



EDCs & Plastic baby bottles

Ms. SIMON, PhD student

*Laboratory of Food Analysis of Marie-Louise
SCIPPO, FARAH – Veterinary Public Health,
Department of Food Sciences, CART, University of
Liège*

Plastics: what's dangerous?



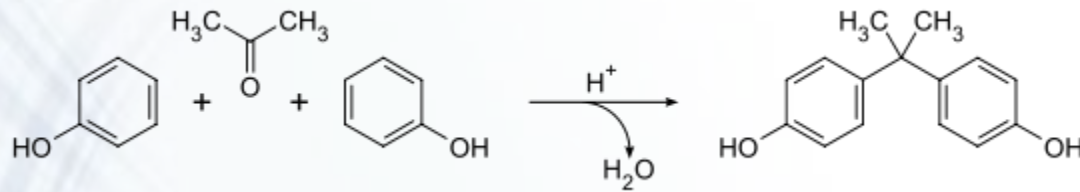
Food contaminants



**Migration des
substances
d'emballage
dans les
aliments**

What is Bisphenol A

- *Made Man chemical*



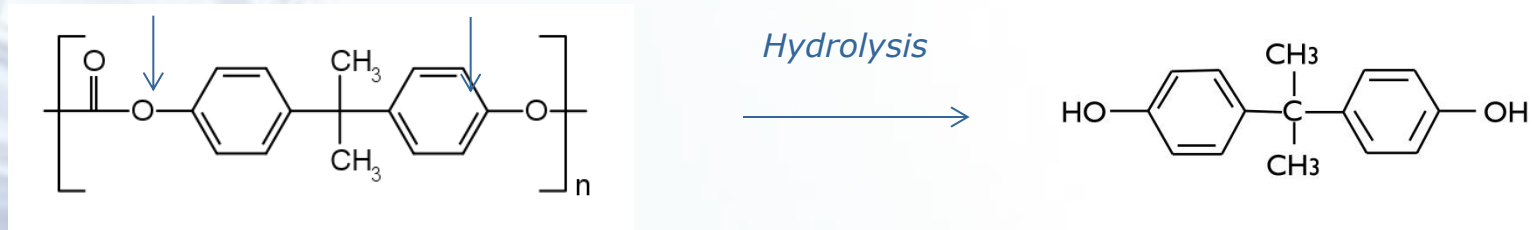
- *Used as the building block for notably polycarbonate plastic*

- *Durability*
- *Clarity*
- *Impact resistance*
- *Heat resistance*



Migration of BPA from polycarbonate material

- *Studies have found solid evidence that BPA does migrate from PC plastics into the food, drink or water in contact.*



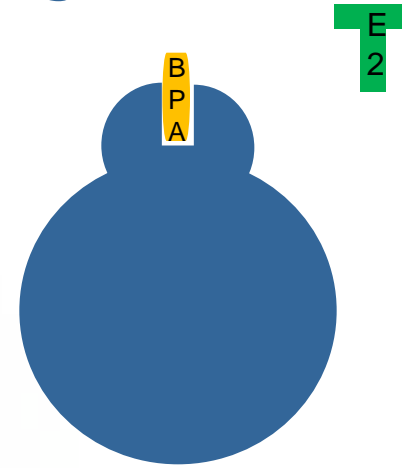
- *Heat*
- *Contact with acidic or basic compounds*
- *...*

Bisphenol A: an endocrine disruptor

- Mimics the female hormone estrogen



Normal condition



In presence of BPA

- *BPA has been linked to :*
 - *Breast and prostate cancer risk*
 - *Early puberty*
 - *Brain and thyroid dysfunction*
 - *Heart disease*
 - *Infertility in male and female*
 - *obesity*

Regulation

- *2011: European Commission decided to ban the use of polycarbonate to manufacture baby bottles*



- *Why are babies more susceptible to BPA?*
 - *Brain is still developing*
 - *Lack of enzymes to inactivate BPA*
 - *Daily BPA intake (expressed per kg of body weight) more or less ten times higher than Adults*

Alternatives to polycarbonate baby bottles

- *Polypropylene*
- *Polyamide*
- *Polyethersulfone*
- *Tritan co-polyester*
- *Silicone*



Are alternatives to polycarbonate **HEALTHY** ?

Objectives

Table 1. Migrants from different type of baby bottles detected by GC-MS (with index of recognition >80%).

Migrant	CAS	Quality	SML (mg kg ⁻¹)	Polypropylene (n = 149)			Polyamide (n = 28)			Silicone (n = 5)		
				n	Range (µg kg ⁻¹)	Average (µg kg ⁻¹)	n	Range (µg kg ⁻¹)	Average (µg kg ⁻¹)	n	Range (µg kg ⁻¹)	Average (µg kg ⁻¹)
2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (TXIB)	6846-50-0	100	5 ^a	72	1-62	5	3	2	2	5	14-574	159
2,2-Bis(4-hydroxyphenyl)propane (BPA)	80-05-7	100	0.6 ^b				17 ^c	1-1005	106			
2,4,6-Trimethyl benzaldehyde	487-68-3	90	n.a.							1	94	
2,4-Dimethyl benzaldehyde	15764-16-6	87	60	6	21-62	47				1	94	
2,4-Di- <i>tert</i> -butyl phenol	96-76-4	100	60	133	1-419	49	1	3		4	26-221	103
2,6-Diisopropyl-naphthalene (DIPN)	241 57-81-1; 38640-62-9	100	n.a.	69	1-23	5	6	1-2	1	5	4-23	12
2,6-Di- <i>tert</i> -butyl- <i>p</i> -benzoquinone	719-22-2	97	60							2	341-382	361
2-Butoxyethyl acetate	112-07-2	86	60	6	139-778	354						
2-Methylnaphthalene	91-57-6	80	60	1	3		1	3				
2-Propenamido,2-methyl- <i>N</i> -phenyl	1611-83-2	86	n.a.	7	90-132	105						
2-Propenoic acid,3-(4-methoxyphenyl)-2-ethylhexyl ester	5466-77-3	95	n.a.							1	175	
2-Propenoic acid-2-ethylhexyl ester	103-11-7	86	0,05							3	24-72	76
3,5,5-Trimethyl-2-cyclohexen-1-one	78-59-1	91	60							1	88	
4-Ethylbenzaldehyde	4748-78-1	91	60							1	92	
4- <i>Tert</i> -butylcyclohexyl acetate	32210-23-4	90	n.a.							1	145	
9-Octadecenamido (oleamide)	301-02-0	93	60	2	227-2487	1357						
9-Octadecenoic acid, methyl ester	112-62-9	99	60	12	18-294	65						
Acetic acid, 2-ethylhexyl ester	103-09-3	86	60							4	23-76	51
Alpha-methylstyrene	98-83-9	86	0.05									
Benzaldehyde-4-methylthio	3446-89-7	90	n.a.							1	33	
Benzoic acid, 4-ethoxy-ethyl ester	23676-09-7	91	3,6							1	23	
Benzophenone	119-61-9	100	0.6	39	1-286	43	2	2	2	5	11-637	184
Butylated hydroxytoluene (BHT)	128-37-0	100	3	14	1-156	44				3	1-3	2
Camphor	76-22-2	96	60 ^d							3	18-147	87
Cyclododecene	1501-82-2	97	n.a.				17	6-63	29			
Cyclohexanone	108-94-1	93	60							1	109	
Cyclohexanone-5-methyl-2-(1-methylethyl)	10458-14-7		60							2	20-128	74
Decanoic acid 2-ethylhexyl ester	73947-30-5	86	60	8	28-170	113						
Dodecanoic acid 1-methylethyl ester	10233-13-3	83	60	16	29-3131	570				3	356-1464	739
Dodecanoic acid 2-ethylhexyl ester	20292-08-4	86	60	9	15-1220	692						
Dodecanoic acid, methyl ester	111-82-0	91	60							1	45	
Erucamide	112-84-5	100	60	9	138-791	303				2	73-160	116
Eucalyptol	470-82-6	91	60	2	237-391	314				2	149-589	369
Hexadecanoic acid	57-10-3	99	60	7	1590-2965	2347				1	9540	
Hexadecanoic acid methyl ester	112-39-0	97	60	7	19-98	49						

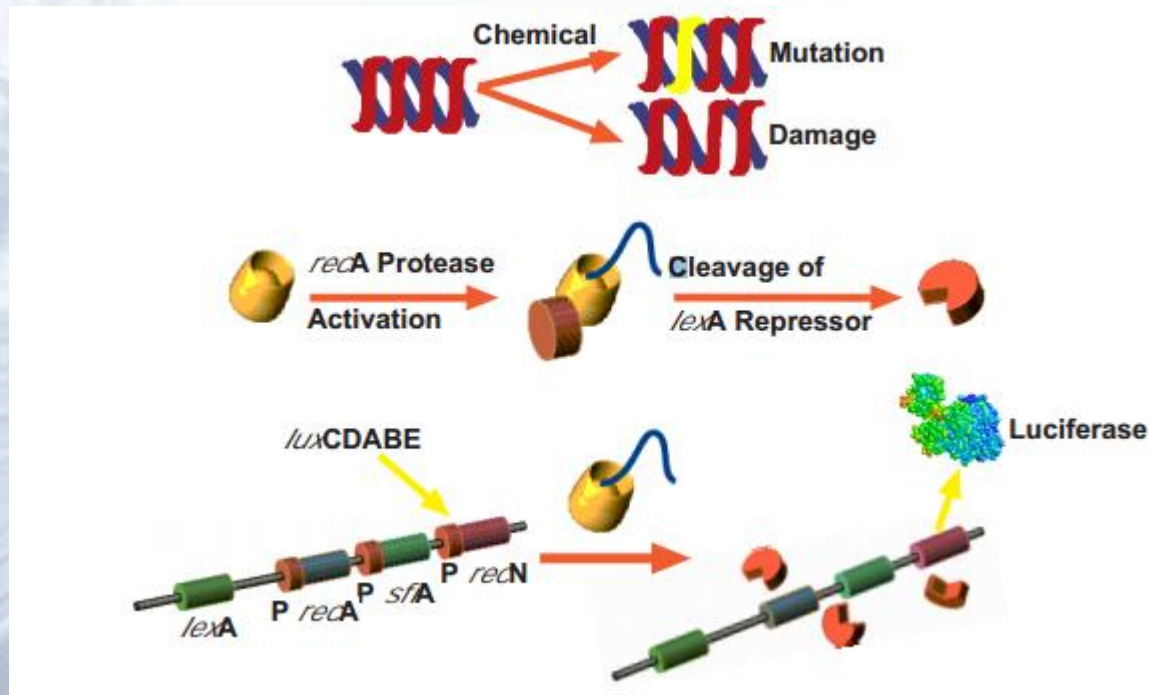
(continued)

Protocols

- *Biological activity*
 - *Reporter gene assays*
 - *ER1 (Davis University, Californie USA)*
 - *ER2 (University of Liège, Belgium)*
 - *AR (University of Liège, Belgium)*
 - *GR (University of Liège, Belgium)*
 - *PR (University of Liège, Belgium)*
 - *PPAR γ (Biodetector system, Netherlands)*
 - *TR β (Biodetector system, Netherlands)*
 - *AhR (Davis University, Californie USA)*
 - *38 substances*
 - *4 concentrations in DMSO (dilution 10 to 10) starting from 100 mM or solubility threshold*
 - *A final concentration of 1 % of DMSO in culture medium*
 - *Test the agonistic (substance only)*
 - *the antagonistic effect (co-exposure with the reference standard close to EC50 value).*

Protocols

- *genotoxicity*
 - *Based on a reporter gene assay*
 - *Recombinant bacteria carrying Luciferase gene*
 - *Induced by SOS response*
 - *+ Cytotoxicity*



Screening Compounds for Genotoxicity and Cytotoxicity: An Automated Bioluminescent *Salmonella typhimurium* Test in Microplate Format Jari Meriläinen and Jorma Lampinen, Thermo Labsystems, P.O. Box 100, FIN-01621 Vantaa, Finland



Results and discussion

plasticizers

- A group of additives, increasing the plasticity or fluidity of a material
 - Phthalates
 - concern on reproductive and developmental toxicity and the possible endocrine disrupting potency of the phthalates
 - Experimental animals and human exposure data
 - 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (TXIB)
 - No long term effect known

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TR β		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT
diisobutyl phthalate	ni	++	-	+	-	-	++	-	+	-	++	-	+	-	+	-	-
dibutyl phthalate	0,3	++	-	-	+	-	+	-	+	-	+	-	+	-	+	?	?
Diethylhexylphthalate	1,5	++	++	+	+	-	++	-	-	-	++	-	+	-	++	-	-
TXIB	5	++	-	+	-	-	-	-	+	-	+	-	-	-	-	-	-

Antioxydants

- To prevent the various effects such as oxidation reactions taking place due to different weathering conditions
 - 2,4-Di-tert-butylphenol
 - Unknown for long term effect
 - Cytotoxic compound
 - 2,6-diisopropylnaphthalene (DIPN)
 - Unknown for long term effect
 - Butylated hydroxytoluene (BHT)
 - Unknown for long term effect

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TRβ		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT		
2,4-Di-tert-butyl phenol	60	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DIPN	ni	+	-	+	-	-	?	-	-	-	?	+	-	+	-	-	-
BHT	3	-	?	-	-	-	-	-	-	-	+	-	+	-	-	-	?

UV absorbers

- *Against the degradation of plastic by ultraviolet energy*
 - *Benzophenone*
 - *Information on adverse health effect of its derivates: impact on thyroid axe*
 - *2-Propenoic acid,3-(4-methoxyphenyl)-2-ethylhexyl ester*
 - *Known for estrogenic androgenic and progesteronic effect in vitro and in vivo*
 - *Adverse effect on the development of the reproductive organs*

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TRβ		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT
Benzophenone	0,6	++	-	++	-	-	+	-	++	-	+	-	-	-	+	-	?
2-Propenoic acid,3-(4-methoxyphenyl)-2-ethylhexyl ester	ni	++	-	+	-	-	-	-	+	-	++	-	++	-	++	+	-

Chemical intermediates

- *Basic building block to manufacture high performance plastics*

- *Bisphenol A*

- *A possible involvement in early puberty, prostate and breast cancer and behavioral disorders, especially from early-life exposures.*
- *A possible association between BPA, diabetes and cardiovascular diseases*

- *Bisphenol S*

- *Mimic female hormone like BPA*
- *association between BPS and cardiovascular disease*

- *Alpha-methylstyrene*

- *No long term effect known*

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TRβ		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT
<i>Bisphenol A</i>	0,6	++	-	++	-	-	+	-	+	-	+	-	?	+	?	-	-
<i>Alpha-methylstyrene</i>	0,05	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-
<i>Bisphenol S</i>	0,6	++	-	++	-	-	+	-	++	-	++	-	-	+	+	-	?

flavour and fragrances agents

- *mask unpleasant odours*
 - *Sixteen substances*
 - *Six of them didn't show any reaction on seven receptors*
 - *2-methylnaphtalene and naphtalene*
 - *Acetic acid, 2-ethylhexyl ester*
 - *Cyclohexanone-5-methyl-2-(1-methylethyl)*
 - *Eucalyptol*
 - *Octadecanoic acid, ethyl ester*

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TR β		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT
2,4,6-Trimethyl benzaldehyde	ni	-	++	-	++	-	?	-	++	-	++	-	-	-	+	-	-
4-ethylbenzaldehyde	60	-	-	-	?	-	-	-	+	-	-	-	+	-	++	-	-
4-Tert-butylcyclohexyl acetate	ni	+	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-
Camphor	60	++	-	-	-	-	?	-	-	-	++	-	-	-	+	-	-
Cyclododecene	ni	+	-	-	?	-	?	-	?	-	?	-	-	-	-	-	-
dodecanoic acid 1-methylethyl ester	60	/	/	-	++	-	-	-	?	-	++	-	+	-	++	/	/
Dodecanoic acid, methyl ester	60	++	-	-	+	-	?	-	?	-	++	-	+	-	++	-	?
Hexadecanoic acid methyl ester	60	+	-	-	++	-	?	-	?	-	-	-	-	-	-	-	-
Octadecanoic acid	60	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-

Other additives groups

– 2-Propenoic acid-2-ethylhexyl ester

- Cosmetic agent
- No long term effect known

– Oleamide

- Cosmetic agent
- Unknown long term effect

– Trimethyl-2-cyclohexen-1-one

- a naturally occurring substance found in canberries
- No long term effect known

Migrant	SML (mg/kg)	ER1		ER2		AR		GR		PR		TbR		PPARY		AhR	
		AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT	AGO	ANT
2-Propenoic acid-2-ethylhexyl ester	0,05	-	-	-	?	-	-	-	-	-	-	-	-	+	-	-	-
9-octadecenamide (oleamide)	60	-	-	-	-	-	-	-	?	-	-	-	-	+	-	+	-
3,5,5-Trimethyl-2-cyclohexen-1-one	60	-	?	-	-	-	?	-	?	-	+	-	-	-	+	-	-

Vitotox

- *None of the tested compounds fulfilled all criteria for a positive result in genotoxicity testing*
- *A screening assay for DNA damage, but not a mutagenicity assay*
 - *Good correlation with AMES test*
- *More tests are required to complete the full genotoxic profile of the compounds*

Conclusions

- *None of the compounds tested fulfilled all criteria for a positive result*
- *Qualitative data on the biological activity of the chemical migration products from plastic baby bottles.*
 - *A lot of compound reacted on one or several receptor.*

Perspectives

- *Characterization of the dose-response relationship of certain compounds*
- *Test the activity of global migration*
- *Test of certain substances on a in vivo model*



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