

EXPOSICION HUMANA A COMPUESTOS ORGANICOS PERSISTENTES Y NO PERSISTENTES

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Hospital Clínico. Universidad de Granada
Granada

VIGILANCIA BIOLÓGICA DE LA EXPOSICIÓN
A SUSTANCIAS QUÍMICAS
EN LA POBLACIÓN ESPAÑOLA



Contenido

- C. Orgánicos persistentes lipofílicos
- Alquilfenoles
- Bisfenol-A y otros bisfenoles
- Ftalatos
- Parabenes
- Benzofenonas
- Triclosán
- Filtros UV: canfenos y oxicinamatos
- PFOS y PFOA
- Y que mas?...

Organoclorados y cáncer de mama

Desde 1984 más de 40 estudios tratando de asociar los niveles en sangre y tejido adiposo de compuestos organoclorados (DDT y PCBs) y el riesgo de cáncer de mama

Resultados conflictivos

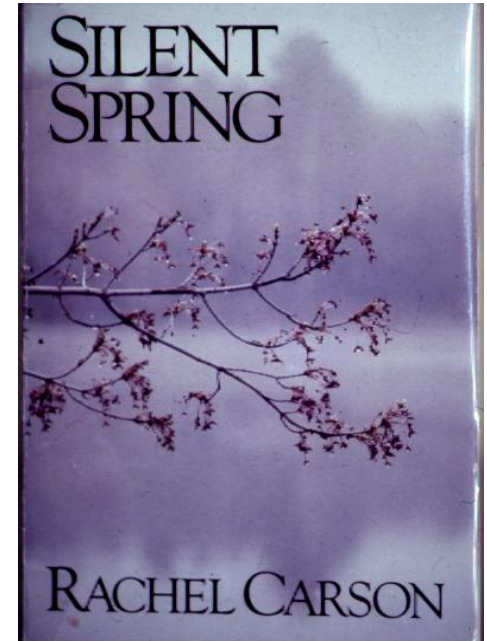
Cáncer es una enfermedad multifactorial

Largo periodo de incubación

Dificultades en la medida de exposición

¿Que compuesto químico?

Medida de exposición/Medida de Efecto



Pesticide Residues and Breast
Cancer: The Harvest of a
Silent Spring?

*David J. Hunter, Karl T. Kelsey**

Journal of the National Cancer Institute, Vol. 85, No. 8, April 21, 1993

Estimación del riesgo en cáncer de mama (OR)

Estudios universitarios	6.48 (2.09-19.07)*
Antecedentes familiares	5.02 (1.99-12.70)
Exposición química ambiental	3.80 (1.37-10.56)
Clase social elevada/CB	3.19 (1.49-6.85)
Consumo de tabaco	2.23 (1.21-4.14)
Cosumo alcohol	1.99 (1.16-3.43)
Estudios secundarios/NE	1.98 (1.11-3.51)
Edad de menarquia >12	1.88 (1.10-3.22)
Lactancia (>34meses)	0.43 (0.24-0.77)
Número hijos 4-5	0.40 (0.20-0.81)
Casada/soltera	0.31 (0.11-0.81)
Número hijos >6	0.23 (0.10-0.57)

*OR (IC 95%) para los factores de riesgo (protección) conocidos

Cancer Causes and Control 15: 591–600, 2004.
© 2004 Kluwer Academic Publishers. Printed in the Netherlands.

591

Breast cancer risk and the combined effect of environmental estrogens

Jesús M. Ibarluzea¹, Mariana F. Fernández², Loreto Santa-Marina¹, Maria F. Olea-Serrano², Ana M. Rivas², Juan J. Aurrekoetxea¹, José Expósito³, Miguel Lorenzo⁴, Pablo Torné⁵, Mercedes Villalobos⁶, Vicente Pedraza⁶, Annie J. Sasco⁷ & Nicolas Olea^{2,*}

Riesgo de cáncer de mama: Carga química (TEXB-alfa) en mujeres con BMI < 28.6 kg/m² (mediana) postmenopausicas

TEXB,
Ibarluzea
et al.
(2004),
CCC 13,
591-600

OR = 5.67 (95% CI 1.59-20.21)

.. cuando el cuarto cuartil (>197.51 pM Ee/g lipid)
se compara con el primer cuartil(<0.25 pM Ee/g lipid)

Fernandez
et al.
(2007)
Eur J
Cancer

p trend <0.01

¿Cuales son los contaminantes ambientales responsables de TEXB?:

Residuo de compuestos químicos en tejido mamario

Botella B, Environ Res
96: 34-40, 2004

17 pesticidas organoclorados (OC)

Cerrillo I, Environ Res.
98: 233-239, 2005

37 bifenilos policlorados (PCB)

Fernandez MF,
Chemosphere. 66:377-
383, 2006

10 PCBs hidroxilados y dioxin-like PCB,
15 dioxinas y furanos,

Carreno J, Environ Res.
103(1):55-61 . 2007

8 bifenilos polibromados (PBB)

Fernandez MF,
Reproductive
Toxicology 24(2):259-
64, 2007

11 esterres de PBBs (PBDE)

Lopez-Espinosa MJ,
Environ Res 106(1):1-
6., 2008

Exposure of women to organochlorine pesticides in Southern Spain[☆]

Begoña Botella, Jorge Crespo, Ana Rivas, Isabel Cerrillo, Maria Fátima Olea-Serrano,
and Nicolás Olea*

Environmental Research 96 (2004) 34–40

Exposición a pesticidas Organoclorados: Tejido mamario

Chemosphere 62 (2006) 1917–1924

Environmental and lifestyle factors
for organochlorine exposure among women living
in Southern Spain

I. Cerrillo ^a, M.F. Olea-Serrano ^b, J. Ibarluzea ^c, J. Exposito ^d,
P. Torne ^e, J. Laguna ^f, V. Pedraza ^a, N. Olea ^{a,*}

Residues of studied pesticides in adipose tissue (N = 458)

Pesticide	Mean ^a	SD ^a	Median ^a	Percentage
<i>o,p'</i> -DDT	14.01	65.35	^b	17.46
<i>p,p'</i> -DDT	13.74	32.92	^b	22.27
<i>o,p'</i> -DDD	62.34	147.81	^b	20.52
<i>p,p'</i> -DDE	501.14	496.63	392.31	97.38
∑ DDTs	659.98	744.35	496.06	98.25
Endosulfan I	1.82	10.14	^b	21.39
Endosulfan II	7.82	28.65	^b	11.13
Endosulfan-ether	1.79	7.06	0.31	50.43
Endosulfan-lactone	1.48	9.06	^b	15.93
Endosulfan-diol	4.79	22.58	^b	29.69
Endosulfan-sulfate	9.34	64.20	^b	10.04
∑ Endosulfans	38.83	159.82	9.00	69.65
Aldrin	10.51	27.08	^b	30.34
Dieldrin	6.52	31.04	^b	22.49
Endrin	13.84	39.90	^b	11.57
Lindane	17.91	60.57	^b	39.30

^a ng g⁻¹ of lipid.

^b Below detection limit.

Table 2
Concentrations of PCDD/F, WHO_{PCDD/F}-TEQ and WHO_{PCDD/F}-TEQ₂₀₀₅ as pg g⁻¹ fat in adipose tissue samples (n= 20) from women living in Southern Spain

Congeners	Mean (SD) (pg g ⁻¹ fat)	G. Mean (GSD) (pg g ⁻¹ fat)	≥ LOQ (%)	P5 (pg g ⁻¹ fat)	P25 (pg g ⁻¹ fat)	P50 (pg g ⁻¹ fat)	P75 (pg g ⁻¹ fat)	P95 (pg g ⁻¹ fat)	ΣCongeners (%)	WHO _{PCDD/F} -TEQ (%)	WHO _{PCDD/F} -TEQ ₂₀₀₅ (%)
2,3,7,8-TCDD	2.05(0.97)	1.87(1.53)	100	0.77	1.56	1.79	2.45	4.96	0.46	9.7	10.6
1,2,3,7,8-PeCDD	6.29(3.32)	5.59(1.64)	100	2.01	3.99	5.34	7.45	15.7	1.4	29	31.6
1,2,3,4,7,8-HxCDD	4.40(2.08)	3.99(1.57)	100	1.86	2.96	3.96	5.99	9.43	0.97	2.1	2.3
1,2,3,6,7,8-HxCDD	55.6(26.2)	49.3(1.72)	100	12.5	37.0	49.8	74.4	112	12.3	26	28.3
1,2,3,7,8,9-HxCDD	7.48(3.43)	6.78(1.64)	100	2.09	4.48	7.10	10.3	14.0	1.7	3.5	3.9
1,2,3,4,6,7,8-HpCDD	53.3(29.2)	45.2(1.84)	100	14.2	26.5	44.6	74.6	112	12	2.6	2.8
OCDD	292(148)	265(1.54)	100	150	186	235	369	723	66	0.15	0.47
2,3,7,8-TCDF	0.56(0.58)	0.45(2.01)	95	0.01	0.28	0.40	0.75	2.67	0.14	0.27	0.29
1,2,3,7,8-PeCDF	0.27(0.25)	0.27(1.93)	80	nq	0.1	0.23	0.37	0.94	0.07	0.06	0.04
2,3,4,7,8-PeCDF	9.52(5.28)	8.43(1.64)	100	3.51	5.98	8.26	10.7	24.6	2.1	22	14.6
1,2,3,4,7,8-HxCDF	4.67(2.69)	4.17(1.59)	100	2.11	2.98	4.00	4.94	13.2	1.0	2.2	2.4
1,2,3,6,7,8-HxCDF	3.72(2.31)	3.28(1.61)	100	1.47	2.48	3.15	3.80	11.2	0.80	1.7	1.9
2,3,4,6,7,8-HxCDF	1.14(0.50)	1.03(1.58)	100	0.50	0.73	1.01	1.46	2.11	0.26	0.55	0.61
1,2,3,7,8,9-HxCDF	nq	nq	0	nq	nq	nq	nq	nq	0	0	0
1,2,3,4,6,7,8-HpCDF	3.44(2.27)	2.96(1.70)	100	1.43	2.08	2.64	3.86	9.46	0.72	0.17	0.18
1,2,3,4,7,8,9-HpCDF	0.09(0.16)	0.34(1.27)	25	nq	nq	nq	0.18	0.42	0.08	0	0.005
OCDF	1.46(1.16)	1.63(1.58)	80	nq	0.97	1.29	1.69	4.19	0.4	0	0.002
ΣPCDD/F	446(206)	410(1.51)	100	254	287	360	563	1010			
WHO _{PCDD/F} -TEQ	21.5(9.27)	19.6(1.58)	100	7.12	14.0	20.0	27.9	42.0			
WHO _{PCDD/F} -TEQ ₂₀₀₅	19.6(8.43)	17.9(1.58)	100	6.49	12.8	18.0	26.3	37.3			

Abbreviations: mean (SD): arithmetic mean (standard deviation); G. mean (GSD): geometric mean (geometric standard deviation); ≥ LOQ: limit of quantification; P5: percentile 5; P25: percentile 25; P50: percentile 50; P75: percentile 75. P95: percentile 95. TCDD: tetrachlorodibenzo-*p*-dioxin; PeCDD: pentachlorodibenzo-*p*-dioxin; HxCDD: hexachlorodibenzo-*p*-dioxin; HpCDD: heptachlorodibenzo-*p*-dioxin; OCDD: octachlorodibenzo-*p*-dioxin; TCDF: tetrachlorodibenzofuran; PeCDF: pentachlorodibenzofuran; HxCDF: hexachlorodibenzofuran; HpCDF: heptachlorodibenzofuran; OCDF: octachlorodibenzofuran; ΣPCDD/Fs: sum of polychlorinated dibenzo-*p*-dioxins and dibenzofurans; WHO_{PCDD/F}-TEQ and WHO_{PCDD/F}-TEQ₂₀₀₅: Based on World Health Organization toxic equivalency factors for dibenzo-*p*-dioxins and dibenzofurans in 1997 (Van den Berg et al., 1998) and 2005 (Van den Berg et al., 2006), respectively; nq: below limit of quantification.

Exposición a dioxinas: Tejido mamario



Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere



Dioxins in adipose tissue of women in Southern Spain

M.J. Lopez-Espinosa ^a, H. Kiviranta ^b, P. Araque ^a, P. Ruokojärvi ^b, J.M. Molina-Molina ^a, M.F. Fernandez ^a, T. Vartiainen ^{b,c}, N. Olea ^{a,*}

Table 3
Concentration and frequency (%) of OH-PCB congeners in adipose tissue samples of women from Southeast Spain

Congeners	Mean	SD	Median	%	P5	P25	P75	P95
OH-PCB 107/118	0.3	0.72	<LOQ	20	<LOQ	<LOQ	<LOQ	1.57
OH-PCB 138	5.31	8.88	3.3	70	<LOQ	<LOQ	5.08	14.8
OH-PCB 180	1.96	3.84	<LOQ	25	<LOQ	<LOQ	0.78	10.4
Σ OH-PCB	7.79	12.1	4.05	–	<LOQ	2.78	6.05	20.3

Concentrations in pg/ g of lipid. OH-PCB: hydroxy-polychlorinated biphenyl. P5, P25, P75, P95 percentiles.

Exposición a PCBs: Tejido mamario



Available online at www.sciencedirect.com



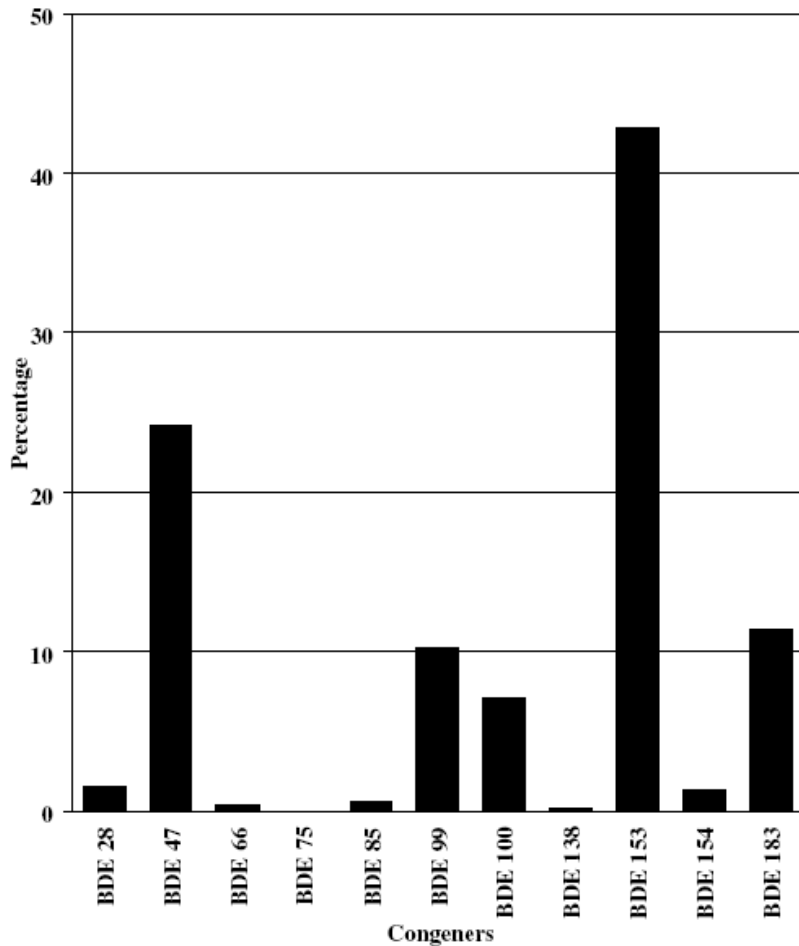
Chemosphere 71 (2008) 1196–1205

CHEMOSPHERE

www.elsevier.com/locate/chemosphere

Polychlorinated biphenyls (PCBs) and hydroxy-PCBs in adipose tissue of women in Southeast Spain

M.F. Fernandez ^{a,*}, H. Kiviranta ^b, J.M. Molina-Molina ^a, O. Laine ^b,
M.J. Lopez-Espinosa ^a, T. Vartiainen ^{b,c}, N. Olea ^a



Exposición a PBBs y PBDEs: Tejido mamario

Chemosphere xxx (2006) xxx–xxx

CHEMOSPHERE

www.elsevier.com/locate/chemosphere

PBDEs and PBBs in the adipose tissue of women from Spain

M.F. Fernandez ^a, P. Araque ^a, H. Kiviranta ^b, J.M. Molina-Molina ^a,
P. Rantakokko ^b, O. Laine ^b, T. Vartiainen ^{b,c}, N. Olea ^{a,*}

^a Laboratory of Medical Investigations, Clínico University Hospital, University of Granada, 18071 Granada, Spain

^b Department of Environmental Health, National Public Health Institute, P.O. Box 95, FI-70701 Kuopio, Finland

^c Department of Environmental Sciences, University of Kuopio, P.O. Box 1627, FI-70211 Kuopio, Finland

¿Cuales son los xenoestrógenos responsables de TEXB?:

Residuo de compuestos químicos en tejido mamario

Botella B, Environ Res
96: 34-40, 2004

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103(1):55-61 . 2007

8 bifenilos polibromados (PBB)

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64, 2007

11 esteres de PBBs (PBDE)

2 alquilfenoles

Lopez-Espinosa MJ,
Environ Res 106(1):1-
6., 2008

5 bisfenol-A y derivados clorados

Table 1

Concentrations of 4-nonylphenol and 4-octylphenol (ng g^{-1} adipose tissue) in adipose tissue samples from women living in Southern Spain.

	n (%)	>LOD			
		Mean (SD)	25th	Median	75th
4-Nonylphenol	20/20 (100)	82 (127)	40	57	69
4-Octylphenol	4/20 (23.5)	5.5 (2.1)	4.2	4.5	7.7

n (%) = Number of subjects (percentage of detection); LOD = limit of detection; SD = standard deviation

Exposición a Alquilfenoles: Tejido mamario

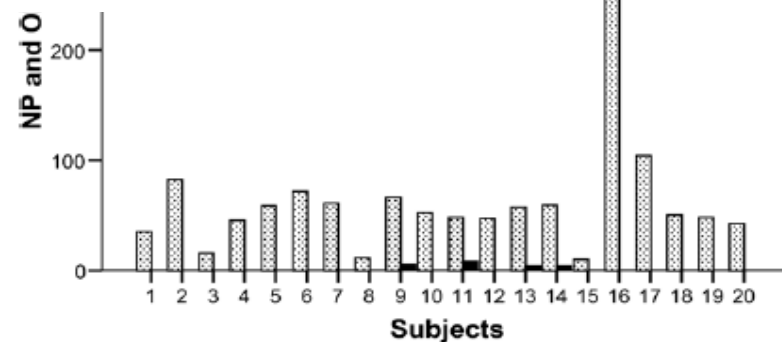


Fig. 2. Individual concentrations (ng g^{-1} adipose tissue) of 4-nonylphenol (NP) and 4-octylphenol (OP) in adipose tissue samples.



ELSEVIER

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Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere



Nonylphenol and octylphenol in adipose tissue of women in Southern Spain

M.J. Lopez-Espinosa^{a,b}, C. Freire^a, J.P. Arrebola^a, N. Navea^{a,c}, J. Taoufik^{c,a}, M.F. Fernandez^a, O. Ballesteros^c, R. Prada^a, N. Olea^{a,*}

Alquilfenoles

Nonil y octilfenol

Alquilfenol etoxilados:
mono, di, tri... etoxilados

Detergentes

Anti-oxidantes

Anti-amarilleantes del plástico

Nonoxynol: espermicida

Inertes en pesticidas



Exposición a bisfenoles: tejido mamario

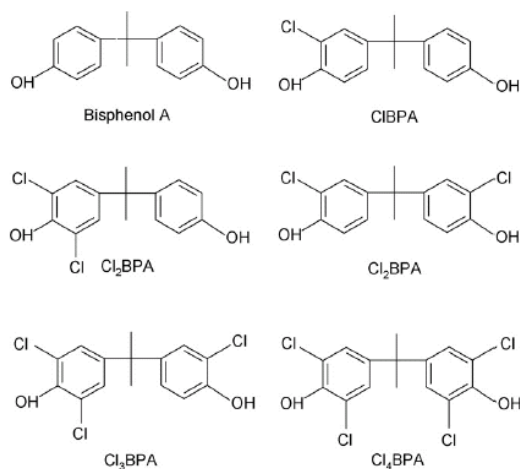


Fig. 1. Structural formula of bisphenol-A and chlorinated derivatives.



Table 2
Concentrations of BPA (ng/g) and chlorinated derivatives in adipose tissue samples

	n (%)	>LOD					
		Mean (\pm S.D.)	Median	5th	25th	75th	95th
BPA	11/20 (55)	5.83 (3.48)	4.79	2.07	3.54	7.12	11.88
Cl-BPA	3/20 (15)	3.05 (0.28)	3.14	2.82	2.94	3.21	3.26
Cl ₂ -BPA	16/20 (80)	9.21 (9.26)	7.77	2.61	5.62	8.83	21.49
Cl ₃ -BPA	2/20 (10)	0.74 (0.15)	0.74	0.66	0.69	0.80	0.84
Cl ₄ -BPA	0/20 (0)	<LOD	<LOD	–	–	–	–
Σ BPA	16/20 (80)	9.00 (9.22)	8.12	0	1.93	9.60	28.25

n (%), number of subjects (percentage of detection); LOD, Limit of detection.

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Reproductive Toxicology xxx (2007) xxx–xxx

Reproductive
Toxicology

www.elsevier.com/locate/reprotox

Bisphenol-A and chlorinated derivatives in adipose tissue of women

M.F. Fernandez^{a,*}, J.P. Arrebola^a, J. Taoufiki^b, A. Navalón^b,
O. Ballesteros^b, R. Pulgar^a, J.L. Vilchez^b, N. Olea^a

^a Laboratory of Medical Investigations, San Cecilio University Hospital,
University of Granada, 18071 Granada, Spain

^b Research Group of Analytical Chemistry and Life Sciences, Department of Analytical Chemistry,
University of Granada, 18071 Granada, Spain

BPA (como DES) es estrogénico

"Really?"

Yes...
desPLEX[®]
to prevent ABORTION, MISCARRIAGE and
PREMATURE LABOR

*recommended for routine prophylaxis
in ALL pregnancies . . .*

96 per cent live delivery with **desPLEX**
in one series of 1200 patients*—
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No gastric or other side effects with **desPLEX**
— in either high or low dosage^{2,4,5}

(Each **desPLEX** tablet starts with 25 mg. of diethylstilbestrol, U.S.P., which is then ultramicronized to smooth and accelerate absorption and activity. A portion of this ultramicronized diethylstilbestrol is even included in the tablet coating to assure prompt help in emergencies. **desPLEX** tablets also contain vitamin C and certain members of the vitamin B complex to aid detoxification in pregnancy and the effectuation of estrogen.)

For further data and a generous trial supply of **desPLEX**, write to:
Medical Director

REFERENCES

1. Canerio, E. M., et al.: *Am. J. Obst. & Gynec.* 65:1299, 1953.
2. Gitman, L., and Kaplowitz, A.: *N. Y. St. J. Med.* 50:2823, 1950.
3. Kannak, K. J.: *South. M. J.* 45:1166, 1952.
4. Peña, E. F.: *Med. Times* 82:921, 1954; *Am. J. Surg.* 87:95, 1954.
5. Bore, J. W.: *J. Nat. M. A.* 43:20, 1951; 45:223, 1953.

GRANT CHEMICAL COMPANY, INC., Brooklyn 26, N.Y.

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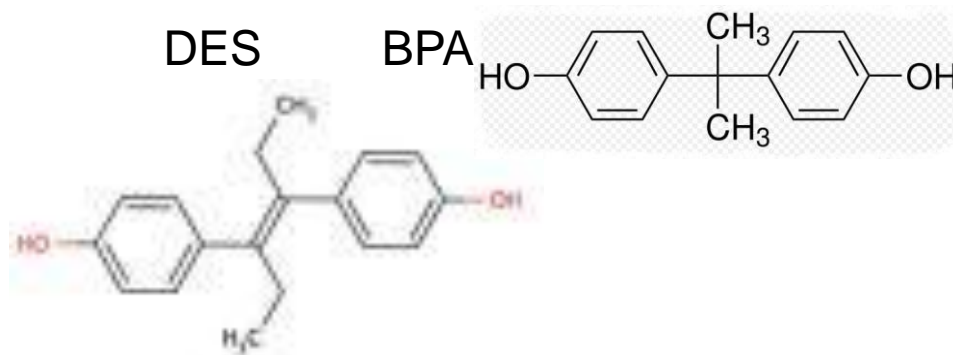
Am. J. Obst. & Gyn.
June, 1956

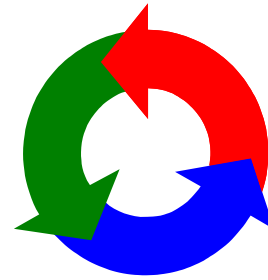
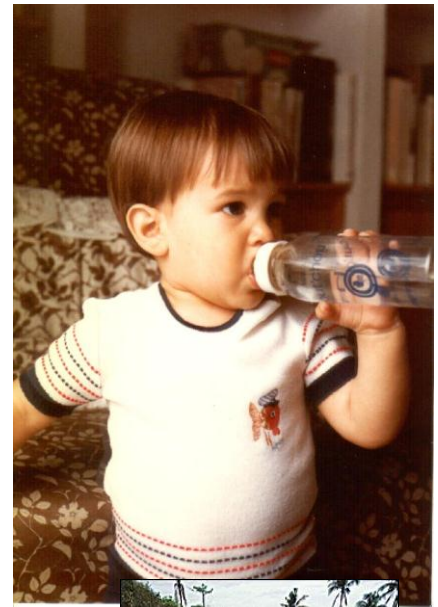
Figure 6-1 An ad promoting diethylstilbestrol addressed to obstetricians.



Wellcome Images

E. C. Dodds y W. Lawson,
"Synthetic Œstrogenic Agents
without the Phenanthrene Nucleus",
Nature, 137 (1936), 996.





MARTES 22 DE MAYO DE 2007

General Electric vende su filial de Cartagena al grupo Saudi Basic Industries Corporation (SABIC) por 11.600 millones de dólares

Producción anual de BPA en Cartagena: 250.000 Tm/año (Lexam y Ultem)



سابك
عندنا

OR (IC 95%) para los factores de riesgo (protección) conocidos y TEXTB

Antecedentes familiares	5.02 (1.99-12.70)	TEXTB
Clase social elevada/CB	3.19 (1.49-6.85)	
Consumo de tabaco	2.23 (1.21-4.14)	TEXTB
Consumo alcohol	1.99 (1.16-3.43)	TEXTB
Estudios secundarios/NE	1.98 (1.11-3.51)	
Edad de menarquia >11	1.88 (1.10-3.22)	
Lactancia (>34meses)	0.43 (0.24-0.77)	TEXTB
Número hijos 4-5	0.40 (0.20-0.81)	TEXTB
Casada/soltera	0.31 (0.11-0.81)	
Número hijos >6	0.23 (0.10-0.57)	TEXTB



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ScienceDirect

journal homepage: www.ejconline.com



2 Analysis of population characteristics related to the total
3 effective xenoestrogen burden: A biomarker of xenoestrogen
4 exposure in breast cancer ☆

⁵ Mariana F. Fernandez^{a,*}, Loreto Santa-Marina^b, Jesus M. Ibarluzea^b, Jose Exposito^c,
⁶ Juan J. Aurrekoetxea^b, Pablo Torne^d, Juan Laguna^e, Ana I. Rueda^d, Vicente Pedraza^f,
⁷ Nicolas Olea^{a,f}

INMA

Seguimiento de 3.500 mujeres embarazadas y sus hijos.

Cohortes ya establecidas y de nueva creación en 6 Comunidades Autónomas.

Seguimiento durante al menos dos décadas.



Table 2
Residues of DDTs in placenta extracts

Pesticide	Mean ^a	±SD	Median ^a	Maximum ^a	Frequency (%)
<i>p,p'</i> -DDT	1.02	1.47	0.50	8.66	59.00
<i>o,p'</i> DDT	0.60	0.78	0.50	3.55	58.94
<i>p,p'</i> -DDE	2.37	2.80	1.78	28.29	96.03
<i>o,p'</i> -DDD	1.42	2.47	0.50	19.01	56.70
∑DDTs	5.23	5.28	3.69	31.50	99.33

^a ng/g of placenta.

Table 3
Residues of endosulphan in placenta extracts

Pesticide	Mean ^a	±SD	Median ^a	Maximum ^a	Frequency (%)
E-I	0.67	1.37	0.28	11.16	58.95
E-II	0.40	1.30	–	12.90	24.50
E-ether	0.12	0.19	0.10	1.39	52.32
E-diol	5.11	5.23	4.46	26.23	76.86
E-lactone	0.81	2.43	–	27.31	43.30
E-sulphate	0.68	1.44	–	8.29	47.70
∑Endosulphans	8.79	8.42	7.06	49.78	98.30

E = endosulphan; – = <LOD.

^a ng/g of placenta.

Table 4
Residues of aldrin, endrin and dieldrin in placenta extract

Pesticide	Mean ^a	±SD	Median ^a	Maximum ^a	Frequency (%)
Aldrin	0.24	0.60	–	4.79	26.49
Endrin	0.70	1.32	–	8.83	33.11
Dieldrin	0.25	0.59	–	3.68	22.51

– = <LOD.

^a ng/g of placenta.



Available online at www.sciencedirect.com



Placenta xx (2006) 1–8

PLACENTA

Organochlorine Pesticides in Placentas from Southern Spain and Some Related Factors[☆]

M.-J. Lopez-Espinosa^a, A. Granada^a, J. Carreno^a,
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Accepted 27 September 2006

Exposición a Pesticidas OC: Placenta

Determination of Bisphenol A and its chlorinated derivatives in placental tissue samples by liquid chromatography–tandem mass spectrometry

I. Jiménez-Díaz^{a,b}, A. Zafra-Gómez^a, O. Ballesteros^{a,*}, N. Navea^b, A. Navalón^a, M.F. Fernández^b, N. Olea^b, J.L. Vílchez^a

Journal of Chromatography B 2010

Exposición a Bisfenol-A y otros bisfenoles: Placenta

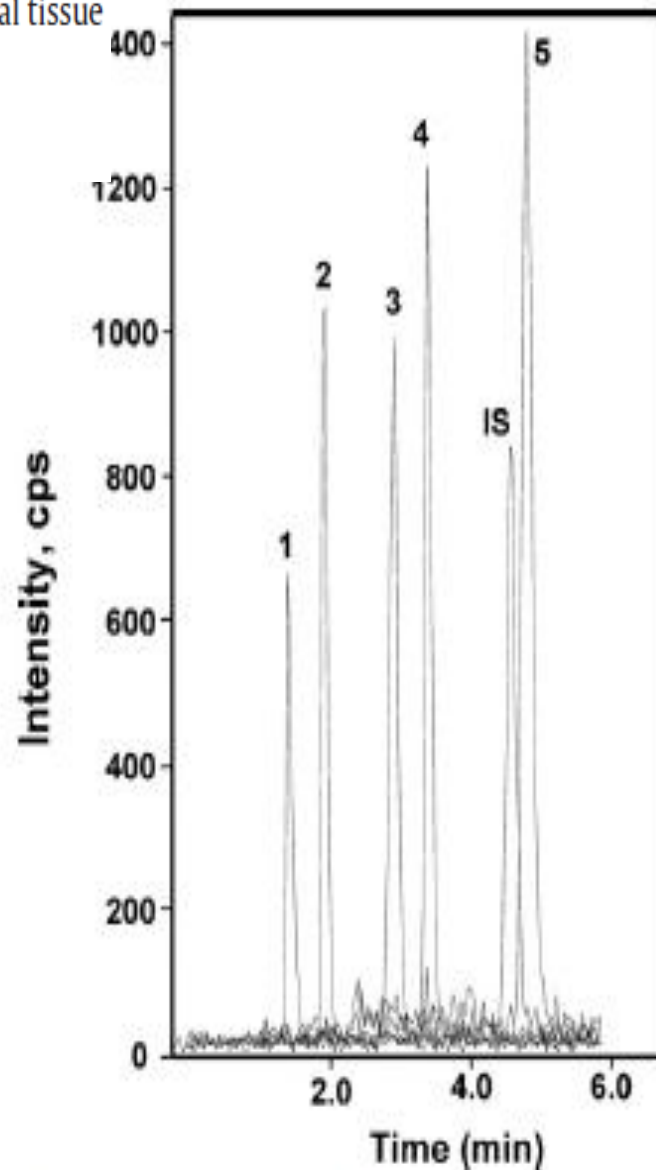


Fig. 1. MRM mode chromatogram of a standard mixture of the target compounds in a spiked placental tissue sample in MRM mode (10.0 ng g^{-1} of each compound). Peak identification: (IS) Internal Standard (1) Cl_4 -BPA; (2) Cl_3 -BPA; (3) Cl_2 -BPA; (4) Cl -BPA; (5) BPA.

Urinary concentrations of phthalates and phenols in a population of Spanish pregnant women and children

Casas L, Fernández MF, Llop S, Guxens M, Ballester F, Olea N, Basterrechea Irurzun M, Santa Marina L, Riaño I, Tardón A, Vrijheid M, Calafat AM, Sunyer J on behalf of the INMA Project. Environ Inter, 2011 (In press)

	Pregnant women			Children		
	3rd trimester			4 years old		
	n	% <LOD	Median	n	% <LOD	Median
BPA	120	9.0	2.2	30	3.3	4.2

Exposición a bisfenol-A: Orina



News Release

2008-59
April 18, 2008
For immediate release

***Government of Canada Takes Action on
Another Chemical of Concern: Bisphenol A***

OTTAWA - The Honourable Tony Clement, Minister of Health, and the Honourable John Baird, Minister of the Environment, today announced that the Government is taking action to protect the health of Canadians and the environment from another chemical of concern.

**European Commission: EU Ban on Bisphenol A
in Baby Bottles Next Year**

Friday, 26 November 2010

Exposición a bisfenoles

Latas con recubrimiento interior (envases alimentarios)

Xenoestrogens Released from Lacquer Coatings in Food Cans

José Antonio Brotons, María Fátima Olea-Serrano, Mercedes Villalobos, Vicente Pedraza, and Nicolás Olea

Laboratorio de Investigaciones Médicas, Universidad de Granada, 18071 Granada, Spain

to human exposure to xenoestrogens. *Key words:* bisphenol-A, food containers, lacquer coating, xenoestrogens. *Environ Health Perspect* 103:608–612 (1995)



Exposición a BPA: Origen sanitario

Estrogenicity of Resin-based Composites and Sealants Used in Dentistry

Nicolás Olea,¹ Rosa Pulgar,² Pilar Pérez,¹ Fátima Olea-Serrano,³ Ana Rivas,³ Arantzazu Novillo-Fertrell,³ Vicente Pedraza,¹ Ana M. Soto,⁴ and Carlos Sonnenschein⁴

¹Laboratory of Medical Investigation, Department of Radiology, School of Medicine, ²Department of Medical Odontology, School of Dentistry, and ³Department of Nutrition, School of Pharmacy, University of Granada, 18071 Granada, Spain; ⁴Department of Anatomy and Cellular Biology, Tufts University, School of Medicine, Boston, MA 02111 USA

Environ Health Perspect 104:298–305 (1996)



Exposición a BPA y ftalatos: Medioambiente hospitalario

Table 1. Distribution of the urinary concentrations of phenols ($\mu\text{g/L}$)^a in hospitalized premature infants.

Compound	Species	No. of infants	No. < LOD	Geometric mean (SD)	Median	Range		NHANES 2003–2004 ^b	
						Minimum	Maximum	Median	95th percentile
BP-3	Total	42	2	3.4 (4.8)	2.4	< LOD (0.4)	176	17.2	227
	Free	36	17	NA	NA	< LOD (0.4)	4.1		
BPA	Total	41	0	30.3 (5.2)	28.6	1.6	946	3.7	16.0
	Free	37	3	1.8 (3.2)	1.7	< LOD (0.4)	17.3		
MePB	Total	41	0	203 (4.7)	243	10.1	4,010	43.9 ^c	680 ^c
	Free	34	0	32 (4.9)	23	2.2	515		
PrPB	Total	42	0	16.8 (4.9)	17.0	1.3	1,360	9.1 ^c	279 ^c
	Free	37	0	2.6 (5.2)	1.7	0.3	171		
TCS	Total	42	34	NA	NA	< LOD (2.3)	16.7	5.9	148
	Free	37	36	NA	NA	< LOD (2.3)	3.4		

^aThe total concentrations are the sum of the free plus conjugated species of each phenol. We calculated geometric means and medians if the frequency of detection was > 60%. The estimated concentrations of free species must be interpreted with caution because at the time of the collection of the urine specimens, we did not prescreen the sampling materials for the presence of these phenols. ^bData from 314 children 6–11 years of age from NHANES (National Health and Nutrition Examination Survey) 2003–2004 for BP-3 (Calafat et al. 2008a), BPA (Calafat et al. 2008c), and TCS (Calafat et al. 2008b). ^cData from a group of 100 adults (Ye et al. 2006).

Exposure to Bisphenol A and Other Phenols in Neonatal Intensive Care Unit Premature Infants

Antonia M. Calafat,¹ Jennifer Weuve,^{2,3} Xiaoyun Ye,¹ Lily T. Jia,¹ Howard Hu,⁴ Steven Ringer,⁵ Ken Huttner,⁶ and Russ Hauser^{3,7}

¹Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ²Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, Illinois, USA; ³Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA; ⁴Schools of Public Health and Medicine, University of Michigan, Ann Arbor, Michigan, USA; ⁵Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; ⁶Neonatology Unit, and ⁷Vincent Memorial Obstetrics and Gynecology Service, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

Exposición a bisfenoles ftalatos

Papel y cartón reciclados (envases alimentarios)

Food Additives and Contaminants, January 2007; 24(1): 95–102



Oestrogenicity of paper and cardboard extracts used as food containers

M.-J. LOPEZ-ESPINOSA¹, A. GRANADA¹, P. ARAQUE¹, J.-M. MOLINA-MOLINA¹,
M.-C. PUERTOLLANO¹, A. RIVAS², M. FERNÁNDEZ¹, I. CERRILLO¹,
M.-F. OLEA-SERRANO², C. LÓPEZ³ & N. OLEA¹

¹Laboratory of Medical Investigations, San Cecilio University Hospital, University of Granada, E-18071 Granada, Spain, ²Department of Nutrition and Food Sciences and ³Department of Physical Chemistry, University of Granada, E-18071 Granada, Spain

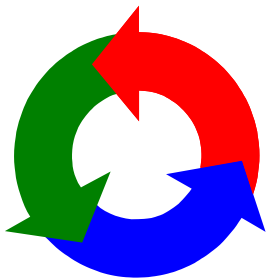
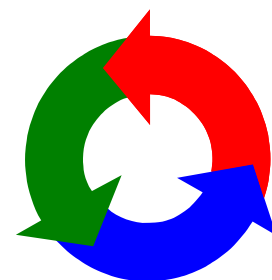


Table I. Estimated values of oestrogenicity (pM oestradiol equivalents Eeq g⁻¹ of cardboard or paper) and the frequency of positive samples in the E-Screen assay of paper and cardboard extracts.

	Total samples (<i>n</i> = 40)	Cardboard (<i>n</i> = 32)	Paper (<i>n</i> = 8)
Arithmetic mean	60.52	64.24	45.61
Geometric mean	11.97	13.33	7.78
Median	18.69	21.51	16.80
Standard deviation	12.55	13.02	12.09
Range	0.01–355.50	0.01–355.50	0.08–280.90
Frequency (%)	90.00	90.63	87.50

Table II. Levels and frequency of BPA, DBP and DEHP (ng g⁻¹ of cardboard or paper) in samples.

Residues	Total samples (<i>n</i> = 40)	Cardboard (<i>n</i> = 32)	Paper (<i>n</i> = 8)
<i>BPA</i>			
Arithmetic mean	97.34	115.32	25.43
Geometric mean	2.38	2.74	1.35
Median	0.52	0.52	0.49
Standard deviation	16.33	17.68	12.72
Range	0.05–1817.00	0.05–1817.00	0.08–188.00
Frequency (%)	45.00	46.88	37.50
<i>DBP</i>			
Arithmetic mean	713.17	706.32	740.49
Geometric mean	37.39	20.97	377.63
Median	121.84	75.62	548.55
Standard deviation	35.61	41.65	3.95
Range	0.10–10774.00	0.10–10774.00	29.10–3049.00
Frequency (%)	67.50	59.38	100
<i>DEHP</i>			
Arithmetic mean	3901.56	706.32	740.49
Geometric mean	341.74	302.11	559.54
Median	893.48	814.44	2751.84
Standard deviation	23.27	22.53	31.36
Range	0.52–61013.00	0.52–61013.00	1.53–10198.00
Frequency (%)	77.50	78.13	75.00



Exposición a bisfenoles y ftalatos: Agua embotellada



PET = Riesgo de presencia de ftalatos



Endocrine disruptors in bottled mineral water: total estrogenic burden and migration from plastic bottles

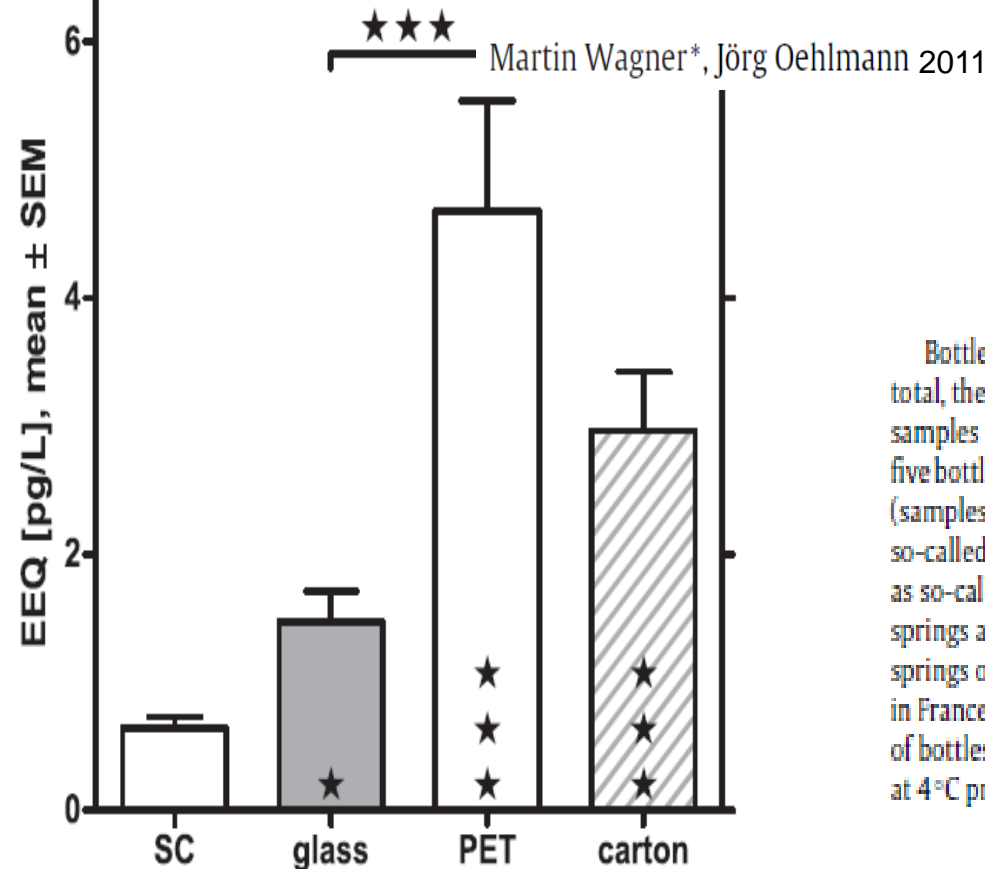
Martin Wagner • Jörg Oehlmann

3 & 7

Environ Sci Pollut Res (2009) 16:278–286

DOI 10.1007/s11356-009-0107-7

Endocrine disruptors in bottled mineral water: Estrogenic activity in the E-Screen[☆]



Bottled mineral water was purchased at local retailer stores. In total, the analyzed water samples comprised 18 products (coded as samples 1 to 18) from 13 different companies, including water from five bottlers that was packed in glass and plastic bottles made of PET (samples 1+2, 3+4, 5+6, 7+8, 9+10). With the exception of one so-called table water (bottled tap water), the products are marketed as so-called mineral water. These products originate from natural springs and are not processed or altered beyond deferrization. The springs of the products are located in different geographic regions in France, Germany, and Italy. Of each product, a sufficient number of bottles from the same lot ($n=10-12$) was purchased and stored at 4°C prior to analysis.

Fig. 4. Influence of the packaging material on the estrogenic activity of bottled water. Pooled analysis of products from the same springs bottled either in glass (sample 1, 3, 5, 7, 9) or plastic (PET, samples 2, 4, 6, 8, 10). Water bottled in PET contains significantly higher estrogenicity compared to water from glass (*** $p < 0.001$). Significant differences compared to the solvent control (SC, * $p < 0.05$, *** $p < 0.001$).



CLASIFICACION PLASTICOS



Poli-etileno tereftalato



Poli-etileno de alta densidad



Cloruro de polivinilo



Poli-etileno de baja densidad



Polipropileno



Poliestireno



Otros

Los materiales y objetos plásticos pueden estar compuestos de diferentes capas de materias plásticas unidas entre sí por medio de adhesivos. Los materiales y objetos plásticos pueden también estar impresos o recubiertos con un revestimiento orgánico o inorgánico. Los materiales y objetos plásticos impresos o recubiertos, al igual que los unidos entre sí por medio de adhesivos, deben quedar incluidos en el ámbito de aplicación del presente Reglamento. Los adhe-

REGLAMENTO (UE) N° 10/2011 DE LA COMISIÓN

de 14 de enero de 2011

sobre materiales y objetos plásticos destinados a entrar en contacto con alimentos

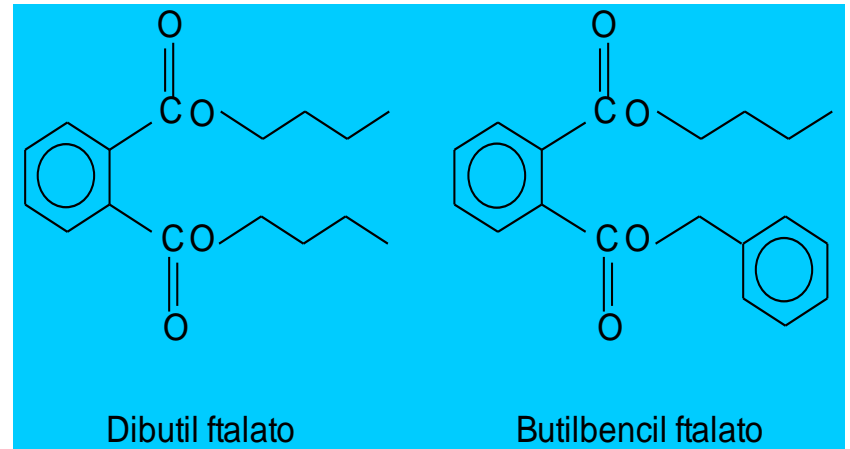
(Texto pertinente a efectos del EEE)

Exposición a ftalatos

Butilbencilftalato (BBP)

Dibutilftalato (DBP)

Dietilhexilftalato (DEHP)



Plastificantes desde 1930

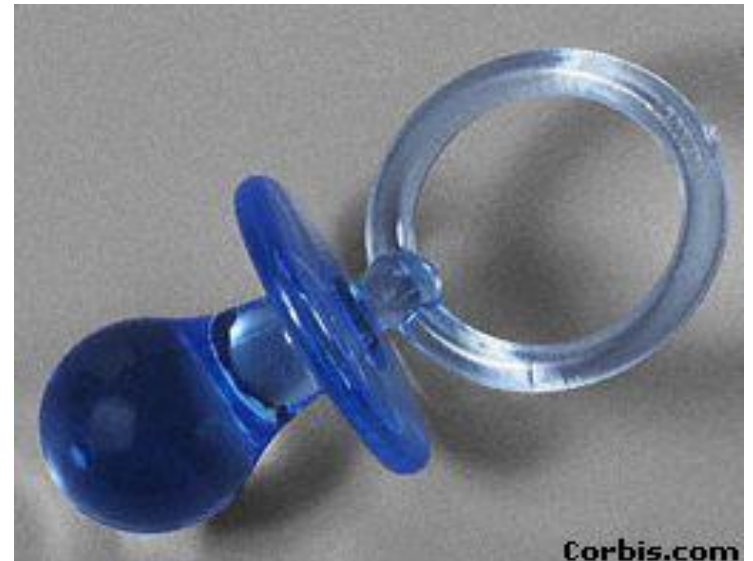
Tintas para plástico

Tratamiento de suelos

Antioxidantes alimentación (Lácteos)

Envases alimentarios

Tetinas y mordedores infantiles



['CASO CONTADOR'](#) | Acusaciones

La batalla de los plásticos



Contador, ahora con 'plásticos'

En la orina del ciclista se ha detectado una sustancia plástica, muy común en las transfusiones de sangre

di-(2-ethylhexyl)phthalate (DEHP)

	Pregnant women			Children		
	3rd trimester			4 years old		
	n	% <LOD	Median	n	% <LOD	Median
Phthalates						
MCNP	118	3.4	2.8	19	0	4.0
MCOP	118	2.5	4.0	19	0	7.5
MECPP	118	0	32.2	19	0	115.0
MEHHP	118	0	17.3	19	0	57.4
MEOHP	118	0	15.7	19	0	44.6
MEHP	118	15.1	4.4	19	0	6.2
MCPP	118	2.5	1.5	19	0	6.1
MiBP	118	0	29.9	19	0	41.9
MBP	118	0	27.5	19	0	30.2
MBzP	118	0.8	10.5	19	0	33
MEP	118	0	324	19	0	755

Exposición a ftalatos: Orina

Urinary concentrations of phthalates and phenols in a population of Spanish

pregnant women and children Casas L, et al. on behalf of the INMA Project. Environ Inter, 2011 (In press)

Sexy for her.

For baby, it could really be poison.



What Are You Smelling?
 It's not just a bottle of 100 percent
 baby lotion. Cosmetics, hair conditioners,
 perfume, and even baby oil can contain
 chemicals that may be harmful to your
 baby. The Environmental Protection Agency
 (EPA) has found that many of these
 chemicals are also found in household
 products like cleaning supplies, paint,
 and pesticides. Some of these chemicals
 are known to be carcinogenic, meaning
 they can cause cancer. Others can harm
 your baby's developing organs and
 nervous system. To protect your baby,
 choose products that are labeled as
 "fragrance-free" or "paraben-free." And
 always use products as directed.

WASH YOUR FACE
 Gentle cleanser
 Soap-free cleanser
 Baby soap
 Oil-free cleanser
 Baby wash
 Baby shampoo
 Baby conditioner
 Baby lotion
 Baby cream
 Baby powder
 Baby oil
 Baby sunscreen

DEODORANT
 Gentle deodorant
 Baby deodorant
 Baby powder
 Baby cream
 Baby lotion
 Baby oil
 Baby sunscreen

SKIN CARE
 Gentle cleanser
 Baby cleanser
 Baby lotion
 Baby cream
 Baby powder
 Baby oil
 Baby sunscreen

HAIR CARE
 Gentle shampoo
 Baby shampoo
 Baby conditioner
 Baby lotion
 Baby cream
 Baby powder
 Baby oil
 Baby sunscreen

PERFUME
 Gentle perfume
 Baby perfume
 Baby lotion
 Baby cream
 Baby powder
 Baby oil
 Baby sunscreen

Sorpresa!!

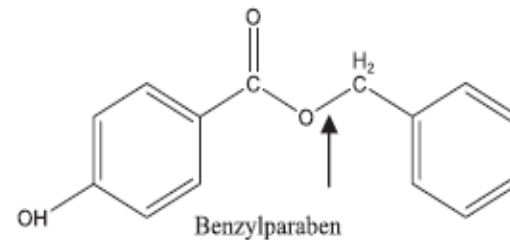
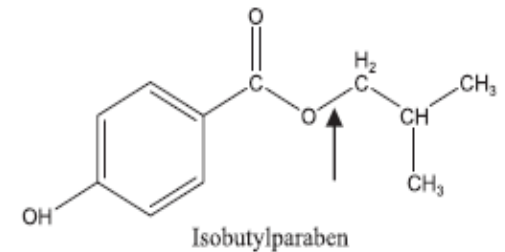
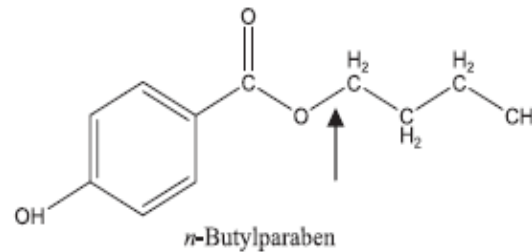
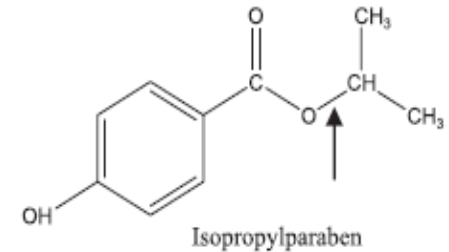
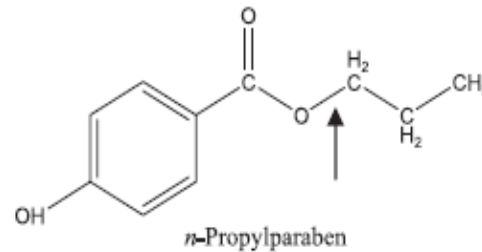
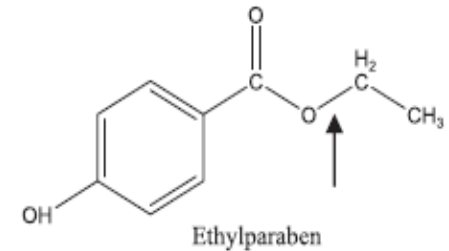
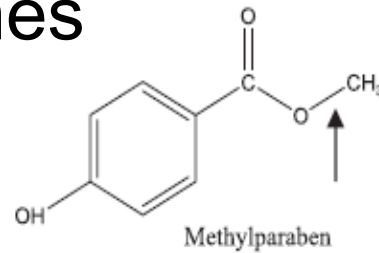
Exposición a ftalatos:
No solo plásticos.
Perfumería
y Cosmética

Exposición a Ftalatos y parabenes



algunos parece
que ya se han enterado

Exposición a parabenes



Benzylparaben

Butylparaben

Ethylparaben (E214)

iso-Butylparaben.

Iso-Propylparaben.

Methylparaben (E218)

Propylparaben (E216)

JOURNAL OF APPLIED TOXICOLOGY

J. Appl. Toxicol. 2008; 28: 561-578

Review

Paraben esters: review of recent studies of endocrine toxicity, absorption, esterase and human exposure, and discussion of potential human health risks

Exposición a parabenos: Placenta

Producto	Frecuencia	Concentración (ng/g)
Butiparaben (BPB)	16% (8/50)	0.2 - 0.6
Etilparaben (EPB)	66% (33/50)	0.2 - 5.3
Metilparaben (MPB)	96% (48/50)	0.1 - 10.0
Propilparaben (PPB)	90% (45/50)	0.2 - 2.2

A new liquid chromatography–tandem mass spectrometry method for determination of parabens in human placental tissue samples

I. Jiménez-Díaz^{a,b}, F. Vela-Soria^a, A. Zafra-Gómez^{a,*}, A. Navalón^a, O. Ballesteros^a, N. Navea^b, M.F. Fernández^b, N. Olea^b, J.L. Vílchez^a

Exposición a parabenes: Orina

	Embarazadas			Niños		
	3r Trimestre			4 años old		
Producto	n	% <LOD	Median ng/g	n	% <LOD	Median ng/g
B-PB	120	9.9	2.4	30	16.7	1.2
E-PB	120	12.4	8.8	30	20	8.1
M-PB	120	0	191	30	0	150.0
P-PB	120	1.7	29.8	30	0	21.5

Exposición a triclosán (TCS)

HOW TO AVOID TRICLOSAN

Forgo antibacterial soap.

The American Medical Association says not to use it at home.

Watch for triclosan (and triclocarban) in personal care products.

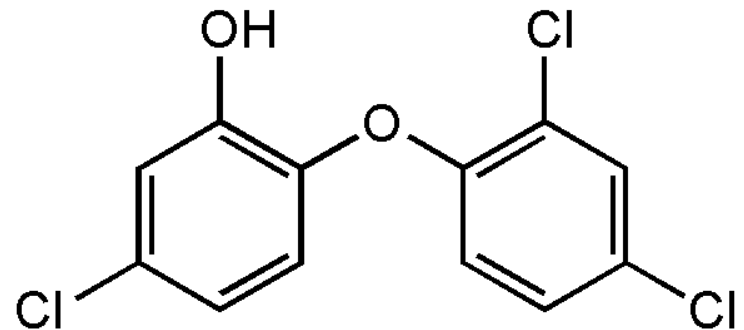
Read ingredient labels or use Skin Deep to find products free of triclosan and triclocarban, its chemical cousin.

Avoid “antibacterial” products.

Triclosan is used in everyday products like toothbrushes, toys, and cutting boards that may be labeled “antibacterial,” or make claims such as “odor-fighting” or “keeps food fresher, longer.”

Triclosan may be in these products:

soap and dishwashing liquid	phones
towels	kitchenware and plastic food containers
mattresses	shoes
sponges	flooring and carpets
personal care products	cutting boards
shower curtains	clothing and fabrics
toothbrushes	toys



Exposición a TCS y Clorofenoles: Orina

	Pregnant women			Children		
	3rd trimester			4 years old		
	n	% <LOD	Median	n	% <LOD	Median
Phenols						
TCS	120	40.5	6.1	30	63.3	1.2

	Pregnant women			Children		
	3rd trimester			4 years old		
	n	% <LOD	Median	n	% <LOD	Median
Phenols						
2.4-DCP	120	9.1	1.1	30	0	3.1
2.5-DCP	120	0	16.5	30	0	55.6

Urinary concentrations of phthalates and phenols in a population of Spanish pregnant women and children Casas L, et al. on behalf of the INMA Project. Environ Inter, 2011 (In press)

¿Que mas compuestos químicos investigar?
¿Qué se debería añadir a la lista?

- Filtros UV: benzofenonas, canfenos y oxicinamatos
- PFOS y PFOA
- Aromas sintéticos
- Residuos de fármacos
- entre otros.....

Exposición a filtros UV



Benzophenone-3 (BP-3)
Octyl-methoxycinnamate (OMC)
3-(4-methylbenzylidene) camphor (4-MBC)

....se absorben por la piel y modifican los niveles hormonales

Journal of Investigative Dermatology (2004) **123**, 57–61

Systemic Absorption of the Sunscreens Benzophenone-3, Octyl-Methoxycinnamate, and 3-(4-Methyl-Benzylidene) Camphor After Whole-Body Topical Application and Reproductive Hormone Levels in Humans

Nadeem Rezaq Janjua^{*}, Brian Mogensen^{*}, Anna-Maria Andersson[†], Jørgen Holm Petersen[†], Mette Henriksen^{*}, Niels E Skakkebæk[†] and Hans Christian Wulf^{*}

Exposición a filtros UV

Table 3
Reported use of UV filters in cosmetic products and detection in human milk.

	Reported use (n = 53) ^a						Detection in milk (n = 54) ^a		Correlation of reported use and detection (n = 53)
	Sunscreens		Other cosmetics		All products		Number of positive milk samples	% of total	
	Number of women reporting use	% of total	Number of women reporting use	% of total	Number of women reporting use	% of total			
All UV filters ^b	29	54.72	32	60.38	41	77.36	46	85.19	p = 0.0104
Ethylhexyl-methoxycinnamate (EHMC)	25	47.17	26	49.06	35	66.04	42	77.78	p = 0.0799
Octocrylene (OCT)	21	39.62	2	3.77	23	43.40	36	66.67	p = 0.0401
4-Methylbenzylidene camphor (4-MBC)	14	26.42	0	0	14	26.42	11	20.37	p = 0.0488
Homosalate (HMS)	8	15.09	0	0	8	15.09	3	5.56	p = 0.3943
Benzophenone-3 (Bp-3)	1	1.89	6	11.32	7	13.21	7	12.96	p = 1.0000
Benzophenone-2 (Bp-2)	0	0	10	18.87	10	18.87	0	0	nca
Octyl-dimethyl-PABA (OD-PABA)	0	0	1	1.89	1	1.89	1	1.85	nca
3-Benzylidene camphor (3-BC)	0	0	0	0	0	0	0	0	nca

^a One woman did not complete the questionnaire. Her milk data were excluded from correlation statistics.

^b Reported use (questionnaire) or detection (chemical analysis), respectively, of any of the eight UV filters. nca; no correlation analysis.

Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: Correlation of UV filters with use of cosmetics

Margret Schlumpf^{a,*}, Karin Kypke^b, Matthias Wittassek^c, Juergen Angerer^{c,1}, Hermann Mascher^d, Daniel Mascher^d, Cora Vökt^e, Monika Birchler^e, Walter Lichtensteiger^a

Chemosphere 81 (2010) 1171–1183

Table 4
Concentrations of UV filters, musk fragrances, parabens and phthalate metabolites in human milk.

	Cohort 2004 ^a		Cohort 2005 ^a		Cohort 2006 ^a		All Cohorts ^a				
	Total N = 13		Total N = 21		Total N = 20		Total N = 54		Median	95%	Range
	Mean ± SD	N pos.	Mean ± SD	N pos.	Mean ± SD	N pos.	Mean ± SD	N pos.			
UV filters	ng g ⁻¹ lipid		ng g ⁻¹ lipid		ng g ⁻¹ lipid		ng g ⁻¹ lipid				
Ethylhexyl-methoxy cinnamate	35.31 ± 17.22	13	19.60 ± 25.05	9	25.98 ± 23.09	20	27.50 ± 22.15	42	18.41	73.31	2.10–79.85
Octocrylene	22.57 ± 25.46	7	15.08 ± 10.08	9	39.63 ± 25.21	20	30.18 ± 24.51	36	28.32	70.64	4.70–134.95
4-Methyl-benzylidene camphor	19.00	1	14.50 ± 6.76	3	25.84 ± 14.53	7	22.12 ± 12.80	11	18.70	43.15	6.70–48.37
3- Benzylidene camphor	0	0	0	0	0	0	0	0			
Homosalate	0	0	0	0	29.37 ± 27.64	3	29.37 ± 27.64	3	15.50	56.63	11.40–61.20
Benzophenone-3	117.00	1	35.48 ± 48.63	5	71.18	1	52.23 ± 50.69	7	26.70	120.08	7.30–121.40
Benzophenone-2	0	0	0	0	0	0	0.00	0			
Octyldimethyl-PABA	49.00	1	0	0	0	0	49.00	1			
Musk fragrances ^b	ng g ⁻¹ lipid		ng g ⁻¹ lipid		ng g ⁻¹ lipid		ng g ⁻¹ lipid				
Musk xylene	4.01 ± 8.42	13	1.67 ± 1.34	20	3.72 ± 7.89	14	2.93 ± 6.17	47	1.34	5.67	0.25–31.60
Musk ketone	2.26 ± 3.25	12	0.83 ± 1.00	16	2.34 ± 4.54	6	1.60 ± 2.77	34	0.64	6.47	0.25–12.00
Galaxolide (HHCB)	35.83 ± 24.51	10	55.40 ± 67.33	21	68.15 ± 58.94	14	55.02 ± 57.87	45	36.13	165.57	6.09–309.66
Tonalide (AHTN)	16.25 ± 16.19	2	14.09 ± 9.96	4	8.96	1	13.97 ± 9.96	7	10.23	28.47	4.80–28.80
Phantolide (AHDI)	15.30	1	0	0	0	0	15.30	1			
Habanolide					15.00 ± 0.00	2	15.00 ± 0.00	2	15.00	15.00	15.00–15.00
Parabens ^c			ng mL ⁻¹		ng mL ⁻¹		ng mL ⁻¹				
Methyl-paraben			2.69 ± 2.52	8	1.50 ± 0.84	6	2.18 ± 2.02	14	1.00	5.40	1.00–8.00
Ethyl-paraben			1.33 ± 0.24	4	1.20 ± 0.24	4	1.26 ± 0.23	8	1.30	1.50	1.00–1.50
Propyl-paraben			1.50 ± 0.41	4	1.25 ± 0.35	2	1.42 ± 0.38	6	1.50	1.88	1.00–2.00
Butyl-paraben			0	0	0	0	0	0			
Phthalate metabolites ^d					ng mL ⁻¹		ng mL ⁻¹				
MEHP (DEHP)					34.05 ± 26.00	20	34.05 ± 26.00	20	26.20	74.98	9.60–122.00
MnBP (DnBP)					7.88 ± 6.21	20	7.88 ± 6.21	20	5.95	15.27	1.20–29.80
MiBP (DiBP)					26.61 ± 18.03	20	26.61 ± 18.03	20	24.25	55.28	2.60–66.20
7OH-MMeOP (DiNP)					1.12 ± 0.30	6	1.12 ± 0.30	6	1.20	1.43	0.60–1.50

^a Mean, standard deviation (SD), median, 95 percentile (95%) and range represent values from positive samples, with number (N pos.) of positive samples. The total number of samples analyzed (N) is shown on top of each cohort. Values < LOD = 0.

^b Synthetic musks analyzed but <LOD: (a) In all cohorts: polycyclic musks: Cashmeran (DPMI), Celestolide (ADBI), Traseolide (ATII). (b) In cohort 2006: macrocyclic musks: musk MC4, musk NN, Exalton, Exaltolid, Muscon, Ambrettolid, Civetton.

^c Total N = 41 (cohort 2005 + cohort 2006).

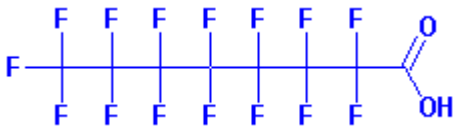
^d Total N = 20 (cohort 2006). Phthalate metabolites analyzed but <LOD: 5OH-MEHP, 5oxo-MEHP, 5cx-MEPP, 2cx-MMHP, MBzP (BBzP), 7oxo-MMeOP (DiNP), 7cx-MMeHP (DiNP).

Exposición alquilos perfluorados (PFOS)

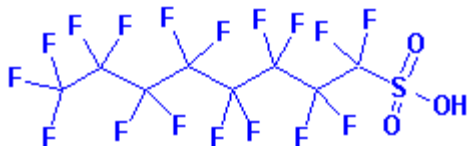
Tejidos aislantes: Goretex
Utensilios de cocina: Tefal



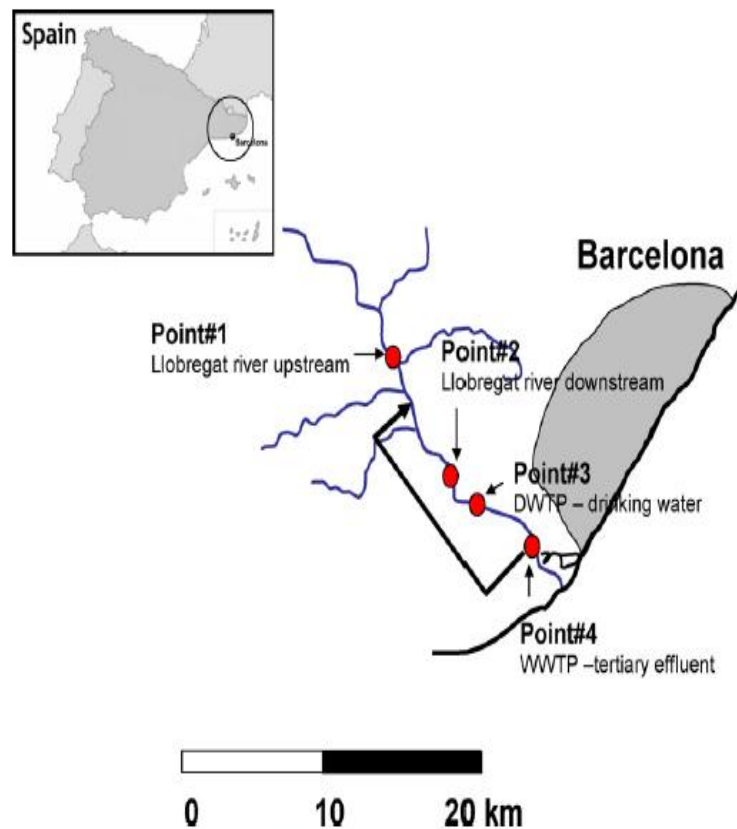
Perfluorooctanoic acid (PFOA or C8)
CAS No: 335-67-1. Molecular formula:



Perfluorooctane sulphonic acid (CAS No. 1763-23-1)



Exposición a residuos de fármacos: Presencia medioambiental



Talanta 83 (2010) 410–424

Fully automated determination of 74 pharmaceuticals in
waste waters by online solid phase extraction–liquid
chromatography–electrospray–tandem mass spectrometry

Rebeca López-Serna^a, Sandra Pérez^a, Antoni Ginebreda^a, Mira Petrović^{a,b,*}, Damià Barceló^{a,c}

Fig. 8. Sampling location.

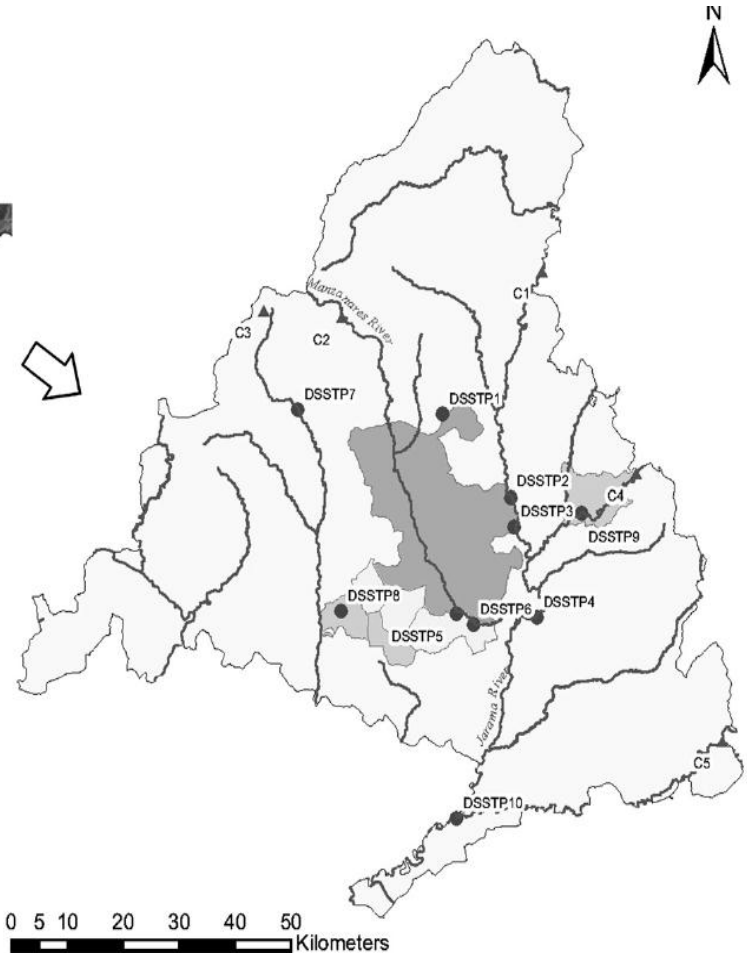
Table 3
Average concentrations and relative standard deviation (expressed in brackets) for target pharmaceuticals in drinking water, superficial water (2 points) and effluent wastewater in the Llobregat River basin (NE Spain).

Therapeutic groups	Compounds	Concentration (ng L ⁻¹) ^a				
		Point #1 – Llobregat River upstream to the spill point	Point #2 – Llobregat River downstream to the spill point	Point #3 – drinking water	Point #4 – WVE tertiary treatment	
Analgesics and antiinflammatories	Ketoprofen	<i>n.d.</i>	3.18 (1.56)	<i>n.d.</i>	57.73 (0.55)	
	Naproxen	81.05 (0.27)	67.38 (0.27)	<i>n.d.</i>	72.17 (0.33)	
	Ibuprofen	186.68 (0.33)	134.75 (0.32)	3.71 (0.15)	43.57 (0.60)	
	Indomethacin	16.27 (0.18)	37.75 (0.29)	<i>n.d.</i>	93.88 (0.52)	
	Diclofenac	89.53 (0.25)	176.78 (0.31)	<i>n.d.</i>	421.50 (0.26)	
	Mefenamic acid	<i>n.d.</i>	6.76 (0.30)	12.82 (2.24)	17.38 (0.63)	
	Acetaminophen	307.00 (0.59)	146.67 (0.91)	<i>n.d.</i>	77.83 (1.77)	
	Salicylic acid	208.17 (0.07)	333.17 (0.61)	201.20 (0.23)	674.33 (0.26)	
	Propyphenazone	3.25 (1.11)	11.10 (0.68)	<i>n.d.</i>	22.55 (0.88)	
	Phenylbutazone	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Phenazone	5.90 (1.57)	40.27 (0.58)	<i>n.d.</i>	56.30 (0.28)	
	Codeine	45.85 (0.8)	109.68 (0.41)	<i>n.d.</i>	350.12 (0.45)	
	Lipid regulators	Clofibric acid	8.40 (0.36)	24.25 (1.10)	<i>n.d.</i>	22.43 (0.16)
		Bezafibrate	15.89 (0.34)	67.32 (0.47)	0.11 (2.24)	217.50 (0.50)
		Fenofibrate	23.85 (0.36)	82.08 (0.49)	<i>n.d.</i>	293.67 (0.64)
Gemfibrozil		1.90 (0.39)	2.14 (0.57)	<i>n.d.</i>	8.58 (0.54)	
Mevastatin		<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
Pravastatin		<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
Atorvastatin		2.99 (1.19)	2.39 (1.10)	27.60 (2.24)	2.71 (1.32)	
Psiquiatric drugs	Paroxetine	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	7.30 (0.91)	
	Fluoxetine	<i>n.d.</i>	<LOQ	2.74 (2.24)	15.87 (0.25)	
	Diazepam	<i>n.d.</i>	6.52 (0.64)	<i>n.d.</i>	18.92 (0.23)	
	Lorazepam	22.58 (0.14)	41.27 (0.23)	<i>n.d.</i>	114.92 (0.26)	
	Carbamazepine	31.28 (0.29)	58.43 (0.30)	<i>n.d.</i>	156.83 (0.24)	
	Loratadine	3.68 (1.68)	2.51 (0.80)	10.48 (1.14)	6.99 (1.08)	
	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>		
Histamine H2 receptor antagonists	Famotidine	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Ranitidine	33.87 (0.40)	61.23 (0.70)	<i>n.d.</i>	197.67 (1.20)	
	Cimetidine	17.33 (2.45)	<i>n.d.</i>	<i>n.d.</i>	32.05 (1.17)	
Tetracycline antibiotics	Tetracycline	<i>n.d.</i>	29.00 (0.91)	<i>n.d.</i>	171.47 (1.06)	
	Doxycycline	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Oxytetracycline	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	42.12 (0.86)	
	Chlorotetracycline	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
Macrolide antibiotics	Erythromycin	50.38 (0.55)	174.73 (0.42)	<i>n.d.</i>	677.00 (0.28)	
	Azithromycin	14.73 (0.34)	71.67 (0.70)	17.00 (0.58)	1031.67 (0.53)	
	Tilmicosin	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Roxythromycin	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	3.90 (0.43)	
	Clarithromycin	42.60 (0.27)	88.83 (0.35)	3.67 (0.22)	237.83 (0.23)	
	Josamycin	1.82 (0.60)	0.81 (1.56)	1.41 (0.77)	3.03 (0.58)	
	Tylosin	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	7.17 (0.57)	
Sulfonamide antibiotics	Spiramycin	39.90 (0.44)	68.32 (0.44)	20.54 (0.92)	141.58 (0.33)	
	Sulfamethoxazol	39.70 (0.23)	78.38 (0.37)	<i>n.d.</i>	140.48 (0.46)	
	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>		
Fluoroquinolones	Sulfadiazine	<i>n.d.</i>	13.40 (1.17)	<i>n.d.</i>	20.38 (0.56)	
	Sulfamethazine	1.68 (2.45)	112.27 (1.55)	4.08 (2.24)	373.84 (1.92)	
	Danofloxacin	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Enoxacin	4.83 (1.56)	4.65 (1.57)	16.04 (0.96)	8.27 (1.13)	
	Ofloxacin	23.28 (0.24)	75.017 (0.48)	15.30 (0.73)	276.67 (0.46)	
	Ciprofloxacin	8.32 (0.79)	28.02 (0.90)	13.28 (0.68)	151.25 (1.43)	
	Enrofloxacin	5.82 (0.56)	40.12 (0.84)	18.93 (0.79)	255.67 (0.35)	
	Norfloxacin	15.83 (0.31)	15.17 (0.86)	32.88 (0.94)	63.72 (1.02)	
	Flumequine	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
Other antibiotics	Trimethoprim	16.43 (0.24)	33.53 (0.34)	0.51 (2.24)	65.92 (0.37)	
	Nifuroxazide	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Chloroamphenicol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Metronidazole	<i>n.d.</i>	44.88 (0.92)	<i>n.d.</i>	211.83 (0.74)	
Beta blockers	Atenolol	38.40 (0.43)	63.17 (0.48)	<i>n.d.</i>	117.82 (0.56)	
	Betaxolol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Carazolol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Pindolol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Nadolol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Timolol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Sotalol	15.28 (0.30)	44.32 (0.94)	<i>n.d.</i>	91.98 (0.30)	
	Metoprolol	54.47 (0.15)	327.40 (1.91)	38.48 (0.30)	96.8 (0.25)	
	Propranolol	<i>n.d.</i>	14.94 (0.39)	<i>n.d.</i>	51.60 (0.30)	
	Salbutamol	<i>n.d.</i>	4.87 (1.70)	<i>n.d.</i>	27.05 (0.30)	
Beta agonists	Clenbuterol	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Butalbital	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
Barbiturates	Pentobarbital	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	
	Phenobarbital	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	

Exposición a residuos de fármacos: Presencia medioambiental

Population

- 160.000 - 180.000
- 180.001 - 205.000
- >205.000
- Less than 160.000



Environment International 36 (2010) 195–201

Fig. 1. Map of the study area and sample site locations (DSSTP and C) in the Community of Madrid.

Pollution by psychoactive pharmaceuticals in the Rivers of Madrid metropolitan area (Spain)

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Table 4

Psychoactive pharmaceutical and metabolite concentrations (ng/L) downstream STPs (bold: maximum, underlined: minimum).

			Jarama			Manzanares		Guadarrama		Henares	Tajo	
		DSSTP1 ^a	DSSTP2	DSSSTP3	DSSTP4	DSSTP5	DSSTP6	DSSTP7	DSSTP8 ^a	DSSTP9	DSSTP10	Median values
Antidepressives	Citalopram	43	<u>[3]</u>	32	b.D.L.	58	b.D.L.	13	120	b.D.L.	b.D.L.	43
	Fluoxetine	16	b.D.L.	13	18	22	b.D.L.	<u>8</u>	44	11	12	14
	Venlafaxine	225	68	43	68	387	40	<u>46</u>	347	43	<u>22</u>	57
Anxiolytics	Nordiazepam	34	24	21	26	52	20	b.D.L.	76	<u>19</u>	<u>26</u>	26
	Oxazepam	30	17	45	28	108	12	b.D.L.	129	<u>[6]</u>	b.D.L.	30
	7-aminoflunitrazepam	b.D.L.	b.D.L.	55	b.D.L.	b.D.L.	b.D.L.	b.D.L.	b.D.L.	b.D.L.	b.D.L.	55
Anticonvulsants	Carbamazepine	1160	b.D.L.	184	273	b.D.L.	82	<u>35</u>	b.D.L.	20	45	82

b.D.L.: below detection limit.

^a Waste-dominated streams.

The data presented here demonstrate that current sewage treatment technologies of the STPs of Madrid rivers cannot effectively remove fluoxetine, citalopram, venlafaxine, nordazepam, oxazepam or carbamazepine, thus discharging them into rivers. We have not

pharmaceuticals in the rivers of Madrid are higher than the contamination found in other geographical areas. Two factors can be responsible for this: the high population density of the Madrid metropolitan area (average >2000 inhabitants/km², Madrid Institute of Statistics, 2007) and the low flow rate of our Mediterranean rivers.

Table 5

Results obtained from the two developed methods for the effluent samples analysed during the performed monitoring campaign (n=5).

Compound	SRM			IDA		
	Range (ng/L)	Mean (ng/L)	Median (ng/L)	Range (ng/L)	Mean (ng/L)	Median (ng/L)
Furosemide	729–1132	884	830	783–1192	983	987
Clofibric acid	37–44	39	41	36–51	42	39
Bezafibrate	40–110	80	97	50–130	97	105
Hydrochlorothiazide	2262–3988	3324	3788	2346–3893	3373	3810
Ketoprofen	120–260	177	162	140–275	218	239
Naproxen	140–1380	780	693	140–1150	717	910
Diclofenac	890–1440	1097	950	1160–1440	1293	1251
Fenoprofen	<MQL	<MQL	<MQL	<MQL	<MQL	<MQL
Indomethacine	160–390	275	241	170–330	235	297
Mefenamic acid	40–60	50	51	50–60	53	52
Ibuprofen	–	–	–	100–340	180	119
Diuron	140–290	203	207	110–260	203	219
Chlorophene	<MQL	<MQL	<MQL	<MQL	<MQL	<MQL
Gemfibrozil	580–3550	2323	2640	470–3090	2123	2710

Evaluation of various liquid chromatography-quadrupole-linear ion trap-mass spectrometry operation modes applied to the analysis of organic pollutants in wastewaters

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Conclusión

Un nuevo escenario en la **exposición ambiental**

- Niveles bajos de exposición, pero múltiples residuos químicos
- Interacciones sinérgicas, aditivas y/o antagónicas entre ellos y los sistemas de homeostasis interna (por ejemplo, hormonas)
- Necesidad de ir mas allá de la cuantificación de uno, o unos pocos residuos: Cuantificar la actividad biológica y las consecuencias de la exposición combinada
- Mientras tanto: PRECAUCION