Universidad y Salud
ARTÍCULO ORIGINAL

DOI: https://doi.org/10.22267/rus.222403.278

Exposición intrauterina a disruptores endocrinos (ftalatos): fuentes de exposición y cuantificación de metabolitos urinarios

Intrauterine exposure to endocrine disruptors (phthalates): sources of exposure and quantification of urinary metabolites

Carlos Alberto Gómez-Mercado[1*] orcid.org/0000-0003-4123-2812

Natalia Escobar[2] orcid.org/0000-0001-7796-1983

María C. González[2] orcid.org/0000-0003-0853-7753

Manuela Lince[2] orcid.org/0000-0001-7874-2109

María C. Vásquez[2] orcid.org/0000-0001-5258-9505

Catalina María Arango-Alzate[2] orcid.org/0000-0001-5134-9294

Angela M. Segura-Cardona[1] orcid.org/0000-0002-0010-1413

Gregory Mejía-Sandobal[3] orcid.org/0000-0003-4236-3320

Albino Barraza-Villareal[4] orcid.org/0000-0002-9020-4175

1. Escuela de Graduados, Universidad CES. Medellín, Colombia.
2. Facultad de Medicina, Universidad CES. Medellín, Colombia.
3. Facultad de Medicina Veterinaria y Zootecnia, Universidad CES. Medellín, Colombia.
4. Centro de Investigaciones en Salud Poblacional, Instituto Nacional de Salud Pública de México. México.

Fecha de recepción: Octubre 28 - 2019 Fecha de revisión: Junio 25 - 2020 Fecha de aceptación: Agosto 26 - 2022

Gómez-Mercado CA, Escobar N, González MC, Lince M, Vásquez MC, Arango-Alzate CM, et al. Exposición intrauterina a disruptores endocrinos (ftalatos): fuentes de exposición y cuantificación de metabolitos urinarios. Univ. Salud. 2022; 24(3):235-247. DOI: https://doi.org/10.22267/rus.222403.278

Resumen

Introducción: Los ftalatos son disruptores endocrinos usados en la fabricación de múltiples productos de la industria, principalmente plásticos. El periodo fetal representa la principal ventana de vulnerabilidad, y la exposición a ftalatos en esta etapa de vida genera efectos adversos fetales y postnatales. El biomarcador más fiable para medición de ftalatos es la orina. **Objetivo:** Caracterizar las diferentes fuentes de exposición a disruptores endocrinos y cuantificar la concentración urinaria de ftalatos en gestantes. **Materiales y métodos:** Estudio transversal, observacional y descriptivo que incluye 400 gestantes que asistieron a control prenatal en las instituciones de salud Génesis y Metrosalud (Medellín-Colombia). Se caracterizaron fuentes de exposición, se recolectó muestras de orina de todas las gestantes, y cuantificó la concentración de ftalatos de 38 mujeres. **Resultados:** Las medias geométricas de ftalato Di(2-ethylhexyl)phthalate(DEHP), Mono-n-butyl phthalate(MnBP), Mono-2-ethyl-5-hydroxyhexyl phthalate(MEHHP) y Mono-2-ethyl-5-oxohexyl phthalate(MEOHP) fueron 162,72µg/L, 58,5 µg/L, 33,93µg/L y 31,63µg/L respectivamente. **Conclusiones:** La mayoría de las gestantes evaluadas han estado expuestas a lo largo de su vida a fuentes potenciales de disruptores endocrinos, presentes en químicos domésticos, tabaco y uso frecuente de cosméticos faciales y corporales. Las concentraciones de MnBP, MEHHP y MEOHP en orina de las participantes, fueron superiores a los hallazgos a nivel mundial.

Palabras clave: Disruptores endocrinos; orina; embarazo. (Fuente: DeCS, Bireme).

Abstract

Introduction: Phthalates are endocrine disruptors used in the manufacture of various industrial products, mainly plastics. The fetal period represents the principal window of vulnerability, and the exposure to Phthalates in this stage of life generates adverse fetal and post-natal effects. The most reliable biomarker for the assessment of Phthalates is urine. **Objective:** To characterize the different exposure sources of endocrine disruptors and quantify the urinary concentration of Phthalates in pregnant women. **Materials and methods:** A cross-sectional, observational, and descriptive study which included 400 pregnant women who received prenatal care in the Genesis and Metrosalud health institutions (Medellín-Colombia). Exposure sources were characterized and urine samples were collected from all pregnant women and the Phthalate concentration was quantified in 38 women. **Results:** The geometric measures of Phthalate Di(2-ethylhexyl)phthalate(DEHP), Mono-n-butyl phthalate(MnBP), Mono-2-ethyl-5-hydroxyhexyl phthalate(MEHHP) and Mono-2-ethyl-5-oxohexyl phthalate(MEOHP) were 162.72µg/L, 58.5 µg/L, 33.93µg/L and 31.63µg/L respectively. **Conclusions:** The majority of pregnant women that were evaluated were exposed to potential sources of endocrine disruptors throughout their life, which are present in household chemicals, tobacco, and frequent use of facial and body cosmetics. The concentrations of MnBP, MEHHP y MEOHP in urine of participants were higher than those found worldwide.

Keywords: Endocrine disruptors; urine; pregnancy. (Source: DeCS, Bireme).

***Autor de correspondencia**
Carlos Alberto Gómez Mercado
e-mail: klargomez@gmail.com

cosméticos faciales y corporales. Las concentraciones de MnBP, MEHHP y MEOHP en la orina de gestantes son superiores a los hallazgos en el mundo, lo cual, implica iniciar procesos de biomonitoreo y educación en los programas de control prenatal. Este es el primer estudio en Colombia que caracteriza las fuentes de exposición y cuantifica las concentraciones urinarias de ftalatos en gestantes.

Referencias

1. Calafat AM, Valentin-Blasini L, Ye X. Trends in Exposure to Chemicals in Personal Care and Consumer Products. *Curr Environ Health Rep* [Internet]. 2015 Dec 1; 2(4):348-55. DOI: 10.1007/s40572-015-0065-9.
2. National Center for Toxicological Research. Endocrine Disruptor Knowledge Base [Internet]. FDA; 2019 [citado 2019 Oct 24]. Disponible en: http://www.fda.gov/science-research/bioinformatics-tools/endocrine-disruptor-knowledge-base
3. Goldman LR, Koduru S. Chemicals in the environment and developmental toxicity to children: a public health and policy perspective. *Environ Health Perspect* [Internet]. 2000; 108(Suppl 3):443-8. DOI: 10.2307/3454535.
4. Fernández MF, Román M, Arrebola JP, Olea N. Endocrine Disruptors: Time to Act. *Curr Environ Health Rep* [Internet]. 2014; 1(4):325-32. DOI: 10.1007/s40572-014-0025-9.
5. Larsson K, Ljung Björklund K, Palm B, Wennberg M, Kaj L, Lindh CH, *et al*. Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children. *Environ Int* [Internet]. 2014; 73:323-33. DOI: 10.1016/j.envint.2014.08.014.
6. Trasande L, Attina TM, Blustein J. Association Between Urinary Bisphenol A Concentration and Obesity Prevalence in Children and Adolescents. *JAMA* [Internet]. 2012; 308(11):1113-21. DOI: 10.1001/2012.jama.11461.
7. Edlow AG, Chen M, Smith NA, Lu C, McElrath TF. Fetal bisphenol A exposure: concentration of conjugated and unconjugated bisphenol A in amniotic fluid in the second and third trimesters. *Reprod Toxicol Elmsford N* [Internet]. 2012; 34(1):1-7. DOI: 10.1016/j.reprotox.2012.03.009.
8. de Cock M, de Boer MR, Lamoree M, Legler J, Van de Bor M. First year growth in relation to prenatal exposure to endocrine disruptors - a Dutch prospective cohort study. *Int J Environ Res Public Health* [Internet]. 2014; 11(7):7001-21. DOI: 10.3390/ijerph110707001.
9. Heindel JJ. Endocrine disruptors and the obesity epidemic. *Toxicol Sci* [Internet]. 2003 Dec; 76(2):247-9. DOI: 10.1093/toxsci/kfg255.
10. Grün F, Blumberg B. Environmental obesogens: organotins and endocrine disruption via nuclear receptor signaling. *Endocrinology* [Internet]. 2006 Jun; 147(6):S50-5. DOI: 10.1210/en.2005-1129.
11. Gluckman PD, Hanson MA. Developmental origins of disease paradigm: a mechanistic and evolutionary perspective. *Pediatr Res* [Internet]. 2004 Sep; 56(3):311-7. DOI: 10.1203/01.PDR.0000135998.08025.FB.
12. Vafeiadi M, Roumeliotaki T, Myridakis A, Chalkiadaki G, Fthenou E, Dermitzaki E, *et al*. Association of early life exposure to bisphenol A with obesity and cardiometabolic traits in childhood. *Environ Res* [Internet]. 2016 Apr; 146:379-87. DOI: 10.1016/j.envres.2016.01.017.
13. Vafeiadi M, Georgiou V, Chalkiadaki G, Rantakokko P, Kiviranta H, Karachaliou M, *et al*. Association of Prenatal Exposure to Persistent Organic Pollutants with Obesity and Cardiometabolic Traits in Early Childhood: The Rhea Mother-Child Cohort (Crete, Greece). *Environ Health Perspect* [Internet]. 2015 Oct; 123(10):1015-21. DOI: 10.1289/ehp.1409062.
14. Winneke G. Developmental aspects of environmental neurotoxicology: lessons from lead and polychlorinated biphenyls. *J Neurol Sci* [Internet]. 2011 Sep 15; 308(1-2):9-15. DOI: 10.1016/j.jns.2011.05.020.
15. Koch HM, Becker K, Wittassek M, Seiwert M, Angerer J, Kolossa-Gehring M. Di-n-butylphthalate and butylbenzylphthalate — urinary metabolite levels and estimated daily intakes: pilot study for the German Environmental Survey on children. *J Expo Sci Environ Epidemiol* [Internet]. 2007 Jul [citado 2018 Mar 22]; 17(4):378-87. Disponible en: https://www.nature.com/articles/7500526
16. Koch HM, Preuss R, Angerer J. Di(2-ethylhexyl)phthalate (DEHP): human metabolism and internal exposure-- an update and latest results. *Int J Androl* [Internet]. 2006 Feb; 29(1):155-65. DOI: 10.1111/j.1365-2605.2005.00607.x.
17. Janjua NR, Mortensen GK, Andersson A-M, Kongshoj B, Wulf HC. Systemic Uptake of Diethyl Phthalate, Dibutyl Phthalate, and Butyl Paraben Following Whole-Body Topical Application and Reproductive and Thyroid Hormone Levels in Humans. *Environ Sci Technol* [Internet]. 2007 Aug 1 [citado 2018 Mar 24]; 41(15):5564-70. DOI: 10.1021/es0628755.
18. Main KM, Mortensen GK, Kaleva MM, Boisen KA, Damgaard IN, Chellakooty M, *et al*. Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. *Environ Health Perspect* [Internet]. 2006 Feb; 114(2):270-6. DOI: 10.1289/ehp.8075.
19. Zhang Y, Lin L, Cao Y, Chen B, Zheng L, Ge R-S. Phthalate levels and low birth weight: a nested case-control study of Chinese newborns. *J Pediatr* [Internet]. 2009 Oct; 155(4):500-4. DOI: 10.1016/j.jpeds.2009.04.007.
20. Braun JM, Smith KW, Williams PL, Calafat AM, Berry K, Ehrlich S, *et al*. Variability of urinary phthalate metabolite and bisphenol A concentrations before and during pregnancy. *Environ Health Perspect* [Internet]. 2012 May; 120(5):739-45. DOI: 10.1289/ehp.1104139.
21. Hauser R, Duty S, Godfrey-Bailey L, Calafat AM. Medications as a source of human exposure to phthalates. *Environ Health Perspect* [Internet]. 2004 May; 112(6):751-3. DOI: 10.1289/ehp.6804.
22. Schettler T. Human exposure to phthalates via consumer products. *Int J Androl* [Internet]. 2006 Feb; 29(1):134-9. DOI: 10.1111/j.1365-2605.2005.00567.x.
23. Sathyanarayana S. Phthalates and Children's Health. *Curr Probl Pediatr Adolesc Health Care* [Internet]. 2008 Feb 1 [citado 2018 Mar 22]; 38(2):34-49. Disponible en: http://www.cppah.com/article/S1538-5442(07)00102-2/fulltext
24. Ramos JJ, Esteban M, Castaño A. Exposición a ftalatos en niños y adultos. *Rev Salud Ambient* [Internet]. 2015; 15:80-3. Disponible en: https://ojs.diffundit.com/index.php/rsa/article/view/751
25. Matsumoto J, Yokota H, Yuasa A. Developmental increases in rat hepatic microsomal UDP-glucuronosyltransferase activities toward xenoestrogens and decreases during

pregnancy. *Environ Health Perspect* [Internet]. 2002 Feb; 110(2):193-6. DOI: 10.1289/ehp.02110193.

26. Bustamante Montes P, Lizama Soberanis B, Olaíz Fernández G, Vásquez Moreno F. FTALATOS Y EFECTOS EN LA SALUD. *Rev Int Contam Ambient* [Internet]. 2001; 17(4):205-15. Disponible en: https://www.revistascca.unam.mx/rica/index.php/rica/article/view/25362
27. Gomez AL, Delconte MB, Altamirano GA, Vigezzi L, Bosquiazzo VL, Barbisan LF, *et al*. Perinatal Exposure to Bisphenol A or Diethylstilbestrol Increases the Susceptibility to Develop Mammary Gland Lesions After Estrogen Replacement Therapy in Middle-Aged Rats. *Horm Cancer* [Internet]. 2017; 8(2):78-89. DOI: 10.1007/s12672-016-0282-1.
28. Ferguson KK, Meeker JD, Cantonwine DE, Chen Y-H, Mukherjee B, McElrath TF. Urinary phthalate metabolite and bisphenol A associations with ultrasound and delivery indices of fetal growth. *Environ Int* [Internet]. 2016 Sep; 94:531-7. DOI: 10.1016/j.envint.2016.06.013.
29. Myridakis A, Fthenou E, Balaska E, Vakinti M, Kogevinas M, Stephanou EG. Phthalate esters, parabens and bisphenol-A exposure among mothers and their children in Greece (Rhea cohort). *Environ Int* [Internet]. 2015 Oct; 83:1-10. DOI: 10.1016/j.envint.2015.05.014.
30. Harley KG, Berger K, Rauch S, Kogut K, Henn BC, Calafat AM, *et al*. Association of prenatal urinary phthalate metabolite concentrations and childhood BMI and obesity. *Pediatr Res* [Internet]. 2017 Apr 20; 82(3):405-15. DOI: 10.1038/pr.2017.112.
31. Harley KG, Aguilar Schall R, Chevrier J, Tyler K, Aguirre H, Bradman A, *et al*. Prenatal and postnatal bisphenol A exposure and body mass index in childhood in the CHAMACOS cohort. *Environ Health Perspect* [Internet]. 2013 Apr; 121(4):514-20. DOI: 10.1289/ehp.1205548.
32. Lee B-E, Park H, Hong Y-C, Ha M, Kim Y, Chang N, *et al*. Prenatal bisphenol A and birth outcomes: MOCEH (Mothers and Children's Environmental Health) study. *Int J Hyg Environ Health* [Internet]. 2014 Mar; 217(2-3):328-34. DOI: 10.1016/j.ijheh.2013.07.005.
33. Braun JM, Lanphear BP, Calafat AM, Deria S, Khoury J, Howe CJ, *et al*. Early-life bisphenol a exposure and child body mass index: a prospective cohort study. *Environ Health Perspect* [Internet]. 2014 Nov; 122(11):1239-45. DOI: 10.1289/ehp.1408258.
34. Hoepner LA, Whyatt RM, Widen EM, Hassoun A, Oberfield SE, Mueller NT, *et al*. Bisphenol A and Adiposity in an Inner-City Birth Cohort. *Environ Health Perspect* [Internet]. 2016 Oct; 124(10):1644-50. DOI: 10.1289/EHP205.
35. Maresca MM, Hoepner LA, Hassoun A, Oberfield SE, Mooney SJ, Calafat AM, *et al*. Prenatal Exposure to Phthalates and Childhood Body Size in an Urban Cohort. *Environ Health Perspect* [Internet]. 2016 Apr; 124(4):514-20. DOI: 10.1289/ehp.1408750.
36. Buckley JP, Engel SM, Braun JM, Whyatt RM, Daniels JL, Mendez MA, *et al*. Prenatal Phthalate Exposures and Body Mass Index Among 4- to 7-Year-old Children: A Pooled Analysis. *Epidemiology* [Internet]. 2016 May; 27(3):449-58. DOI: 10.1097/EDE.0000000000000436.
37. Sabaredzovic A, Sakhi AK, Brantsæter AL, Thomsen C. Determination of 12 urinary phthalate metabolites in Norwegian pregnant women by core-shell high performance liquid chromatography with on-line solid-phase extraction, column switching and tandem mass spectrometry. *J Chromatogr B* [Internet]. 2015 Oct 1 [citado 2018 Nov 27]; 1002:343-52. Disponible en: http://www.sciencedirect.com/science/article/pii/S1570023215301689
38. Tribunal de Núremberg. Código de Ética Médica de Núremberg, Resolución 181. 1947. Disponible en: https://www.san.gva.es/documents/151744/228971/36codigodenuremberg.pdf
39. Manzini JL. Declaración de Helsinki: Principios éticos para la investigación médica sobre sujetos humanos. *Acta Bioeth* [Internet]. 2000; 6(2):321-34. DOI: 10.4067/S1726-569X2000000200010.
40. Invima. Resolución No°8430 [Internet]. 1993 Oct 4 [citado 2016 Apr 27]. Disponible en: https://www.invima.gov.co/resoluciones-medicamentos/2977-resolucion-no-8430-del-4-de-octubre-de-1993.html
41. Buckley JP, Herring AH, Wolff MS, Calafat AM, Engel SM. Prenatal exposure to environmental phenols and childhood fat mass in the Mount Sinai Children's Environmental Health Study. *Environ Int* [Internet]. 2016 May; 91:350-6. DOI: 10.1016/j.envint.2016.03.019.
42. Buckley JP, Engel SM, Mendez MA, Richardson DB, Daniels JL, Calafat AM, *et al*. Prenatal Phthalate Exposures and Childhood Fat Mass in a New York City Cohort. *Environ Health Perspect* [Internet]. 2016 Apr; 124(4):507-13. DOI: 10.1289/ehp.1509788.
43. Botton J, Philippat C, Calafat AM, Carles S, Charles M-A, Slama R, *et al*. Phthalate pregnancy exposure and male offspring growth from the intra-uterine period to five years of age. *Environ Res* [Internet]. 2016 Nov; 151:601-9. DOI: 10.1016/j.envres.2016.08.033.
44. Agay-Shay K, Martinez D, Valvi D, Garcia-Esteban R, Basagaña X, Robinson O, *et al*. Exposure to Endocrine-Disrupting Chemicals during Pregnancy and Weight at 7 Years of Age: A Multi-pollutant Approach. *Environ Health Perspect* [Internet]. 2015 Oct; 123(10):1030-7. DOI: 10.1289/ehp.1409049.
45. Smarr MM, Grantz KL, Sundaram R, Maisog JM, Kannan K, Louis GMB. Parental urinary biomarkers of preconception exposure to bisphenol A and phthalates in relation to birth outcomes. *Environ Health Glob Access Sci Source* [Internet]. 2015 Sep 11; 14(1):73. DOI: 10.1186/s12940-015-0060-5.
46. Arbuckle TE, Davis K, Marro L, Fisher M, Legrand M, LeBlanc A, *et al*. Phthalate and bisphenol A exposure among pregnant women in Canada -- results from the MIREC study. *Environ Int* [Internet]. 2014 Jul; 68:55-65. DOI: 10.1016/j.envint.2014.02.010.
47. Arbuckle TE, Marro L, Davis K, Fisher M, Ayotte P, Bélanger P, *et al*. Exposure to free and conjugated forms of bisphenol A and triclosan among pregnant women in the MIREC cohort. *Environ Health Perspect* [Internet]. 2015 Apr; 123(4):277-84. DOI: 10.1289/ehp.1408187.
48. Sakhi AK, Sabaredzovic A, Papadopoulou E, Cequier E, Thomsen C. Levels, variability and determinants of environmental phenols in pairs of Norwegian mothers and children. *Environ Int* [Internet]. 2018 May 1 [citado 2020 Sep 30]; 114:242-51. Disponible en: http://www.sciencedirect.com/science/article/pii/S0160412017317555
49. Callan AC, Hinwood AL, Heffernan A, Eaglesham G, Mueller J, Odland JØ. Urinary bisphenol A concentrations in pregnant women. *Int J Hyg Environ Health* [Internet]. 2013 Nov 1 [citado 2020 Nov 3]; 216(6):641-4. Disponible en:

http://www.sciencedirect.com/science/article/pii/S1438463912001241

50. Tefre de Renzy-Martin K, Frederiksen H, Christensen JS, Boye Kyhl H, Andersson A-M, Husby S, *et al*. Current exposure of 200 pregnant Danish women to phthalates, parabens and phenols. *Reproduction* [Internet]. 2014; 147(4):443-53. DOI: 10.1530/REP-13-0461.
51. Ashrap P, Watkins DJ, Calafat AM, Ye X, Rosario Z, Brown P, *et al*. Elevated concentrations of urinary triclocarban, phenol and paraben among pregnant women in Northern Puerto Rico: Predictors and trends. *Environ Int* [Internet]. 2018; 121(Pt 1):990-1002. DOI: 10.1016/j.envint.2018.08.020.
52. Huang Y-F, Pan W-C, Tsai Y-A, Chang C-H, Chen P-J, Shao Y-S, *et al*. Concurrent exposures to nonylphenol, bisphenol A, phthalates, and organophosphate pesticides on birth outcomes: A cohort study in Taipei, Taiwan. *Sci Total Environ* [Internet]. 2017 Dec 31; 607-608:1126-35. DOI: 10.1016/j.scitotenv.2017.07.092.
53. Ding G, Wang C, Vinturache A, Zhao S, Pan R, Han W, *et al*. Prenatal low-level phenol exposures and birth outcomes in China. *Sci Total Environ* [Internet]. 2017 Dec 31; 607-608:1400-7. DOI: 10.1016/j.scitotenv.2017.07.084.
54. Irvin EA, Calafat AM, Silva MJ, Aguilar-Villalobos M, Needham LL, Hall DB, *et al*. An estimate of phthalate exposure among pregnant women living in Trujillo, Peru. *Chemosphere* [Internet]. 2010 Sep 1 [citado 2020 Nov 3]; 80(11):1301-7. Disponible en: http://www.sciencedirect.com/science/article/pii/S0045653510007228
55. Gómez-Mercado CA, Mejía-Sandoval G, Segura-Cardona ÁM, Arango-Alzate CM, Hernandez-Gonzalez SI, Patiño-García DF, *et al*. Exposición a Bisfenol A (BPA) en mujeres embarazadas y su relación con la obesidad en sus hijos: Revisión sistemática. *Rev Fac Nac Salud Pública* [Internet]. 2018 Mar 14 [citado 2020 May 25]; 36(1):66-74. Disponible en: https://revistas.udea.edu.co/index.php/fnsp/article/view/326797
56. Ye X, Pierik FH, Hauser R, Duty S, Angerer J, Park MM, *et al*. Urinary metabolite concentrations of organophosphorous pesticides, bisphenol A, and phthalates among pregnant women in Rotterdam, the Netherlands: The Generation R study. *Environ Res* [Internet]. 2008 Oct 1 [citado 2020 Nov 15]; 108(2):260-7. Disponible en: http://www.sciencedirect.com/science/article/pii/S0013935108001552
57. Völkel W, Colnot T, Csanády GA, Filser JG, Dekant W. Metabolism and kinetics of bisphenol a in humans at low doses following oral administration. *Chem Res Toxicol* [Internet]. 2002 Oct; 15(10):1281-7. DOI: 10.1021/tx025548t.
58. Pottenger LH, Domoradzki JY, Markham DA, Hansen SC, Cagen SZ, Waechter JM. The relative bioavailability and metabolism of bisphenol A in rats is dependent upon the route of administration. *Toxicol Sci* [Internet]. 2000 Mar; 54(1):3-18. DOI: 10.1093/toxsci/54.1.3.
59. Wormuth M, Scheringer M, Vollenweider M, Hungerbühler K. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? *Risk Anal* [Internet]. 2006 Jun; 26(3):803-24. DOI: 10.1111/j.1539-6924.2006.00770.x.
60. Petersen JH, Breindahl T. Plasticizers in total diet samples, baby food and infant formulae. *Food Addit Contam* [Internet]. 2000 Feb; 17(2):133-41. DOI: 10.1080/026520300283487.
61. Graham PR. Phthalate ester plasticizers--why and how they are used. *Environ Health Perspect* [Internet]. 1973 Jan; 3:3-12. DOI: 10.1289/ehp.73033.
62. Latini G. Monitoring phthalate exposure in humans. *Clin Chim Acta* [Internet]. 2005 Nov; 361(1-2):20-9. DOI: 10.1016/j.cccn.2005.05.003.
63. Frederiksen H, Skakkebaek NE, Andersson A-M. Metabolism of phthalates in humans. *Mol Nutr Food Res* [Internet]. 2007 Jul; 51(7):899-911. DOI: 10.1002/mnfr.200600243.