Union (EU) and US Environmental Protection Agency (USEPA) priority pollutant list (Directive 2004/107/CE; USEPA, 2005; WHO, 2010). Several factors affect the mechanisms through which PM and PAHs are absorbed/adsorbed by humans, namely age and metabolism of the subject, routes of exposure (inhalation, ingestion, and dermal) and environmental conditions (temperature, moisture, solar radiation, wind speed, and precipitation rates). Inhalation is the main exposure route to PM and PAHs, however ingestion and dermal contact are also relevant (Kim et al., 2015; Ma and Harrad, 2015). Assessment of total exposure to PAHs is very difficult, and therefore biomonitorization assumes a crucial role in the determination of total exposure dose (Kim et al., 2013a). Determination of monohydroxyl-PAHs (OH-PAHs; hydroxylated PAH metabolites resulting from the metabolization process controlled by cytochrome P450 family of enzymes) reflect a more accurate estimation of total PAHs intake, though it should be preferentially combined with data retrieved from environmental monitoring (Chen et al., 2018; Kim et al., 2013a; Oliveira et al., 2017a).

Children encompass all human beings below the legal age of majority, which frequently corresponds to the nineteen years old, unless national law defines a different age (UNICEF, 2018). Children are one of the most susceptible subgroups of the population, because their respiratory, immune, reproductive, central nervous and digestive systems are not fully developed (Burtscher and Schüepp, 2012; Salvi, 2007), which makes them at higher risks for the potential health effects induced by air pollution (Chen et al., 2018; Franklin, 2007; Pongpiachan and Paowa, 2014; Schüepp and Sly, 2012; WHO, 2010; Zhou et al., 2013; Zwozdziak et al., 2016). Due to their size, physiology and activity level, children inhalation rates are higher than adults exhibiting also higher oxygen consumption and resting metabolic rate per unit of body weight (Salvi, 2007). Education is a fundamental component of child's social development, with an increased length and time permanence of children at schools. Children spend per day up to 10 h of their daily time at school environments, principally in indoor areas, which raises interest in characterizing the health relevant air pollutants in these microenvironments. Prenatal exposure to traffic-related air pollution, including PM and PAHs, has been associated with different changes in child behavior and neurodevelopment: decreasing of intelligence quotient and brain-derived neurotrophic factor, reduction of left hemisphere white matter and increasing of attention deficit hyperactivity disorder (Sram et al., 2017). Moreover, pediatric pre-hypertension has been also associated with environmental exposure to PM since systemic oxidative stress and inflammation cause autonomic nervous system imbalance and arterial vascular dysfunction and/or vasoconstriction (Kelishadi et al., 2011). Therefore, protection against potential health risks associated with exposure to PM and PAHs at schools requires reliable information about their real levels of exposure. Thus, there is a need to evaluate the available information regarding the levels of PM and PAHs in the indoor air of school environments and in the outdoor air of the respective surrounding areas. This assessment, combined with the available information on the levels of biomarkers of exposure to PAHs, will allow a comprehensive characterization of children exposure to PAHs at schools. Some reviews were found in the literature concerning specific indoor air pollutants and respiratory diseases among children (Annesi-Maesano et al., 2013; Breysse et al., 2010; de Gennaro et al., 2014; Fuentes-Leonarte et al., 2009; Le Cann et al., 2011; Millman et al., 2008; Salvi, 2007). Also, previous works (Daisey et al., 2003; Mendell and Heath, 2005; de Gennaro et al., 2014; Salthammer et al., 2016) reviewed the literature on indoor air quality (IAQ), ventilation and thermal conditions in schools. However, a comprehensive review with emphasis on the carcinogenic (possible/probable) PAH levels and on their biomarkers of exposure in children at school environments is still needed in order to fully estimate their potential health effects. Thus, the present work aims to critically review the available information on children environmental exposure to PM and PAHs in indoor and outdoor air of school environments and their total exposure to PAHs through the assessment of PAH biomarkers of exposure. Pollutant levels and their main sources are presented and discussed by the geographical location of the schools, being the reported concentrations compared with the existent national and international guidelines. The main health evidences of schoolchildren exposure to PM and PAHs at schools are also reviewed.

2. Methods

The available scientific literature within the last decade (2007–2017) was searched in the Thomson Reuters ISI Web of Knowledge, Science Direct, PubMed, Scielo, and Google Scholar databases by combining at least two of the following keywords: schools, children, IAQ, PM, PAHs, biomarkers of exposure, urinary PAH metabolites, and health effects. The search yielded 92 and 27 studies on indoor and/or outdoor levels of PM and PAHs at school environments, respectively. A total of 17 studies reported the levels of urinary PAH biomarkers of exposure in children at schools. Due to the limited number of works available, the search was extended to include all the studies that assessed the levels of urinary PAH metabolites in children, regardless of the environment. Overall 71, 52, and 65% of the collected studies on airborne PM and PAHs, and urinary PAH metabolites were performed in children with 6 to 13 years old attending at primary/elementary schools, respectively. Limited studies exist for preschool children (3–5 years) as well as for young teenagers (> 14 years), being the available information also included in this review.

3. Particulate matter

Particles are generally classified according to their aerodynamic diameter: ≥2.5 μm (coarse fraction), ≤2.5 μm (fine fraction, $PM_{2.5}$) and ≤0.1 μm (ultrafine particles) (WHO, 2006, 2013). PM is directly emitted into the air (primary source) or formed in the atmosphere (secondary sources) during reactions with precursors (ammonia, sulfur dioxide, oxides of nitrogen and non-methane volatile organic

compounds) (WHO, 2013; Zhang et al., 2015). PM is originated from a variety of outdoor natural (suspended crustal materials, volcanic ash, sea salts, pollen, spores, bacteria, plant and animal debris) and anthropogenic (combustion of fossil fuels, industrial and waste incineration, biomass burning, and agricultural operations) sources (EEA, 2017; WHO, 2006, 2013). The major source of primary ambient PM_{10} and $PM_{2.5}$ in the 28 European countries emission inventories were those released from the commercial, institutional and households sector (42% for PM_{10} and 22% for $PM_{2.5}$), followed by the energy sector with emissions from production, distribution, and industries (22% for PM_{10} and 15% for $PM_{2.5}$), by agriculture (15% for PM_{10} and 4% for $PM_{2.5}$), and non-road and road transport (13% for both fractions; EEA, 2017). However, studies that included PM speciation and source apportionment have been revealing that 40–71% of PM_{10} and 37–82% of $PM_{2.5}$ are made up of secondary particles being combustion of biomass (13–24% of PM_{10} and 11–21% of $PM_{2.5}$), and vehicle exhaust and non-exhaust emissions (18–31% of PM_{10} and up to 37% of $PM_{2.5}$) the most important sources in the urban and suburban areas (Amato et al., 2015; Belis et al., 2013). Emissions from re-suspension of crustal/mineral dust (7–18% of PM_{10} and 2–15% of $PM_{2.5}$), sea/road salts (7–13% of PM_{10} and 2–3% of $PM_{2.5}$), and industrial sources (4–11% of PM_{10} and 5–12% in $PM_{2.5}$) were the lowest contributors to secondary PM mass concentrations (Amato et al., 2015; Belis et al., 2013; Liang et al., 2016). The infiltration of outdoor air indoors depends on penetration efficiency and indoor deposition rates (Morawska et al., 2013). Major indoor sources of PM include human activities (cooking, sweeping, dusting and vacuuming), combustion processes (wood and fossil fuel burning), tobacco smoke, building materials (carpeting, flooring, paint, and plastics), and the use of various consumer products including aerosols, detergents, sprays, cosmetics, etc. (Breysse et al., 2010; Destaillats et al., 2008; Kim et al., 2015; Morawska et al., 2017).

3.1. Exposure levels and major sources of PM and ultrafine particles

Fig. 1 summarizes the available data (Table 1S, Supplementary material) on PM_{10} and $PM_{2.5}$ concentrations in indoor and outdoor school environments, organized by continent. Most of the studies were conducted in Europe (54%) and Asia (26%) whereas in America there were only 16% of the studies (performed in USA, Mexico, Brazil and Colombia); Africa and Oceania are the least characterized continents (4%) (Table 1S, Figs. 1S and 2S of Supplementary material). Regarding the American continent, USA was the most well characterized country (8%) comparatively with the central (4%) and southern (4%) countries; no study was found in Canadian schools (Table 1S, Figs. 1S and 2S of Supplementary material). Recently, WHO also highlighted the huge gap in monitoring and reporting air pollutants in low and middle-income regions (WHO, 2016a). PM_{10} and $PM_{2.5}$ were the most commonly studied fractions of PM both indoors and outdoors and were reported in 64 and 76% of the available studies, respectively. Only a very small fraction, i.e., 13% of the available studies on PM levels at schools included the environmental monitoring of PM_1 ($PM \leq 1\ \mu m$), being those studies restricted to Asian (Mohammadyan and Shabankhani, 2013; Song et al., 2011; Sughis et al., 2012) and European (Branco et al., 2014; Dorizas et al., 2013; Madureira et al., 2012; Oliveira et al., 2015a, 2015b, 2016a; Polednik, 2013; Rovelli et al., 2014; Zwozdziak et al., 2016) countries (Table 1S and Fig. 3S of Supplementary material).

Overall, the inter-continent decreasing order of the reported indoor PM_{10} levels was: Europe (n = 23, median of 105.0 $\mu g/m^3$) > Asia (n = 15, 86.0 $\mu g/m^3$) > Africa (n = 2, 49.9 $\mu g/m^3$) > America (n = 4, 34.6 $\mu g/m^3$); data are inexistent for Oceania (Fig. 1a). Regarding school outdoor environments PM_{10} levels, the inter-continent comparison was: Africa (n = 2, 86.8 $\mu g/m^3$) > Asia (n = 29, 74.0 $\mu g/m^3$) > America (n = 8, 47.9 $\mu g/m^3$) ≈ Europe (n = 22, 46.6 $\mu g/m^3$); again, no information exists for Oceania schools (Fig. 1b). Despite the limited information available for American schools (16%), PM_{10} levels in the indoor and outdoor air of North American (i.e., USA) schools were predominantly lower (overall median between 17.2 and 22.1 $\mu g/m^3$ and 18.8–41.0 $\mu g/m^3$, respectively) than the concentrations reported for Central American schools (47.1–68.2 $\mu g/m^3$ indoors and 54.8–106.9 $\mu g/m^3$ outdoors; Table 1S, Supplementary material). At South American schools, information is only available for ambient air, being the concentrations of PM_{10} (84.7 $\mu g/m^3$; Castro et al., 2009) also mostly higher than the levels found in North American schools, but in a closer range with the concentrations reported for Mexican schools (Table 1S and Figs. 1S and 2S, Supplementary material). Regarding Asian schools, PM_{10} levels varied between 66.7 and 591 $\mu g/m^3$ and 31–1578 $\mu g/m^3$ in the indoor and outdoor air, respectively (Tables 1S of Supplementary material). In the case of China, the most characterized Asian country, the available data indicated that the highest concentrations of PM_{10} (in the indoor and outdoor air of school environments) were reported in the northern comparatively with the eastern and southern regions of the country; the lowest concentrations were observed in schools from Taiwan (Table 1S and Fig. 1S of Supplementary material). These findings are corroborated by the Asian Air Quality Index available on Real-time Air Quality Index Visual Map where the northern regions of China, as well as, some Indian cities present very unhealthy (201–300 $\mu g/m^3$) and hazardous (> 300 $\mu g/m^3$) air pollution levels (AAQI, 2018). According to the report of the Clean Air Initiative for Asian Cities Center (CAI-Asia, 2010), PM_{10} continues to be a major and critical pollutant for most of the Asian countries with an annual concentration average of 89.5 $\mu g/m^3$, which is about 4.5 times higher than the WHO Air Quality Guideline of 20 $\mu g/m^3$ (Table 2S) (CAI-Asia, 2010). Among the 230 cities included in this report, about 135 (i.e., 60% of the cities) presented PM_{10} annual averages higher than 70 $\mu g/m^3$. In what concerns to European schools, concentrations of PM_{10} ranged from 7.5 to 229 $\mu g/m^3$ indoors and between 21 and 166 $\mu g/m^3$ outdoors, being the reported outdoor levels predominantly lower than the ones found at Asian schools but in a close range with the concentrations determined at American schools (Table 1S of the Supplementary material).

For indoor $PM_{2.5}$, the identified median levels were: Asia (n = 10, 75.3 $\mu g/m^3$) > Europe (n = 41, 35.0 $\mu g/m^3$) > Africa (n = 2, 20.35 $\mu g/m^3$) > America (n = 4, 15.2 $\mu g/m^3$) > Oceania (n = 1, 6.7 $\mu g/m^3$) (Fig. 1a). Regarding ambient $PM_{2.5}$, the respective order of concentrations was Asia (n = 18, 39.95 $\mu g/m^3$) > Europe (n = 32, 29.0 $\mu g/m^3$) > America (n = 11, 17.5 $\mu g/m^3$) > Oceania (n = 1, 11.6 $\mu g/m^3$); no data are available for Africa (Fig. 1b). Asian schools presented $PM_{2.5}$ concentrations ranging between 17 and 163 $\mu g/m^3$ indoors and from 15.3 to 242 $\mu g/m^3$ outdoors (Table 1S of Supplementary material). As observed for PM_{10}, Chinese schools situated in the northern region of the country also presented concentrations that were predominantly higher than in the eastern and southern regions (Table 1S and Fig. 2S of Supplementary material). Recently, Lu et al. (2019) showed that the implementation of the Air Pollution Prevention and Control Action Plan in China caused a sharp decreasing trend (over 30%) in the ambient $PM_{2.5}$ levels in several cities between the period of 2013–2017. However, the northern and central Chinese provinces (Beijing, Tianjin, Hebei, Henan, Hubei, and Shandong) continue to be the areas that present the highest concentrations of $PM_{2.5}$ (Lu et al., 2019). Despite that most of the Asian countries have already adopted the National Ambient Air Quality Standards for PM_{10}, only Bangladesh, India, Singapore, and Sri Lanka implemented guidelines for ambient levels of $PM_{2.5}$ till 2010 (CAI-Asia, 2010). At European countries, levels of $PM_{2.5}$ varied between 5.14 and 100 $\mu g/m^3$ and between 6.1 and 115 $\mu g/m^3$ in the indoor and outdoor of schools, respectively (Table 1S and Fig. 2S of Supplementary material). Despite the higher number of studies concerning European schools (54%), no general tendency could be found because concentrations varied significantly among countries; still, the reported levels were predominantly lower than the concentrations found at Asian schools (Table 1S). Regarding the American continent, $PM_{2.5}$ concentrations were predominantly lower at North American (7.6–10.2 $\mu g/m^3$ indoors versus 8.8–16.6 $\mu g/m^3$ outdoors)

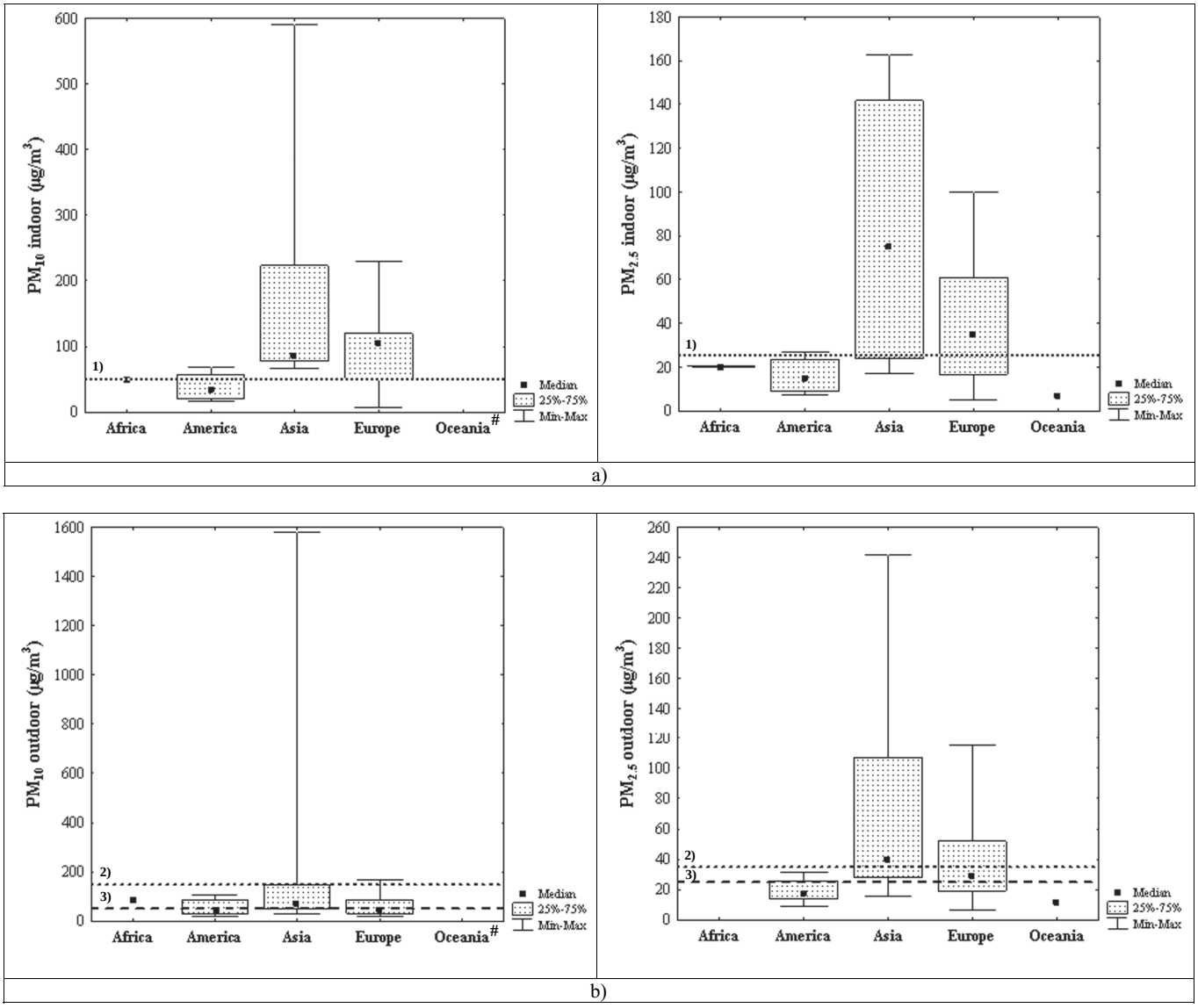


Fig. 1. Summary (median, 25–75 percentiles, and range) of the reported environmental concentrations of PM_{10} and $PM_{2.5}$ in the indoor (a) and outdoor (b) air of schools organized by continent.
1) Portuguese guidelines for indoor air quality over an averaging time of 8-h (50 µg/m^3 for PM_{10} and 25 µg/m^3 for $PM_{2.5}$; Portuguese Regulation, 2013).
2) US EPA guidelines for ambient air over an averaging time of 24-h (150 µg/m^3 for PM_{10} and 35 µg/m^3 for $PM_{2.5}$; USEPA, 2010).
3) WHO guideline for ambient air over an averaging time of 24-h (50 µg/m^3 for PM_{10} and 25 µg/m^3 for $PM_{2.5}$; WHO, 2006).
#Information not available (Table 1S, Supplementary material).

than at Central American schools (20.2–26.7 µg/m^3 indoors versus 17.5–31.1 µg/m^3 outdoors) (Table 1S, Supplementary material). Concentrations of $PM_{2.5}$ (17.1–24.3 µg/m^3; Jacobson et al., 2014; Riguera et al., 2011) at South American schools, as observed for PM_{10}, were slightly higher than the levels reported in North American schools but similar with the concentrations found at Mexican schools (Table 1S and Figs. 1S and 2S, Supplementary material). However, it should be bear in mind that the available data from all the previous studies are not enough to fully represent a specific country or continent and inter/intra comparisons should be made with caution. Furthermore, the available studies focus on different fractions of PM and were performed using different methodologies which included real-time instantaneous and continuous monitoring devices that were used with different sampling time [60 s (Mohammadyan and Shabankhani, 2013; Zhang and Zhu, 2012) to 96 h (Zora et al., 2013)] and different detection methods (laser photometry, beta gauge method, and gravimetric detection; Table 1S, Supplementary material), which further complicate the comparison. Inter-continental divergence is mostly attributed to different levels of economic development, and social and cultural dissimilarities while intra-continent heterogeneity depends more on the geographic location of cities (urbanization and planning, school's location, type of construction and used materials, etc.), climate and seasonal metrological conditions. Variation in PM_{10} and $PM_{2.5}$ distribution profiles among continents also reflect the predominance of different PM sources. However, authors are unanimous on reporting higher concentrations of PM in schools situated in the vicinity of industrial complexes and in the proximity of roads with heavy traffic emissions (Alvarado-Cruz et al., 2017; He et al., 2010; Jyethi et al., 2014; Kim et al., 2013b; Li et al., 2011; Sughis et al., 2012; Trasande et al., 2015; Zora et al., 2013). Only 21 and 31% of the studies assessed, respectively, the levels of PM_{10} and $PM_{2.5}$ concomitantly in the indoor and outdoor air of schools, (Table 1S, Supplementary material). Based on these studies, the indoor-to-outdoor (I/O) ratios were determined in different school environments (Fig. 2). PM levels at European schools seem to predominantly originate from

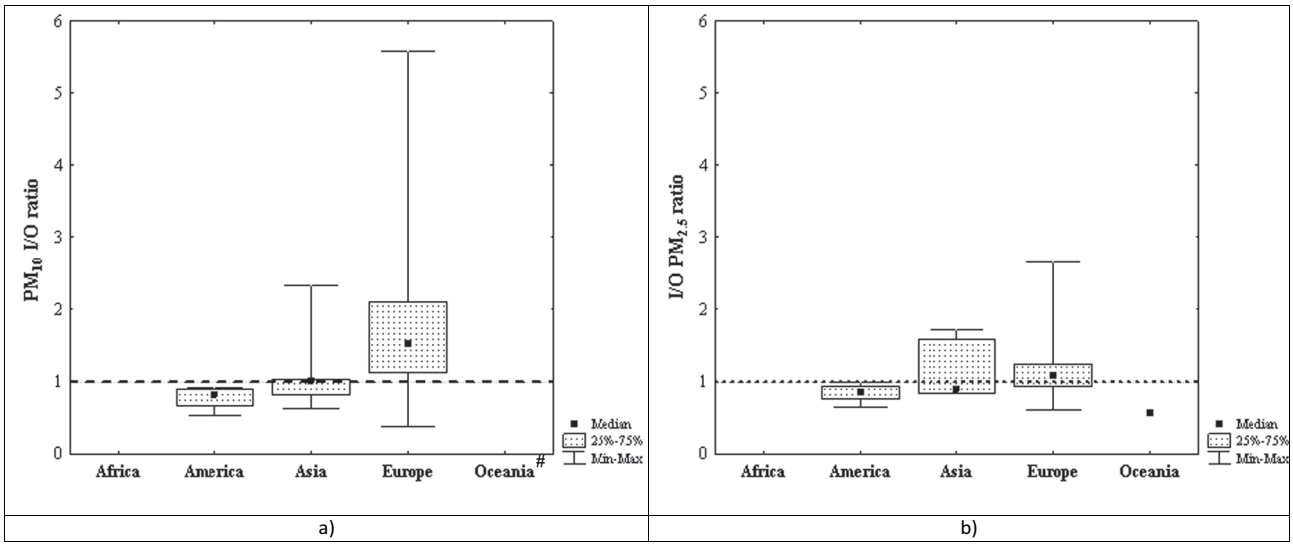


Fig. 2. Indoor-to-outdoor ratios of the reported PM_{10} (a) and $PM_{2.5}$ (b) levels in school environments. Only studies that concomitantly monitored PM_{10} and $PM_{2.5}$ levels indoors and outdoors were considered.
[#]Information not available (Table 1S, Supplementary material).

indoor sources [median (range): 1.5 (0.4–5.6) for PM_{10} and 1.1 (0.6–2.7) for $PM_{2.5}$] while outdoor air penetration was the major source of PM in American classrooms [0.8 (0.5–0.9) for PM_{10} and 0.9 (0.6–1.0) for $PM_{2.5}$]. Regarding Asian schools, median values of I/O ratios were 1.0 (0.6–2.3) for PM_{10} and 0.9 (0.8–1.7) for $PM_{2.5}$ thus revealing the contribution of both indoor and outdoor sources; no information is available for the remaining continents. Only 3% of the available studies (i.e. 1 Asian and 2 European works) reported the concentrations of PM_1 in the indoor and outdoor air of schools with I/O ratios varying between 0.8 and 1.3 (Table 1S and Fig. 3S, Supplementary material). The wide range of I/O ratios is a consequence of different occupancy rates, activities conducted inside the classrooms, physical characteristics of buildings (energy efficiency, permeability, particle size-specific profile), site specificity, the type of ventilation (natural vs. mechanical, duration and frequency), but also of seasonal meteorology. The major sources of PM in school indoor environments are occupants, classroom furnishings (whiteboards, tables, chairs, etc.), and the use of air-conditioning and heating systems (Destaillats et al., 2008; Morawska et al., 2017). Other human tasks such as cooking, cleaning, as well as schoolchildren playing activities, the use of printers and photocopy machines also constitute important sources of PM indoors at schools (Destaillats et al., 2008; Morawska et al., 2013, 2017; Salthammer et al., 2016). In that regard, Amato et al. (2014) evaluated the sources of $PM_{2.5}$ (by active high volume sampling over continuous 24 h) at 39 Spanish primary schools and found that 47% of indoor $PM_{2.5}$ concentrations were generated indoors mainly due to dust re-suspension of sandy playgrounds (13%) and a combined mixture (34%) of organic (skin flakes, cloth fibers, possible condensation of volatile organic compounds) and particles from chalk and building deterioration. These authors (Amato et al., 2014) also reported predominantly higher levels of PM mineral composition at schools with unpaved playgrounds comparatively with those that have paved playgrounds. Additionally, they described poor IAQ in classrooms that were directly oriented to the street rather than to the interior of playgrounds. Some works characterizing Spanish schoolchildren also reported higher concentrations of $PM_{2.5}$ and other traffic related air pollutants, such as black carbon and nitrogen dioxide, in the indoor air of classrooms than in the respective outdoor areas, being the reported levels strongly influenced by the proximity to local traffic emission sources (Reche et al., 2015; Rivas et al., 2014, 2015, 2018). Outdoor air penetration impacts the indoor air of classrooms, principally if natural ventilation is used throughout the day (including during class hours). Ambient air infiltration is strongly dependent on ventilation rates of classrooms, building characteristics, construction materials and season. Higher contributions are expected if windows and doors are directly facing streets and major traffic roads. Based on the existent information, a higher number of studies, including the simultaneous evaluation of indoor and outdoor levels of PM at schools are needed, principally in the less characterized continents (Africa, America, and Oceania; Figs. 1S–3S of Supplementary material) to better identify the major sources of PM and to propose measures to reduce children exposure at schools. Recently, Rivas et al. (2018) discussed the potential interventions that may strongly contribute to reduce the impact of traffic related air pollutants in the air quality of urban schools. The most important actions were identified as being raising awareness in all school community (teachers, students, and parents) about the potential impact of air pollution on children health, replacement of private cars by public transport to commute to school, the use of low-emitting cleaning products to clean classrooms at the end of the school day (with open doors/windows), and the regular cleaning and/or replacement of sandy playgrounds (Rivas et al., 2018).

Overall, the indoor and outdoor levels of PM_{10} at schools varied between 7.5 $\mu g/m^3$ (French schools from rural areas; active sampling over 2–4 days with gravimetric determination; Liaud et al., 2014) to 591 $\mu g/m^3$ (Pakistani schools at a high polluted region; portable laser-aerosol analyzer over 24 h; Sughis et al., 2012) and from 20.4 $\mu g/m^3$ (American elementary schools situated in low traffic areas; active sampling over 96 h with gravimetric determination; Zora et al., 2013) to 1578 $\mu g/m^3$ (dusty days at Iranian elementary schools; automatic monitoring over 1 h with determination by the Beta Gauge method; Neisi et al., 2017), respectively. Concentrations of $PM_{2.5}$ reported for studies conducted in school environments varied between 5.14 $\mu g/m^3$ (urban Belgium schools; real-time particle count over 3 h; Saenen et al., 2016) to 163 $\mu g/m^3$ (Sughis et al., 2012) in the indoor air while corresponding outdoor levels ranged between 6.1 $\mu g/m^3$ (French primary schools; Flamant-Hulin et al., 2010) to 242 $\mu g/m^3$ (Chinese schools; Bae et al., 2010) (active sampling with gravimetric determination; Table 1S). Regarding PM_1 in school environments, concentrations varied between 7.3 $\mu g/m^3$ (Pakistani school; Sughis et al., 2012) to 114 $\mu g/m^3$ (Portuguese primary schools; aerosol spectrometry over 8 h with detection by laser scattering optical counting; Madureira et al., 2012) indoors and from 8.4 $\mu g/m^3$ (Pakistani schools at a low polluted area; Sughis et al., 2012) to 91 $\mu g/m^3$ (Madureira et al., 2012) outdoors

(Table 1S).

A total of 28% and 35% of the studies [1 African, 4 American (2 Mexican, 1 Brazilian and 1 Colombian), 12 Asian, and 9 European for PM_{10}; 3 American (1 USA and 2 Mexican), 12 Asian, and 17 European for $PM_{2.5}$] reported ambient PM_{10} and $PM_{2.5}$ concentrations that exceeded the World Health Organization (WHO) guidelines of 50 and 25 $\mu g/m^3$ (24-h mean), respectively (Table 2S, Supplementary material). The highest exceedances were observed in Asian schools [overall median (range): 74.0 (31–1578) $\mu g/m^3$ for PM_{10} and 39.95 (15.3–242) $\mu g/m^3$ for $PM_{2.5}$; Fig. 1b] where 95% of the studies (reporting environmental levels) exceeded the WHO guidelines, with medians being 1.5 times (0.6–32) higher for PM_{10} and 1.6 times (0.6–9.7) higher for $PM_{2.5}$; only the studies performed by Chen et al. (2011, 2012) reported PM_{10} concentrations lower than the WHO limit value (Table 1S, Supplementary material). It is important to enhance the undeniable impact of the Air Pollution Prevention and Control Action Plan policy implemented in 2013 in China that caused a decreasing trend in the ambient levels of $PM_{2.5}$ in almost all the principal Chinese cities (Lu et al., 2019). Regarding US EPA guidelines for ambient air (150 $\mu g/m^3$ for PM_{10} and 35 $\mu g/m^3$ for $PM_{2.5}$ over an averaging time of 24-h; USEPA, 2010; Table 2S, Supplementary material), it was found that American schools presented concentrations that were well below the limits (Fig. 1b). American and European schools presented outdoor PM_{10} [overall median (range): 47.9 (18.8–107) $\mu g/m^3$ and 46.6 (21.0–166) $\mu g/m^3$, respectively] and $PM_{2.5}$ [17.5 (8.80–31.1) $\mu g/m^3$ and 29.0 (6.10–115) $\mu g/m^3$] levels that were lower than the concentrations reported at Asian schools (Fig. 1b). However, 46 and 53% of the American and European studies that recorded ambient PM_{10} and/or $PM_{2.5}$ concentrations at schools also exceeded the WHO limits (Table 1S, Supplementary material). Regarding IAQ, WHO recommends the use of the already available outdoor guidelines since, in the presence of relevant indoor sources, concentrations are usually higher in indoor areas comparatively with the respective outdoor spaces (WHO, 2010). Portugal is among the few countries with established IAQ guidelines for the indoor air in public buildings, which were updated in 2013 (Portuguese Regulation, 2013). The PM limits were re-defined according to WHO guidelines for indoor air with the values of 25 and 50 $\mu g/m^3$ for $PM_{2.5}$ and PM_{10}, respectively (8-h mean versus 24-h period suggested by WHO; Table 2S, Supplementary material). Among the studies that concern children exposure to PM at school indoor environments, a total of 39 studies (1 South African, 1 South American, 11 Asian, and 26 European) reported PM_{10} and/or $PM_{2.5}$ levels that exceeded the defined IAQ guidelines (Table 1S, Supplementary material). Moreover, PM was included in the list of priority pollutants that should be considered of greatest importance in the process of revising and/or updating WHO air quality guidelines, mostly due to the new and recent large body of health burden especially from short-term exposure and since the evidence of its effects on cardiorespiratory health and mortality has increased substantially (WHO, 2016b).

Concerning PM distribution profile, it was found that the majority of PM_{10} fraction was composed by 43% and 54% of $PM_{2.5}$ for the indoor and outdoor air, respectively (Almeida et al., 2011; Bae et al., 2010; Chen et al., 2011, 2012; Demircigil et al., 2014; Diapouli et al., 2008; Ekmekcioglu and Keskin, 2007; Elbayoumi et al., 2013; Ferreira and Cardoso, 2013, 2014; Fromme et al., 2007, 2008; Jovanović et al., 2014; Madureira et al., 2012, 2015, 2016; Mohammadyan and Shabankhani, 2013; Naidoo et al., 2013; Neisi et al., 2017; Oliveira et al., 2015a, 2016b; Saenen et al., 2016; Sarnat et al., 2012; Scheepers et al., 2012; Song et al., 2011; Sughis et al., 2012; Wallner et al., 2012; Zora et al., 2013; Table 1S, Supplementary material) and that this fraction seems to have a strong contribution of PM_1 (64% indoors versus 65% outdoors; Madureira et al., 2012; Mohammadyan and Shabankhani, 2013; Oliveira et al., 2015a, 2015b, 2016a; Song et al., 2011; Sughis et al., 2012; Zwozdziak et al., 2016; Table 1S, Supplementary material). Therefore, more studies characterizing PM_1 concentrations in school indoor and outdoor environments are needed.

3.2. Health impact on children

PM health effects are directly related with its ability to easily penetrate the human respiratory system (WHO, 2013). It is well documented that the size of particles determines the place of deposition within the thoracic region (Brugha and Grigg, 2014; Kim et al., 2015; WHO, 2006). Coarse particles can deposit in the tracheobronchial tree while fine fractions and ultrafine particles can reach the lowest parts of respiratory tract, where they can deposit in the conducting airways and gas exchange regions of lungs; the smallest ones can be moved into the circulatory system (Kim et al., 2015). The smaller the particle size, the higher the toxicity through mechanisms of oxidative stress and inflammation in human cardio-respiratory system (Brugha and Grigg, 2014; Chen et al., 2011, 2012; Lippmann, 2014). It is well known that children have a lesser nasal contribution to breathing, making less efficient particle uptake in the nasal airways, and deposition in the lower respiratory tract thus may be greater (Maynard, 2015). Recently, the Lancet Commission on pollution and health estimated that exposure to $PM_{2.5}$ was responsible for an increase of 20% in human deaths (from 3.5 to 4.2 million deaths till 2015) and it is expected to increase > 50%, thus reaching 6.6 million deaths in 2050, during the next three decades with sharpest increases for southern and eastern Asian countries (Landrigan et al., 2017). Exposure to PM has been associated with higher rates of cardio-respiratory morbidity and mortality in humans, being responsible for 3% of cardiopulmonary and 5% of lung cancer deaths diagnosed worldwide; long-term exposure to $PM_{2.5}$ is directly related with increments of 6–13% in cardiopulmonary mortality (WHO, 2013). Fine particles have a profound negative impact on human health and ecosystems, being their effects strongly dependent on the properties, size, and chemical composition of the aerosols (Zhang et al., 2015). Recently, the WHO Regional Office for Europe developed the software AIRQ$^+$ (WHO, 2018) to estimate the effects of exposure to air pollutants on public health. The methodologies and concentration-response functions used by AIRQ$^+$ are based on the systematic review of all studies available until 2013 and their respective meta-analysis. The available information on the indoor levels of PM_{10} and $PM_{2.5}$ at school environments from American, Asian, and European countries was used to estimate the magnitude of exposure on the health of children; schools from Africa and Oceania were not considered due to the scarce information available (Table 1S, Supplementary material). Data related with the population (children under 14 years) were taken from the latest revision on world population prospects (United Nations, 2017) and health end-points baseline incidences were retrieved from European Health Information Gateway (EHIG, 2018). PM_{10} and $PM_{2.5}$ global median concentrations by continent were determined with the information available in the literature for school environments (Table 1S, Supplementary material) and assuming a 24-h daily basis, which was used to represent median annual concentrations in each continent. Information collected from the available literature mostly corresponds to the environmental monitoring of 6–13 years old children; limited studies exist for younger (preschool) children. Although, it is expected that the youngest children be more susceptible to the potential health effects of exposure to airborne pollutants (Giorgini et al., 2016; Kelishadi et al., 2011; Ngoc et al., 2017), it was assumed that school environmental (indoors and outdoors) exposure to PM would affect all children regardless of their age. AIRQ$^+$ model considers air pollution monitoring data as proxy indicator of population exposure and does not account for multiple exposure routes and multipollutant scenarios. Also, AIRQ$^+$ determinations carry some uncertainties once the model was constructed with data obtained from studies performed mainly in Western Europe and North America, which may increase prediction errors. However, it is believed that the model can provide valuable information on the health effects of PM on young children. All the information needed for AIRQ$^+$ model application is presented in Table 3S, Supplementary material. The number of attributable proportions (AP) and the number of excess cases for long- and short-term

Table 1
Attributable proportion and number of excess cases of long- and short- term health end-points (expressed as %) estimated by AIRQ$^+$ software (WHO, 2018) for American, Asian, and European children due to PM_{10} and $PM_{2.5}$ exposure at school environments.

Continent	Health end-point	Pollutant	Relative risk	Attributable proportion (%)	Number of excess cases
			Median (95% confidence interval)		
America	Long-term health effects				
	Post-neonatal infant mortality, all cause	PM_{10}	1.04 (1.02–1.07)	5.57 (2.85–9.41)	96 (49–162)
	Mortality due to acute lower respiratory infection for children	$PM_{2.5}$	–	6.72 (2.91–11.8)	1 (0–1)
	Short-term health effects				
	Hospital admissions: respiratory diseases	$PM_{2.5}$	1.02 (0.99–1.04)	[a]	[a]
Asia	Long-term health effects				
	Post-neonatal infant mortality, all cause	PM_{10}	1.04 (1.02–1.07)	22.8 (12.2–36.0)	4656 (2501–7353)
	Mortality due to acute lower respiratory infection for children	$PM_{2.5}$	–	42.9 (29.1–53.6)	20 (14–26)
	Short-term health effects				
	Hospital admissions: respiratory diseases	$PM_{2.5}$	1.02 (0.99–1.04)	9.03 (−0.91–18.0)	2307 (−232–4592)
Europe	Long-term health effects				
	Post-neonatal infant mortality, all cause	PM_{10}	1.04 (1.02–1.07)	28.3 (15.5–43.7)	131 (71–202)
	Mortality due to acute lower respiratory infection for children	$PM_{2.5}$	–	22.5 (16.0–28.6)	0
	Short-term health effects				
	Hospital admissions: respiratory diseases	$PM_{2.5}$	1.02 (0.99–1.04)	1.86 (−0.18–3.9)	31 (−3–65)

[a] Global median concentrations of PM_{10} and/or $PM_{2.5}$ were below the available WHO air quality guidelines (Fig. 1).

health effects of PM_{10} and $PM_{2.5}$ on schoolchildren are exhibited in Table 1. The AP estimated for the total number of post-neonatal deaths (all causes) attributed to long-term exposure to PM_{10} at classrooms were 28, 23, and 6% for European, Asian, and American schools, which corresponds to a total of 131, 4656, and 96 post-neonatal deaths annually, respectively. $PM_{2.5}$ long-term health effects on schoolchildren were estimated through the determination of mortality rates due to acute lower respiratory infection in children with < 5 years old. The number of excess cases was higher at Asian (AP of 42.9%, 20 excess cases) than in European (AP of 22.5%) and American (AP of 6.72%) schoolchildren (Table 1).

Short-term exposure to PM_{10} is known to increase the number of hospital admissions due to the aggravations of respiratory function; all-cause of daily mortality increases 0.2–0.6% per 10 μg/m^3 (Kim et al., 2015; WHO, 2013). Based on the recent findings reported by Lu et al. (2019), the implementation in 2013 of an Air Pollution Prevention and Control Action Plan in China caused a decrease of 25–30% in the ambient levels of $PM_{2.5}$ (2013–2017), which was directly associated with a reduction of 10.7% in total mortality and represented a saving of almost $194,000 million in health care services. AIRQ$^+$ would allow to estimate the incidence of asthma symptoms among asthmatic children, however no data were available related with the frequencies of occurrence; there is only information on the mortality due to diseases of respiratory system for European and Asian children (2.08 versus 74.74 deaths per 100,000; EHIG, 2018). $PM_{2.5}$ short-term health effects on schoolchildren was determined with the number of hospital admissions related with respiratory diseases and a total of 2307 (AP of 9.03%) and 31 (AP of 1.86%) cases are annually predicted due to the levels of $PM_{2.5}$ reported at Asian and European schools, respectively (Table 1). Asthma is a complex chronic disease influenced by environmental and genetic factors that affects 334 million people worldwide, being the most common disease among children (Heinrich, 2011; Report asthma, 2014). It results from a chronic inflammation of airways and constitutes the cause of substantial burden principally in the countries with elevated prevalence rates (Australia, New Zealand, some African, Middle-East, South American, and Western European) thus reducing the quality of life of affected people (Report asthma, 2014). PM is recognizably one of the most relevant pollutants that may promote and/or aggravate the symptoms of asthma (Annesi-Maesano et al., 2007, 2012, 2013; Breysse et al., 2010; WHO, 2013). The International Study of Asthma and Allergies in Childhood (ISAAC) estimated that about 14% of the world children population had already asthmatic symptoms; disability and premature death were higher among pre-adolescents (10–14 y) (Report asthma, 2014). Many studies reported that children exposed to increased levels of PM, mainly $PM_{2.5}$, present a higher risk for the development and/or aggravation of cardio-respiratory diseases including chronic obstructive pulmonary disease, lung cancer, exacerbations of asthma and cystic fibrosis, regular cough, among other respiratory infections and allergic diseases, thus leading to a greater use of rescue medication, doctor visits and hospital admissions (Annesi-Maesano et al., 2007, 2013; Brugha and Grigg, 2014; Freitas et al., 2009; Kim et al., 2015; Lee et al., 2014; Liu et al., 2013; Simoni et al., 2010; Zhao et al., 2008; Zora et al., 2013). In that regard, some authors observed a significant reduction in some lung function parameters including forced vital capacity, forced expiratory volumes, and peak expiratory flow of schoolchildren (Gao et al., 2013; Jacobson et al., 2014; Mustapha et al., 2011; Reddy et al., 2012; Sarnat et al., 2012; Spira-Cohen et al., 2011; Zhou et al., 2013). Much emphasis has been placed on the formation of oxidative free radicals in the lung, because of interactions between particles and lung lining fluid and/or lung cells, which play an important role in subsequent oxidative stress and inflammatory response (Bae et al., 2010; Chen et al., 2011, 2012; Maynard, 2015). Some studies have demonstrated that exposure to PM, with special emphasis on $PM_{2.5}$, is associated with high arterial blood pressure and constitutes an increased risk for many cardiovascular diseases including heart failure, stroke, and myocardial infarction (Giorgini et al., 2016; Trasande et al., 2015; Sughis et al., 2012). Buoli et al. (2018) found strong evidences of an increased risk of attention deficit hyperactive disorder in children exposed to PM_{10} among other air pollutants. Other authors reported that children (7–10 years) attending schools in high polluted areas presented a smaller growth in the long-term change in working memory and attention than children from less polluted schools, thus suggesting that traffic related air pollution may have negative consequences in the cognitive development, i.e., learning, school achievement, and behavior of children (Sunyer et al., 2015). A strong association between environmental exposure to $PM_{2.5}$ during pregnancy and an increased risk of young children to develop autism spectrum disorders was also observed (Buoli et al., 2018). Environmental exposure to PM has been also associated with the increased risk of human skin diseases, especially atopic dermatitis, eczema and skin aging (Annesi-Maesano et al., 2007; Ngoc et al., 2017; Song et al., 2011). In addition, pre- and post-neonatal exposure to PM has also been associated with increased vulnerability to the development of cardiorespiratory diseases (Brugha and Grigg, 2014; Kelishadi et al., 2011; Koppen et al., 2011).

4. Polycyclic aromatic hydrocarbons

PAHs are a large group of organic compounds that have gathered

relevant environmental and health concern during last decades due to toxic, mutagenic, and carcinogenic properties of some of them (ATSDR, 1995; IARC, 2010; Kamal et al., 2015; Kim et al., 2013a; WHO, 2010, 2013). PAHs are constituted of fused benzene rings and their physicochemical properties make them widely distributed in the environment, being air and food the major routes of exposure for non-occupational scenarios. Airborne PAHs are found in the air gaseous phase and bound to PM. PAHs distribution among air gas and particulate phases is dependent on the volatility of the compound, ambient moisture and temperature, and on the concentration of airborne free radicals (Dat and Chang, 2017; Lohmann and Lammel, 2004; Tsapakis and Stephanou, 2005). Among the several hundreds of compounds, special attention has been given to the 16 PAHs classified as priority pollutants (USEPA, 2005): naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz(a)anthracene, chrysene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(a) pyrene, dibenz(a,h)anthracene, benzo(ghi)perylene and indeno (1,2,3–cd)pyrene. The International Agency for Research on Cancer (IARC) classified benzo(a)pyrene as carcinogenic to humans (group I; IARC, 2010), benz(a)anthracene, dibenzo(a,l)pyrene), and dibenz(a,h) anthracene as probable carcinogens (group 2A; IARC, 2010), and naphthalene, chrysene, benzo(b)fluoranthene, benzo(j)fluoranthene, benzo(k)fluoranthene and indeno(1,2,3-c,d)pyrene as possible carcinogens (group 2B; IARC, 2002, 2010). PAHs are considered to cause reproductive, developmental, cardiorespiratory, and immune toxic effects in humans (ATSDR, 1995). There are enough evidences that prenatal exposure to carcinogenic PAHs is associated with intrauterine growth restriction in humans (Kamal et al., 2015; WHO, 2010). PAHs (and other volatile organic compounds) are important sources of oxidative stressors that interact with lipids during lipid peroxidation. Some PAH congeners are already recognized as endocrine-disrupting chemicals (WHO, 2013). PAHs present low water solubility and marked lipophilicity, which increases with the number of rings of the compounds and strongly contributes to their environmental bioaccumulation. Therefore, exposure to PAHs poses a serious threat to human health, principally for the most susceptible groups of the population such as young children. PAHs are formed during pyrolysis and incomplete combustion of organic matter, being originated from both natural (volcanic eruptions and forest fires) and anthropogenic sources (ACGIH, 2005; Dat and Chang, 2017; Kamal et al., 2015; UNECE, 1998). Energy production sector, such as burning of fossil fuels, petroleum, coal tar, gas, and wood, constitutes the primary source of PAHs worldwide (Dat and Chang, 2017; Kamal et al., 2015; Kim et al., 2013a). The major sources of benzo(a)pyrene among the European countries were the emissions from the commercial, institutional and households sector (75%), followed by agriculture through field burning of agricultural residues (12%), the energy production and distribution (5%), the emissions from industrial processes and product use (4%), and the energy use in industry (2%); road transported and waste sectors accounted with 1% each for the total benzo(a)pyrene emissions (EEA, 2017). PAHs are used as intermediates in the production of many pharmaceutical, lubricating, and plasticizing industries (Kamal et al., 2015). Considering indoor air, tobacco smoke is one of the major sources of PAHs (Castro et al., 2011; Slezakova et al., 2009, 2014), particularly in the industrialized countries, whereas in the developing ones open fires of wood and/or other combustion materials (coal, agricultural residues or dung) for cooking or heating purposes are typically more dominant (Chen et al., 2015; Dat and Chang, 2017; Ravindra et al., 2008). Emission characteristics, transformation and persistence of airborne PAHs depend on environmental conditions (temperature, moisture, precipitation, solar radiation, concentration of atmospheric oxidants, e.g. ozone, hydroxyl and nitrate radicals) and combustion parameters, namely burned material, temperature and humidity, and oxygen supply (Dat and Chang, 2017; Tsapakis and Stephanou, 2005, 2007; Tham et al., 2008). PAHs persistence increases with molecular weight and they are not easily degraded under natural conditions (Haritash and Kaushik, 2009). Limited information exists on technologies of partial and/or entire removal of PAHs from the environment (Dat and Chang, 2017; Polidori et al., 2013; Rosbach et al., 2013).

4.1. Levels of exposure and sources

The available studies on PAH levels (indoors and/or outdoors) at school environments are presented in Table 2. Most of the reports were conducted in European (56%) and Asian (33%) schools while only 7 and 4% of the works were performed in American and African schools, respectively (Fig. 4S, Supplementary material). No information was found for Oceania and South American schools. All the researches included the assessment of PM-bound PAHs, except the work of Boudehane et al. (2016), but only 37% of them included the monitorization of the gas phase or the simultaneous characterization of gaseous and particulate phases (Table 2). This fact can be explained because PAHs with higher toxic and carcinogenic (known, possible/probable) properties are predominantly found in the particulate phase (Krugly et al., 2014; Oliveira et al., 2015a, 2015b, 2016a). Still, naphthalene, a possible carcinogen to humans (group 2B; IARC, 2002) as well as acenaphthene, fluorene, phenanthrene, and anthracene have been predominantly found in the airborne gaseous phase (Dat and Chang, 2017), thus enhancing the importance of monitoring both particulate and gaseous fractions. Considering concomitantly assessment of indoor and outdoor air of school environments, as previously observed for PM levels characterization, a total of 59% of the studies were found (Table 2).

Particulate-bound PAHs were determined by active sampling over at least 8 h and 74% of the available studies were almost exclusively dedicated to the assessment of PAH levels in PM_{10} and/or $PM_{2.5}$ fractions (Table 2). Overall, a total of five studies [one performed in a Central American (Mexico), one in an Asian (India) and three at European (France and Portugal) schools] reported the levels of PM_{10}-bound ΣPAHs, with mean values ranging between 0.39 and 61.7 (median 0.89) ng/m^3 indoors and from 0.83 to 103 (median 2.38) ng/m^3 outdoors.

$PM_{2.5}$ was the most well characterized PM fraction at schools [59% of studies: one performed in a Central American (USA), four at Asian (China), and eleven at European (France, Italy, Lithuania, Poland, and Portugal) schools]. Overall, the reported ΣPAHs mean concentrations varied between 0.27 and 53.2 (median 6.2) ng/m^3 and 1.08–388 (median 36.8) ng/m^3 in the indoor and outdoor air of school environments, respectively (Table 2 and Fig. 4S of Supplementary material). The reported PM-bound concentrations were predominantly higher at Asian than at European schools [median (range) of 30.5 (0.80–60.0) ng/m^3 versus 3.11 (0.23–61.7) ng/m^3 indoors and 46.7 (1.12–388) ng/m^3 versus 3.37 (0.83–52.9) ng/m^3 outdoors, respectively; Table 2; Fig. 4S, Supplementary material].

Among the 27 studies concerning the levels of PAHs at school environments, only 4 studies included PAHs associated with lower fraction, i.e. PM_1 (Liaud et al., 2014; Oliveira et al., 2015a, 2015b, 2016a). Mean levels of PM_1-bound ΣPAHs ranged between 0.23 and 5.4 ng/m^3 indoors and from 1.4 to 2.5 ng/m^3 outdoors (Table 2). The outcomes of the available data (Liaud et al., 2014; Oliveira et al., 2015a, 2015b, 2016a) showed that PAHs were predominantly found in the finer fractions of PM with PM_1-bound congeners representing 66–85% and 55–86% of $PM_{2.5}$-bound PAHs, respectively in the indoor and outdoor air (Table 2). This information reinforces the importance of analyzing the lowest fractions of PM in future studies. Recently, Dat and Chang (2017) also demonstrated that lighter PAHs (2–3 rings) were mostly bound to coarse PM while high molecular weight compounds, the more toxic, mutagenic, and carcinogenic PAHs, were predominantly bound to the finest fraction of PM ($PM_{2.5}$ and PM_1). Furthermore, children exposure to PAHs might enhance and/or aggravate PM health effects with the finest fraction reaching the deepest regions of the lungs and entering in the circulatory systems. Thus, the evaluation of PAHs in the

Table 2
PAH concentrations (mean ± SD and/or range, expressed as ng/m^3) reported in indoor and outdoor air of school environments.

Continent	Country, city	Methodology[#]	Note	Children		Analysed phase	No. of PAHs	ΣPAHs indoor	ΣPAHs outdoor	Reference
				n	Age					
Africa	Algeria, Quargla	Passive sampling (21 days); GC–MS	Primary schools			Gas	17	45–63	54 ± 7	Boudehane et al. (2016)
America, North	USA, Southern California	LVS (24 h); HPLC-FLD	Elementary, middle, and secondary schools	300	9–16	Gas $PM_{2.5}$ Total air ($PM_{2.5}$ + gas)	15		94.1–151 0.42–1.78 94.5–152	Eiguren-Fernandez et al. (2007)
America, Central	Mexico	HVS and LVS (24 h); GC–MS	Elementary schools* in urbanized and industrial area	150	7–10	PM_{10}	17		2.38 2.16–2.80	Alvarado-Cruz et al. (2017)
Asia	China, Beijing	MVS (24 h); GC–MS	n.r. Non-haze fog days Haze fog days			$PM_{2.5}$	14		 36.8 388	Gao et al. (2016)
	China, Taiwan	HVS (72 h); GC–MS	Community center including elementary schools	369	5–12		16			Hu et al. (2011)
			High-exposure areas			Gas PM** Total air (PM** + gas)		8.65 0.69 9.35	7.60 1.29 8.89	
			Low-exposure areas			Gas PM** Total air (PM** + gas)		6.00 0.90 6.90	4.60 1.20 5.80	
	China, Xi'an	LVS (8 h); GC–MS	Middle school			$PM_{2.5}$	25	50.3–112	49.6–140	Wang et al. (2017c)
	China, Xi'an	LVS (8 h); GC–MS	Middle school			$PM_{2.5}$		49.7 ± 16.3; 50.8 ± 27.8	52.2 ± 18.0	Wang et al. (2017b)
	China, Xi'an	Personal cascade impactor (12 h); GC–MS	Middle school	50	12–14	TSP	16	60.0 ± 20.0 4.9–162	77.7 ± 32.3 14.0–173	Xu et al. (2015)
						$PM_{2.5}$	16	53.2 ± 21.8	72.9 ± 35.7	
	India, Delhi	HVS (24 h); HPLC-UV	Primary schools in the proximity of industrial and heavy traffic roads			PM_{10}	10		103 ± 50.4 38.1–217	Jyethi et al. (2014)
	Saudi Arabia, Jeddah	Active sampling device (24 h); GC–MS	Primary schools*	184	10–14	Total air (PM** + gas)	14			Trasande et al. (2015)
			Near the oil refinery Near a ring road Background						36.7 ± 17.3 30.3 ± 8.2 12.3 ± 7.5	
	Thailand, Bangkok	Personal air sampling (8 h); HPLC-FLD	Primary schools* Urban	180	9–13	PM**	10			Ruchirawat et al. (2007)
			Playground					11.3 ± 5.2 2.64–25.54	41.1 ± 10.2 12.01–99.95	
			Classroom					7.03 ± 1.03 5.06–9.39		
	Thailand, Chonburi		Rural							
			Playground					0.91 ± 0.36 0.28–1.92	1.17 ± 0.40 0.31–2.91	
			Classroom					0.84 ± 0.49 0.28–2.31		
	Thailand, Bangkok	Personal air sampling (8 h); HPLC-FLD	Primary schools* Urban	184	8–13	PM**	10		5.78 ± 1.08 2.10–25.54	Tuntawiroon et al. (2007)
	Thailand, Chonburi		Rural						1.12 ± 0.19 0.28–2.31	

(*continued on next page*)

Table 2 (*continued*)

Continent	Country, city	Methodology[#]	Note	Children		Analysed phase	No. of PAHs	ΣPAHs indoor	ΣPAHs outdoor	Reference
				n	Age					
Europe	France, Strasbourg	3-stage cascade impactor (96 h); HPLC-FLD-PAD	School (n.r.) in a rural area			PM_{10}	16	0.39		Liaud et al. (2014)
						$PM_{2.5}$		0.27		
						PM_1		0.23		
	Italy, Rome	LVS (24 h); GC–MS	n.r.			$PM_{2.5}$	11	2.79 ± 1.36		Romagnoli et al. (2016)
	Italy, Rome	LVS (24 h); GC–MS	Elementary school	5	8–11	$PM_{2.5}$	8			Gatto et al. (2013)
			Summer					0.63 ± 0.3	1.08 ± 0.56	
								0.21–1.32	0.36–2.56	
			Winter					6.0 ± 3.9	9.1 ± 4.5	
								1.6–16	4.2–18.5	
	Italy, Rome	LVS and MVS (24 h); GC–MS	n.r.			$PM_{2.5}$	8			Romagnoli et al. (2014)
			Winter					1.8-8.3	7.0–9.5	
			Spring					0.3–1.0	0.4–1.2	
	Italy, Taranto	LVS (24 h); GC–MS	Primary school			$PM_{2.5}$	8	1.51–2.36		Di Gilio et al. (2017)
	Lithuania, Kaunas	Personal air sampling (8 and 24 h); GC–MS	Primary schools			TSP	15	19.9–80.3		Krugly et al. (2014)
			Urban, winter			$PM_{2.5}$	15	20.3–131	40.7–121	
						Gas	15	35.6–80.6		
	Poland, Silesia	LVS (24 h); HPLC-FLD	Kindergartens, spring			$PM_{2.5}$	15			Błaszczyk et al. (2017)
	Dąbrowa, Górniczas		Urban	125				36.1	52.9	
								14.6–72.9	18.0–118	
	Złoty Potok		Rural	25				31.4	39.3	
								25.0–89.5	22.8–108	
	Portugal, Aveiro	LVS and MVS; GC–MS	Primary school, city center			PM_{10}		0.89 ± 0.65	0.83 ± 0.42	Alves et al. (2014)
	Portugal, Porto	LVS (24 h); HPLC-FLD-PAD	Primary schools			$PM_{2.5}$	18	2.8–54	6.4–48	Oliveira et al. (2017b)
	Portugal, Porto	LVS (24 h); HPLC-FLD-PAD	Preschool	173	3–5	Total air	18	34.4	31.1	Oliveira et al. (2017a)[a]
						(TSP + gas)		26.1–151	2.79–46.9	
						Gas		32.7	28.3	
								24.1–149	2.18–43.7	
						TSP		1.68	2.81	
								1.36–1.99	0.281–17.3	
	Portugal, Chaves		Preschool	44	3–5	Total air	18	62.7	15.1	
						(TSP + gas)		52.6–85.3	6.20–19.2	
						Gas		60.8	11.7	
								50.7–83.9	4.91–16.0	
						TSP		1.90	3.37	
								0.87–2.48	1.12–3.50	
	Portugal, Porto	LVS (24 h); HPLC-FLD-PAD	Preschool	173	3–5	Total air	18	63.3	28.2	Oliveira et al. (2016a)
						($PM_{2.5}$ + gas)		25.1–149	2.68–47.9	
						Gas		61.9	26.6	
								23.9–149	1.94–43.6	
						$PM_{2.5}$		1.45	1.62	
								1.18–2.23	0.744–4.27	
						$PM_{1.0}$		0.96	1.40	
								0.96–1.62	0.74–2.36	
	Portugal, Chaves		Preschool	44	3–5	Total air	18	69.4	21.4	
						($PM_{2.5}$ + gas)		51.4–84.1	5.11–30.5	
						Gas		65.1	16.9	
								50.7–83.7	4.54–17.1	
						$PM_{2.5}$		4.23	4.55	
								2.60–7.77	2.70–10.5	
						$PM_{1.0}$		3.11	2.52	
								2.59–5.44	1.63–4.70	

(*continued on next page*)

Table 2 (*continued*)

Continent	Country, city	Methodology[#]	Note	Children		Analysed phase	No. of PAHs	ΣPAHs indoor	ΣPAHs outdoor	Reference
				n	Age					
	Portugal, Porto	LVS (24 h); HPLC-FLD-PAD	Preschool	173	3–5	Total air ($PM_{2.5}$ + gas)	18	35 24–40		Oliveira et al. (2015a)[b]
						Gas		30 17–36		
							$PM_{2.5}$		6.2 3.0–7.6	
								8.9 4.0–13		
	$PM_{1.0}$		4.7 1.9–6.0							
	Portugal, Porto	LVS (24 h); HPLC-FLD-PAD	Preschool	173	3–5	Total air ($PM_{2.5}$ + gas)	18	54.4 27.8–82.0		Oliveira et al. (2015b)
						Gas		44.5 27.1–66.1		
						$PM_{2.5}$		6.89 0.721–15.9	7.73 2.22–9.88	
						$PM_{1.0}$		5.40 0.534–14.7		
	Serbia	LVS (24 h); GC–MS	Primary school, downtown			PM_{10}	16	61.7 ± 61.4 10.2–199		Jovanović et al. (2014)
	Serbia	LVS (24 h); GC–MS	n.r.			Total air (PM + gas)	16			Živković et al. (2015)
			Winter					36.9-272[b]	27.0-132[b]	
Summer							88.4–422[b]	202–1017[b]		

n.r. – authors did not report any information related with the type of school and/or schoolchildren (number of participants and their age);

[#] Methodology [sampling devices (time of sampling) detection methods] used: LVS – low volume samplers; MVS – medium volume samplers; HVS – high volume samplers. HPLC-FLD – high performance liquid chromatography with fluorescence detection; HPLC-UV - high performance liquid chromatography with ultra-violet detection; HPLC-FLD-PAD - high performance liquid chromatography with fluorescence and photodiode array detection; GC–MS – gas chromatography with mass detection.

[*] The type of school was estimated according with the age of schoolchildren reported by the authors (kindergartens/preschools ≤ 6 years, elementary/primary schools 6–13 years, middle/secondary schools 13–16 years, and high schools ≥ 16–17 years).

[**] Authors did not report the fraction of PM collected and analysed.

[a] Data is presented in medians.

[b] Data is presented as the range of percentile 25 to percentile 75.

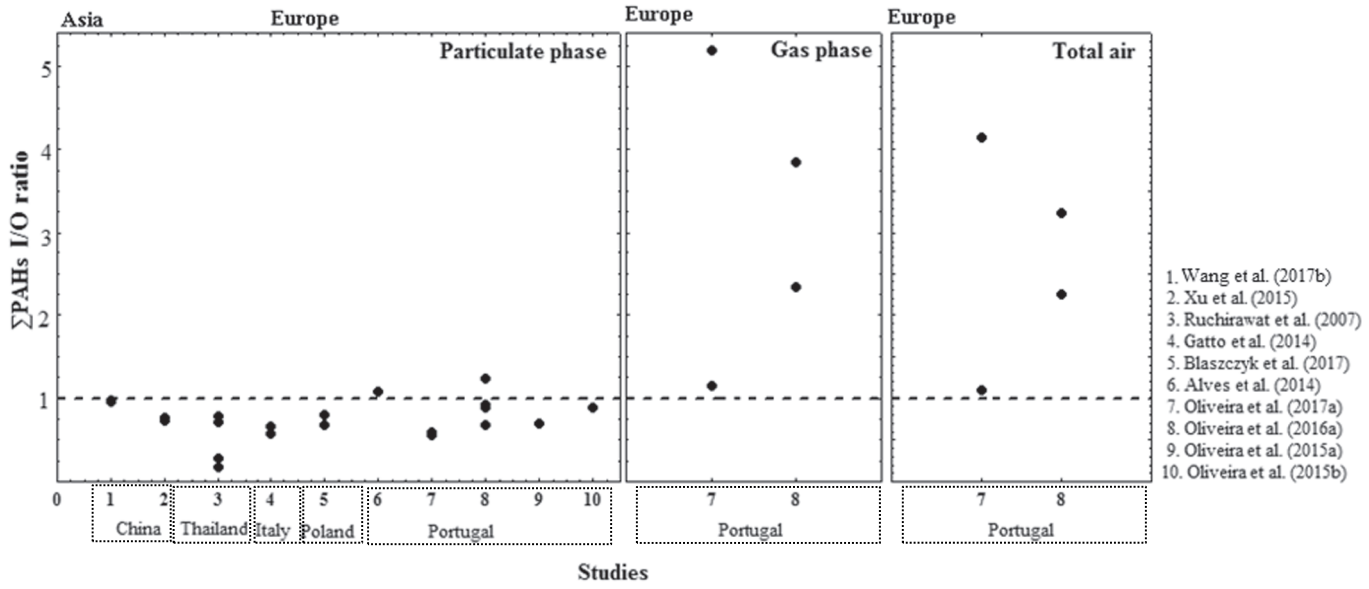


Fig. 3. Indoor-to-outdoor ratios of the reported PAH concentrations in particulate and gas phases, as well as in the total air of schools. Only studies that concomitantly monitored levels indoors and outdoors were considered.

smallest particulate fractions, such as PM_1 and $PM_{2.5}$, is highly health relevant.

Regarding the content of PAHs in the gas phase, determined by active sampling except in Boudehane et al. (2016), ΣPAH levels ranged between 30.0 and 65.1 (median 38.6) ng/m^3 and from 11.7 to 121 (median 27.4) ng/m^3 in the indoor and outdoor air of schools, respectively (Table 2). Despite the composition of airborne gas phase have been frequently neglected, some authors have emphasized its strong contribution to the total airborne (gas + PM) concentrations of PAHs (Eiguren-Fernandez et al., 2007; Oliveira et al., 2015a, 2015b, 2016a, 2017b); gaseous PAHs accounted for up to 81.8–97.8% of total ΣPAHs indoors and 77.5–99.6% in the outdoor air of schools. Airborne gaseous PAHs are frequently present at significantly higher concentrations than in PM fractions (Dat and Chang, 2017; Eiguren-Fernandez et al., 2007; Oliveira et al., 2015a, 2015b, 2016a, 2017b). Levels of ΣPAHs in the total air (i.e., gas and particulate phases) of schools ranged between 34.4 and 69.4 (median 58.5) ng/m^3 and 12.3–122 (median 29.2) ng/m^3 for the indoor and outdoor air, respectively. Compounds with 2–3 aromatic rings (naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, and anthracene) were predominantly found in the airborne gas phase while compounds with 5 and more rings [benzo(b)fluoranthene, benzo(j)fluoranthene, benzo(k) fluoranthene, benzo(a)pyrene, dibenzo(ah)anthracene, dibenzo(al) pyrene, benzo(ghi)perylene, indeno (123-cd)pyrene] were almost entirely bound to particles; PAHs with 4 rings, namely fluoranthene, pyrene, benz(a)anthracene, and chrysene, were distributed between both phases.

Data from the available studies (that concomitantly assessed indoors and outdoors) were used to determine I/O ratios of ΣPAHs at school environments (Fig. 3); information was not organized by continent due to the scarce number of reports (a total of 10 works performed in Chinese, Italian, Polish, Portuguese, and Thai schools; Table 2). In general, the outdoor concentrations of PM-bound PAHs were higher than those indoors (I/O ratios < 1), except for two works (Alves et al., 2014; Oliveira et al., 2016a), which highlight the strong contribution of outdoor sources, mostly from infiltration of ambient emissions. Road vehicle emissions are an important source of PAHs in urban areas, being the compounds with 4–6 rings the most abundant ones in PM principally in the smallest fractions (Eiguren-Fernandez et al., 2007; Krugly et al., 2014; Liaud et al., 2014; Oliveira et al., 2015a, 2015b, 2016a). Many countries face the common environmental problem of high PAHs air pollution, especially in the major cities with a large population, high dependency on fossil fuels and elevated levels of traffic congestion. In 2015, 20% of the urban population in EU-28 was exposed to annual benzo(a)pyrene levels that exceeded the targeted guideline of 1.0 ng/m^3 (Directive 2004/107/CE), with 85% of the population being exposed to concentration above the annual estimated reference level of 0.12 ng/m^3 (EEA, 2017). According to EEA (2017), the ambient air levels of benzo(a)pyrene in EU-28 resulted firstly from the emissions of commercial, institutional, and households fuel combustion (75%) and secondly from the agricultural waste burning (15%). Domestic combustion of coal and wood are important sources of benzo(a)pyrene principally in some eastern (e.g. Poland) and in some regions of southern (e.g. Bulgaria and Austria) countries (EEA, 2017), while the contribution of agricultural waste burning was more significant in southern European countries. The contribution of road transports only accounted with 1% of the total emission of benzo(a)pyrene (EEA, 2017). Since PAH concentrations are higher in urban areas with high population density (and principally during the winter; Dat and Chang (2017); Gatto et al. (2013); Romagnoli et al. (2014)) children attending schools situated in urban areas, in the vicinity of heavily trafficked streets and/or industrial areas are at higher risk (Oliveira et al., 2015b, 2016a, 2017a; Ruchirawat et al., 2007; Trasande et al., 2015; Tuntawiroon et al., 2007). Tuntawiroon et al. (2007) reported ambient ΣPAH levels that were 20-fold greater for schools in proximity to roadsides in Bangkok than for provincial schools (30.39 ± 5.80 versus 1.50 ± 0.28 ng/m^3). In the specific case of two works (Oliveira et al., 2016a, 2017a) that included the simultaneous assessment of exposure to PAHs in the particulate, gaseous and total air in Portuguese (Oporto Metropolitan area) school environments, the reported I/O ratios were higher than unity for gaseous PAHs (median of 3.1; range: 1.2–5.2) and for total air ΣPAHs (median of 2.7; range: 1.1–4.1), thus revealing the existence of relevant indoor sources of mainly low molecular weight PAHs (Fig. 3). Authors are aware that conclusions taken only from these two studies cannot be generalized, still, the achieved findings are in line with the conclusions reported by other authors (Krugly et al., 2014; Moreau-Guigon et al., 2016) for different indoor environments. PAHs occur as complex mixtures and their compositional profiles may vary significantly. The re-emission and sorption of gaseous PAHs from indoor surfaces, re-suspension of indoor dust, and emissions from human activities including cooking, (e.g., in canteens and snack-bars), cleaning, children handicrafts account for the higher levels of PAH in

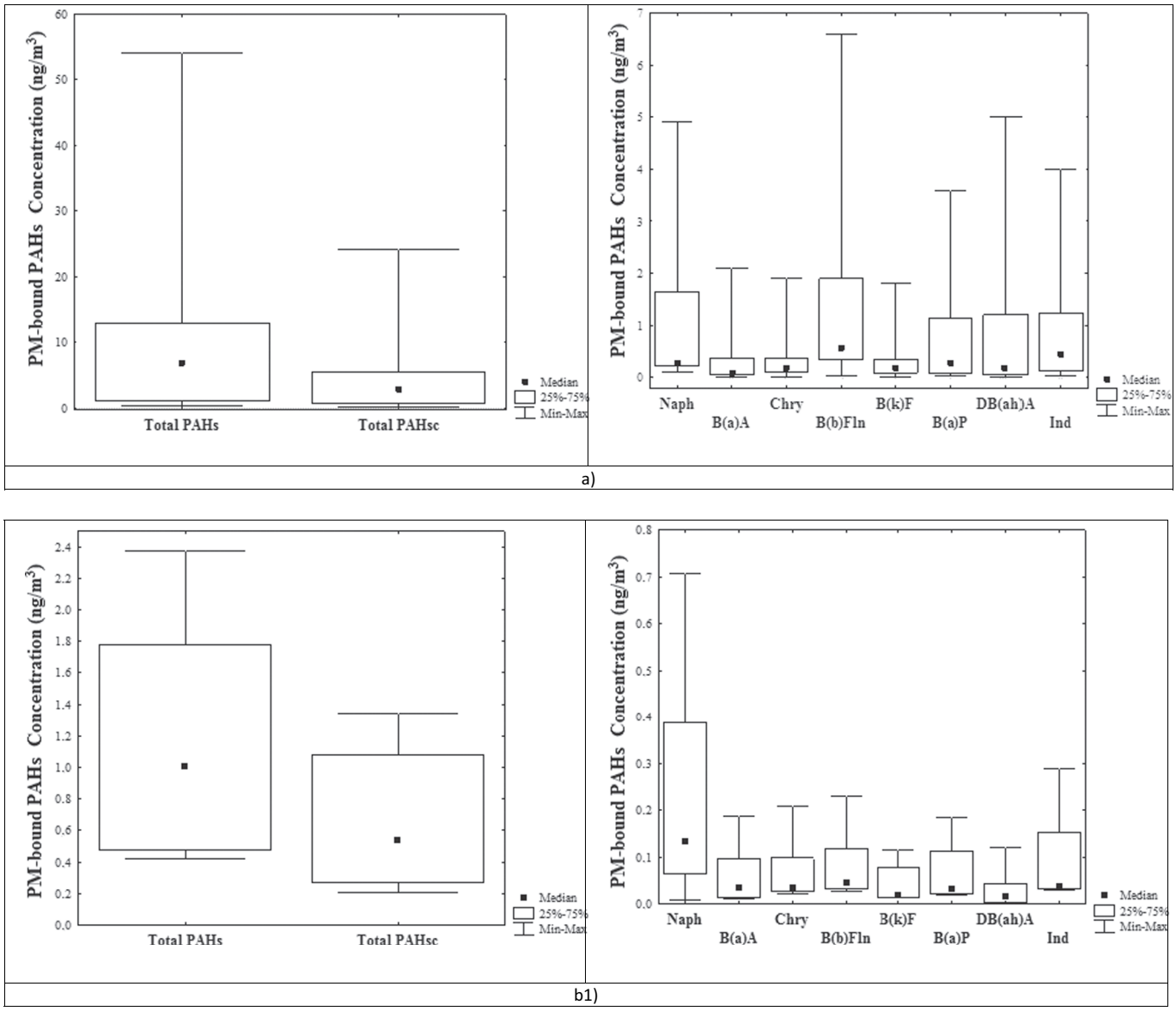


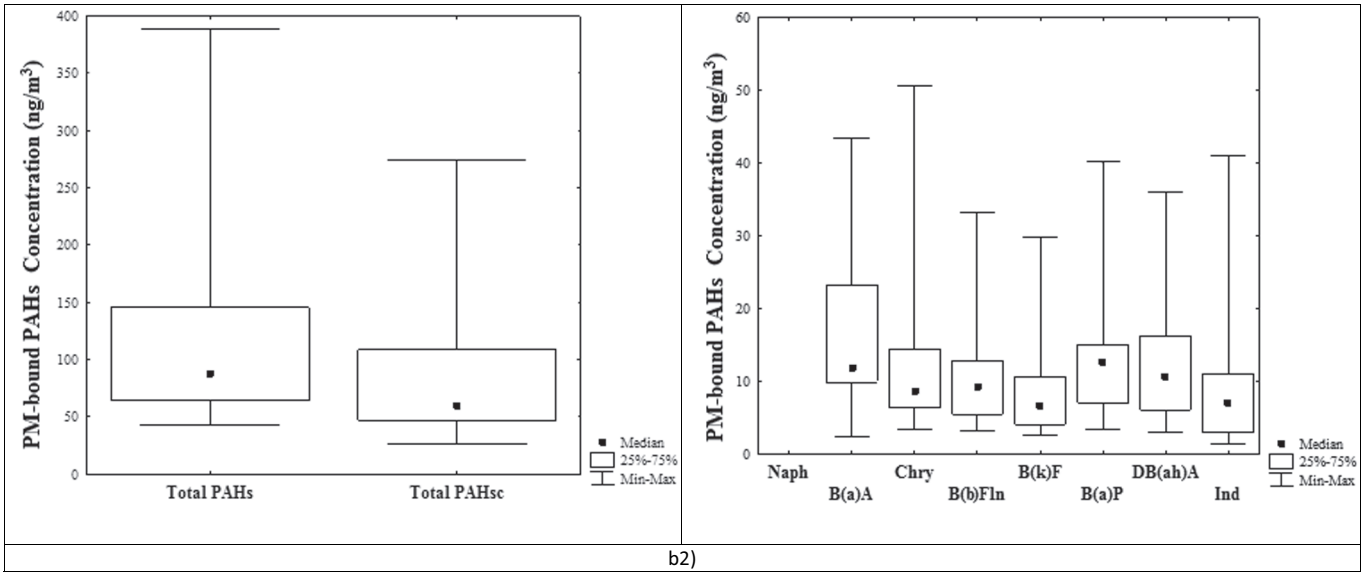
Fig. 4. Particulate-bound concentrations of total PAHs, total carcinogenic PAHs, and individual carcinogenic compounds in the indoor air of European (a) and outdoor air of American (b1), Asian (b2), and European (b3) schools. There were no or insufficient data characterizing the other continents for statistical treatment. B(a)A – benz(a)anthracene; B(a)P – benzo(a)pyrene; B(b)Fln – benzo(b)fluoranthene; B(j)Fln – benzo(j)fluoranthene; B(k)Fln – benzo(k)fluoranthene; Chry – chrysene; DB(ah)A – dibenz(ah)anthracene; Ind – indeno(123-cd)pyrene;.Naph – naphthalene.
Notes: All the studies that reported mean or median concentrations of particulate-PAHs regardless of the fraction were considered; in some studies concentrations of B (b)Fln and/or B(j)Fln and/or B(k)Fln are reported together.

the indoor air of school environments (Alves et al., 2014; Gatto et al., 2013; Krugly et al., 2014; Morawska et al., 2017). The regular use of heating systems and some electronic equipment (such as printers) are also relevant indoor sources of PAHs at schools (Destaillats et al., 2008; Heinrich, 2011). These findings support the need to include both gas phase and fine fractions of PM in the environmental and personal monitoring of schoolchildren.

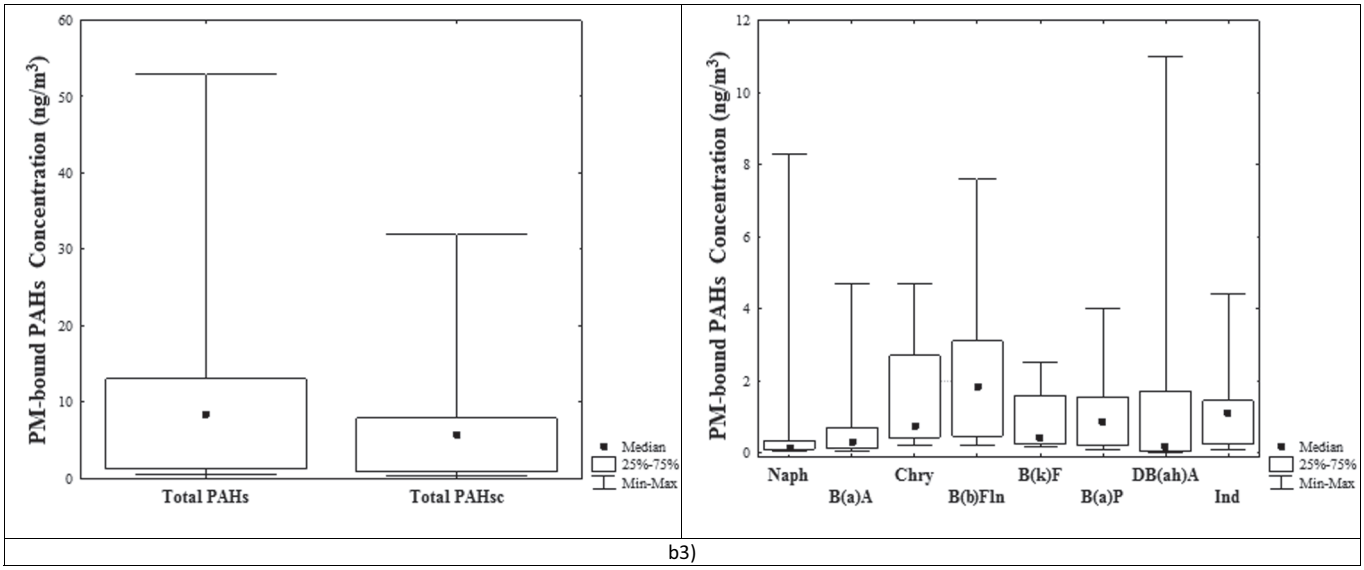
4.2. Assessment of carcinogenic risks on children

Benzo(a)pyrene and possible/probable carcinogenic PAHs may induce cancer through a mutagenic mechanism that involves metabolic activation to reactive diol-epoxides that covalently bind to cellular macromolecules such as proteins and the DNA molecules to form adducts (Gao et al., 2018; Kim et al., 2013a). The formation of DNA adducts is believed to be the first step in the initiation of carcinogenic processes, being then converted into mutations after cell replication (WHO, 2010). Mutations in critical tumor oncogenes and tumor suppressor genes have been identified in lung tumors from humans exposed to PAHs or PAH-containing mixtures (WHO, 2010). PAHs also play an undeniable role in inflammatory processes thus contributing to the aggravation of cardiorespiratory diseases (Bae et al., 2010; Kamal et al., 2015; Kim et al., 2013a).

The concentrations of total carcinogenic PAHs ($\Sigma PAHs_{carc}$) and its contribution to PM-bound and total air (PM and gas phases) ΣPAHs in the indoor and outdoor air of European and in the ambient air of American and Asian schools are presented in Figs. 4 and 5; there were no or insufficient data for statistical treatment of the other continents. Overall the contribution of carcinogenic compounds was predominantly lower in the indoor air (30–40% of ΣPAHs) comparatively with outdoor areas (35–96% ΣPAHs). The compounds that contributed the most for $\Sigma PAHs_{carc}$ (PM-bound and total air) indoors were naphthalene (9.7%



b2)



b3)

Fig. 4. (*continued*)

versus 85%), benzo(b)fluoranthene (20% versus 2%), indeno(123-cd) pyrene (16% versus 3%), and benzo(a)pyrene (10% versus 2%); the other compounds accounted with < 10% of $\Sigma PAHs_{carc}$ (Figs. 4a and 5a). Regarding schools' ambient air, naphthalene is by far the compound that contributed the most for $\Sigma PAHs_{carc}$ followed by benzo(b)fluoranthene, chrysene, and indeno(123-cd)pyrene at American schools; benzo(a)pyrene, benzo(a)anthracene, and dibenz(a,l)anthracene at Asian schools; and benzo(b)fluoranthene, indeno(123-cd)pyrene, benzo (a)pyrene, and chrysene at European schools (Figs. 4b and 5b). I/O ratios of PM-bound carcinogenic compounds varied between 0.08 for benz(a)anthracene to 0.87 for naphthalene, thus revealing the strong impact of outdoor air penetration in the indoor levels of carcinogenic (possible/probable) PAHs. Therefore, PM-bound PAHs have an undeniable role in ambient air pollution and on the IAQ of schools. Total air I/O ratios ranged between 0.29 and 1.4, which reflect the contribution of both indoor and outdoor sources. According to WHO (2010), the interactions between PAHs in mixtures are complex and highly unpredictable because of the inhibitory, additive, and synergistic effects. Due to its carcinogenic potency and its abundance in the environment, benzo(a)pyrene has been defined as an indicator of human exposure to carcinogenic PAHs. Indoor levels of benzo(a)pyrene accounted with 10 and 2% of $\Sigma PAHs_{carc}$ at European schools, respectively in PM-bound and total air PAHs, while outdoors, it varied between 5.5 (American) and 21% (Asian) and from 0.02 (American) to 4.5% (European schools) of $\Sigma PAHs_{carc}$, respectively (Figs. 4 and 5). The median concentrations of ambient PM-bound benzo(a)pyrene were 12.5 (3.3–40.2) ng/m^3 at Asian, 0.49 (0.07–4.0) ng/m^3 at European, and 0.03 (0.02–0.11) ng/m^3 at North American schools. A total of 31% of the studies [performed in Asian (China and India: Gao et al., 2016; Jyethi et al., 2014; Wang et al., 2017b, 2017c) and European (Italy, Portugal, Serbia, and Poland: Błaszczyk et al., 2017; Oliveira et al., 2017a; Romagnoli et al., 2014; Živković et al., 2015) schools] reported levels that exceeded the target guideline of 1 ng/m^3 settled for PM_{10} fraction (Table 2S). Recently, EEA concluded that 14-member states reported benzo(a)pyrene concentrations that exceeded the annual target value in 2015, with exceedances being more predominant in central and eastern European countries (EEA, 2017). In its last report concerning IAQ, WHO (2010) stated that no threshold could be defined for PAHs and emphasized that all indoor exposures are considered relevant to human health. PAHs, and more specifically naphthalene, are among the selected pollutants, however a guideline value of 10 μg/m^3 (maximum average concentration) is only defined for naphthalene

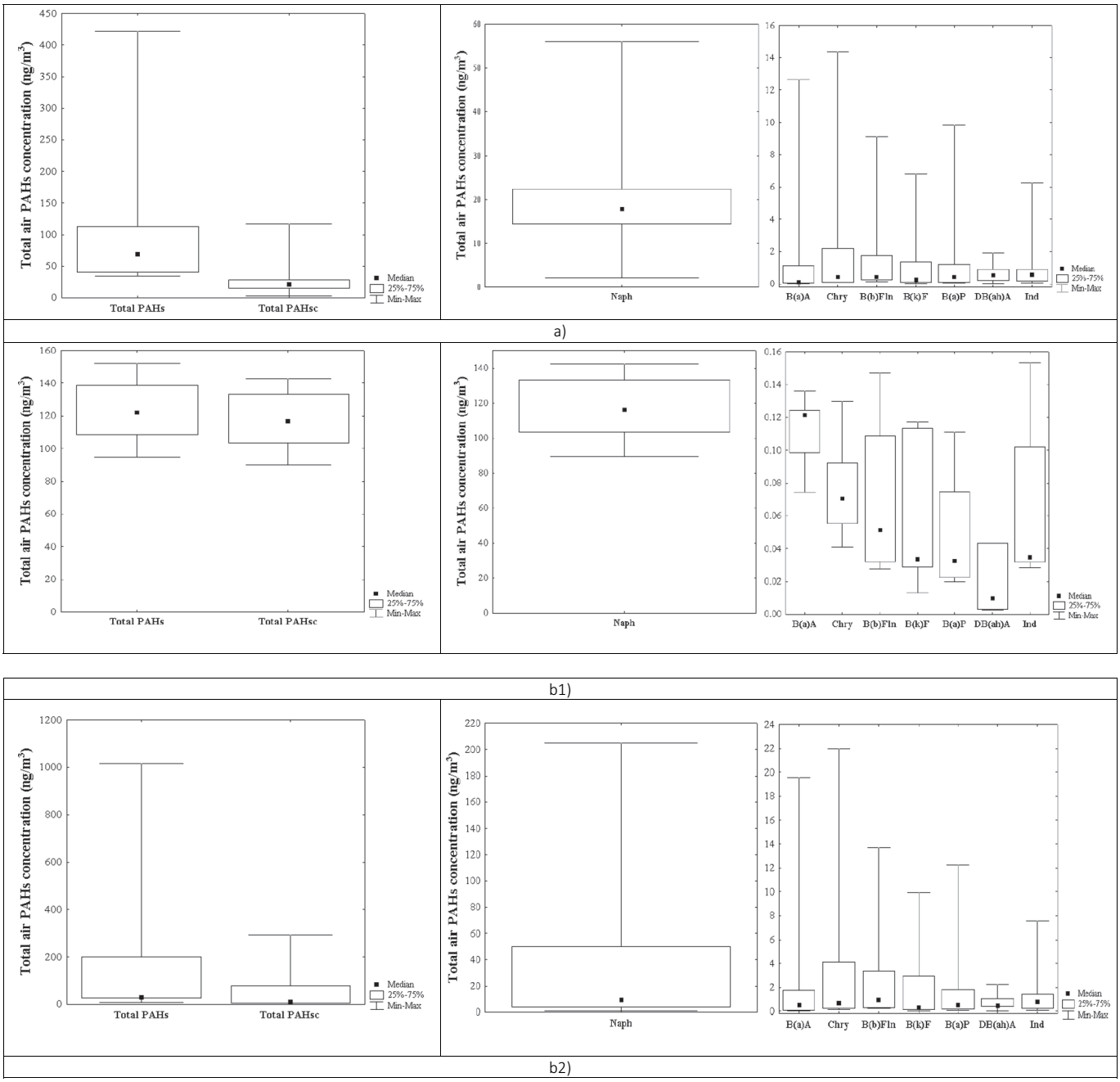


Fig. 5. Total air (i.e., gas and particulate phases) concentrations of total PAHs, total carcinogenic PAHs, and individual carcinogenic compounds in the indoor air of European (a) and outdoor air of American (b1) and European (b2) schools. There were no or insufficient data characterizing the other continents for statistical treatment.
B(a)A – benz(a)anthracene; B(a)P – benzo(a)pyrene; B(b)Fln – benzo(b)fluoranthene; B(j)Fln – benzo(j)fluoranthene; B(k)Fln – benzo(k)fluoranthene; Chry – chrysene; DB(ah)A – dibenz(ah)anthracene; Ind – indeno(123-cd)pyrene;.Naph – naphthalene.
Notes: in some studies concentrations of B(b)Fln and/or B(j)Fln and/or B(k)Fln are reported together.

(Table 2S; WHO, 2010). Naphthalene is known to cause ophthalmologic and dermal changes, hemolytic anemia, liver and neurological damages, respiratory tract lesions and tumors in the upper respiratory tract of animals (Sarigiannis et al., 2011; WHO, 2010). WHO threshold for naphthalene was never exceeded in indoor school environments (overall median of 17.8 ng/m^3). Despite no guidelines are defined for benzo(a)pyrene in the indoor air of buildings, WHO (2010) stated that levels above 1.0 ng/m^3 predicted a greater genomic frequency of translocations, micronuclei and DNA fragmentation. The concentrations of benzo(a)pyrene in the indoor air of some Asian (overall median of 3.10; 3.1–4.7 ng/m^3) and European (overall median of 0.75; 0.02–3.6 ng/m^3) schools exceeded the recommended guideline of 1.0 ng/m^3 (Błaszczyk et al., 2017; Oliveira et al., 2017a; Romagnoli et al., 2014; Wang et al., 2017b, 2017c).

The carcinogenic potency of a given PAH compound can be assessed based on its benzo(a)pyrene equivalent concentration (i.e. B(a)Peq). Calculation of B(a)Peq concentration for a given PAH compound requires the use of its toxic equivalent factor (TEF), which represents its relative carcinogenic potency by using benzo(a)pyrene as the reference compound to adjust its original concentration. The median values of the total TEF-adjusted concentrations (ΣTEF-PAHs) reported in the literature for Asian and European schools are presented in Fig. 6; no data

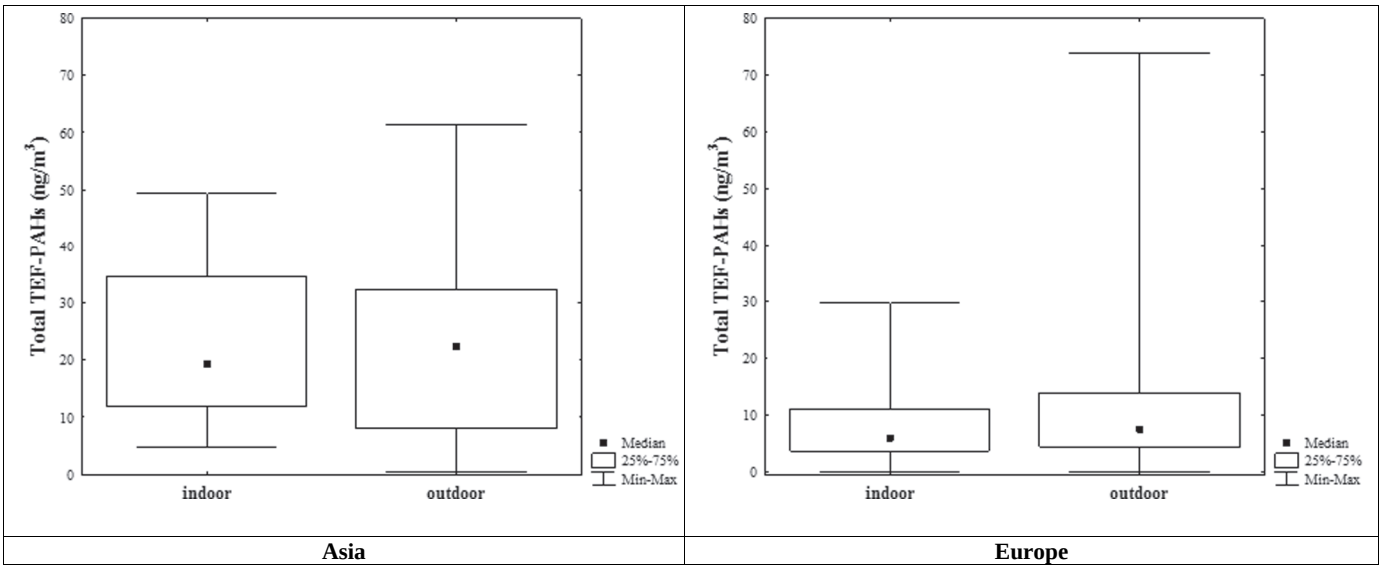


Fig. 6. Levels of total TEF-adjusted concentrations of PAHs in Asian and European schools.

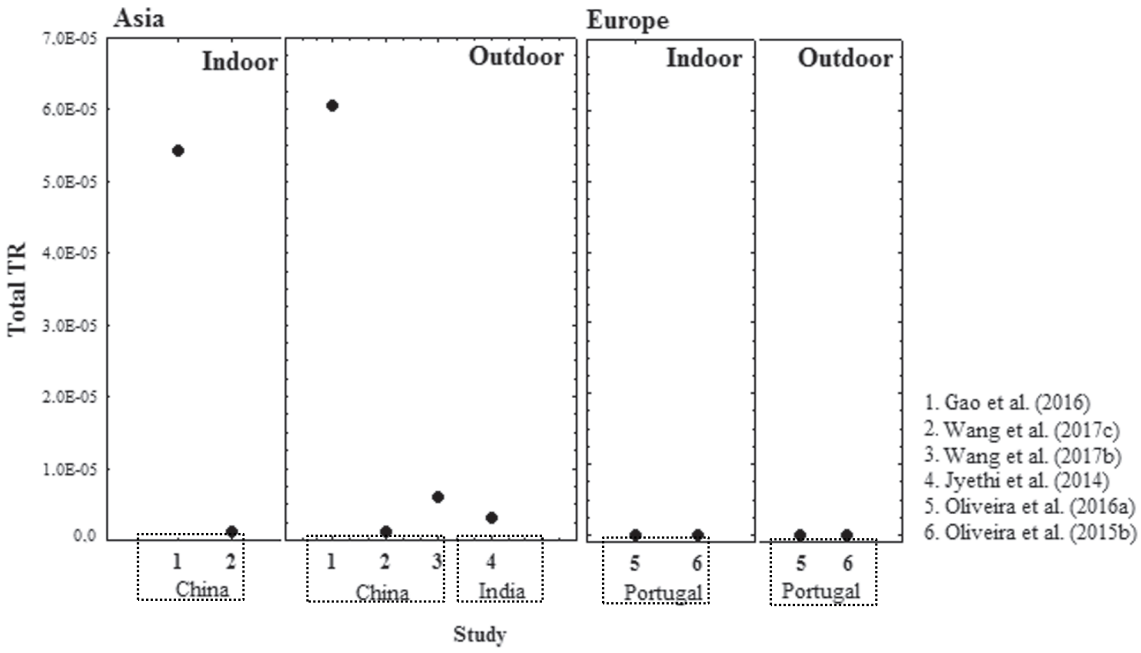


Fig. 7. Levels of total carcinogenic risks (TR) reported in the indoor and outdoor air of Asian and European schools.

characterizing the other continents were found. Overall, levels were predominantly higher in Asian than in European school environments. Concentrations were slightly lower in school indoor environments than in outdoor areas [median (range): 19.4 (4.70–49.4) ng/m^3 versus 22.4 (0.43–61.3) ng/m^3 for Asian schools and 6.06 (0.04–29.8) versus 7.59 (0.04–74.0) ng/m^3 for European schools]. Based on the available epidemiological evidences in coke-oven workers, WHO specified a unit risk of 8.7×10^{-5} per ng/m^3 of benzo(a)pyrene (i.e., PAH mixture) to cause an increased risk of lung cancer, which corresponds to 1 additional cancer case in 100,000 individuals exposed to 0.12 ng/m^3 of benzo(a)pyrene (WHO, 2010). Assuming that children spend approximately 7-h at school indoor areas and 1-h outdoors and considering the median ΣTEF-PAHs reported, the corresponding lung cancer risks were assessed as being 5.1×10^{-4} (1.2×10^{-4}–1.29×10^{-3}) for Asian and 1.6×10^{-4} (1.0×10^{-6}–7.8×10^{-4}) for European schools indoors with values, respectively, of 8.2×10^{-5} (1.6×10^{-6}–2.2×10^{-4}) and 2.8×10^{-5} (1.5×10^{-7}–2.7×10^{-4}) in the outdoor air of schools. The estimated values at Asian and European schools were, respectively, 50 and 16 times higher than WHO health guideline of 10^{-5}, emphasizing the importance of indoor exposure. Children lung cancer risks were though estimated assuming a similar distribution of carcinogenic PAHs in all indoor areas as in occupational environments. This assumption may not be always correct, but it is expected that associated uncertainties are unlikely to be large (WHO, 2010).

The carcinogenic risks (TR) associated with the exposure to PAHs can be determined according to the methodologies provided by US EPA (USEPA, 2018). Fig. 7 exhibits the reported data on total carcinogenic risks associated with children inhalation exposure to PAHs in the indoor and outdoor air of Asian and European schools; data was inexistent for other continents. Total carcinogenic risks represent the incremental probability of a subject to develop cancer, over a lifetime (70 years) because of continuous exposure to PAHs (USEPA, 1989). Children total carcinogenic risks were predominantly higher at Asian than at European schools [1.3×10^{-6} to 5.4×10^{-5} (median 1.3×10^{-6}) indoors

Table 3
Monohydroxyl-PAH concentrations (mean ± SD and/or range, expressed as μmol/mol creatinine except when indicated otherwise[#]) reported in children at school age (n = number of enrolled children).

Continent	Country, city	n (age, years)	Note	Metabolite[**]					Reference
				OHNaph	OHFlu	OHPhen	OHPy	ΣOHPAHs	
America, North	USA, Harlem, Bronx, Washington	113 (5)	Dominican ethnicity	1OHNaph 2970 (113–138,000) 2OHNaph 4680 (246–52,900)				7651	Orjuela et al. (2012)[#]
			African American	1OHNaph 2890 (82–67,700) 2OHNaph 2470 (150–10,300)				5360	
	USA, New York City, Manhattan, Bronx	222 (5)	Dominican ethnicity	1OHNaph 2539 (199–3225)[a] 2OHNaph 4675 (3943–5543)[a]	2OHFlu 269 (232–314)[a] 3OHFlu 110 (94–128)[a] 9OHFlu 235 (204–271)[a]	1OHPhen 166 (144–191)[a] 2OHPhen 49 (42–58)[a] 3OHPhen 152 (131–175)[a] 4OHPhen 32 (28–38)[a]	1OHPy 155 (133–182)[a]	8382	Miller et al. (2010)[#]
			African American ethnicity	1OHNaph 3569 (2613–4874)[a] 2OHNaph 3262 (2741–3882)[a]	2OHFlu 32 (261–393)[a] 3OHFlu 14 (114–173)[a] 9OHFlu 31 (54–1801)[a]	1OHPhen 166 (138–203)[a] 2OHPhen 58 (47–71)[a] 3OHPhen 185 (150–228)[a] 4OHPhen 46 (37–58)[a]	1OHPy 169 (136–210)[a]	7532	
America, Central	Mexico	150 (7–10)	Elementary schools[d] in urbanized and industrial area				1OHPy 0.0185 (0.006–0.046)[b]	0.0185	Alvarado-Cruz et al. (2017)
	Mexico, Chiapas, San Luis Potosí	321 (3 − 13)	Local communities				1OHPy nd – 4.82	nd – 4.82	Domínguez-Cortinas et al. (2013)
	Mexico, Chiapas, Quintana Roo, Oaxaca, San Luis Potosí	256 (6–12)	Public schools				1OHPy (0.10–4.50)	0.10–4.50	Jasso-Pineda et al. (2015)
	Mexico, Chiapas, Quintana Roo, Oaxaca, San Luis Potosí	258 (3–13)	Primary and elementary schools				1OHPy (0.08–4.40)	0.08–4.40	Martínez-Salinas et al. (2010)
	Mexico, Juarez	135 (6–12)	Public school				1OHPy 1.20 ± 1.10	1.20	Ochoa-Martinez et al. (2016)
	Mexico, Chiapas, Oaxaca, Quintana		Communities that use biomass fuels to cook and heat homes				1OHPy (3500–4500)	3500–4500	Pérez-Maldonado et al. (2014)[#]
	Mexico, San Luis Potosí	55 (6–12)	Public school				1OHPy 0.25 ± 0.15	0.25	Pérez-Maldonado et al. (2017)
Asia	Afghanistan, Kabul, Ningarhar	13 (2–9)	Urban and rural areas			1OHPhen 1343 (46.6–6865) 2 + 9OHPhen 731 (46.3–2903) 3OHPhen 1133 (19.3–8925) 4OHPhen 114 (4.0–976)	1OHPy 3167 (71.4–16,288)	6488	Hemat et al. (2012)[#,**]

(*continued on next page*)

Table 3 (*continued*)

Continent	Country, city	n (age, years)	Note	Metabolite**					Reference
				OHNaph	OHFlu	OHPhen	OHPy	ΣOHPAHs	
	China, Chongqing	1230 (6–12)	Primary schools Urban area	2OHNaph 2901 (2.57–130,392)	2OHFlu 971 (1.74–85,787)	9OHPhen 3181 (18.57–43,764)	1OHPy 224 (1.77–1652)	7277	Liu et al. (2017)#,*
	China, Guangzhou	35 (4–6)	Elementary school Non-polluted area	2OHNaph 1.81 (0.13–58.14)	2OHFlu 1.38 (0.73–13.20)	2OHPhen 0.25 (0.07–1.31) 3OHPhen 0.08 (nd-0.30) 4OHPhen 0.07 (0.01–2.05) 9OHPhen 2.27 (0.21–19.39)	1OHPy 0.10 (nd-0.41)	5.96	Fan et al. (2012)*
		39 (6–7)	Kindergarten Polluted area	2OHNaph 5.92 (0.22–29.51)	2OHFlu 2.90 (0.10–15.46)	2OHPhen 0.14 (0.03–2.84) 3OHPhen 0.28 (nd-1.20) 4OHPhen 0.14 (0.01–1.32) 9OHPhen 1.64 (0.15–11.95)	1OHPy 0.55 (0.04–1.87)	11.6	
	China, Lanzhou Xigu, Yuzhong	160	Areas with large petrochemical complex				1OHPy 0.42 (0.067–2.05)	0.42	Yu et al. (2016)
	China, Taiwan	369 (5–12)	Community center including elementary schools				1OHPy		Hu et al. (2011)
			High-exposure areas				0.194 ± 0.143 0.186 ± 0.148	0.194 0.186	
			Low-exposure areas				1OHPy 0.113 ± 0.082 0.122 ± 0.089	0.113 0.122	
	China, Taiwan, Taipei	453 (3)	Male Female				3720 3450	3720 3450	Wang et al. (2017a) #
	Iran, Shiraz Paramont Sadra	120 (9–12)	Primary schools Urban area Suburban area				1OHPy 0.64 (0.08–2.93) 0.89 (0.06–3.60)	0.64 0.89	Shahsavani et al. (2017)c
	Saudi Arabia, Jeddah	204 (10−12)	Primary schools[d] Near an oil refinery			1OHPhen 0.122 2 + 9OHPhen 0.052 3OHPhen 0.113 4OHPhen 0.027	1OHPy 0.176	0.49	Alghamdi et al. (2015)c,*
			Near a major highway			1OHPhen 0.113 2 + 9OHPhen 0.058 3OHPhen 0.126 4OHPhen 0.028	1OHPy 0.144	0.47	

(*continued on next page*)

Table 3 (*continued*)

Continent	Country, city	n (age, years)	Note	Metabolite**					Reference
				OHNaph	OHFlu	OHPhen	OHPy	ΣOHPAHs	
			Near the Red Sea			1OHPhen 0.098 2 + 9OHPhen 0.047 3OHPhen 0.085 4OHPhen 0.020	1OHPy 0.098	0.35	
	Saudi Arabia, Jeddah	184 (10–14)	Primary schools[d] Near an oil refinery Near a ring road Background			1OHPhen 0.378 (0.22–0.48)[b] 0.346 (0.23–0.57)[b] 0.26 (0.17–0.40)[b]	1OHPy 0.14 (0.11–0.23)[b] 0.18 (0.098–0.29)[b] 0.099 (0.068–0.22)[b]	1.26 0.53 0.36	Trasande et al. (2015)[c,*]
	Thailand, May Province Om Koi Mae Chaem	200 (10–14)	Elementary schools[d] Smoke-haze episode				1OHPy 0.70 (0.02–8.48) 0.24 (0.02–2.92)	 0.70 0.24	Naksen et al. (2017)[*]
	Thailand Bangkok Chonburi	180 (9–13)	Primary schools[d] Urban area Rural area				1OHPy 0.18 ± 0.01 (0.04–0.55) 0.10 ± 0.01 (0.02–0.47)	 0.18 0.10	Ruchirawat et al. (2007)
	Thailand Bangkok Chonburi	184 (8–13)	Primary schools[d] Urban area Rural area				1OHPy 0.22 ± 0.02 (0.03–0.99) 0.12 ± 0.11 (0.02–0.43)	 0.22 0.12	Tuntawiroon et al. (2007)
	Japan, Tokyo, Kanagawa	134 (3–6)	Kindergarten				1OHPy 0.066 (0.02–1.25)	0.066	Mori et al. (2009, 2011)[c]
Europe	Germany, Dortmund Hörde, Duisburg	948 (5–9)	Vicinity of a coke oven plant				1OHPy 0.157 (0.030–1.07)	0.157	Wilhelm et al. (2007)[c,*]
	Germany, Borken		Rural town				0.081 (0.026–0.559)	0.081	
	Portugal Porto	173 (3–5)	Preschools Boys Girls	1OHNaph + 1OHAce 4.42 3.90	2OHFlu 0.216 0.124	1OHPhen 0.055 0.056	1OHPy 0.057 0.066	4.75 4.15	Oliveira et al. (2017a)[*]
	Chaves	44 (3–5)	Boys Girls	3.49 3.73	0.324 0.221	0.085 0.138	0.117 0.184	4.02 4.27	
	Spain, Granada	174 (4)	Urban area Rural area				1OHPy 0.060 ± 0.040 0.054 ± 0.055	0.060 0.054	Freire et al. (2009)

nd - not detected.

** 1OHAce: 1-hydroxyacenaphthene; 2OHFlu: 2-hydroxyfluorene; 3OHFlu: 3-hydroxyfluorene; 9OHFlu: 9-hydroxyfluorene; 1OHNaph: 1-hydroxynaphthalene; 2OHNaph: 2-hydroxynaphthalene; 1OHPhen: 1-hydroxyphenanthrene; 2OHPhen: 2-hydroxyphenanthrene; 3OHPhen: 3-hydroxyphenanthrene; 4OHPhen: 4-hydroxyphenanthrene; 9OHPhen: 9-hydroxyphenanthrene; 1OHPy: 1-hydroxypyrene.

* Concentrations are expressed as median.

Concentrations are expressed in ng/L urine.

[a] Concentrations expressed as 95% confidence interval.

[b] Concentrations expressed as percentile 25–75% confidence interval.

[c] Data was originally expressed as μg/g creatinine and converted to μmol/mol creatinine: concentration reported/1.72 for OHPhen and concentration reported/1.93 for OHPy.

[d] The type of school was estimated according with the age of schoolchildren reported by the authors (kindergartens/preschools ≤6 years, elementary/primary schools 6–13 years, middle/secondary schools 13–16 years, and high schools ≥16–17 years).

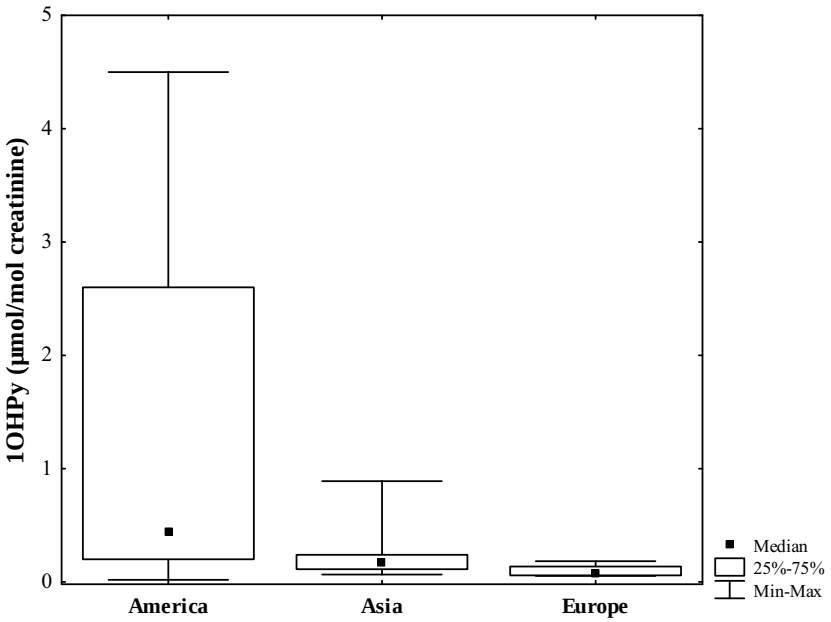


Fig. 8. Concentrations of urinary 1OHPy (median, 25–75 percentiles, and range; µmol/mol creatinine) in American, Asian and European schoolchildren. There were no or insufficient data characterizing the other continents for statistical treatment.

and 1.3×10^{-6} to 6.1×10^{-5} (median 4.7×10^{-6}) outdoors versus 5.9×10^{-9} to 1.1×10^{-8} (median 6.5×10^{-9}) indoors and 1.1×10^{-8} to 2.2×10^{-8} (median 1.3×10^{-8}) outdoors] Gao et al. (2016), Jyethi et al. (2014), Oliveira et al. (2015b, 2016a), Wang et al. (2017b, 2017c). Only one study (Oliveira et al., 2017a) determined the total carcinogenic risks associated with schools indoor and outdoor air exposure (weighted by the respective time spent in each environment), reporting values that varied between 3.2×10^{-7} to 2.2×10^{-5} (median of 1.8×10^{-6}). US EPA defined an acceptable risk level of total carcinogenic risks in the range of 10^{-4} to 10^{-6}, being the risks lower than 10^{-6} considered negligible. Overall the median carcinogenic risks reported in the literature are negligible, with maximum risks being within the US EPA acceptable range. Children spend a significant part of their time at schools (approximately 35–40 h a week during 9–10 months per year), which might result in long-term exposure to PAH levels that may put them at a higher risk of suffering the respective health consequences. All risk estimations discussed in this work were based on the concentrations reported by several authors in schools from different cities (and continents) and therefore a large variability might be associated with these estimations. Additionally, estimated cancer risks in children cannot be extended to lifetime without the correction for proportioning the exposure duration to the averaging time spent at schools (approximately 9–12 years).

4.3. PAHs biomonitoring

Environmental monitoring of PAHs is a complex task and usually does not capture total exposure, i.e., inhalation, ingestion, and dermal uptake, reason why it is important to use suitable biological markers (e.g., metabolites) to estimate total exposure. In the human body, cytochrome P450 IA is a family of enzymes that metabolize PAHs into electrophilic intermediates in order to expedite their excretion from the organism. Bile, faeces, urine, and milk are the principal elimination routes of PAH metabolites, however special attention has been given to urine since it is the easiest, cheapest, and less invasive matrix, which is particularly important for young children. Biomonitoring studies are very relevant in children because the absorbed dose of PAHs may be quite different from the adults mostly due to different physiology, metabolism and behaviors. Young children frequently play on the floor and hand-to-mouth activities may be a relevant source of PAHs. Dermal exposure also constitutes an important route of exposure, principally in the youngest ones. Data on children total exposure of PAHs have been slowly emerging but information is still limited. All the studies performed since 2007, regardless of the environment (please see Methods section for details), are presented in Table 3. Only 26 studies were found worldwide with 54% of the works characterizing Asian children; the remaining 46% characterized European, North and Central American children; no information exists for African, South American, and Oceania children (Table 3; Fig. 5S of Supplementary material). A total of 65% of the studies (17 studies) were performed in school environments and/or included children attending local schools. For each work, the reported mean or median concentrations of all PAH metabolites were added to estimate the levels of total PAH metabolites (ΣOH-PAHs) in the urine of schoolchildren (Table 3). Overall median of ΣOH-PAH levels was 0.36 µmol/mol creatinine, with concentrations ranging between 0.018 µmol/mol creatinine for 7–10 years old Mexican children (Alvarado-Cruz et al., 2017) to 11.6 µmol/mol creatinine for 6–7 years old Chinese children attending kindergartens situated in a polluted area (Fan et al., 2012). The studies performed by Orjuela et al. (2012), Miller et al. (2010), Hemat et al. (2012), Liu et al. (2017), Pérez-Maldonado et al. (2014), and Wang et al. (2017a) reported an overall schoolchildren median levels of urinary ΣOH-PAH of 5360 (3450–8382) ng/L of urine and cannot be compared directly with the other since normalization with creatinine was not performed (Table 3). It is important to point out that ΣOH-PAH levels are obviously dependent on the number of PAH metabolites considered, which varied from study to study. Still, it can be used to estimate the total PAHs exposure since it reflects the contribution of several compounds. Urinary 3-hydroxybenzo(a)pyrene is the main metabolite of the only known carcinogenic PAHs, benzo(a)pyrene, however, it has been detected in very low levels in humans (Fan et al., 2012; Miller et al., 2010). Low detection rates of this high molecular weight biomarker have been attributed to the complex biological metabolic process that culminates in its elimination mostly through faeces (Likhachev et al., 1992). 1-Hydroxypyrene (1OHPy), the major metabolite of pyrene, is one of the most abundant PAHs in different matrices (air, food, etc.; Cirillo et al., 2006; Gomes et al., 2013; Slezakova et al., 2009, 2014; Oliveira et al., 2017a, 2017b). 1OHPy is known as the urinary PAH biomarker of exposure

and, thus, it was analysed in all the reported studies (Table 3) except in one (Orjuela et al., 2012). A total of 69% of the available studies considered 1OHPy, solely, as the biomarker of exposure to PAHs. Children urinary concentrations of 1OHPy ranged between 0.018 and 4.82 (median of 0.186) μmol/mol creatinine and from 155 to 4500 (median of 3167) ng/L (Table 3). American children presented median urinary 1OHPy levels that were, respectively, ca. six and two times higher than the median levels reported for European (0.45 versus 0.07 μmol/mol creatinine; $p \leq 0.001$) and Asian (0.45 versus 0.18 μmol/mol creatinine; $p = 0.005$) children (Fig. 8). Asian children presented concentrations that were two times higher than those found in European children (0.18 versus 0.07 μmol/mol creatinine; $p = 0.005$; Fig. 8). There are no reference guidelines available for urinary PAH metabolites; only a benchmark level of 0.24 μmol 1OHPy/mol creatinine was proposed for non-smoking and non-occupationally exposed people (Jongeneelen, 2001). All the studies concerning American children were performed in Mexican communities and the reported 1OHPy urinary concentrations largely exceeded (up to twenty times) the proposed benchmark level (Table 3); 95% of children living in Chiapas state (Mexico) presented urinary levels of 1OHPy above that proposed guideline (Domínguez-Cortinas et al., 2013). Therefore, the highest levels of urinary 1OHPy were found in Mexican children from rural and indigenous communities with agriculture activity that used biomass combustion as principal energy source for cooking and heating home (Domínguez-Cortinas et al., 2013; Jasso-Pineda et al., 2015; Martínez-Salinas et al., 2010; Pérez-Maldonado et al., 2014). Data from the literature also revealed that some Asian children presented urinary 1OHPy levels that were 2–4 times higher than the proposed reference value (Table 3); exceedances were observed in Chinese (6–7 years) and Iranian (9–12 years) children attending kindergartens and primary schools (Fan et al., 2012; Shahsavani et al., 2017; Yu et al., 2016). Higher levels were also reported in rural Thai children, principally during a smoke-haze episode caused by biomass burning (Naksen et al., 2017). Some authors have demonstrated that 1OHPy is the metabolite that contributes less for ΣOH-PAHs (Fan et al., 2012; Liu et al., 2017; Miller et al., 2010; Oliveira et al., 2017a; Trasande et al., 2015). Since pyrene is one of the most abundant PAHs in different matrices, its lower contribution to urinary ΣOH-PAHs is directly associated with its biological process of metabolization in the human body and with the higher molecular weight of pyrene comparatively with lighter PAH congeners (Li et al., 2012). Therefore, the inclusion of other, i.e., lighter metabolites is crucial to better estimate PAHs total exposure. Urinary hydroxynaphthalenes, 1- and 2-hydroxylnaphthalene, are the major metabolites of naphthalene (Li et al., 2012). These biomarkers have been described as the metabolites that contribute the most for PAHs total internal dose, accounting with 51–91% of ΣOH-PAHs in schoolchildren, followed by hydroxyfluorenes and hydroxyphenanthrenes (Table 3). Studies that simultaneously assessed children environmental exposure to PAHs at school environments and the urinary levels of PAH metabolites are limited (Alghamdi et al., 2015; Alvarado-Cruz et al., 2017; Hu et al., 2011; Oliveira et al., 2017a; Ruchirawat et al., 2007; Trasande et al., 2015; Tuntawiroon et al., 2007) with scarce information for other metabolites than 1OHPy (Alghamdi et al., 2015; Oliveira et al., 2017a; Trasande et al., 2015). Oliveira et al. (2017a) observed a similar distribution profile between the levels of PAHs in the total (PM + gas) indoor air of Portuguese kindergartens and the urinary levels of PAH metabolites in preschool children (3–5 years). Hu et al. (2011) reported higher concentrations of pyrene in ambient total air (PM + gas) and urinary 1OHPy levels in children (5–12 years) living in Chinese communities located in close vicinity to a power plant comparatively with those living at > 5 km away from the power plant. Additionally, children attending schools situated near industrial complex areas as well as in the proximity of urban zones, which are strongly affected by traffic emissions, are regularly exposed to higher concentrations of airborne PAHs and presented elevated levels of urinary 1OHPy comparatively with schoolchildren from rural communities (Fan et al., 2012; Ruchirawat et al., 2007; Trasande et al., 2015; Tuntawiroon et al., 2007). Moreover, pyrene and phenanthrene increments of 1 ng/m^3 in the outdoor total air of schools were directly associated with increases of 3.5 and 1.0% of schoolchildren (10–12 years) urinary levels of 1OHPy and total hydroxyphenanthrenes, respectively (Alghamdi et al., 2015). Positive associations were also found between naphthalene and acenaphthene concentrations in the indoor air of kindergartens with children urinary concentrations of 1-hydroxynaphthalene and 1-hydroxyacenaphthene (Oliveira et al., 2017a). Therefore, exposure to PAHs at school environments seems to have a strong contribution to children urinary levels of PAH biomarkers. Additionally, the potential health risks associated with the exposure to PM and/or PAHs cannot be considered separately but together since synergetic and cumulative effects may occur. In that regard, Bae et al. (2010) found evidences of a synergistic effect of exposure to high levels of PM, PAH and oxidative stress in Chinese and Korean schoolchildren (9–12 years). The concentrations of urinary hydroxynaphthalenes in 5 years old children were positively associated with the occurrence and frequency of chromosomal aberrations, which are established markers of cancer risks in humans (Orjuela et al., 2012). A more recent study (Wang et al., 2017a) found that 1OHPy concentrations were positively related with the levels of immunoglobulin E and 8-hydroxy-2′-deoxyguanosine, which is one biomarker of oxidative stress. Thus, children exposure to PAHs was associated with the aggravation of asthma symptoms (Wang et al., 2017a). Jasso-Pineda et al. (2015) detected higher DNA damage levels in the blood cells of Mexican children that were heavily exposed to chemical mixtures, including PAHs and pesticides; significant correlations between urinary 1OHPy and DNA damage were reported. Wenten et al. (2009) evaluated the occurrence of incident respiratory-related school absence records and DNA damage in elementary schoolchildren and found that glutathione S-transferases, particularly the GSTP1 haplotype, were associated with respiratory-related school absences. Some works (Peluso et al., 2013; Rusconi et al., 2011) have been conducted in children attending schools at Sarroch (Sardinia Island - Italy), a place where one of the world's largest power plants and the second largest European oil refinery and petrochemical park is located. Rusconi et al. (2011) found that children living in Sarroch showed an increased prevalence in wheezing symptoms, bronchial inflammation and in MDA–deoxyguanosine adducts of 83%, and a decrease in lung function comparatively with children living in a background area. Two years later, Peluso et al. (2013) conducted a cross-sectional study to evaluate the prevalence of MDA–deoxyguanosine adducts in the nasal epithelium of children (6–14 years) attending primary and secondary schools and reported higher levels of MDA–deoxyguanosine adducts in children from Sarroch. Tuntawiroon et al. (2007) reported significantly higher levels of carcinogen-DNA adduct in the peripheral lymphocytes of schoolchildren from Bangkok than in those from provincial areas. Furthermore, DNA strand breaks were significantly higher, while the DNA repair capacity [which is inversely correlated with the number of dicentric chromosomes or chromosomal breaks (deletions) per metaphase] was lower in schoolchildren from Bangkok (Tuntawiroon et al., 2007). Some genetic polymorphisms have also been detected in glutathione-*S*-transferases and cytochrome P450 enzymes involved in the metabolism of PAHs (Ruchirawat et al., 2007).

5. Final remarks and future perspectives

Data from the available studies revealed the strong contribution that IAQ of schools have on children total exposure to PM and PAHs and on the respective potential health risks. Authors are aware that data retrieved from the available works varied in geographical location and may not represent the exposure levels of a specific country or an entire continent. Additionally, different fractions of PM as well as different periods of air sampling and different measurement methodologies, and/or temporal coverage were considered, which may have introduced a

high variability to the global data comparison. However, it is believed that, despite all the limitations, this approach contributes to deeper the knowledge on schoolchildren environmental exposure to PM and PAH at schools, with the characterization of exposure levels among different countries, the identification of major local sources, and the assessment of children total exposure to PAHs. Available data indicated that Asian children have been exposed to higher levels of PM and PAHs at school environments, with increased values of total TEF and total TR and higher urinary levels of total PAH metabolites. Therefore, the available data suggest that Asian children are at a higher risk to suffer from the burden of diseases that can be promoted and aggravated by the exposure to PM and PAHs. Despite the limited number of studies, consistent evidences also proved that environmental monitoring of PAHs should include both gas and PM phases. The use of PM-bound benzo(a) pyrene as the only marker of exposure to carcinogenic PAHs may not be enough. There is a clear need: i) to revise the established international guideline by including other health-relevant PAHs (possible/probable carcinogens) rather than only benzo(a)pyrene and ii) to define airborne guidelines for PAHs in the gas phase (with particular attention for naphthalene) and in the smallest fractions of PM ($PM_{2.5}$ and PM_1). There are enough evidences that children attending schools from urban areas are exposed to higher concentrations of airborne PM and PAHs, being the urinary levels of PAH metabolites also increased. Children attending schools at urban and polluted areas also presented early markers of genotoxic damage and a lower capacity to repair DNA, leading to the higher prevalence of chromosomal aberrations and deletions in comparison with schoolchildren from rural, i.e., less urbanized areas. However, the mechanisms by which environmental exposure to PM and PAHs might promote and aggravate children cardiorespiratory diseases and increase their predisposition to develop cancer later in life remain unknown. Therefore, there is a need to implement strategies that may contribute to pollution mitigation and prevention and to provide healthier school environments for children. To achieve that, city planning at urban polluted areas should be rethought to reduce children exposures at schools and surrounding areas. The new schools should be constructed away from trafficked roads with materials, paints, and furniture with low emission profiles of volatile organic compounds; whenever possible, classrooms should face the calmest street around the school and greener areas should be created preferentially near children playground areas (Rivas et al., 2018; Miri et al., 2018). More attention should be given to optimization of classrooms' ventilation (natural and/or mechanical; automatic system for window opening based on IAQ sensors data, etc.). The development and installation inside classrooms of low cost and portable sensors for PM and the main carcinogenic compounds, combined with the installation of effective air filtration devices, would be highly relevant and would strongly contribute to improve air quality, especially at the schools located near highly trafficked freeways, refineries and other important sources of these pollutants. Moreover, portable monitors to measure air pollutants closer to or at the point of human contact have been emerging, which may help to increase the representativeness of the exposure data. Since exposure to PAHs is directly associated with environmental (indoor and outdoor) levels of PM, principally the smallest fractions, the synergistic effects of PM and PAHs on children's health should be addressed in future studies. Thus, to fully understand the health implications of PM and PAHs in children, more studies including both environmental monitoring and children biomonitoring are needed, principally in the less characterized geographical areas.

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Appendix A. Supplementary data

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