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Abstract: Particulate matter (PM) composition has a key role in a wide range of health outcomes, such as asthma, chronic obstructive pulmonary disease, lung cancer, cardiovascular disease, and death, among others. Because of its location and orography, Montcada i Reixac, a municipality located in the Barcelona metropolitan area (Catalonia, Spain), means an interesting case study to investigate air pollution. The area is also characterized by the presence of different industrial emission sources, including a cement factory and a large waste management plant, as well as an intense traffic. In this study, PM10 levels and trace elements, ions, and carbonaceous particles were determined for a long time period (2013-2016) in this highly polluted area. PM10 samples were collected during six consecutive days in two campaigns (cold and warm) per year. A number of elements (As, Ba, Be, Bi, Ca, Cd, Ce, Co, Cr, Cs, Cu, Dy, Er, Eu, Fe, Ga, Gd, Ge, Hf, Hg, Ho, K, La, Li, Hg, Mg, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Sn, Sr, Tb, Th, Ti, Tl, U, V, W, Y, Yb, and Zr), ions (Cl-, SO42-, NO3-, and NH4+), and carbonaceous content (total carbon, organic plus elemental carbon, and CO32-), were analysed. These data were used to identify the PM10 main components: mineral matter, sea spray, secondary inorganic aerosols, organic matter plus elemental carbon, trace elements or indeterminate fraction. Although a clear seasonality (cold vs. warm periods) was found, there were no differences between working days and weekends. However, some traffic-related elements (i.e., Co, Cr, Mn, and Sb) showed significantly higher concentrations in weekdays.

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February 7, 2018

Dear Prof. Domingo:

We are pleased to submit to your consideration for publication in **Environmental Research**, the manuscript entitled *Main components of PM10 in an area influenced by a cement plant in Catalonia, Spain: Seasonal and daily variations* (Rovira et al.).

We also state that out study does not include human subjects.

Hoping that you will find the manuscript interesting for the readers of **Environmental Research**, we look forward to hearing from you.

Sincerely,

Dr. Martí Nadal

HIGHLIGHTS

- Constituents and main components of airborne PM_{10} near a cement plant were studied.
- A clear seasonality was found, with higher levels in winter.
- A daily pattern was not observed, when comparing weekdays and weekends.
- Road traffic had a significant contribution to PM_{10} levels.

Main components of PM_{10} in an area influenced by a cement plant in Catalonia, Spain: Seasonal and daily variations

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ABSTRACT

Particulate matter (PM) composition has a key role in a wide range of health outcomes, such as asthma, chronic obstructive pulmonary disease, lung cancer, cardiovascular disease, and death, among others. Because of its location and orography, Montcada i Reixac, a municipality located in the Barcelona metropolitan area (Catalonia, Spain), means an interesting case study to investigate air pollution. The area is also characterized by the presence of different industrial emission sources, including a cement factory and a large waste management plant, as well as an intense traffic. In this study, PM_{10} levels and trace elements, ions, and carbonaceous particles were determined for a long time period (2013-2016) in this highly polluted area. PM_{10} samples were collected during six consecutive days in two campaigns (cold and warm) per year. A number of elements (As, Ba, Be, Bi, Ca, Cd, Ce, Co, Cr, Cs, Cu, Dy, Er, Eu, Fe, Ga, Gd, Ge, Hf, Hg, Ho, K, La, Li, Hg, Mg, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Sn, Sr, Tb, Th, Ti, Tl, U, V, W, Y, Yb, and Zr), ions (Cl^-, SO_4^{2-}, NO_3^-, and NH_4^+), and carbonaceous content (total carbon, organic plus elemental carbon, and CO_3^{2-}), were analysed. These data were used to identify the PM_{10} main components: mineral matter, sea spray, secondary inorganic aerosols, organic matter plus elemental carbon, trace elements or indeterminate fraction. Although a clear seasonality (cold vs. warm periods) was found, there were no differences between working days and weekends. However, some traffic-related elements (i.e., Co, Cr, Mn, and Sb) showed significantly higher concentrations in weekdays.

Keywords

PM_{10}, characterization, trace elements, ions, carbon, cement plant

1. Introduction

Nowadays, air pollution, especially in cities and metropolitan areas, is one of the most challenging problems that governments and local authorities must face. Road traffic, industrial activities (e.g., power plants, cement factories, waste incineration facilities, etc.) or the presence of harbours and airports, are pointed out as potentially important sources of air pollution in urban areas (Amato et al., 2016; Chen et al., 2017; Grigoratos and Martini, 2015; Kalaiarasan et al., 2016; Kholdebarin et al., 2015; Mateos et al., 2018; Pant et al., 2016; Sánchez-Soberón et al., 2015; Squizzato et al., 2017; Tao et al., 2017; Tolis et al., 2015; Wang et al., 2017). Among others, particulate matter below 10 μm of diameter (PM_{10}) is one of the pollutants that receive most of the attention. Particulate matter (PM) presents a wide variety of constituents, such as metals and trace elements, organic compounds, and acids (Cassee et al., 2013; Sánchez-Soberón et al., 2015, 2016). Not only PM composition, but also its size, depend on different parameters, such as weather, season of the year, and emission sources (Cassee et al., 2013). PM composition has a key role in a wide range of health effects, which include –but are not limited to– asthma, chronic obstructive pulmonary disease, lung cancer, cardiovascular disease, premature birth, low birth weight, and even death (Deepak and Devi, 2016; Ebisu et al., 2016; Falcon-Rodriguez et al., 2016; Franchini et al., 2016; Maleki et al., 2016; Morakinyo et al., 2016; Morales-Suárez-Varela et al., 2017; Wang et al., 2016).

Montcada i Reixac is a municipality (34,802 inhabitants in 2016) located in Catalonia (NE Spain). Since it is located in the metropolitan area of Barcelona (4,793,592 inhabitants in 2016), it means an interesting case study to investigate air pollution. The zone is also characterized by a particular orography, being located in a river basin flanked by hills. There is also a wide variety of industrial emissions sources, two dense highways (daily crossed by around 50,000 and 160,000 vehicles), a waste treatment facility which manages approximately 240,000 tons of organic waste/year (Vilavert et al., 2014), and a cement plant with an annual capacity of 900,000 tons of clinker (Rovira et al., 2016, 2011; Sánchez-Soberón et al., 2015). In addition, a municipal waste incinerator was operating in the zone until 2004, when it ceased to operate (Schuhmacher and Domingo, 2006). Altogether, this makes this zone an area of a special environmental interest, and

consequently, various studies and environmental surveys have been conducted in recent years (Abad et al., 2003; Domingo et al., 1999a, 1999b, 2000; Gallego et al., 2016; Meneses et al., 1999; Nadal et al., 2002, 2009; Rovira et al., 2016; Schuhmacher et al., 1997, 1998a, 1998b, 2006; Schuhmacher and Domingo, 2006; Vilavert et al., 2012, 2014). Despite these investigations, the inhabitants of Montcada i Reixac are still concerned regarding air quality and possible health outcomes.

In this study, PM_{10} levels, constituents (trace elements, ions, and carbon) and main components were studied for a long time in an area influenced by a cement plant in Montcada i Reixac. Seasonal and daily variations were also studied in detail. To the best of our knowledge, this is the first study facing in deep, and for a long period of time, the PM_{10} characterization in this complex area.

2. Materials and methods

2.1. Study area and sampling

Sampling points (41°28'11"N; 2°11'04"E) were located in "Can Sant Joan", a neighbourhood of Montcada i Reixac. The studied area is located in the Besòs river basin, with a cement plant situated at approximately 600 m from the sampling point and two highways nearby. Additional details on the area of study are available elsewhere (Rovira et al., 2011, 2016). A daily (between 0:00 am to 11:59 pm) PM_{10} sample was collected for 6 consecutive days, in two periods per year, between 2013 and 2016. Sampling campaigns were carried out in October and December of 2013, July and November of 2014, October and December of 2015, and July and December of 2016. Meteorological data during the sampling campaigns are summarized in Table 1. A high volume sampler MicroPNS HVS16 PM10 (MCZ, Bad Nauheim, Germany), which allows the sampling of daily PM_{10} levels with the reference method UNE EN 12341, was used. A volume around 1630 m^3 was collected for each sample in quartz microfiber filters (QFFs) of 150 mm of diameter, being previously heated at 200°C for 4 hours to remove any volatile organic compound. Before and after sampling, QFFs were acclimated at 25ºC and 40% relative humidity. Then, at the same conditions, they were weighed until the weight of each filter was stabilized.

2.2. Trace elements

A ¼ fraction of each QFF was digested with 2 mL of 65% nitric acid (Suprapur, E. Merck, Darmstadt, Germany) and 3 mL of hydrofluoric acid (37.5% Panreac, Barcelona, Spain) in a Teflon vessel for 8 hours at room temperature and 8 hours at 80°C. The digested solution was evaporated until dryness on a sand bath at 250ºC. The residue was dissolved in 2.5 mL of nitric acid and made up to 25 mL with ultrapure water. They were kept at -20°C until analysis (Mari et al., 2009).

The concentrations of aluminium (Al), arsenic (As), barium (Ba), beryllium (Be), bismuth (Bi), cadmium (Cd), cerium (Ce), cobalt (Co), chromium (Cr), caesium (Cs), copper (Cu), dysprosium (Dy), erbium (Er), europium (Eu), gallium (Ga), gadolinium (Gd), germanium (Ge), hafnium (Hf), holmium (Ho), lanthanum (La), lithium (Li) mercury (Hg), manganese (Mn), molybdenum (Mo), niobium (Nb), neodymium (Nd), nickel (Ni), lead (Pb), praseodymium (Pr), rubidium (Rb), antimony (Sb), scandium (Sc), selenium (Se), samarium (Sm), tin (Sn), strontium (Sr), terbium (Tb), thorium (Th), titanium (Ti), thallium (Tl), uranium (U), vanadium (V), tungsten (W), yttrium (Y), ytterbium (Yb) and zirconium (Zr), were determined by inductively coupled plasma mass spectrometry (ICP-MS, Perkin Elmer Elan 6000). Rhodium was used as internal standard. In turn, the levels of barium (Ba), calcium (Ca), iron (Fe), potassium (K), magnesium (Mg) and sodium (Na) were determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES, Perkin Elmer Optima 3200RL).

Detection limits were 0.01 ng/m^3 for Bi, Ce, Cs, Dy, Er, Eu, Gd, Ho, La, Nb, Nd, Pr, Sm, Ta, Tb, U, W, Y and Yb; 0.03 ng/m^3 for Cd, Pb, Tl, and Rb; 0.06 ng/m^3 for Co, Cu, Hf, Mn, Mo, Sn, Sr, Th and Zr; 0.13 ng/m^3 for As, Be, Hg, Li, Ni and Sb; 0.25 ng/m^3 for Ga; 0.31 ng/m^3 for Cr, Ge and V; 0.63 ng/m^3 for Se; 1.25 ng/m^3 for Sc; 3.13 ng/m^3 for Ba and Fe; 6.25 ng/m^3 for Ti and Zn; 15.6 ng/m^3 for Ca; 31.3 ng/m^3 for Al and Mg; 123 ng/m^3 for Na; and 156 ng/m^3 for K.

Quality control/quality assurance of the analytical process was carried out through the analysis of duplicate samples, blanks, and standards (Loamy clay, National Institute of Standards and Technology, LCS-4).

2.3. Ions

The soluble portion of another QFF piece was extracted with 15 mL of ultrapure water for 12 h of axial agitation, and 3 rounds of ultrasound at 60°C for 10 min. The resulting extract was filtered with a 0.47 μm membrane filter. For the analysis of Cl^-, SO_4^{2-} and NO_3^-, an ion chromatograph (Dionex D-300) was used, while the determination of ammonium (NH_4^+) was made by the reaction of Berthelot, whereby indofenol is formed and subsequently determined by spectrophotometry at a wavelength of 640 nm (Patton and Crouch, 1977). Detection limits were 0.002 $\mu g/m^3$ for Cl^-; 0.02 $\mu g/m^3$ for NO_3^-; 0.10 $\mu g/m^3$ for SO_4^{2-} and 0.008 $\mu g/m^3$ for NH_4^+.

2.4. Total (TC), organic (OC) and elemental (EC) carbon

For the analysis of total carbon (TC), a piece of filter (2.8 cm^2) was burnt through combustion with an oxygen atmosphere at a temperature of 1,000°C. The resulting gases (CO_2, SO_2 and NO_X), dragged by a stream of helium, were analysed by gas chromatography (Thermo EA 1108 CHNS-O Carlo Erba Instruments) (Tiessen and Moir, 2000a, 2000b). For the analysis of organic carbon (OC) plus elemental carbon (EC), a sample was previously digested in a HCl atmosphere to remove the carbon from carbonates (CC), being subsequently analysed with the same methodology used to determine TC. The detection limit was 0.01 $\mu g/m^3$. The OC was calculated from the ratio reported by Pérez et al. (2008), according to which, OC = 0.7 (OC + EC). For organic (OM) matter calculation, the level of OC was multiplied by a factor of 1.6 (Malm et al., 1994; Russell, 2003; Turpin and Lim, 2001).

2.5 Indirect determinations

The concentrations of carbonates (CO_3^{2-}) were determined indirectly from the stoichiometric ratio: $CO_3^{2-} = 1.5Ca + 2.5Mg$ (Querol et al., 2001). Similarly, silicon oxide (SiO_2) was calculated from the following stoichiometry: $2Al_2O_3 = SiO_2$ (Querol et al.,

2001). Levels of aluminium oxide (Al_2O_3) were calculated assuming that all the aluminium was present in oxide form (Querol et al., 2001).

PM was classified into 6 main components: 1) mineral matter (sum of CO_3^{2-}, SiO_2, Al_2O_3, Ti, P, Mn, Mg, K, Fe, and Ca), 2) sea spray (sum of Na and Cl^-), 3) organic matter and elemental carbon (OM+EC), 4) secondary inorganic aerosols (sum of SO_4^{2-}, NH_4^+, and NO_3^-), 5) trace elements (the sum of the remaining elements), and 6) indeterminate (the difference between PM concentrations and the sum of the other main components) (Sánchez-Soberón et al., 2015).

2.7. Statistics

For the statistical analysis, values below the detection limit (LD) were assumed to be equal to one-half of that limit (ND = ½ LD). Statistical significance was established using firstly the Levene test to establish whether data showed a parametric distribution. Subsequently, the ANOVA or Kruskal-Wallis tests were applied. A difference was considered as statistically significant when the probability was lower than 0.05 ($p<0.05$).

3. Results and discussion

3.1. Elements, carbon, ions and indirect determinations

PM_{10} levels in each sampling campaign are depicted in Fig. 1. PM_{10} concentration showed a mean value of 30 μg/m^3, ranging from 14 to 65 μg/m^3. The 5th, 25th, 75th and 95th percentiles were 17, 20, 36, and 63 μg/m^3, respectively. Significantly higher levels were found in December 2013, December 2015 and December 2016 than those noted in July 2014, December 2014 and October 2015. Periods with greater values were anticyclone episodes, typical of winter in Mediterranean areas. In general terms, statistically similar (p=0.810) PM_{10} levels were found between July (23 μg/m^3) and October campaigns (23 μg/m^3), both presenting concentrations significantly lower (p<0.001) than those in December (38 μg/m^3). PM_{10} levels were similar (p=0.450) irrespective of the day of sampling, being mean levels 31 and 29 μg/m^3 in working days and weekends, respectively.

The daily (24 h) PM_{10} limit, which can be only exceeded 35 times a year and set at 50 $\mu g/m^3$ (European Union Parlament and Council, 2008), was overpassed in 2 of the 6 samples analysed in December 2013, and 1 of 6, in December 2015. According to the Catalan air quality network (Generalitat de Catalunya, 2017), PM_{10} mean annual levels in this same location were: 25 $\mu g/m^3$ in 2013 and 2016, and 28 $\mu g/m^3$ in 2014 and 2015, overpassing 6, 11, 8 and 4 times the daily threshold limit (50 $\mu g/m^3$) during 2013, 2014, 2015 and 2016, respectively.

The concentrations of trace elements in PM_{10} samples collected from 2013 to 2016 are shown in Table 2. Sodium (2,684 ng/m^3), Ca (1,495 ng/m^3), K (783 ng/m^3), Fe (641 ng/m^3) and Al (537 ng/m^3) were the elements with the greatest concentrations. Contrastingly, Be, Ge, Hg, Ho, Se and Tb were below their respective detection limits in most of the samples. In general terms, higher levels were found in the surveys of December and October than in July, with a few exceptions (i.e., Cd, Li, Sc and Se). Clear seasonal trends were observed for Cu, Pb, Sb and Sn, all of them presenting statistically significant differences among campaigns (July < October < December). Twenty elements (Al, As, Bi, Ca, Cr, Cu, Er, Hf, La, Nb, Pb, Sb, Sm, Sn, Th, U, W, Y, Yb and Zr) showed significantly different concentrations of PM_{10} between July and October campaigns ($p<0.05$). Moreover, significant differences between July and December were observed for As, Bi, Ca, Ce, Cr, Cs, Cu, Fe, K, Mo, Nb, Ni, Pb, Rb, Sb, Sn, Tl, U and W ($p<0.05$). Finally, only for a few elements (namely, Cu, Fe, Pb, Sb, and Sn) the difference in PM_{10} levels between October and December campaigns reached a level of statistical significance ($p<0.05$).

A specific analysis of daily trends in PM_{10} levels was conducted, with only a few elements presenting significantly different concentrations when comparing working days and weekends: Co (0.35 vs. 0.20 ng/m^3), Cr (6.16 vs. 3.61 ng/m^3), Mn (12.8 vs. 7.89 ng/m^3), and Sb (3.94 vs. 2.64 ng/m^3). Since the activity of the cement plant is continuous throughout the week, the main difference between weekdays and weekends is the reduction of road traffic in the highways crossing the area. In addition, all these elements (Co, Cr, Mn, and Sb) have been related to road traffic emissions according to data from the scientific literature, being linked to wear brakes, brake linings, tyres, fossil fuels and lubricants combustion, and/or engine abrasion (Bosco et al., 2005; Ogunbileje et al., 2013; Saradhi et al., 2014; Schauer et al., 2006; Taiwo et al., 2014; Golokhvast et al., 2015;

Valotto et al., 2015; Wawer et al., 2015; Yu et al., 2014). Therefore, the PM content of Co, Cr, Mn and Sb might be a good surrogate to study the contribution of traffic in polluted areas with similar characteristics to our case study. Furthermore, the potential contribution of other emission sources cannot be disregarded, as some of these elements (Co, Cr, and Mn) may be also related to mineral fraction or cement dust (Gupta et al., 2012; Saradhi et al., 2014; Valotto et al., 2015).

The levels of total carbon (TC), organic plus elemental carbon (OC+EC), carbonates (CO_3^{2-}) and ions (Cl^-, SO_4^{2-}, NH_4^+ and NO_3^-), as well as indirect determinations (OM, SiO_2, and Al_2O_3) calculated in the eight sampling campaigns between 2013 and 2016, are summarized in Table 3. The carbonaceous content (TC, OC+EC and OM) of PM_{10} samples showed a strong seasonal pattern (December>October>July), with significant differences among sampling campaigns. In contrast, no significant differences in carbonaceous content (TC, OC+EC and OM) were noted between working days and weekends. Regarding carbonates (CO_3^{2-}), levels in July were significantly lower ($p<0.05$) than in December and October. By contrast, ions (Cl^-, SO_4^{2-}, NH_4^+ and NO_3^-) did not show notable differences among campaigns, with the only exception of NH_4^+, whose values were significantly higher in December ($p<0.05$). Like PM_{10} concentrations, the levels of ions (Cl^-, SO_4^{2-}, NH_4^+ and NO_3^-) were not significantly different when comparing weekdays and weekends.

Pearson's correlations were calculated for all trace elements, ions, total carbon and PM_{10} total concentrations (Supplementary Information, Fig. S1). PM_{10} showed high Pearson's coefficients with TC (0.925; R^2=0.855), Sn (0.844; R^2=0.713) and Sb (0.793; R^2=0.628), all of them at $p<0.001$. In addition, TC was highly and positively correlated ($p<0.001$) with OC+EC (0.986; R^2=0.972), as well as with a number of elements: Sn (0.855; R^2=.783), Sb (0.843; R^2=0.711), Pb (0.780; R^2=0.609), Cu (0.764; R^2=0.583), Cr (0.709; R^2=0.503), and Fe (0.687; R^2=0.472). As above commented, all these elements are related to road traffic emissions (e.g., brake wear, fuel combustion, tyre), a fact that points out traffic as one of the main contributors to Total Carbon (TC) content in PM.

3.2. PM_{10} main components

PM_{10} main components in air samples collected around the cement plant, according to the sampling period and season, are depicted in Fig. 2 and 3, as well as in Supplementary Information (Fig. S2). The percentage of mineral matter decreased from 28-39% in 2013 to 8-16% during the period 2014-2016. In July, the levels of mineral matter (2.31 $\mu g/m^3$) were significantly lower than those registered in October (5.41 $\mu g/m^3$) and December (7.89 $\mu g/m^3$) campaigns. Sea spray, with a mean overall contribution of 5% (range: 1-10%) did not show significant differences in concentrations between sampling periods (1.46, 1.74, and 1.32 $\mu g/m^3$ in July, October and December, respectively). The relative contribution of sea spray was lower in the December (3%) campaigns than in the October (8%) and July (6%) surveys. Regarding the OM+EC fraction, significant differences were observed among sampling months, with a profile inversely proportional to ambient temperature (17.5, 8.61 and 4.34 $\mu g/m^3$ in December, October and July, respectively). The relative contribution of OM+EC fraction showed the same trends, with significant differences according to the season (46%, 37% and 19% in December, October and July, respectively). These results are in agreement with the presence of more combustion processes and less dispersion of pollutants during cold seasons. Similarly, the concentrations of secondary inorganic aerosols (4.35, 4.07, and 4.99 $\mu g/m^3$ in July, October and December) were not significantly different among campaigns. However, a significantly higher relative contribution was noted in July (19%) than in December (15%). Finally, for the trace elements fraction, a significant increase of levels was noted in parallel with the decrease of the ambient temperature (0.05, 0.09, 0.13 $\mu g/m^3$, in July, October and December, respectively). Trace elements owned a relative contribution of 0.2% in July campaigns, and 0.4% in October and December surveys. When comparing weekdays and weekends, no significant differences were noted in the levels of main PM components, with the only exception of secondary inorganic aerosols, whose relative contribution was 14% and 16% in weekdays and weekends, respectively. However, despite the relative contribution was different, total levels of secondary inorganic aerosols did not show significant differences between working days (4.46 $\mu g/m^3$) and weekends (4.85 $\mu g/m^3$).

The dendrogram (Supplementary Information Fig. S2) with all the data set showed two main groups. The first one was mainly formed by samples obtained in anticyclone periods (December 2013, 2015 and 2016), while the other included the rest of sampling

periods. In turn, the anticyclone group was divided in two sub-groups: 1) December 2013, and 2) December 2015 and December 2016. Similarly, the second main group was also divided in two subgroups: 1) warm season campaigns (July 2014 and 2016), and 2) colder surveys (October 2013 and 2015, and December 2014). The same classification was obtained after applying a principal component analysis (PCA), whose plots explained 81.1% of the data variance in a 3-D model (Fig. 4). Cold periods (December campaigns) were characterized by high scores of OM+EC and trace elements due to combustion process, while July campaigns (especially in 2014) showed a great score of sea spray and indeterminate component. An explanation could be the difference in wind regimes according to the season, as winds blowing from the sea are increased in summer in this Mediterranean area. In addition, both 2013 campaigns had high scores of mineral matter.

4. Conclusions

In the current study, the main PM_{10} components of samples collected near a cement plant were investigated. The concentrations of a number of trace elements, ions, and carbonaceous fraction content were analysed. Some parameters, including PM_{10} levels and main components, showed significant differences among sampling campaigns. Most of them were related to seasonal patterns (cold vs. warm periods), likely due to differences in emission sources and meteorological conditions. Higher levels of PM_{10} and its components were detected in the samplings conducted in December, when the area is affected by anticyclone episode conditions. Contrastingly, PM_{10} levels and most of its components were lower during summer (July campaigns) or in rainy periods (December of 2014 and October of 2016). Despite the area is subjected to an important industrial activity, traffic might have a significant contribution on the surrounding environment, given the strong correlation among PM_{10} levels, TC and several traffic-related trace elements (e.g., Sn, Sb, Cu, Cr, and Fe). Although no significant differences in PM_{10} main components were noted between weekdays and weekends, the levels of some traffic-related elements (e.g., Co, Cr, Mn, and Sb) were decreased in the weekend. To the best of our knowledge, this is the longest PM_{10} characterization survey in an area concurrently influenced by a cement plant and traffic.

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Appendix. Supplementary material

Supplementary data associated with this article can be found in the online version.

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Table 1

Meteorological conditions in each sampling campaign.

Period	Mean Temperature (ºC)	Minimum Temperature (ºC)	Maximum Temperature (ºC)	Rainfall during sampling (mm)	Rainfall the week before sampling (mm)	Relative humidity (%)
October 2013	21.0	17.6	25.2	0.0	3.0	76
December 2013	9.7	3.7	15.5	0.0	0.0	70
July 2014	22.8	15.8	31.4	0.0	0.8	65
December 2014	6.7	0.5	15.1	0.3	34.3	65
October 2015	18.1	9.5	27.8	7.9	46.8	67
December 2015	10.5	3.4	16.4	0.3	0.0	79
July 2016	24.2	17.6	30.7	0.0	1.4	56
December 2016	8.0	-0.3	17.0	0.0	2.1	75

Table 2

Levels of trace elements (ng/m^3) in PM_{10} samples collected near a cement plant in 8 campaigns performed between 2013 and 2016.

	Oct 2013 *n=6*	Dec 2013 *n=6*	Jul 2014 *n=6*	Dec 2014 *n=6*	Oct 2015 *n=6*	Dec 2015 *n=6*	Jul 2016 *n=6*	Dec 2016 *n=5*
Al	624 ± 114	2.596 ± 539	91.0 ± 48.1	134 ± 98.0	186 ± 82.3	201 ± 71.5	261 ± 135	140 ± 113
As	0.63 ± 0.09	0.52 ± 0.15	0.19 ± 0.07	0.40 ± 0.15	0.33 ± 0.12	0.69 ± 0.16	0.19 ± 0.08	0.33 ± 0.10
Ba	ND	ND	8.39 ± 4.39	15.4 ± 10.7	19.3 ± 1.46	35.2 ± 9.82	17.9 ± 12.0	26.0 ± 7.81
Be	0.08 ± 0.03	ND	ND	ND	ND	ND	ND	ND
Bi	1.59 ± 0.50	3.97 ± 2.06	0.24 ± 0.16	0.36 ± 0.34	0.47 ± 0.22	0.72 ± 0.46	0.62 ± 0.54	1.64 ± 1.01
Ca	2686 ± 825	4.744±1.076	391 ± 142	867 ± 608	767 ± 81.3	1150 ± 373	612 ± 234	596 ± 199
Ce	1.29 ± 0.48	0.68 ± 0.24	ND	0.21 ± 0.13	0.49 ± 0.93	1.76 ± 2.18	0.05 ± 0.03	0.39 ± 0.07
Cd	0.68 ± 0.35	2.12 ± 0.76	0.19 ± 0.09	0.33 ± 0.08	0.27 ± 0.06	0.44 ± 0.12	0.54 ± 0.22	0.44 ± 0.12
Co	0.27 ± 0.09	0.45 ± 0.27	0.15 ± 0.02	0.12 ± 0.07	0.18 ± 0.05	0.54 ± 0.35	0.33 ± 0.09	0.37 ± 0.22
Cr	6.26 ± 1.23	8.48 ± 3.07	3.26 ± 0.53	3.35 ± 2.79	3.82 ± 2.14	8.06 ± 3.62	3.73 ± 1.34	7.31 ± 4.46
Cs	0.09 ± 0.06	0.12 ± 0.04	0.02 ± 0.01	0.04 ± 0.03	0.03 ± 0.01	0.05 ± 0.01	0.04 ± 0.02	0.03 ± 0.01
Cu	42.6 ± 9.50	41.4 ± 18.2	9.62 ± 14.8	22.2 ± 16.3	18.9 ± 3.76	38.8 ± 8.6	16.7 ± 6.06	58.7 ± 20.6
Dy	0.06 ± 0.02	0.15 ± 0.04	0.02 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0.01 ± 0.01
Er	0.05 ± 0.02	0.11 ± 0.03	0.01 ± 0.01	ND	0.01 ± 0.01	0.01 ± 0	0.01 ± 0.00	0.01 ± 0.00
Eu	0.10 ± 0.05	0.42 ± 0.11	ND	ND	ND	0.01 ± 0.01	0.01 ± 0.00	0.01 ± 0.00
Fe	407 ± 103	627 ± 197	313 ± 84.2	516 ± 285	518 ± 84.3	1250 ± 266	628 ± 209	912 ± 367
Ga	ND	ND	0.89 ± 0.21	0.35 ± 0.28	0.58 ± 0.05	1.28 ± 0.31	0.26 ± 0.20	0.47 ± 0.16
Gd	0.21 ± 0.07	0.29 ± 0.07	0.02 ± 0.01	0.01 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.01 ± 0.01	0.01 ± 0.01
Ge	ND	ND	ND	ND	ND	0.19 ± 0.08	ND	ND
Hf	0.30 ± 0.11	0.71 ± 0.10	ND	0.08 ± 0.05	0.05 ± 0.03	0.10 ± 0.04	0.08 ± 0.13	0.04 ± 0.02
Hg	ND	ND	ND	ND	ND	0.08 ± 0.03	ND	ND
Ho	0.01 ± 0.01	0.03 ± 0.01	ND	ND	ND	ND	ND	ND
K	1600 ± 662	3093 ± 871	309 ± 202	ND	186 ± 80.2	478 ± 63.1	188 ± 85.0	216 ± 139
La	0.47 ± 0.17	1.04 ± 0.22	0.15 ± 0.04	0.10 ± 0.03	0.18 ± 0.07	0.24 ± 0.04	0.16 ± 0.09	0.11 ± 0.02
Li	0.64 ± 0.31	0.84 ± 0.28	0.29 ± 0.07	0.21 ± 0.09	0.29 ± 0.19	ND	0.68 ± 0.36	0.3 ± 0.09
Mg	56.2 ± 51.3	85.6 ± 26.0	32.1 ± 42.5	ND	ND	ND	48.8 ± 30.8	105 ± 25.1
Mn	6.98 ± 3.95	6.87 ± 3.33	7.85 ± 2.30	9.83 ± 5.34	9.47 ± 2.22	22.8 ± 6.84	10.7 ± 3.31	15.1 ± 7.00
Mo	1.06 ± 0.23	2.04 ± 0.61	2.39 ± 0.35	0.92 ± 0.48	1.92 ± 0.26	2.88 ± 0.99	0.10 ± 0.16	0.96 ± 0.65
Na	904 ± 473	1494 ± 450	ND	62.2 ± 14.5	1371 ± 388	905 ± 196	779 ± 514	700 ± 535
Nb	0.25 ± 0.04	0.89 ± 0.19	ND	0.09 ± 0.05	0.06 ± 0.04	0.07 ± 0.04	0.04 ± 0.02	ND
Nd	0.36 ± 0.15	14.95 ± 4.51	0.11 ± 0.03	0.04 ± 0.02	0.10 ± 0.04	0.13 ± 0.04	0.12 ± 0.07	0.05 ± 0.02
Ni	4.07 ± 0.91	6.96 ± 2.42	ND	2.14 ± 1.16	4.01 ± 0.88	7.31 ± 2.04	4.89 ± 1.00	5.57 ± 4.02
Pb	11.9 ± 3.20	16.8 ± 3.04	3.16 ± 1.62	10.8 ± 5.66	8.36 ± 4.14	17.6 ± 3.49	4.60 ± 1.52	17.8 ± 6.56
Pr	0.10 ± 0.04	0.24 ± 0.06	0.03 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.01	0.03 ± 0.02	0.01 ± 0.01
Rb	3.55 ± 1.57	4.90 ± 1.23	0.51 ± 0.13	0.65 ± 0.20	0.46 ± 0.13	0.79 ± 0.08	0.86 ± 0.34	0.70 ± 0.17
Sb	3.88 ± 0.90	5.76 ± 1.94	1.62 ± 0.59	2.63 ± 2.13	2.44 ± 0.67	5.83 ± 1.92	1.60 ± 0.89	4.38 ± 1.92
Sc	2.03 ± 2.30	2.69 ± 1.15	2.56 ± 1.71	1.90 ± 1.04	1.03 ± 1.02	ND	0.93 ± 2.27	0.06 ± 0.13
Se	ND	ND	ND	ND	ND	ND	ND	ND
Sm	0.08 ± 0.03	0.18 ± 0.04	0.02 ± 0.01	ND	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.01 ± 0.01
Sn	4.32 ± 1.42	8.05 ± 2.38	1.86 ± 0.74	4.09 ± 2.82	4.36 ± 0.88	7.81 ± 1.84	3.57 ± 1.63	6.97 ± 2.28
Sr	7.52 ± 4.37	21.2 ± 3.67	3.03 ± 0.12	2.57 ± 1.14	2.61 ± 0.50	2.70 ± 0.48	4.77 ± 1.63	2.59 ± 0.51
Ta	0.05 ± 0.01	0.25 ± 0.35	ND	ND	0.07 ± 0.15	0.01 ± 0.02	ND	ND
Tb	0.01 ± 0.01	0.03 ± 0.01	ND	ND	ND	ND	ND	ND
Th	0.15 ± 0.04	0.33 ± 0.10	ND	ND	0.04 ± 0.03	0.03 ± 0.02	ND	ND
Ti	46.8 ± 14.4	70.9 ± 20.3	24.1 ± 8.12	21.5 ± 14.9	22.0 ± 5.93	32.6 ± 4.30	42.1 ± 16.3	29.7 ± 9.61
Tl	0.04 ± 0.04	0.07 ± 0.03	0.02 ± 0.00	0.02 ± 0.01	0.02 ± 0.02	0.06 ± 0.01	0.01 ± 0.01	0.04 ± 0.05
U	0.09 ± 0.02	0.15 ± 0.04	0.02 ± 0.00	0.05 ± 0.02	0.05 ± 0.01	0.04 ± 0.01	0.02 ± 0.01	0.02 ± 0.01
V	6.86 ± 3.02	23.5 ± 8.95	6.57 ± 3.79	6.09 ± 2.04	8.41 ± 3.47	16.4 ± 3.14	9.42 ± 1.35	5.40 ± 5.03
W	0.33 ± 0.34	0.61 ± 0.39	0.08 ± 0.03	0.10 ± 0.11	0.12 ± 0.07	3.36 ± 3.12	ND	0.55 ± 0.73
Y	0.24 ± 0.10	0.60 ± 0.17	0.10 ± 0.03	0.05 ± 0.03	0.06 ± 0.05	0.08 ± 0.02	0.02 ± 0.01	0.05 ± 0.08
Yb	0.03 ± 0.01	0.08 ± 0.02	ND	ND	ND	0.01 ± 0.00	ND	ND
Zr	10.4 ± 4.20	21.3 ± 3.72	2.60 ± 1.35	2.49 ± 1.56	3.87 ± 0.74	3.39 ± 1.17	0.72 ± 0.50	0.90 ± 1.41

Levels in ng/m^3. Oct: October; Dec: December; Jul: July. ND: Not detected.

Table 3

Levels of Total Carbon (TC), organic plus elemental carbon (OC+EC), ions (Cl^-, SO_4^{2-}, NH_4^+ and NO_3^-) and indirect determinations (OM, CO_3^{2-}, SiO_2, and Al_2O_3) in PM_{10} collected in 8 sampling campaigns from 2013 to 2016.

	Oct 2013 n=6	**Dec 2013** n=6	**Jul 2014** n=6	**Dec 2014** n=6	**Oct 2015** n=6	**Dec 2015** n=6	**Jul 2016** n=6	**Dec 2016** n=5
TC	8.01 ± 1.10	17.5 ± 5.61	3.04 ± 0.47	8.00 ± 2.79	5.51 ± 0.90	17.4 ± 3.86	3.77 ± 0.80	13.9 ± 3.95
OC+EC	7.38 ± 1.34	13.9 ± 5.48	2.77 ± 0.43	6.24 ± 2.17	4.74 ± 0.85	16.2 ± 3.90	3.11 ± 0.60	13.2 ± 3.81
OM	8.27 ± 1.49	15.6 ± 6.14	3.10 ± 0.48	6.99 ± 2.44	5.40 ± 4.70	18.6 ± 4.38	3.74 ± 0.97	14.8 ± 4.26
CO_3^{2-}	2.19 ± 1.12	4.83 ± 1.06	0.42 ± 0.10	0.90 ± 0.60	0.77 ± 0.08	1.15 ± 0.37	0.66 ± 0.23	0.70 ± 0.22
SiO_2	0.34 ± 0.06	1.43 ± 0.30	0.07 ± 0.03	0.08 ± 0.05	0.11 ± 0.05	0.11 ± 0.04	0.13 ± 0.07	0.08 ± 0.06
Al_2O_3	1.18 ± 0.22	4.91 ± 1.02	0.23 ± 0.12	0.27 ± 0.16	0.37 ± 0.16	0.38 ± 0.14	0.46 ± 0.25	0.26 ± 0.21
Cl^-	0.69 ± 0.35	0.05 ± 0.03	0.34 ± 0.50	0.13 ± 0.03	0.51 ± 0.73	0.47 ± 0.14	0.33 ± 0.54	1.65 ± 0.71
SO_4^{2-}	2.48 ± 0.74	2.47 ± 0.42	2.16 ± 0.44	1.05 ± 0.09	0.95 ± 0.70	1.85 ± 0.84	1.63 ± 0.76	3.13 ± 0.98
NH_4^+	0.08 ± 0.07	0.24 ± 0.09	0.08 ± 0.08	0.09 ± 0.05	0.22 ± 0.26	0.62 ± 0.06	0.08 ± 0.04	0.15 ± 0.07
NO_3^-	3.31 ± 0.97	5.02 ± 1.29	0.85 ± 0.26	1.13 ± 0.43	1.09 ± 0.50	2.38 ± 0.62	3.92 ± 0.46	1.88 ± 0.24

Levels in $\mu g/m^3$. TC: Total carbon; OC+EC: organic carbon plus elemental carbon; OM: organic matter.
Oct: October; Dec: December: Jul :July

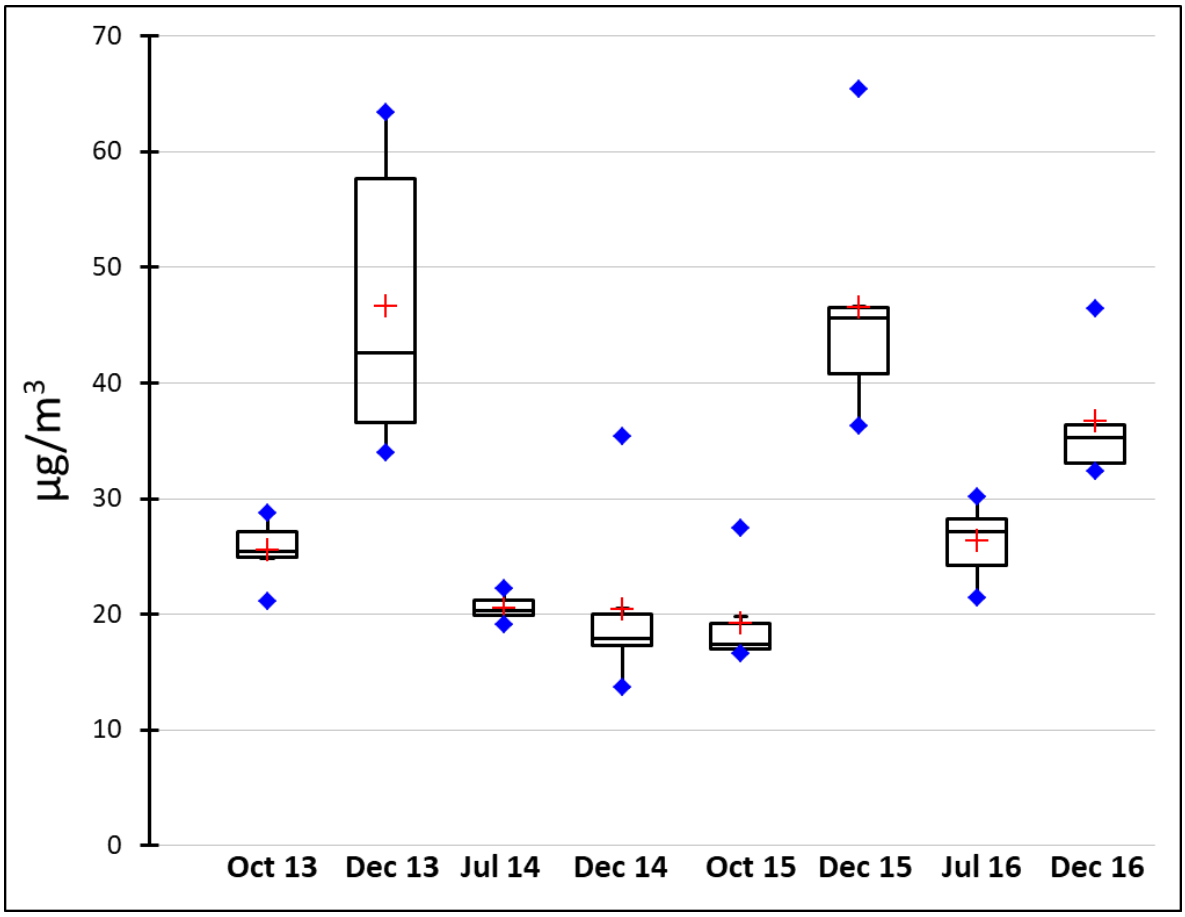

Fig. 1. Box-plot of PM_{10} levels ($\mu g/m^3$) in the eight campaigns performed from 2013 to 2016. Mean levels are marked with a red cross.

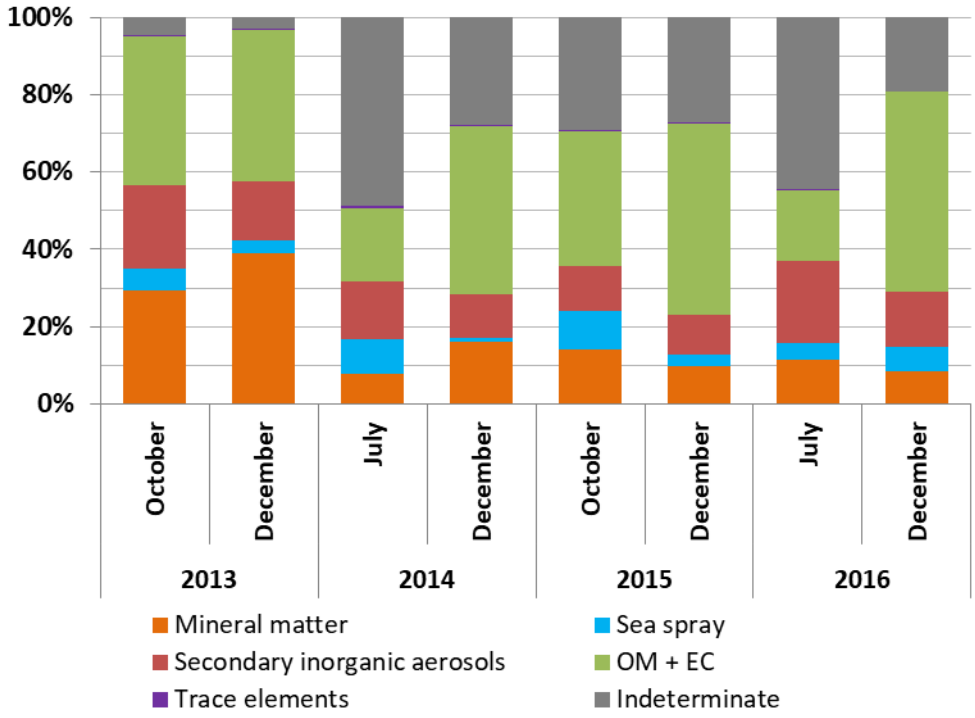

Fig. 2. PM_{10} principal components sampled during 2013 to 2016 near a cement plant.

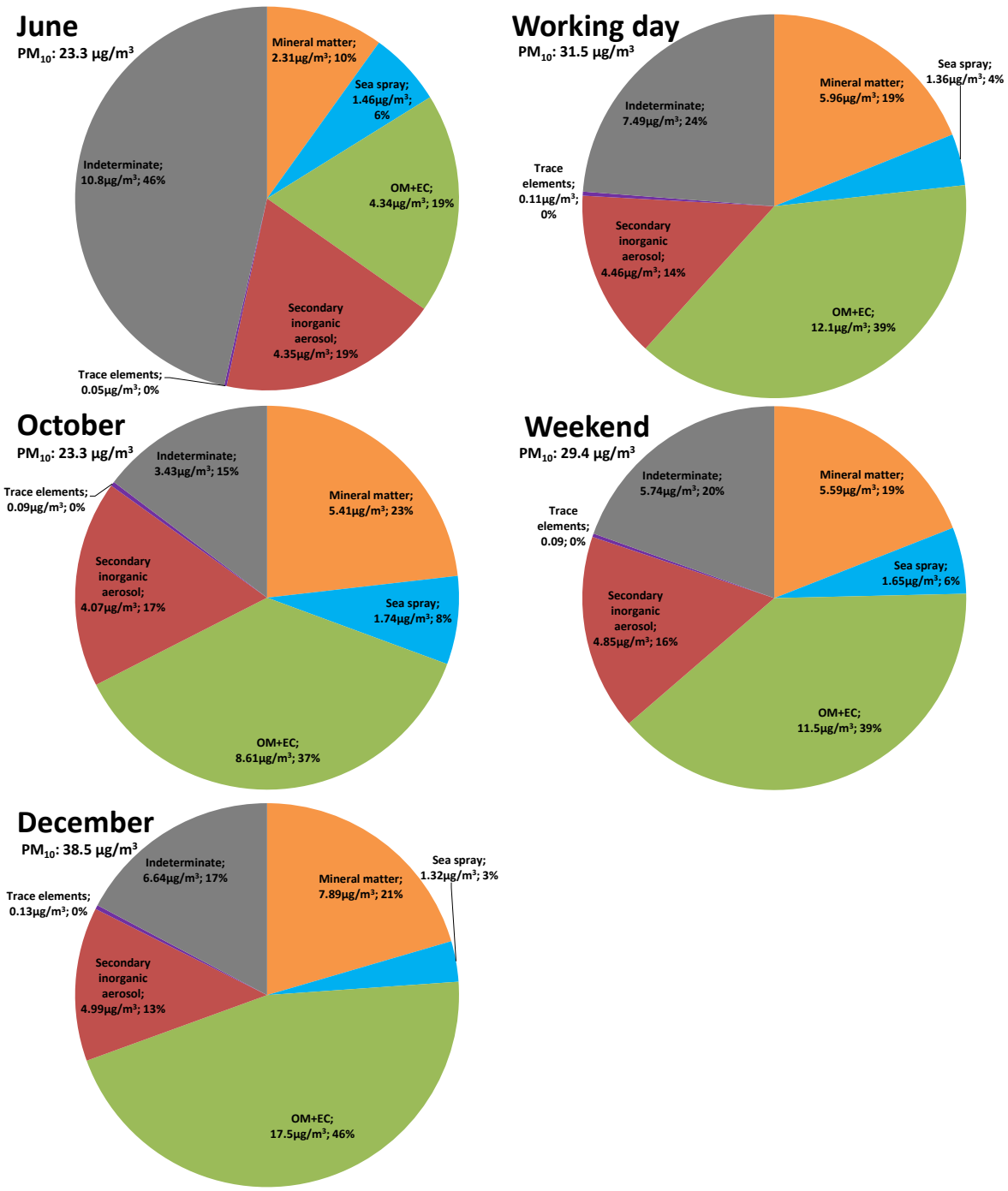

Fig. 3. PM_{10} main components in June, October, and December, and during working days and weekends.

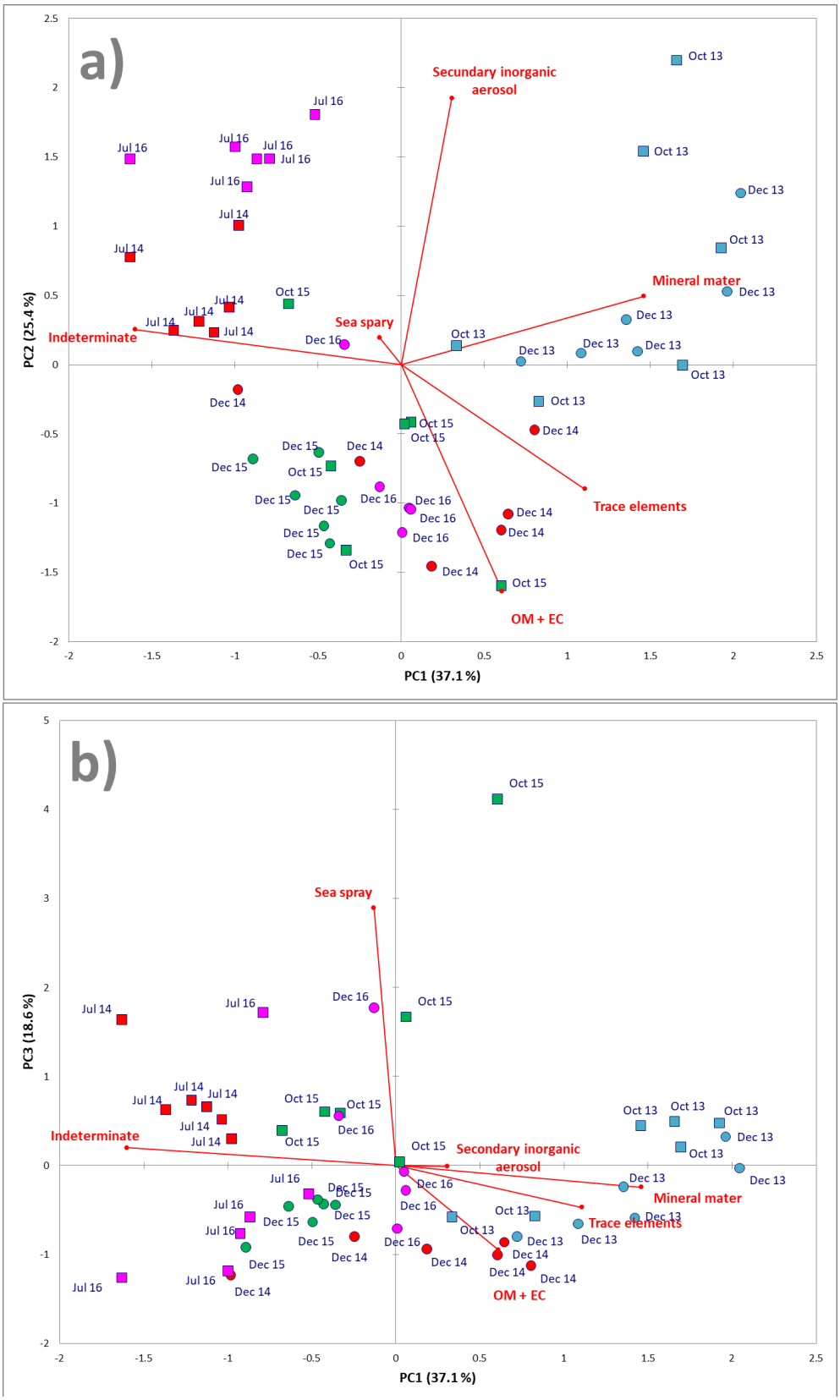

Fig. 4. Principal components analysis with main components of PM_{10} collected around a cement plant between 2013 and 2016.

Supplementary Material

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Abstract: Bisphenol A (BPA) and Di-(2-ethylhexyl) phthalate (DEHP) are two wide spread chemicals classified as endocrine disruptors (ED). The present study aims to estimate the non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP for a pregnant women cohort. In addition, to assess the prenatal exposure for the fetus, a physiologically based pharmacokinetic (PBPK) model was used. It was adapted for pregnancy in order to assess the internal dosimetry levels of EDs (BPA and DEHP) in the fetus. Estimates of exposure to BPA and DEHP from all pathways along with their relative importance were provided in order to establish which proportion of the total exposure came from diet and which came from non-dietary exposures. In this study, the different oral dosing scenarios (dietary and non-dietary) were considered keeping inhalation as a continuous exposure case. Total non-dietary mean values were 0.002 µg/kgbw/day (0.000; 0.004 µg/kgbw/day for 5th and 95th percentile, respectively) for BPA and 0.597 µg/kgbw/day (0.116 µg/kgbw/day and 1.506 µg/kgbw/day for 5th and 95th percentile, respectively) for DEHP. Indoor environments and especially dust ingestion were the main non-dietary contributors to the total exposure of BPA and DEHP with 60% and 81%. However, as expected, diet showed the higher contribution to total exposure with >99.9% for BPA and 63% for DEHP. Although diet was considered the primary source of exposure to BPA and phthalates, it must be taken into account that with non-dietary sources the first-pass metabolism is lacking, so these may be of equal or even higher toxicological relevance than dietary sources.
The present study is in the framework of "Health and environmental-wide associations based on large population surveys" (HEALS) project (FP7-603946).

Cover Letter

Dear Editor,

In the submitted manuscript titled " Pregnant women and prenatal exposure to BPA and DEHP through non-dietary routes: Dermal contact, non-dietary ingestion and inhalation exposure assessment in Reus (Catalonia, Spain) cohort", we present a pregnancy cohort study from Tarragona (Spain). This work is part of one major EU project, Health and Environment-wide Associations via Large population Surveys (HEALS). Presented work is part of ongoing biomonitoring study where we are performing a target cohort study of pregnant women to estimate prenatal and early exposure of selected chemicals. Results presented in this manuscript are the second set of results of non-dietary estimate of two major endocrine disruptors (BPA and DEHP) and internal dosimetry simulation of PBPK model. First set of result titled “Prenatal exposure estimation of BPA and DEHP using integrated external and internal dosimetry: A case study” was published in Environment Research (ER 158 566–575). Results are very interesting and present some new insight on concentration profile of these chemicals in mother and fetus. We hope that presented study covered in this manuscript is of special interest for the general readers of Environmental Research. We hope that manuscript will be considered for review and eventually acceptable for publication in this Journal. We look forward to your feedback.
Sincerely,

Vikas Kumar and Co-Authors

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Pregnant women and prenatal exposure to BPA and DEHP through non-dietary routes: Dermal contact, non-dietary ingestion and inhalation exposure assessment in Reus (Catalonia, Spain) cohort.

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Abstract

Bisphenol A (BPA) and Di-(2-ethylhexyl) phthalate (DEHP) are two wide spread chemicals classified as endocrine disruptors (ED). The present study aims to estimate the non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP for a pregnant women cohort. In addition, to assess the prenatal exposure for the fetus, a physiologically based pharmacokinetic (PBPK) model was used. It was adapted for pregnancy in order to assess the internal dosimetry levels of EDs (BPA and DEHP) in the fetus. Estimates of exposure to BPA and DEHP from all pathways along with their relative importance were provided in order to establish which proportion of the total exposure came from diet and which came from non-dietary exposures. In this study, the different oral dosing scenarios (dietary and non-dietary) were considered keeping inhalation as a continuous exposure case. Total non-dietary mean values were 0.002 $\mu g/kg_{bw}/day$ (0.000; 0.004 $\mu g/kg_{bw}/day$ for 5^{th} and 95^{th} percentile, respectively) for BPA and 0.597 $\mu g/kg_{bw}/day$ (0.116 $\mu g/kg_{bw}/day$ and 1.506 $\mu g/kg_{bw}/day$ for 5^{th} and 95^{th} percentile, respectively) for DEHP. Indoor environments and especially dust ingestion were the main non-dietary contributors to the total exposure of BPA and DEHP with 60% and 81%. However, as expected, diet showed the higher contribution to total exposure with >99.9% for BPA and 63% for DEHP. Although diet was considered the primary source of exposure to BPA and phthalates, it must be taken into account that with non-dietary sources the first-pass metabolism is lacking, so these may be of equal or even higher toxicological relevance than dietary sources.

The present study is in the framework of “Health and environmental-wide associations based on large population surveys” (HEALS) project (FP7-603946).

Keywords: Bisphenol-A; Di-(2-ethylhexyl) phthalate (DEHP); PBPK modeling; exposure assessment.

1. Introduction

Bisphenol A (BPA) and Di-(2-ethylhexyl) phthalate (DEHP) are two high volume industrial chemicals used in a wide variety of consumer products. These compounds are defined as non-persistent Endocrine Disrupters (EDs) and are categorized as chemicals of concern among others by the World Health Organization (WHO, 2010). The exposure to EDs plays a key role in the epigenome shaping of many aspects of the endocrine function (Casati, 2013; Chen et al., 2018). The evidences present in the literature indicate that EDs can affect the different levels of epigenetic control (Sharma et al., 2017) and in some cases can act transgenerationally, if the exposure to EDs occurs during “critical windows of exposure”, especially, the prenatal and the early life period (Casati et al., 2015; Sharma et al., 2016; Watkins et al., 2017). Furthermore, some studies have shown that exposure to these chemicals in the early period of life may cause functional impairment of development and reproduction (Dodson et al., 2012; Meeker, 2012; Sakhi et al., 2014), increase the risk of allergy/asthma (Robinson and Miller, 2015; Sakhi et al., 2014) and also can develop obesity and type 2 diabetes (Casas et al., 2011; De Cock et al., 2014; Myridakis et al., 2016). It is known that fetal exposure is directly related to the mother’s exposure, due to a bi-directional transfer of chemicals between the placenta and fetal plasma (Sharma et al. 2018). Normally placental barrier is considered protective layer against harmful compounds, however, a recent study has found poor barrier mechanism of placenta against some common EDs (Ribeiro et al., 2017).

Phthalates such as DEHP are industrial chemicals, which are used in polyvinyl chloride (PVC) plastics, found in products such as shoes, gloves and packing materials as well as in building materials, floorings and wall coverings. In addition, they are used in pharmaceuticals products, personal care products (PCPs), paints and adhesives (Bao et al., 2015). All of these applications are related to dermal contact, non-dietary ingestion or inhalation exposure sources. Some studies confirm that DEHP is an important contaminant in dust household; people can be exposed to it via dust ingestion, the exposure through this will be higher for workers in PVC industries (Fromme et al., 2004). It is known that babies and young children are the most vulnerable groups with respect to phthalates due to their developmental status (Sathyanarayana et al., 2008; Zhu et al., 2018).

BPA is currently used in polycarbonate plastics, found in materials intended to come into contact with food, like reusable plastic bottles, feeding-bottles, plates, cups, microwave and ovenware (Geens et al., 2009). In addition, we can find BPA in storage containers and epoxy resin linings for food and beverage containers. Furthermore, they are used in thermal papers and paper currencies, medical devices, dental sealants, and PCPs which are related with dermal exposure sources (Geens et al., 2012; Lv et al., 2017). Some studies showed that BPA exposure via dermal route can highly contribute to overall internal exposure (Biedermann et al., 2010; Mielke et al., 2011). Other studies affirm that people who work in offices will be more exposed via dust ingestion or inhalation than others because the levels of BPA in dust offices were almost 5–10 times higher than dust from particular homes (Geens et al., 2009).

The human exposure routes to EDs are multiple (Giulivo et al., 2016). Although the major human route of exposure to BPA and DEHP has been shown by several assessments, including the European Food Safety Authority (EFSA), to be the dietary pathway (EFSA, 2013; Geens et al., 2012; Guo et al., 2013). However, some studies confirm that non-dietary sources need to be more thoroughly characterized (EFSA, 2015; Geens et al., 2012). Estimates of exposure to DEHP and BPA from all pathways

along with their relative importance should be provided in order to establish which proportion of the total exposure comes from diet and which comes from non-dietary exposures. Human exposure to EDs from non-dietary sources, their toxicity, as well as their combined effects, are poorly understood (Larsson et al., 2014).

Although diet was considered the primary source of exposure to BPA and phthalates (Casas et al., 2013; Schettler et al., 2006), there is controversy on whether external exposure resulting from food ingestion is really a good estimate for internal exposure. It is known that dietary exposure contributes around 90 % to internal exposure to total BPA or DEHP and dermal exposure via thermal paper or via cosmetic products may contribute around 10 % (von Goetz et al., 2017). DEHP and BPA, among others EDs, are banned from PCPs and cosmetics in the EU (EC, 2009). However, plastic containers made of PCPs may contain phthalates and BPA with the ability to migrate to the products (Larsson et al., 2014), so it should be considered in the evaluations of exposure to these pollutants. In this study, occupational risk, lifestyle and the use of different PCPs were considered in order to assess the exposure to different pathways (dermal contact, non-dietary ingestion, and inhalation). Sharma et al., (2018) developed a P-PBPK model for BPA including specific pregnancy physiology and both oral and dermal route of exposure. The simulation results were presented to compare the reported data from different cohorts presuming the collection of samples can be from at different time points, in order to explain the inconsistency in biomonitoring data. Moreover, some authors compared the results obtained between real measurements concentrations levels of EDs in the blood reported and the exposure estimates based on PBPK models (Mielke and Gundert-Remy, 2009); the intake estimated were several orders of magnitude lower than the real values in blood reported in the literature. One way to explain this abnormality could be that in the PBPK model they only considered the dietary source, so this could have led to an underestimation of the exposure to these chemicals through non-dietary routes like dermal, inhalation or dust ingestion. However, there are other contributing factors for this difference such as genetic variability, biomonitoring sampling strategy and contamination of sample during analysis. The present study aims to estimate the non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP for a pregnant women cohort. In addition, to assess the prenatal exposure for the fetus, through all routes (diet and non-dietary) a physiologically based pharmacokinetic (PBPK) model was used. The pregnancy PBPK model structure was adapted from Sharma et al., (2018). Previous work has been extended to estimate the aggregate exposure of these EDs to humans to understand the relative importance of nondietary exposure. Parameters and structure of the models were kept same as our previous publications (Sharma et al., 2018; Martínez et al., 2017), except nondietary routes (inhalation and dermal) were included. The present study is in the framework of “Health and environmental-wide associations based on large population surveys” (HEALS) project (FP7-603946) and part of the study has been completed in MODELBIS project (MINECO funded with ref no AGL2016-78942-R).

2. Materials and methods

2.1. Study population

The study population comprises a cohort of pregnant women and ongoing birth cohort. The pregnant women were recruited during the first trimester of pregnancy as part of

the European "HEALS" project. The recruitment of pregnant mothers has started in March 2016 and in the present study 72 mother-child pairs from Reus (Tarragona, Spain) were included. Women were informed of the study during their first visit (12th gestational week) to the University Hospital "Sant Joan de Reus", in Reus (Catalonia, NE Spain). Women were eligible to participate according to the following inclusion criteria: ≥16 years old, intention to deliver at the reference hospital, and no problems with the communication language. This study was approved by the Ethical Committee of Clinical Research of the Hospital and a written informed consent was obtained from the participants.

2.2. Questionnaires and data acquisition

At 20th gestational weeks (GW), a PCPs frequency questionnaire was filled in a face-to-face interview. Different PCPs were included in the questionnaire: a) makeup (face cream, eyeshadow and liquid foundation), b) lipstick, c) body lotion, d) shampoo, e) shower gel, f) hair conditioner, g) toothpaste, h) deodorant and i) spray perfume. In addition, the questionnaires also included in one hand, general characteristics data of the study population, such as maternal age at delivery, twin pregnancy, maternal body mass index (BMI), maternal education, social economic status, country of origin, and marital status. On the other hand, a set of questions targeting to know other sources of these compounds are included, such as maternal smoking, lifestyle, hours spend outdoors and indoors and occupational risk. A description of the characteristics of the study population is shown in Table 1.

2.3. BPA and DEHP non-dietary assessment

2.3.1. Dermal contact exposure

The assessment of exposure of BPA and DEHP through dermal contact for pregnant women population was calculated according to equation 1. We considered all previously PCPs mentioned.

$$\text{Dermal exposure} = \Sigma \left(C_{BPA/DEHP} \cdot PCP_{fr} \cdot PCP_{a} \cdot ABS \cdot R_{f}\right) / BW_{20GW} \quad \text{Eq. 1}$$

Where $C_{BPA/DEHP}$ is the BPA or DEHP concentration in PCPs (in µg/g); PCP_{fr} is the frequency application (in application/day); PCP_{a} is the amount per application (in g/application); ABS is the dermal absorption factor (non-dimensional); R_f is the retention factor for rinse-off products (non-dimensional); and BW_{20GW} is the body weight at 20 gestational weeks (in kg). Dermal exposure is given in $\mu g/kg_{bw}$/day. Data used to assess the dermal exposure of BPA and DEHP are summarized in Table 2.

2.3.2. Non-dietary ingestion exposure

Non-dietary ingestion pathways include, on the one hand, dust ingestion that was calculated according to equation 2.a. On the other hand, exposure through PCPs ingestion was considered. Lipstick and toothpaste ingestion was assessed according to equation 2.b.

$$\text{Non-dietary ingestion exposure } (dust_{ingestion}) = \left(C_{DEHP/BPAdust} \cdot I_{r}\right) / BW_{20GW} \quad \text{Eq. 2.a}$$

$$\text{Non-dietary ingestion exposure } (PCP_{ingestion}) = \left(C_{BPA/DEHP} \cdot PCP_{fr} \cdot PCP_{a} \cdot Ing_{f}\right) / BW_{20GW} \quad \text{Eq. 2.b}$$

Where $C_{BPA/DEHP\ dust}$ is the BPA or DEHP levels in homes dust (in µg/kg); I_r is the Ingestion rate (in kg/day) and $BW_{20\ GW}$ is the body weight at 20 gestational weeks (in kg). PCP_{fr} is the frequency application (in application/day); PCP_a is the amount per application (in g/application) and Ing_f is the ingestion factor (non-dimensional). The total non-dietary exposure is given in µg/kg_{bw}/day. Table 3 provides data used to assess the non-dietary ingestion exposure of BPA and DEHP.

2.3.3. Inhalation exposure

The exposure assessment of BPA and DEHP through inhalation for pregnant women was calculated according to equation 3. We considered levels of BPA and DEHP in the outdoor and indoor air. In this case, three different scenarios were assessed: sleeping (3.a), indoors (3.b) and outdoors (3.c) scenarios.

$$\text{Inhalation exposure}_{\ sleeping} = (C_{DEHP/BPA\ indoor} \cdot Ih_{r\ sleep} \cdot t_{\ sleep}) / BW_{20GW} \quad \text{Eq. 3.a}$$

$$\text{Inhalation exposure}_{\ indoors} = (C_{DEHP/BPA\ indoor} \cdot Ih_{r\ sedentary} \cdot t_{\ indoor}) / BW_{20GW} \quad \text{Eq.3.b}$$

$$\text{Inhalation exposure}_{\ outdoors} = (C_{DEHP/BPA\ outdoor} \cdot Ih_{r\ moderate} \cdot t_{\ outdoor}) / BW_{20GW} \quad \text{Eq.3.c}$$

Where $C_{DEHP/BPA\ indoor}$ is the DEHP or BPA levels in indoor air (in µg/m^3); $C_{DEHP/BPA\ outdoor}$ is the DEHP or BPA levels found in outdoor air (in µg/m^3); $Ih_{r\ sleep}$ is the inhalation rate sleeping (in m^3/min); $Ih_{r\ sedentary}$ is the inhalation rate doing sedentary activities (in m^3/min); $Ih_{r\ moderate}$ is the inhalation rate doing moderate activities (in m^3/min); $t_{\ sleep}$ is the mean of time sleeping (in min); $t_{\ indoor}$ is the mean of time spending indoor (at work and at home) (in min); $t_{\ outdoor}$ is the time spending in doing activity outdoor (in min) and BW_{20GW} is the body weight at 20 gestational weeks (in kg). The total inhalation exposure is given in µg/kg_{bw}/day. Table 4 contains the data used to assess the inhalation exposure of BPA and DEHP.

The concentration levels of BPA and DEHP in different PCPs, in dust and air, were taken from the literature with a preference rule of Spanish values> European values> other available data. To deal with variability and uncertainty of parameters used, probabilistic estimation of the dermal, non-dietary ingestion and inhalation exposure was performed in a probabilistic way. Monte-Carlo simulation is a common approach used to incorporate variability and uncertainty of the parameters used into the estimation of human health exposure (Mari et al., 2009; May et al., 2002; Rovira et al., 2016; Schuhmacher et al., 2001). Table 2, 3 and 4 includes the probabilistic distribution of parameters for the calculation of human health exposure. Monte-Carlo simulation was carried out by Oracle Crystal Ball© software. Exposures were calculated based on the propagation variable of variability and uncertainty given by each parameter probability function until 100,000 iterations.

2.4 Tissue dosimetry model (PBPK).

The basic structure of pregnant PBPK model has been adapted from Sharma et al., (2018) in the current study in order to assess dietary and non-dietary exposure. It comprises plasma, liver, kidneys, fat, brain, skin, placenta, a rest of the body and a fetus compartment. Fetus compartment was subcategorized again into liver, brain, and plasma. All the Physiological parameters during pregnancy are considered to be

dynamic parameters that change due to the growth of mother organs (Abduljalil et al., 2012; Gentry et al., 2003; Loccisano et al., 2013). The source of exposure to fetuses was via a free fraction of chemicals into mother's placenta, considering that fetuses' exposure is directly related to mother's exposure. The placental-fetal unit assumes a bidirectional transfer process describing chemical transfer between mothers' placenta to fetuses' plasma and fetuses' plasma to the mothers. Detailed descriptions of standard and pregnancy-specific model equations are adapted form Sharma et al., (2018). Metabolic kinetic parameters for both mothers and fetuses were previously estimated from in-vitro studies (Martínez et al., 2017; Sharma et al., 2018).

Two different sources of exposure were considered for the current study, dietary exposure and the combination of dietary with non-dietary exposure. The dosing considered being inputs for the PBPK model was estimated using Monte Carlo technique for the exposure assessment. It has been considered the six following exposure scenarios of BPA and DEHP: 5^{th} percentile diet; 5^{th} percentile diet + non-diet; Mean diet; Mean diet+ non-diet; 95^{th} percentile diet, and 95^{th} percentile diet + non-diet. For the current study, the routes of exposure were the following: ingestion and dermal exposure that were divided into three equal doses (with 8 hours of the interval). On the other hand, continuous exposure for inhalation was presumed, considering three different inhalation rates (sleeping time, doing sedentary activities and doing moderate activities).

3. Results and discussion

3.1 Non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP.

The contribution of dermal contact, non-dietary ingestion, and inhalation to the total non-dietary intake from Reus pregnant mothers' cohort was assessed in a probabilistic way using Monte-Carlo simulation. Figure 1, summarizes the contribution of each non-dietary source to the total exposure of BPA and DEHP.

Regarding BPA (Figure 1), the total non-dietary mean value was 0.002 $\mu g/kg_{bw}$/day (0.000 and 0.004 $\mu g/kg_{bw}$/day for 5^{th} and 95^{th} percentile, respectively). Relative mean contributions were 60%, 36% and 4% for non-dietary ingestion, inhalation, and dermal routes, respectively. For DEHP (Figure 1), the total non-dietary mean exposure was 0.597 $\mu g/kg_{bw}$/day (0.116 $\mu g/kg_{bw}$/day and 1.506 µg/kg bw/day for 5^{th} and 95^{th} percentile, respectively). The maximum mean contribution was, again, non-dietary ingestion with 81%, followed by dermal route and inhalation with 15% and 4%, respectively.

For both chemicals, BPA and DEHP, non-dietary ingestion was the highest mean relative contributor with 60% and 81%, respectively, of the total non-dietary exposure. These represented a mean non-dietary ingestion exposure of $9.62 \cdot 10^{-4}$ and 0.485 $\mu g/kg_{bw}$/day for BPA and DEHP, respectively. Non-dietary ingestion route considered the levels of both compounds in homes dust and in PCPs that could be accidentally ingested during their use (lipstick and toothpaste). In both cases, the major contribution (>99.9%) to the total non-dietary ingestion exposure to BPA and DEHP came from home dust ingestion. The average concentration of BPA and DEHP in dust were very high, $2 \cdot 10^3$ and $1.20 \cdot 10^6$ $\mu g/kg_{dust}$, respectively. BPA levels in dust were obtained from Belgian houses (Geens et al., 2009) and phthalate levels in dust came from different

European homes (Wormuth et al., 2006). However, similar BPA and DEHP levels in indoor dust were found worldwide (Das et al., 2014; Fromme et al., 2004; Kubwabo et al., 2016; Loganathan and Kannan, 2011). The high contribution of dust in the total DEHP non-dietary ingestion exposure is due to phthalates, which are used as plasticizers in numerous consumer products, commodities, and building materials. Consequently, phthalates are found in human residential and occupational environments in high concentrations (Wormuth et al., 2006). As well as DEHP, the high contribution of dust in the total BPA non-dietary ingestion exposure is due to BPA is used in a variety of household applications. Through manufacture and usage, these contaminants can leach into the environment and can be deposited in the indoor dust (Geens et al., 2009). It was assumed that consumers accidentally ingest small amounts of PCPs. So, it was estimated the scenario for non-dietary ingestion using information about the amounts cosmetics ingested daily (Table 3), and the DEHP and BPA concentrations in PCP. No much information was available on how much PCPs are ingested daily and also it was not many literature data about concentration levels of these two EDs in different cosmetic products. Only data regarding DEHP in lipstick and BPA in toothpaste content were found. Therefore, it was only considered the accidental ingestion of these two cosmetics, lipstick and toothpaste, during their use. Results showed that the contribution to this kind of ingestion to the total DEHP and BPA non-dietary ingestion were insignificant (0.07% and 0.01% for BPA and DEHP, respectively) compared to total non-dietary ingestion and also with the dietary total intake. However, more bibliographic data is needed to be able to carry out a good exposure assessment.

According to BPA, inhalation was the second greatest contributor to the total exposure with an exposure of $5.90 \cdot 10^{-4}$ $\mu g/kg_{bw}/day$, that meant the 36% of the total non-dietary exposure. In this case, three different scenarios were assessed: indoor, outdoor and sleeping inhalation exposure that showed a contribution to total BPA inhalation exposure of 37%, 51%, and 12%, respectively. Inhalation exposure was lower than the dust exposure; this can be due to BPA has a comparatively low vapour pressure. As a result, concentrations of BPA in the air can be expected to be low and it will be present mainly in the particulate phase, adsorbed to dust (EFSA, 2013). Finally, dermal contact was the exposure route that contributed the least (4%) to the total mean non-dietary BPA exposure, with a dose of $6.39 \cdot 10^{-5}$ $\mu g/kg_{bw}/day$. Among all the PCPs, face cream (39%), shower gel (20%) and body lotion (18%) have the higher contribution. In Europe, BPA is not allowed as an ingredient in cosmetics (Regulation (EC) no. 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products). However, if BPA is present in the packaging (e.g. polycarbonates plastic (PC) packaging), it could migrate into the cosmetic products (EFSA, 2013). It must be taken into account that dermal absorption of BPA can reach 95-100% if BPA is applied dissolved in ethanol, because ethanol may act as a transport mediator for BPA into the skin, thus enhancing the absorption fraction. In addition, this property of dissolving in ethanol can be found in similar compounds in the formulation of creams and body lotions (EFSA, 2013).

Regarding DEHP, dermal contact with a mean value of 0.087 $\mu g/kg_{bw}/day$, was the second greatest contributor to the total non-dietary exposure (15%). In this exposure assessment, perfume and deodorant were the items which contribute more to the total DEHP dermal exposure, with 36% and 33%. The quite high presence of these ED is due to phthalates in general, are added as humectants, emollients, or skin penetration enhancers, which are very common in perfumes and fragrances (Koo and Lee, 2004). Finally, DEHP inhalation (0.025 $\mu g/kg_{bw}/day$) was the item which contributed less (4%) to the DEHP mean non-dietary exposure. Indoor exposure and sleeping inhalation

exposure had a relative contribution of 61% and 36%, respectively. Other authors (Wormuth et al., 2006) found that accidental ingestion of PCPs are the major sources of exposure to DEHP in all consumer groups that we estimated. Although the food is the dominating source of exposure to DEHP in all consumer groups (Wormuth et al., 2006).

Indoor environment (home dust ingestion and inhalation (indoor and sleeping)) were the principal source of BPA and DEHP of non-dietary exposure with a relative contribution of 78% and 85%, respectively. PCPs contribute with 4% and 15% to total mean non-dietary exposure of BPA and DEHP, respectively, almost exclusively through dermal contact. Finally, outdoor environment (trough outdoor inhalation) showed a contribution of 18% and <0.1% to total mean non-dietary exposure for BPA and DEHP, respectively.

3.2 Dietary exposure vs non-dietary exposure

Figure 2, shows the comparison between total dietary exposure and non-dietary (dermal, non-dietary ingestion and inhalation) exposure to BPA and DEHP. Data from the dietary exposure was previously estimated using the same cohort population (Martínez et al., 2017).

Regarding BPA, mean dietary daily intake from Reus (Tarragona, Spain) cohort was 0.715 $\mu g/kg_{bw}$/day (Martínez et al., 2017), and the mean exposure estimated for non-dietary ingestion, inhalation, and dermal contact were $9.62 \cdot 10^{-4}$, $5.90 \cdot 10^{-4}$, $6.39 \cdot 10^{-5}$ $\mu g/kg_{bw}$/day, respectively. In general, in the present study according to non-dietary exposure, the maximum exposure estimated for BPA was 0.0072 $\mu g/kg_{bw}$/day and the 95% of the population were under 0.0040 $\mu g/kg_{bw}$/day. Non-dietary exposure practically did no contribute to the total exposure (0.2%). In other words, diet was the greatest contributor to the total exposure (99.8%) (Figure 2). However, on the one hand, it is important to know that in this study thermal paper was not considered in dermal exposure estimation, which is considered as a potential exposure source for BPA in the EU by the EFSA, 2015. On the other hand, with dermal absorption and inhalation the first-pass metabolism is lacking, so dermal sources may be of equal or even higher toxicological relevance than dietary sources (Lu et al., 2017; Völkel et al., 2002; von Goetz et al., 2017). Considering diet and non-diet sources the mean of the total exposure was 0.72 $\mu g/kg_{bw}$/day and the 5^{th} and 95^{th} percentile of the total exposure were 0.28 and 1.41 $\mu g/kg_{bw}$/day (Figure 2).

Regarding DEHP, Figure 2 shows that non-dietary sources contribute with 37 % of the total exposure. The mean dietary daily intake of DEHP exposure from Reus cohort was 1.00 $\mu g/kg_{bw}$/day (Martínez et al., 2017), and the mean exposure estimated for non-dietary ingestion, inhalation, and dermal contact were 0.485, 0.025, 0.087 $\mu g/kg_{bw}$/day respectively. According to total non-dietary exposure, the maximum dose was 3.86 $\mu g/kg_{bw}$/day and the 95^{th} percentile was 1.51 $\mu g/kg_{bw}$/day, and mean value was 0.60 $\mu g/kg_{bw}$/day. Considering diet and non-diet sources the mean of the total exposure was 1.60 $\mu g/kg_{bw}$/day and the 5^{th} and 95^{th} of the total exposure were 0.52 and 3.52 $\mu g/kg_{bw}$/day, respectively (Figure 2).

EFSA published its comprehensive re-evaluation of BPA exposure and toxicity, in January 2015, and established a tolerable daily intake (TDI) of 4 $\mu g/kg_{bw}$/day for BPA (EFSA, 2015). On the other hand, EFSA and the European Chemicals Agency (ECHA) established the TDI for DEHP to 50 $\mu g/kg_{bw}$/day (ECHA, 2010; EFSA, 2015). Only the non-dietary ingestion estimated data from this study can be compared with this EFSA

and ECHA tolerable values because the TDI values are concerned about “daily intake”. Therefore, in this study, the maximum value estimated for BPA non-dietary ingestion exposure was 0.0052 μg/kg_{bw}/day and the 95% of the population were below 0.0028 μg/kg_{bw}/day. Whereas, for DEHP, the maximum value estimated for non-dietary ingestion exposure was 3.39 μg/kg_{bw}/day and the 95% of the population were under 1.24 μg/kg_{bw}/day. These values for BPA and DEHP estimated in our study were far away from the tolerable values of the EFSA and ECHA. Although BPA and DEHP non-dietary ingestion exposure assessment values were under the tolerable established, it is important to take into account that non-dietary ingestion and, in general, non-dietary levels must be added to the total dietary exposure assessment, in order to make a good exposure estimation.

3.3 Internal dosimetry

The chemicals’ dose inputs considered to run the P-PBPK, were probabilistically estimated by Monte-Carlo simulation (Section 2.4). From probabilistic distribution, six total scenarios were selected for BPA and DEHP: the 5^{th} percentile diet; the 5^{th} percentile diet + non-diet; mean diet; mean diet + non-diet; the 95^{th} percentile diet and the 95^{th} percentile diet + non-diet. The outputs from the model simulation were selected considering the metabolites generated, their toxicity, gestational period and ability to reach the fetus. For this reason, only free BPA and MEHP (a metabolite of DEHP) were considered. The simulation data were taken from pregnant women and fetus for 24 h during the 24th gestational week. This period was selected because at this time fetus organs are more developed and able to incorporate right biological process. This helps us to explain the difference in metabolic processes in mothers and fetuses. Normally, at the early stage of pregnancy, for both BPA and MEHP, fetus plasma concentration level is higher due to low or no metabolic activities in the fetus (Gauderat et al., 2016; Latini et al., 2003). In order to be near to a real scenario, a dietary, and non-dietary (dermal and ingestion) exposure were divided into three equal doses, along with continuous exposure of non-dietary source (inhalation) and were simulated (Figure 3) in the case of BPA. On the other hand, DEHP metabolite MEHP time plasma concentration profile in case of both mother and fetus is showed in Figure 4, the result of single-dose intake of dietary and non-dietary. In this case, inhalation was considered again as continuous exposure, the simulated concentration curves show a sharp peak concentration o within 1 h of intake. It is known that metabolic activity in the fetus is lower compared to mother's metabolism (Heindel et al., 2017). For that reason, concentration levels of both chemicals in the fetus’ plasma were higher than in the mother. Therefore, BPA and MEHP stay longer in the fetal body, which may cause higher risk to fetuses and makes the fetus more vulnerable to the exposure. A similar trend has been observed by Sharma et al., (2018).

4. Conclusions

The aim of this study was to estimate the non-dietary exposure to BPA and DEHP (dermal, non-dietary ingestion and inhalation) to which pregnant women are subjected and the prenatal exposure. This work elucidates the aggregate exposure to BPA and DEHP in both dietary and non-dietary exposure for pregnant women cohort. To assess the prenatal exposure, a PBPK model adapted for pregnancy was used in order to assess the internal dosimetry levels of EDs (BPA and DEHP) in the fetus.

Regarding BPA non-dietary exposure was 0.002 µg/kg_{bw}/day, with the greatest contribution coming from non-dietary ingestion with 60%, followed by inhalation with 36%. Finally, dermal exposure was the one that contributed the least with 4%. However, in this study, the thermal paper was not considered in dermal exposure estimation, which is considered as a potential exposure source for the general population (EFSA, 2015). According to DEHP non-dietary exposure (0.597 µg/kg_{bw}/day), the maximum contributor was non-dietary ingestion with 81%, followed by dermal contact with 15% and inhalation with 4%. As expected, diet was the main contributor to total exposure to both chemicals. Regarding DEHP, non-dietary sources contribute 37% of the total exposure. The non-dietary exposure to BPA practically did no contribute to the total exposure (0.22%). Indoor environment, dust ingestion, and indoor air inhalation was the main contributor to non-dietary exposure to both ED (78% for BPA and 85% for DEHP) meanwhile PCPs contribute in 4% and 15%, for BPA and DEHP, respectively. However, with dermal absorption that passes the first-pass metabolism, dermal sources may be of equal or even higher toxicological relevance than dietary sources (Völkel et al., 2002; von Goetz et al., 2017). Only the non-dietary ingestion estimated data in combination with other dietary exposure from this study can be comparable with EFSA and ECHA tolerable values because the TDI values are concerned about “daily intake”. Although BPA and DEHP non-dietary ingestion exposure assessment values were under the tolerable established, it is important to take into account that non-dietary exposure levels must be added to the total dietary exposure assessment, in order to make a good exposure estimation.

According to internal dosimetry, six different scenarios were considered in order to run the PBPK model. When the simulation considered diet + non-diet scenarios, the concentration levels of BPA and MEHP (main metabolite of DEHP) increased considerably in plasma. In addition, in fetus’ plasma, the concentration of both chemicals reached levels much higher than those seen previously in mothers. The low metabolic activity in fetus led to maintain a continuous concentration in time. Therefore, this can make the fetus more vulnerable to the exposure compared with their mothers.

The ongoing research is to validate the PBPK model with biological samples from this cohort and demonstrate that this methodology allows the determination of BPA and MEHP for monitoring in biological matrices, such as plasma and urine. Finally, demonstrate that PBPK model can predict the prenatal exposure of the child/fetus to EDs. To conclude, on the one hand, strategies must be presented in order to reduce their exposure. Restrictions must be imposed to regulate the production and use of products related especially with childcare and pregnant women.

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Table 1. Characteristics of the study population from Reus cohort, Tarragona (Spain) (n=72).

Characteristics of the study population (n = 72)	**%**
Maternal age at delivery (years)	
< 20	1
20-29	14
30-39	72
>40	13
Twin pregnancy	8
*Maternal pre-pregnancy BMI**	
Underweight (<19kg/m^2)	6
Normal (19-25 kg/m^2)	50
Overweight (>25 kg/m^2)	25
Obese (>30 kg/m^2)	19
*Maternal pregnancy (20 GW) BMI**	
Underweight (<19kg/m^2)	1
Normal (19-25 kg/m^2)	41
Overweight (>25 kg/m^2)	37
Obese (>30 kg/m^2)	21
Maternal education	
Primary	28
Secondary	31
University	41
Social economic status	
Low level (< 9000-19000€/year)	24
Median level (19000-35000€/year)	49
High level (> 35000 €/year)	27
Maternal country of origin	
Spain	76
Other	24
Marital Status	
Living with the father	99
Not living with the father	1
Maternal smoking	
Never smoke	73
Not during pregnancy	9
During pregnancy	18
**BMI= Body mass index*	

Table 2. Monte-Carlo parameter description to assess the total dermal contribution of BPA and DEHP.

Parameter	Symbol	units	Type	Distribution	Reference
DEHP concentration in	C_{DEHP}	-	-	-	-
Lipstick	-	µg/g	T	1.79 (0-6.45)	Guo and Kannan, 2013
Body lotion	-	µg/g	T	0.96 (0-11.3)	Guo and Kannan, 2013
Face cream	-	µg/g	T	0.4 (0-2.45)	Guo and Kannan, 2013
Shampoo	-	µg/g	T	0.1 (0-1.1)	Esteve et al., 2016
Shower gel	-	µg/g	U	9.53-32.4	Guo et al., 2013
Deodorant	-	µg/g	T	4.98 (0-65.3)	Guo and Kannan, 2013
Hair conditioner	-	µg/g	T	0.18 (0-0.39)	Guo and Kannan, 2013
Spray perfume	-	µg/g	T	15 (7-130)	Wormuth et al., 2006
Eye shadow	-	µg/g	T	0.64 (0-1.46)	Guo and Kannan, 2013
BPA concentration in	C_{BPA}	-	-	-	-
Body lotion	-	µg/g	LN[a]	$3.54 \cdot 10^{-04}$, $1.18 \cdot 10^{-02}$, $1.67 \cdot 10^{-01}$	Liao and Kannan, 2014
Face cream	-	µg/g	LN	0.03 ± 0	Cacho et al., 2013
Liquid foundation	-	µg/g	LN[a]	0,0.02,0.04	Liao and Kannan, 2014
Shampoo	-	µg/g	LN	0.09 ± 0	Cacho et al., 2013
Shower gel	-	µg/g	LN	0.07 ± 0	Cacho et al., 2013
PCP frequency	PCP_{fr}	-	-	-	-
Lipstick	-	Application/day	N	0.18 ± 0.34	Present study
Body lotion	-	Application/day	N	0.78 ± 0.41	Present study
Face cream	-	Application/day	N	0.72 ± 0.44	Present study
Liquid foundation	-	Application/day	N	0.42 ± 0.44	Present study
Shampoo	-	Application/day	N	0.62 ± 0.37	Present study
Shower gel	-	Application/day	N	0.92 ± 0.31	Present study
Deodorant	-	Application/day	N	0.94 ± 0.27	Present study
Hair conditioner	-	Application/day	N	0.35 ± 0.28	Present study
Spray perfume	-	Application/day	N	0.68 ± 0.45	Present study
Eye shadow	-	Application/day	N	0.42 ± 0.44	Present study
PCP amount	PCP_a	-	-	-	-
Lipstick	-	g/application	LN[g]	0.01±3.29	Loretz et al., 2005
Body lotion	-	g/application	LN[g]	3.26 ± 2.25	Loretz et al., 2005
Face cream	-	g/application	LN[g]	0.80 ± 2.55	Loretz et al., 2005

Liquid foundation	-	g/application	LN^g	0.33 ± 2.99	Loretz et al., 2006
Shampoo	-	g/application	G	0.38,5.79,2.15	Loretz et al., 2006
Shower gel	-	g/application	G	0.67,4.89,2.84	Loretz et al., 2006
Deodorant	-	g/application	LN^g	0.56 ± 2.41	Loretz et al., 2006
Hair conditioner	-	g/application	LN^g	10.28 ± 2.20	Loretz et al., 2006
Spray perfume	-	g/application	LN^g	0.30 ± 3.36	Loretz et al., 2006
Eye shadow	-	g/application	LN^g	0.01± 3.61	L. J. Loretz et al., 2008
Body weight	BW_{20GW}	kg	LN	71.42 ± 17.15	Present study
Retention factor (rinse off PCP)	R_f	-	-	-	-
Shampoo	-	-	U	0-0.02	EFSA, 2015
Shower gel	-	-	U	0-0.02	EFSA, 2015
Hair conditioner	-	-	U	0-0.02	EFSA, 2015
Ingestion factor lipstick	1-(Ing_f)	-	LN	0.20 ± 0.04	Franzen et al., 2016
DEHP dermal absorption factor	$ABS_{(DEHP)}$	-	U	0.05-0.15	EPA, 2011
BPA dermal absorption factor	$ABS_{(BPA)}$	-	U	0.08-0.10	Demierre et al., 2012

LN = Log-normal; T = Triangular; U = Uniform; G = Gamma; N= Normal distribution. Mean, minimum, and maximum values were used for triangular distributions; Mean and standard deviation were used for log-normal distributions; Geometrical mean and geometrical standard deviation were used in log-normal[g] distributions; minimum and maximum values were used for uniform distributions; Percentile 50,95 and maximum were used in log-normal[a] distributions and location, scale and shape were used for gamma distribution.

Table 3. Monte-Carlo parameter description to assess the total non-dietary ingestion contribution of BPA and DEHP.

Parameter	Symbol	units	Type	Distribution	Reference
DEHP concentration in	C_{DEHP}	-	-		-
Lipstick	-	µg/g	T	1.79 (0-6.45)	Guo and Kannan,2013
Dust indoor	-	µg/kg dust	LN[b]	$1.20 \cdot 10^{6}$	Wormuth et al., 2006
BPA concentration in	C_{BPA}	-	-		-
Toothpaste	-	µg/g	LN[c]	0.35,0.83	Liao and Kannan,2014
Dust indoor	-	µg/kg dust	LN	$2 \cdot 10^{3} \pm 2.1 \cdot 10^{3}$	Geens et al., 2009
PCP frequency	PCP_{fr}	-	-		-
Lipstick	-	Application/day	N	0.18 ± 0.34	Present study
Toothpaste	-	Application/day	N	1.82 ± 0.76	Present study
PCP amount	PCP_{a}	-	-	-	-
Lipstick	-	g/application	LN[g]	0.01 ± 3.29	Loretz et al., 2005
Toothpaste	-	g/application	U	0.79-1.20	McNamara et al., 2007
Dust ingestion rate	I_r	kg/day	N	$3 \cdot 10^{-5} \pm 3 \cdot 10^{-6}$	EPA, 2011
Ingestion factor	Ing_f	-	-	-	-
Lipstick	-	-	LN	0.20 ± 0.04	Franzen et al., 2016
Toothpaste	-	-	U	0-0.10	Angerer et al., 2010
Body weight	BW_{20GW}	kg	LN	71.42 ± 17.15	Present study

LN = Log-normal; T = Triangular; U = Uniform. Mean, minimum, and maximum values were used for triangular distributions; Mean and standard deviation were used for log-normal distributions; Geometrical mean and geometrical standard deviation were used in log-normal[g] distributions; minimum and maximum values were used for uniform distributions; Mean and P95 were used for log-normal[b] distributions; Percentile 50 and 95 were used in log-normal[c] distributions.

Table 4. Monte-Carlo parameter description to assess the total inhalation contribution of BPA and DEHP.

Parameter	Symbol	units	Type	Distribution	Reference
DEHP concentration in	C_{DEHP}	-	-	-	-
Air indoor	-	$\mu g/m^3$	T	0.3 (0.05-0.62)	Wormuth et al., 2006
Air outdoor	-	$\mu g/m^3$	T	0.01 (0-0.05)	Wormuth et al., 2006
BPA concentration in	C_{BPA}	-	-	-	-
Air indoor	-	$\mu g/m^3$	T	0 (0-0.01)	EFSA, 2015
Air outdoor	-	$\mu g/m^3$	LN	0.01 ± 0.01	Salapasidou et al.,2011
Inhalation rate					
sleeping	$Ih_{r\ sleep}$	m^3/min	LN[b]	0,0.01	EPA, 2011
sedentary activity	$Ih_{r\ sedentary}$	m^3/min	LN[b]	0,0.01	EPA, 2011
moderate activity	$Ih_{r\ moderate}$	m^3/min	LN[b]	0.02,0.03	EPA, 2011
Time sleeping	t_{sleep}	min	N	521 ± 52.10	IEC, 2012
Time outdoor	$t_{outdoor}$	min	N	106 ± 10.60	IEC, 2012
Time indoor	t_{indoor}	min	-	1440	-
Body weight	BW_{20GW}	kg	LN	71.42 ± 17.15	Present study

Time indoor= 24 hours – (T_{sleep} + $T_{outdoor}$). LN = Log-normal; T = Triangular. Mean, minimum, and maximum values were used for triangular distributions; Mean and standard deviation were used for log-normal distributions; Mean and P95 were used for log-normal[b] distributions.

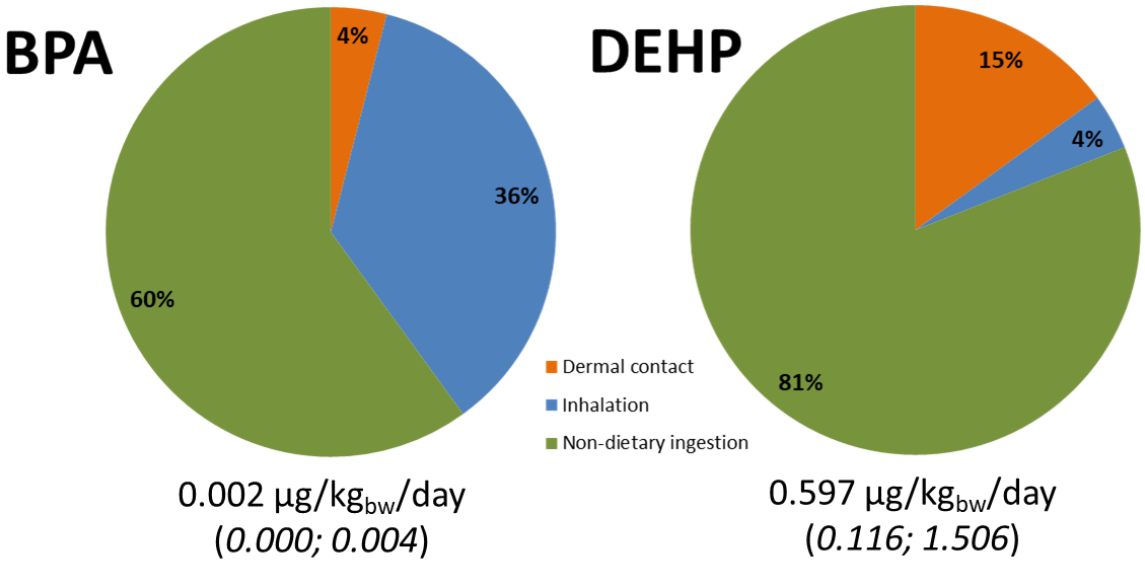


Figure 1. Non-dietary exposure (dermal contact, non-dietary ingestion and inhalation) Reus (Tarragona, Spain) pregnant women cohort exposure to BPA and DEHP exposure. Results are given in mean (5^{th}; 95^{th} *percentile*).

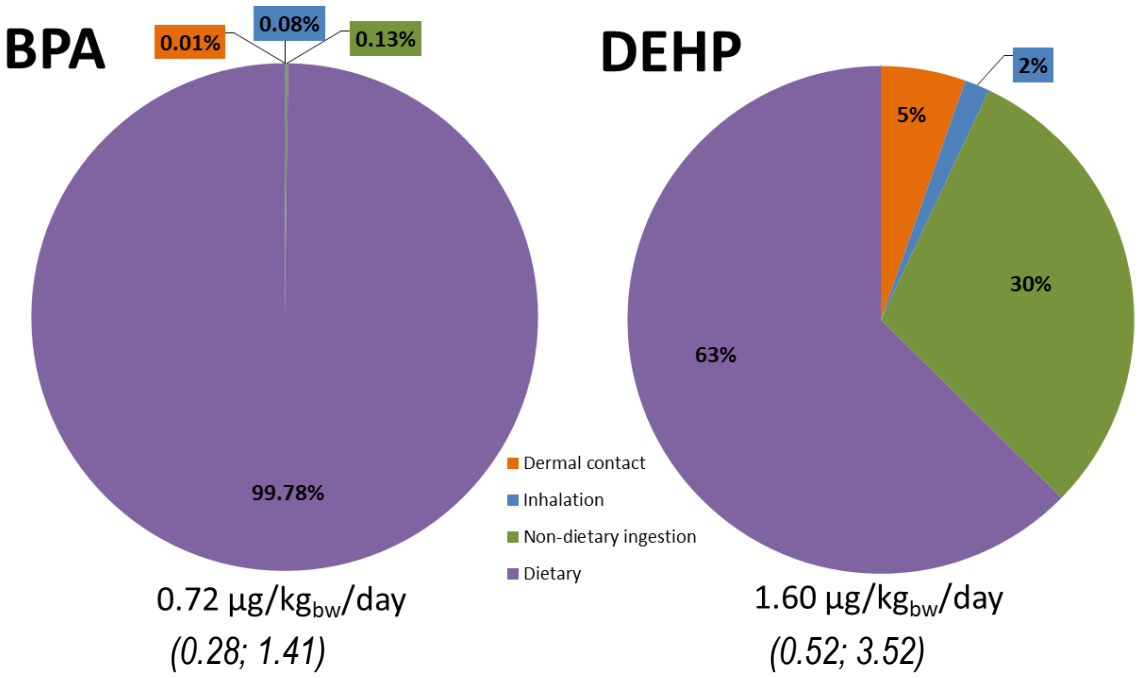
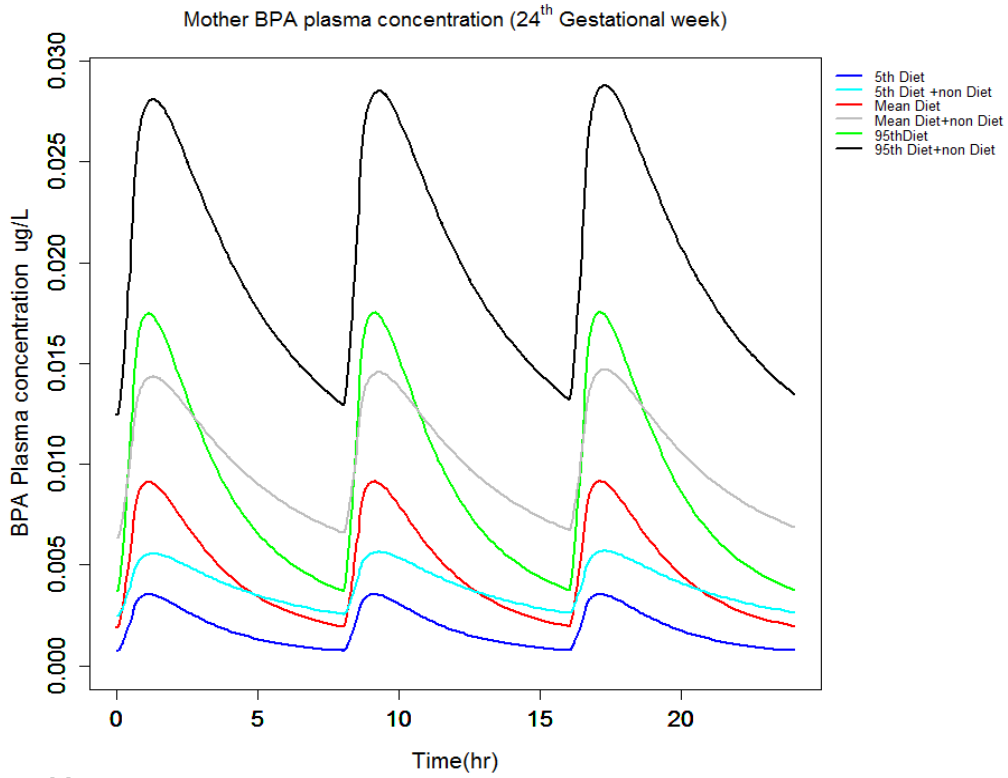


Figure 2. Total mean exposure dietary (Martínez et al., 2017) and non-dietary (dermal, non-dietary ingestion and inhalation) to BPA and DEHP for Reus pregnant women cohort. Results are given in mean (*5th; 95th percentile*).

a)



b)

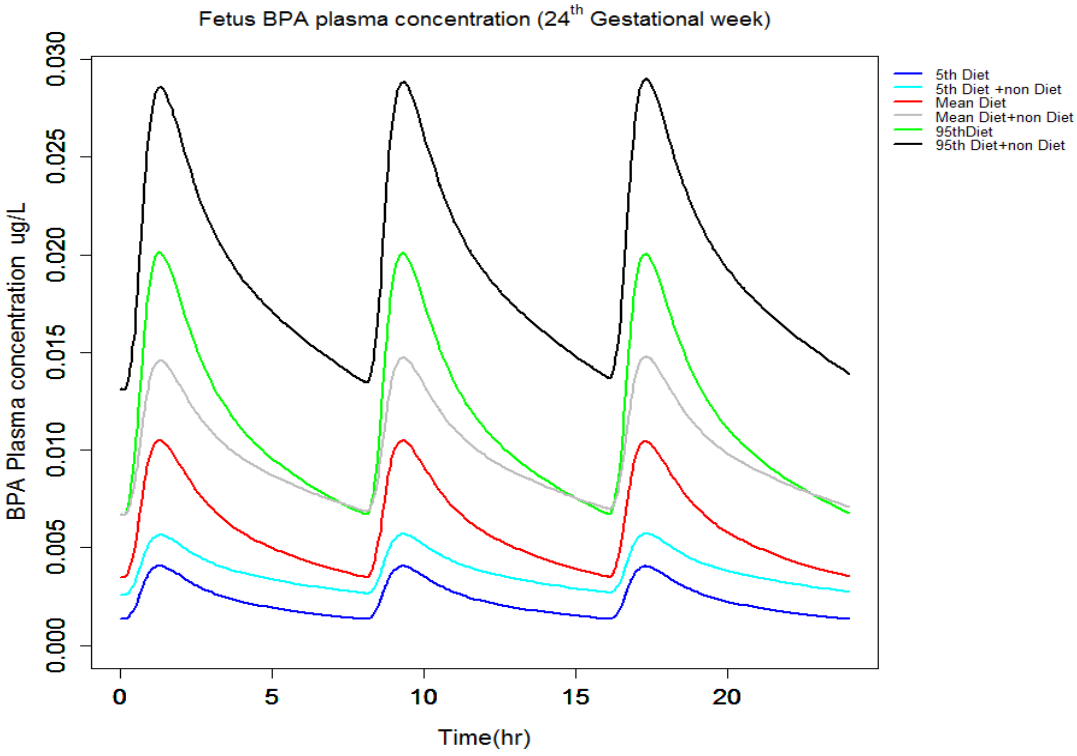
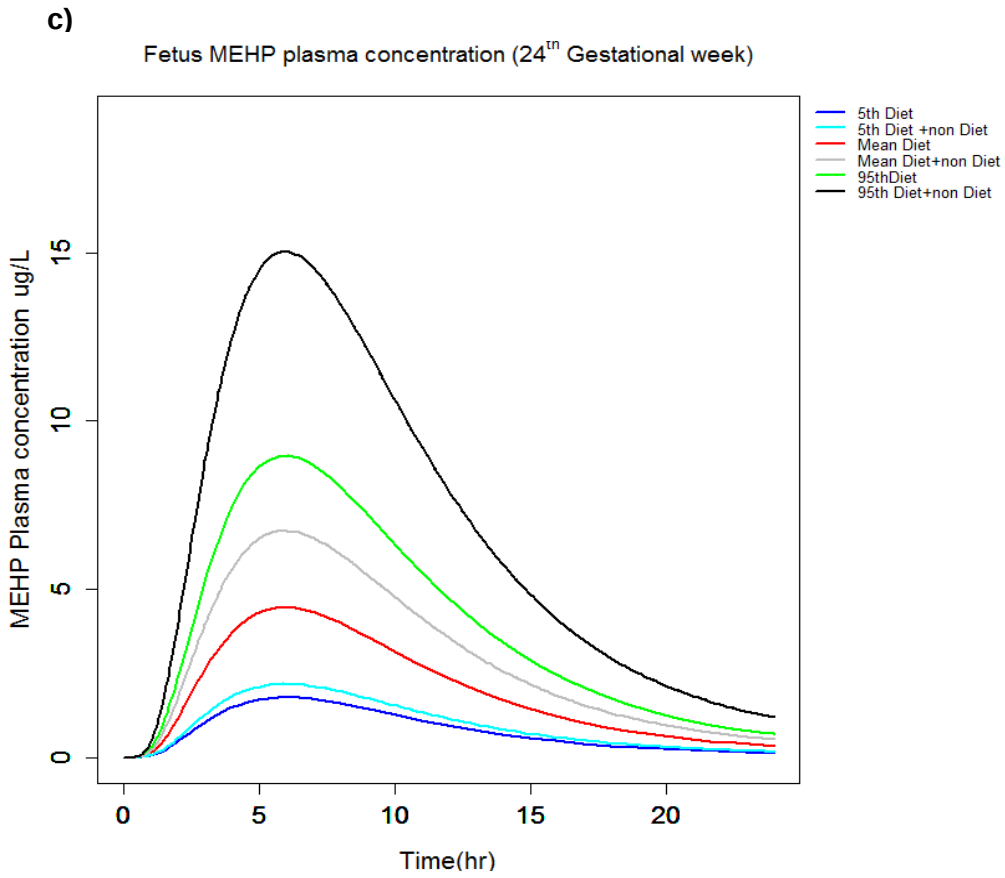


Figure 3. Time versus BPA plasma concentration for mothers a), and fetuses b), considering six different exposure scenarios (the 5th percentile diet; the 5th percentile diet + non-diet; mean diet; mean diet + non-diet; the 95th percentile diet and the 95th percentile diet + non-diet). It was considered three-food intake dose for diet and non-diet (dermal and dust ingestion) keeping inhalation as a continuous exposure.



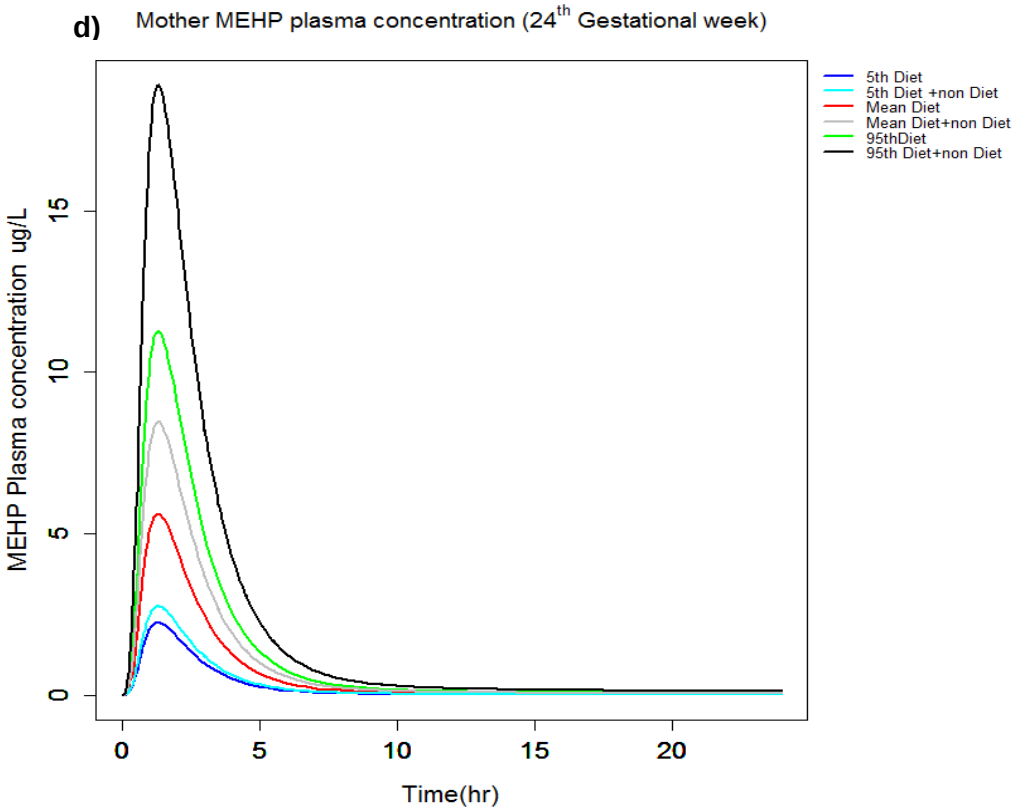


Figure 4. Time versus MEHP plasma concentration for mothers c) and fetuses d), considering six different exposure scenarios (the 5th percentile diet; the 5th percentile diet + non-diet; mean diet; mean diet + non-diet; the 95th percentile diet and the 95th percentile diet + non-diet). It was considered one-food intake dose for diet and non-diet (dermal and dust ingestion) keeping inhalation as a continuous exposure.