UNIVERSITY OF HELSINKI

MUTAGENIC AND OESTROGENIC ACTIVITIES OF COMMERCIALLY PROCESSED FOOD ITEMS AND WATER SAMPLES:

A COMPARISON BETWEEN FINLAND AND NIGERIA

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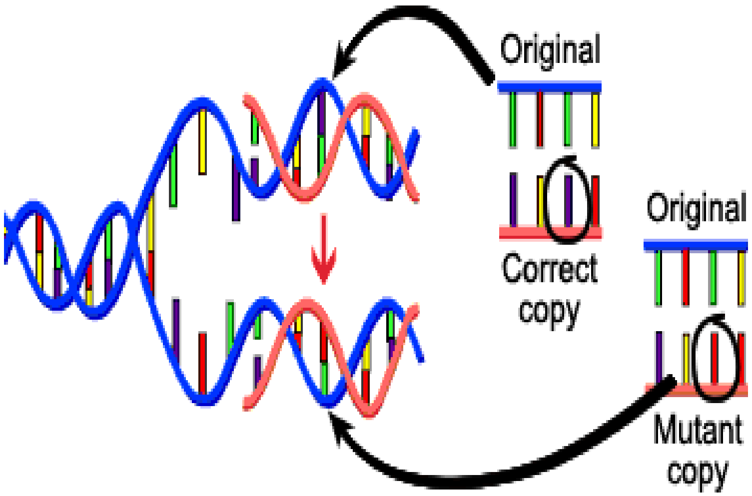
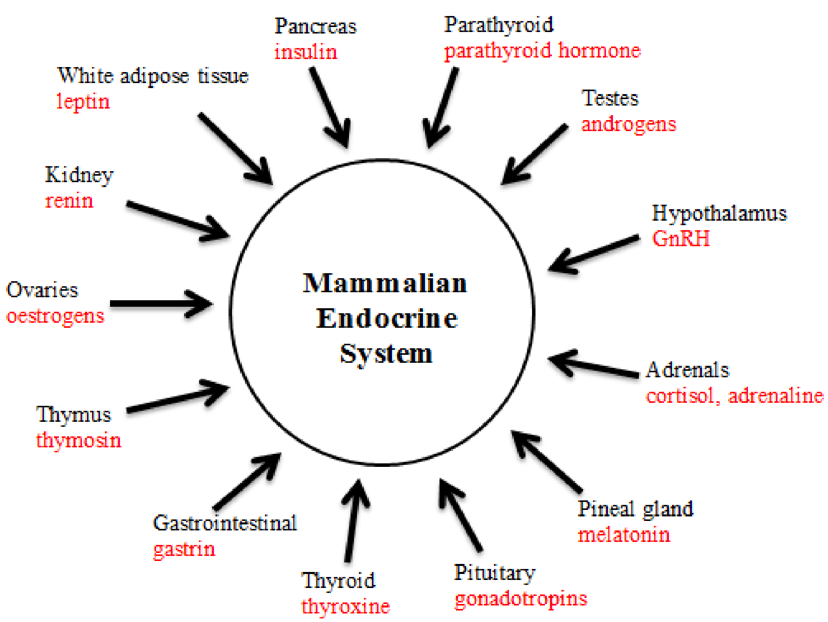
Introduction

What are mutagens?

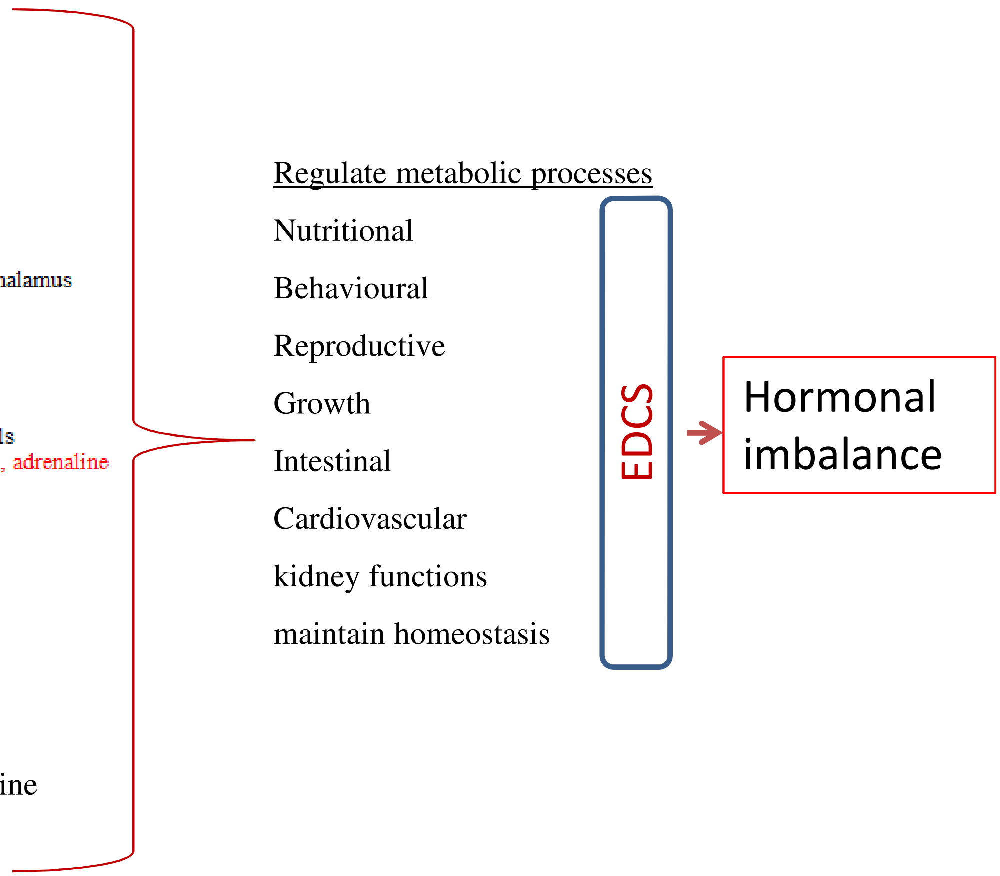
- Mutagens are biological, chemical or physical agent that alters or causes a permanent change (mutation) in the genetic material (usually DNA) of an organism.
- Such mutations are usually the first step in a sequence of events that ultimately leads to the development of cancer.

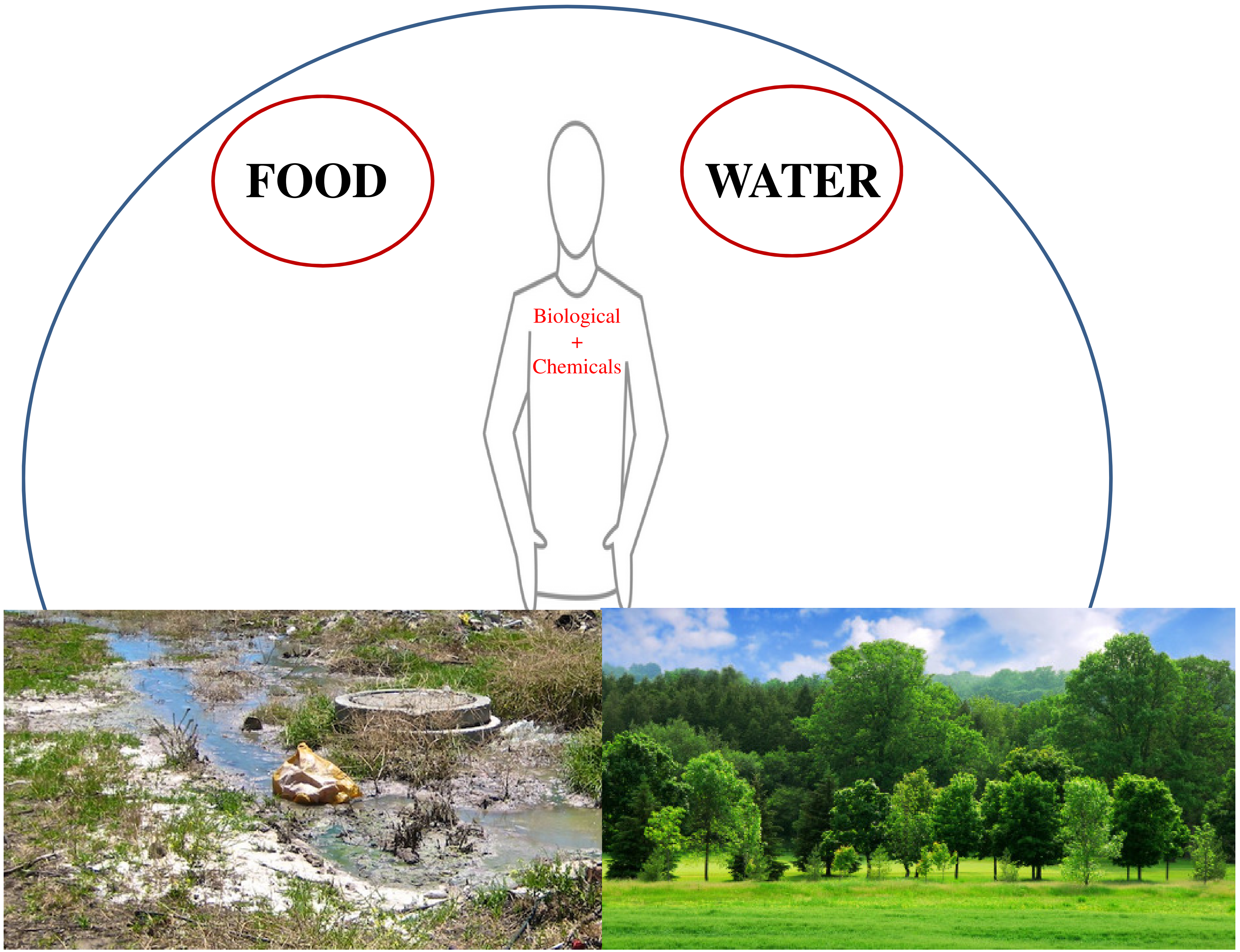


- Endocrine disrupting chemicals (EDCs) are chemical substances that alter the functions of the endocrine system and thereby cause adverse health effects in an intact organism or its progeny (WHO/International Programme on Chemical Safety IPCS, 2002).



Hormone-producing glands and tissues of the endocrine system, with sample hormones [in colour]




FOOD
WATER
Biological
+
Chemicals

Sources/examples of mutagens and xenoestrogens in food

Sources of mutagens in food

1. Substances deliberately added to food

Food additives (e.g. amaranth, allura red, azo dyes)

(Tsuda et al., 2001; Sasaki et al., 2002; Shimada et al., 2010)

2. Substances inadvertently contaminating food

Pesticides (e.g. malathion, chlorpyrifos, lindane)

Country	Pesticides	Reference
United States of America	Chlorpyrifos, melathion etc in meal of pre-school children	Fenske et al., 2002
Spain	Pirimiphos-methyl	Gonzalez-Curbelo et al., 2012
Italy	Average of 3.4 different pesticides per meal (2005-2007). 13 different pesticides in some case	Lorenzin, 2007
Nigeria	DDT, Endrin, Lindane, Diazinon etc	Gwary et al., 2012

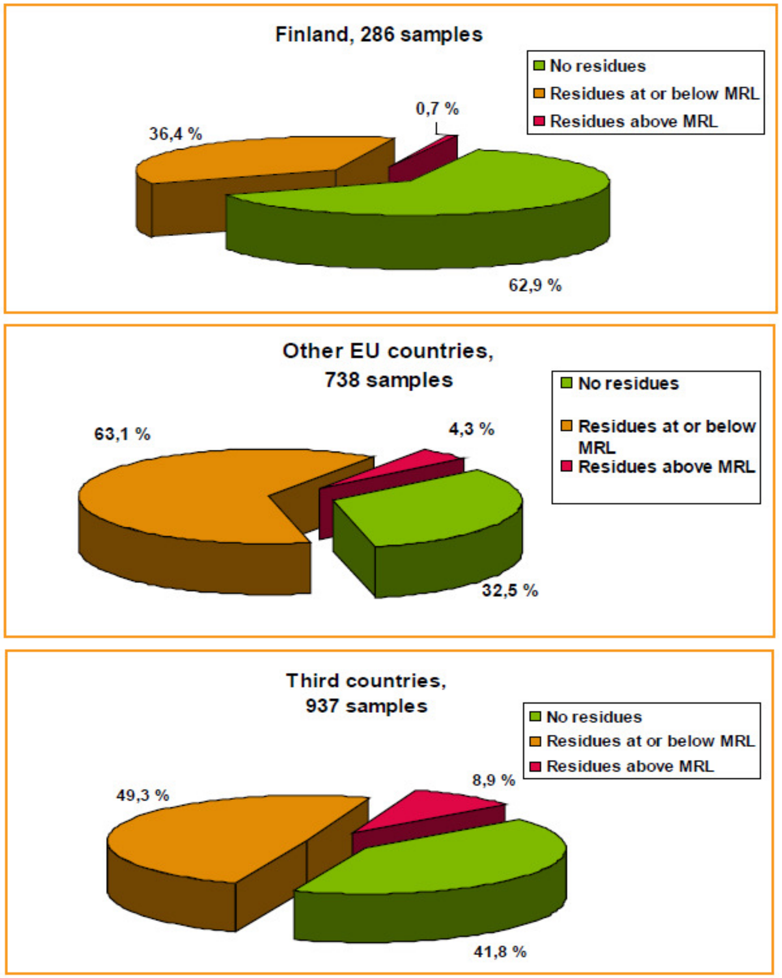


Figure 1. Summary of the results of surveillance sampling. Occurrence of residues by origin of samples. All surveillance samples of national and EU co-ordinated monitoring programs including fruit, vegetables, cereals and processed products.

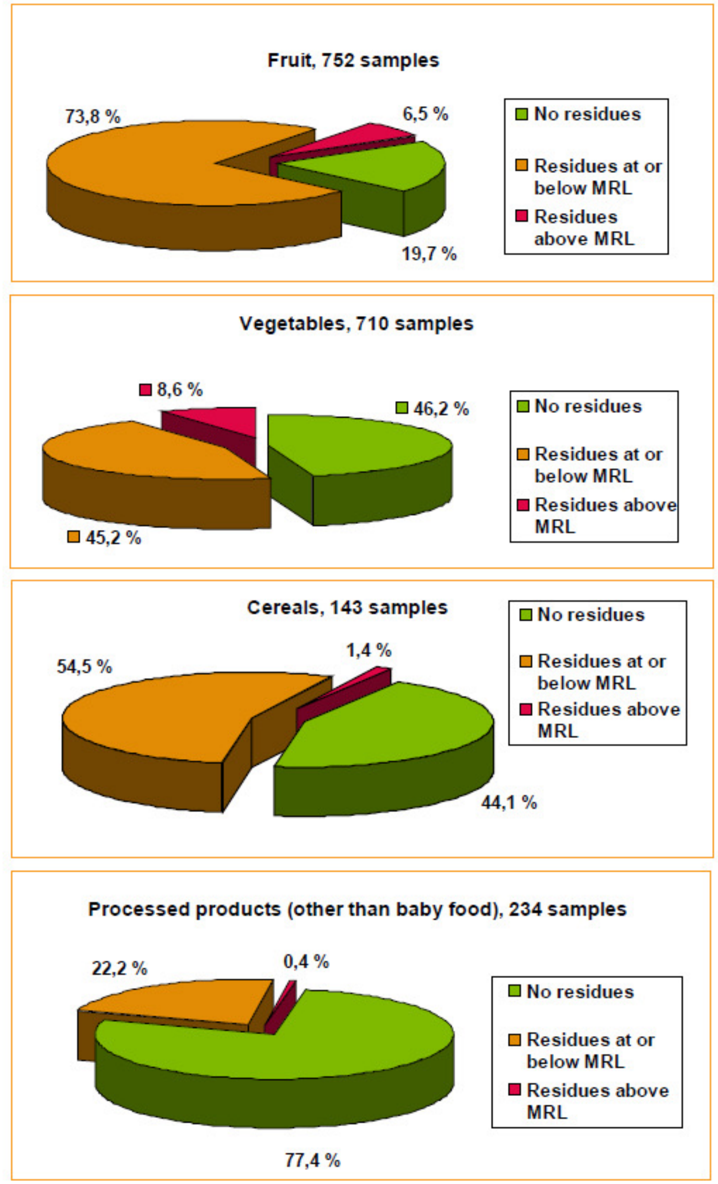


Figure 2. Occurrence of pesticide residues in different types of samples. National and EU co-ordinated programs, surveillance samples only.

Pesticides residue monitoring in Finland, 2008 (EVIRA, 2009)

Table 2. List of pesticides with residues above the MRLs. Surveillance and enforcement samples.

Pesticide	Number of lots with residues >MRL
Dimethoate (sum of dimethoate and omethoate expressed as dimethoate)	29
Carbendazim and benomyl (sum of benomyl and carbendazim expressed as carbendazim)	22
Bromide ion	15
Diazinon	13
Chlorpyrifos	12
Profenofos	11
Carbaryl	9
Fenitrothion	9
Thiophanate-methyl	9
Carbofuran (sum of carbofuran and 3-hydroxy-carbofuran expressed as carbofuran)	8
Cypermethrin (Cypermethrin including other mixtures of constituent isomers (sum of isomers))	8
EPN	7
Methomyl and Thiodicarb (sum of methomyl and thiodicarb expressed as methomyl)	6
Chlorothalonil	5
Dichlorvos	5
Methamidophos	4
Procymidone	4
Propiconazole	4
Triazophos	4
Acetamiprid	3
Metalaxyl (Metalaxyl including other mixtures of constituent isomers including Metalaxyl-M (sum of isomers))	3
Propamocarb (Sum of propamocarb and its salt expressed as propamocarb)	3
Triadimefon (sum of Triadimefon and Triadimenol)	3
Acephate	2
Azoxystrobin	2
Dimethomorph	2
Imidacloprid	2
Methoxyfenozide	2
Tebufenozide	2
Chlorpropham (Chlorpropham and 3-chloroaniline, expressed as Chlorpropham)	1
Cyfluthrin (Cyfluthrin including other mixtures of constituent isomers (sum of isomers))	1
Cyproconazole	1
Deltamethrin (cis-deltamethrin)	1
Diphenylamine	1
Dithiocarbamates (Dithiocarbamates expressed as CS2, including Maneb, Mancozeb, Metiram, Propineb, Thiram and Ziram)	1
Hexaconazole	1
Hydrogen phosphide (phosphides expressed as hydrogen phosphide)	1
Imazalil	1
Lambda-Cyhalothrin	1
Lufenuron	1
Mepanipyrim (Mepanipyrim and its metabolite (2-anilino-4-(2-hydroxypropyl)-6-methylpyrimidine), expressed as Mepanipyrim)	1
Oxadixyl	1
Oxamyl	1
Pendimethalin	1
Pirimiphos-methyl	1
Pyraclostrobin	1
Pyrethrins	1
Pyrimethanil	1
Thiacloprid	1
Tolclofos-methyl	1

Table 2-11: Detection rate and MRL exceedance rate by country of origin and food product

Sample origin	Overall number of samples	% above the LOQ and below the MRL														% above the MRL													
		Number of samples	Apples	Head cabbage	Leek	Lettuce	Peaches	Strawberries	Tomatoes	Oats	Rye	Wine	Cow's milk	Swine meat	Total in %	Number of samples	Apples	Head cabbage	Leek	Lettuce	Peaches	Strawberries	Tomatoes	Oats	Rye	Wine	Cow's milk	Swine meat	Total in %
EU Member States and EFTA countries																													
Austria	121	43	85	23	17	14	0	100	33		0	63	15	0	36	1	0	7.7	0	0	0	0	0		0	0	0	0	0.8
Belgium	293	189	91	24	61	92		88	56		100	100	0	0	65	2	0	0	0	0		3.9	0		0	0	0	0	0.7
Bulgaria	129	57	73	100	100	33	70	36	31	50	50	80	0	0	44	9	0	0	0	42	0	18	6.3	25	0	0	0	0	6.2
Croatia	6	3	100	0					100				0		50	0	0	0					0				0		0
Cyprus	192	69	43	6	0	50	43	33	78			30	7	0	36	11	7.1		11	8.3	4.3	11	0			0	0	0	5.7
Czech Republic	131	54	100	80	0	58	67	100	100	0	21	63	0	6	41	0	0	0	0	0		0	0	0	0	0	0	0	0
Denmark	283	63	18	0	17	45		75	26	0	5		0	0	22	0	0	0	0	0		0	0	0	0		0	0	0
Estonia	112	55	17	88	40	20		50	75	33	89		0	31	49	4	0	0	0	0		22	0	0	0		0	0	3.6
Finland	159	45	47	0	13	0		77	10	6	35		0		28	0	0	0	0	0			0	0	0		0		0
France	570	306	66	9	39	64	86	73	53	47	22	43	0	0	54	8	1.5	4.5	1.1	4.3	0	2.2	0	0	0	0	0	0	1.4
Germany	1169	643	87	21	53	81	33	92	89	0	55	67	36	1	55	2	0	0	0	1.4	0		0	0	0	0	0	0	0.2
Greece	276	113	60	0	13	52	67	48	40	0		28	0	0	41	3	0	0	0	0	1.8	3.7	2.3	0		0	0	0	0.7
Hungary	260	97	59	26	0	40	45	67	55		50	75	0	0	37	2	3.1	0	0	2.5	0	0	0		0	0	0	0	0.8
Iceland	15	2		0		0		50	13						13	1		0		0		50	0						6.7
Ireland	157	59	75	36	36	82		100	67	52			0		38	1	0	9.1	0	0		0	0	0			0		0.6
Italy	1221	634	55	13	11	62	77	72	39	9	0	41	0	0	52	10	0	0	0	2.5	0.4	2.7	2.1	9.1	0	0	0	0	0.6
Latvia	96	14	27	15	8	0		31	0	25	40		0	0	15	1	9.1	0	0	0		0	0	0	0		0		1.0
Lithuania	117	30	38	12	29	38		53	50	25	38		0	0	26	3	0	12	0	0		5.9	0	0	0		0	0	2.6
Luxembourg	67	18	100	33	25	20			50		100	73	0	0	27	0	0	0	0	0			0		0	0	0	0	0
Malta	89	38		21	50	43	63	64	47			64	0	0	43	1		0	0	0	0	9.1	0			0	0	0	1.1
Netherlands	681	333	80	9	38	57	100	92	49	25	0	62	0	13	49	5	0	0	0	3.3	0	2.4	0.5	0	0	0	0	0	0.6
Norway	90	15	43	0	0	25		33	33	18	100		0	0	17	0	0	0	0	0		0	0	0	0		0	0	0
Poland	485	216	77	19	18	69	80	72	63	20	38	0	0	0	45	5	1.0	1.9	0	3.1	0	1.7	2.5	0	0	0	0	0	0.8
Portugal	189	109	67	66	50	62	60	63	54	0	0	60			58	9	25	0	3.8	0	0	4.2	4.2	0	0	0			4.2
Romania	563	133	44	6	9	22	20	17	15	0	13	45	16	14	24	4	0	0	0	6.9	0	0	0	0	0	0	0	0	0.7
Slovakia	92	57	76	92		43	100	33	71	33	43	60	87	0	62	0	0	0		0	0	0	0	0	0	0	0	0	0
Slovenia	228	106	83	0	0	35	82	92	60		0	70	0	0	46	2	0	0	0	2.5	9.1	0	0		0	0	0	0	0.9
Spain	1773	1016	41	45	10	56	77	77	61	0	13	24	2	0	57	16	0	0	1.6	1.0	1.0	1.6	0.9	0	0	0	0	0	0.7
Sweden	103	30	86	8	33	25		100	25	0	93		0	0	29	0	0	0	0	0		0	0	0	0		0	0	0
United Kingdom	695	194	72	31	11	55		98	17	97		0	0	2	28	2	0	0	0	0		2.2	0	1.5		0	0	0	0.3
EU (not specified)	7	3								0	0	75			43	1							0	0	0			0	0
Total	10 369	4744	64	23	33	56	74	75	48	45	44	46	8	3	46	102	1.0	0.9	0.5	2.3	1.0	3.0	0.9	1.3	0	0	0	0	0.9
Third countries																													
Argentina	46	24	57									36			52	1	0									9.1			2.2
Australia	27	19										70			70	0										0			0
Brazil	40	38	95									100			95	0	0									0			0
Chile	124	105	88				97	100				63			85	2	1.7				3	0				0			1.6
China	16	12	80					60				100			75	2	10					20				0			13
Egypt	17	8					0	46	100						47	0					0	0	0						0
FYRM [(a)]	51	18	27	25			100		67			63			35	1	9.1	0			0		0			0			2
Moldova	10	4	33									50			40	0	0									0			0

The 2013 European Union report on pesticide residues in food (EFSA, 2015)

…continuation

Heavy metals and other environmental pollutants (e.g. arsenic, lead, dioxins, polychlorinated dibenzodioxins PCDDs/polychlorinated dibenzofurans PCDFs, PCBs and dioxin-like PCBs)

Food contact materials (FCMs)

3. Process-generated contaminants

Polyaromatic hydrocarbons (PAHs) (e.g. BaA, BaP, BaF, Ch etc)

- Mainly formed in food as a result of processing (grilling, smoking, barbecuing and frying)
- Carcinogens in humans (Samanta et al., 2002)
- Cause mammary tumours in laboratory animals (Hecht, 2002)
  - Heterocyclic aromatic amines (HAAs)
  - *N*-nitrosamines (NAs)
  - Acrylamide (AA)

Table 20: Total dietary exposure to benzo[*a*]pyrene (BaP), PAH2, PAH4 and PAH8 (ng/day) for average and high consumers across Europe[33].

	Average exposure Whole population				*High exposure Sum of P97.5 for cereals and seafood + average exposure for whole population*			
Country	**BaP**	**PAH2**	**PAH4**	**PAH8**	**BaP**	**PAH2**	**PAH4**	**PAH8**
Belgium	232	637	1158	1732	393	1101	2108	3138
Bulgaria	209	560	1020	1526	385	1053	2027	3018
Czech Republic	239	654	1196	1777	426	1207	2328	3449
Denmark	223	617	1135	1690	299	818	1545	2300
Finland	185	535	978	1422	231	623	1155	1693
France	245	655	1220	1814	380	1021	1966	2921
Germany	255	681	1258	1888	422	1194	2311	3439
Hungary	231	647	1168	1716	314	877	1636	2410
Iceland	205	558	1039	1522	694	2232	4486	6568
Ireland	238	646	1188	1793	370	1049	2013	3009
Italy	255	719	1332	1962	487	1502	2943	4322
Netherlands	239	658	1197	1785	535	1687	3318	4886
Norway	252	765	1449	2136	461	1470	2900	4262
Slovakia	244	626	1158	1727	709	1905	3769	5601
Sweden	230	621	1168	1719	364	1003	1949	2876
United Kingdom	188	499	936	1415	315	854	1661	2489
Median EU	235	641	1168	1729	389	1077	2068	3078

EU: European Union

Source: (EFSA, 2008)

Latest news

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Use of not pre

PAH compounds at acceptable level in smoked fish products

Table 5.2 Levels of PAHs in commercially processed Finnish foods and their mutagenic potential only in the presence of the S9 mix.

	PAHs (μg/kg)					Ames test (revt/g)	
Food item	BaP	BaA	Ch	BbF	Sum	TA 100	TA98
Smoked ham	ND	< LOQ	< LOQ	ND	0	201 ± 9.1	34 ± 1.5
	ND	ND	< LOQ	ND	0	174 ± 12.5	32 ± 0.8
	ND	ND	< LOQ	ND	0	189 ± 7.9	37 ± 4.1
Honey-roasted chicken	ND	< LOQ	< LOQ	ND	0	247 ± 11.0	25 ± 2.1
	ND	ND	< LOQ	ND	0	198 ± 15.0	41 ± 6.4
	< LOQ	< LOQ	< LOQ	ND	0	258 ± 9.3	34 ± 4.0
Grilled turkey	ND	0.81	0.84	ND	1.60	297 ± 19.8	45 ± 0.0
	ND	ND	ND	ND	0	225 ± 0.0	39 ± 3.4
	ND	ND	< LOQ	ND	0	188 ± 10.1	27 ± 1.5
Pepper salami	ND	< LOQ	0.88	ND	0.88	241 ± 14.6	32 ± 4.9
	ND	< LOQ	< LOQ	ND	0	168 ± 8.7	30 ± 0.6
	ND	< LOQ	< LOQ	ND	0	200 ± 4.9	34 ± 3.2
Cold-smoked beef	ND	< LOQ	< LOQ	ND	0	209 ± 5.1	39 ± 5.0
	< LOQ	< LOQ	< LOQ	ND	0	188 ± 8.7	28 ± 0.0
	ND	ND	< LOQ	ND	0	188 ± 0.0	29 ± 2.1
Sauna-smoked ham	NA	NA	NA	NA	NA	NA	NA
	ND	ND	< LOQ	ND	0	268 ± 11.2	42 ± 1.2
	ND	ND	< LOQ	ND	0	158 ± 3.8	28 ± 1.2
Smoked fish	4.7	4.5	4.7	4.5	18.40	392 ± 12.0*	51 ± 4.7*
	8.2	15	15	5.8	44	478 ± 41.2*	64 ± 4.9*
	1.0	3.9	3.0	0.8	8.7	401 ± 22.8*	45 ± 2.0*

Key: ND: Not detected; LOQ: Limit of quantification (0.78 μg/kg); LOD: Limit of detection (0.26 μg/kg); NA: Not applicable; asterisk (*): Significantly different from control ($P < 0.05$). Sum: The total sum of benzo[*a*]pyrene, benzo[*a*]anthracene, chrysene and benzo[*b*]fluoranthene.

Table 1. Polycyclic aromatic hydrocarbon (PAH) content ($\mu g\ kg^{-1}$ dry weight) in raw, laboratory, and commercially smoked/grilled fish and meat samples from the Nigerian market.

	Mudfish			Jackfish			Mackerel			Croaker			Suya			Antelope		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
F	7.3	7.1	140.1	0.6	14.0	7.3	2.9	8.6	27.0	0.3	7.1	72.0	1.2	4.2	31.6	0.6	11.1	53.3
Pa	43.3	96.9	485.1	10.2	104.8	74.9	41.4	60.0	269.4	6.6	56.5	372.0	16.6	61.8	246.9	12.4	94.4	210.6
A	5.3	15.3	26.5	1.2	5.0	4.7	6.8	4.4	48.0	0.7	6.3	72.6	1.5	8.1	48.8	0.8	13.6	70.0
Fl	17.3	38.2	115.0	4.0	39.6	39.8	16.4	21.1	100.7	7.0	19.5	169.7	9.7	32.7	122.9	7.9	31.4	121.4
P	3.5	46.5	63.0	4.5	46.0	25.4	17.3	24.6	94.2	6.8	24.1	250.1	9.7	31.7	125.2	7.0	32.1	134.3
BaA	0.8	4.2	39.4	0.3	6.9	7.4	0.9	2.5	12.6	0.2	1.8	17.5	0.4	2.5	15.4	0.4	3.6	19.6
Ch	4.6	7.7	55.2	0.8	15.2	16.3	4.2	5.8	20.0	0.7	3.7	55.4	1.1	4.8	25.6	1.0	7.4	39.6
BbF	1.1	5.9	23.2	0.7	7.3	5.7	0.8	2.0	10.0	0.2	2.8	21.5	0.3	1.6	12.3	0.1	3.6	15.6
BkF	0.6	1.8	15.1	0.4	2.7	2.4	0.3	0.9	6.3	0.1	1.2	13.0	0.1	1.2	6.0	0.2	2.0	6.6
BaP	0.7	2.6	38.0	0.3	3.4	3.0	0.3	0.9	6.6	0.1	1.3	21.5	0.1	1.7	10.1	0.1	2.8	7.9
DBahA	0.3	1.2	3.4	3.6	1.2	0.9	5.6	0.9	1.3	0.9	0.8	2.5	0.1	0.1	1.5	0.1	2.2	0.9
BghiP	1.1	3.0	8.5	0.2	6.6	6.6	7.3	1.4	8.9	1.2	2.7	6.9	1.2	2.1	7.8	0.2	3.1	7.5
IP	0.3	0.4	14.5	n.q.	0.6	1.8	n.q.	1.0	6.4	3.3	1.8	4.6	0.4	1.4	6.5	0.0	3.0	3.8
LMW-PAHs	76.6	204.0	829.6	20.5	209.3	152.1	84.8	118.6	539.3	21.5	113.5	936.4	38.7	138.5	575.3	28.7	182.5	589.7
PAH8	9.4	26.7	197.2	6.3	43.9	44.1	19.3	15.4	72.1	6.8	16.1	142.9	3.7	15.4	85.2	2.1	27.7	101.5
T-PAHs	86.1	230.7	1026.9	26.8	253.2	196.2	104.1	133.9	611.4	28.3	129.6	1079.3	42.4	153.9	660.6	30.9	210.2	691.2
LMW/T-PAHs (%)	89.0	88.4	80.8	76.4	82.7	77.5	81.4	88.5	88.2	75.9	87.6	86.8	91.2	90.0	87.1	93.2	86.8	85.3

Note: Data are mean of two replicate analyses (each one injected twice). A, raw samples; B, laboratory smoked/grilled samples; C, commercially smoked/grilled samples; n.q., not quantifiable for the presence of interference. Fluorene (F), phenanthrene (Pa), anthracene (A), fluoranthene (Fl), pyrene (P), benz[*a*]anthracene (BaA), chrysene (Ch), benzo[*b*]fluoranthene (BbF), benzo[*k*]fluoranthene (BkF), benzo[*a*]pyrene (BaP), dibenz[*a,h*]anthracene (DBahA), benzo[*g,h,i*]perylene (BghiP), indeno[1,2,3-*c,d*]pyrene (IP); LMW-PAHs, low molecular weight PAHs (F + Pa + A + Fl + P); PAH8, BaA + Ch + BbF + BkF + BaP + DBahA + BghiP + IP; T-PAHs, total PAHs (LMW-PAHs + PAH8).

Source: Akpambang et al., 2009

Finnish food items

60 % were non-mutagenic with *Salmonella* Typhimurium TA 100 strain

73 % were non-mutagenic with *Salmonella* Typhimurium TA 98 strain

Processing methods

Smoking oven
Cold smoked
Liquid-smoked
Grilling

Nigerian food items

25 % were non-mutagenic with *Salmonella* Typhimurium TA 100 strain

75 % were non-mutagenic with *Salmonella* Typhimurium TA 98 strain

Processing methods

Wood contact smooking

Poor cooking oil

Deep frying

Mutagens in water samples

- In 1986 and 1988, drinking water in Finland were reported to be mutagenic (Vartiainen and Liimatainen, 1986; Vartiainen et al., 1988).

- This was largely attributed to high levels of the by-products of disinfection (mainly chlorination) stemming from chemical reactions with humic substances

- Seventy-one percent (71%) of water samples with mutagenic outcomes were reported to be contaminated with 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone and several other chlorinated hydroxyl furanones (Kronberg and Vartianien, 1988; Smeds et. al., 1997).

- Consequently in Finland, a linear relationship was reported between exposure to drinking-water mutagenicity and the risk of bladder, kidney, stomach and pancreatic cancers, as well as lymphomas in people consuming the water (Koivusalo et al., 1994, 1995).

http://en.cncnews.cn/news/v_show/32268_Secret_of_Finland’s_drinkable_tap_water__.shtml

- In Nigeria, drinking-water sources have recently been reported to be mutagenic (Adelanwa et al., 2011; Olorunfemi et al., 2014).

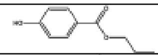
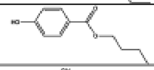
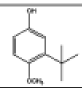
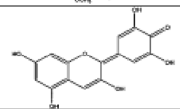
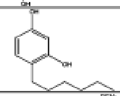
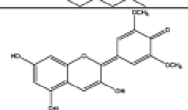
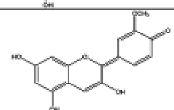
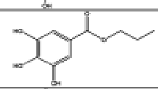
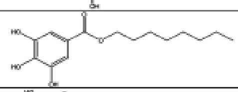
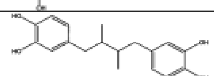
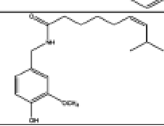
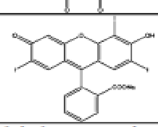
- The sources of mutagen are diverse, ranging from
  - By-product of disinfection
  - Environmental contaminant from pollution
  - Pesticides from agricultural run-off
  - Heavy metals etc

Sources of xenoestrogens in food and drinking water

Xenoestrogens in food

- Plant-based/natural (Phytoestrogen e.g. isoflavones)
- Process-generated contaminant, PAH (Santodonato, 1997)
- Pesticides (e.g. ethylenebisdithiocarbamates) (IARC, 2001; Kontou et al., 2004; Geetanjali and Santosh, 2009).
- Environmental contaminants (e.g. dioxin have been reported to be estrogenic in human cell lines, Boverhof et al., 2006)
- Food additives

Table 3. List of the 13 Food Additives Identified as Potential ERα Ligands by Virtual Screening

Additive	Structure	Predicted $LogP_{o/w}$[b]	Predicted pK_i	Experimental pK_i (K_i)	pEC_{50} (EC_{50})
Propyl 4-hydroxybenzoate[a]		2.53	8.05	3.82 (150 μM)(*6*)	Not tested
Butyl 4-hydroxybenzoate[a]		3.07	7.72	3.98 (105 μM)(*6*)	Not tested
Butyl hydroxyanisole[a]		3.42	8.22	Inactive	5-6 (100-10 μM)(*77, 102*)
Delphinidin		1.43	4.66	Inactive	Inactive
4-Hexylresorcinol		4.26	8.05	Inactive	8.15 (7 nM)
Malvidin		2.87	5.40	Inactive	Inactive
Peonidin		2.46	5.52	Inactive	Inactive
Propyl gallate		1.88	7.06	7.27 (54 nM)	Inactive
Octyl gallate		4.58	7.59	Inactive	Inactive
Nordihydroguaiaretic acid[a]		4.85	7.85	5.52 (3 μM)(*6*)	7.00 (100 nM)(*73*)
Capsaicin		3.51	7.72	Inactive	Inactive
Curcumin		1.44	6.95	Inactive	Inactive
Erythrosine		3.17	5.30	Inactive	Inactive

[a] Additives for which experimental data were already available in the literature. [b] $LogP_{o/w}$ calculated by HINT.

Amadasi et al., 2009

Food contact materials (FCMs)

- FCMs are unintentionally added substances in food
- Their presence usually occurs from leaching of food packaging materials under normal use conditions (ter-Veld et al., 2006; Vandenberg et al., 2007; Le et al., 2008)
- It is also influenced by factors such as storage conditions, sunlight exposure and ambient temperature

- Plasticizers such as a tris(2-ethylhexyl)trimellitate and benzoate mixture have been reported in food (ter Veld et al., 2006)

- Bisphenol A (BPA)

Table 1
Total urinary BPA concentrations of general population ($n = 121$).

	Total BPA concentration in urine		
	µg/l (original)[a]	µg/l (normalized)[b]	µg/g (creatinine)
Arithmetic mean	2.6	3.3	2.8
Geometric mean	1.9	2.6	2.3
Confidence interval (95%)	±0.4	±0.5	±0.4
Minimum	0.5	0.8	0.7
Median	1.8	2.4	2.1
95th percentile	7.9	8.1	7.8
Maximum	13.9	18.9	14.4

[a] Original results with no adjustments.
[b] Results normalized to specific gravity of 1.021.

Experiment 1 remained below the reference limit of 8 µg/l. The trends of the urinary BPA concentration versus time of all volunteers were also very similar when creatinine-adjusted BPA concentrations were used (data not shown).

Table 2
Urinary BPA concentrations of three volunteers during time period of 4–12 months. Spot urine samples were collected 1–2 times a week.

			Urinary BPA (µg/l)[a]					
Volunteer	Months	*n*	AM	GM	Min	Median	95th percentile	Max
V1	12	65	2.4	1.8	0.5	1.7	6.6	16.8
V2	12	80	1.5	1.0	0.3	0.9	4.6	8.8
V3	4	22	4.7	4.2	1.5	4.0	14.2	15.2

Abbreviations: AM, arithmetic mean; GM, geometric mean.
[a] Normalized to specific gravity of 1.021.

Source: (Porras et al., 2014)

Table 2

Concentrations of the phthalates and BPA in 37 food items. Values in bold and italics show median concentrations in different food categories [median lower bound (minimum, maximum)]. Values were given in μg/kg fresh weight. Values less than the LOQ are written as "<specific LOQ value".

Food category	DMP	DEP	DiBP	DnBP	BBzP	DEHP	DCHP	DnOP	DiNP	DiDP	BPA
Quantitation frequency (all products)	12/37	7/37	25/37	23/37	11/37	24/37	4/37	19/37	31/37	14/37	20/37
Grain and grain products	***0.26 (ND, 2.8)***	***ND (ND, 2.1)***	***6.9 (1.0, 24)***	***3.0 (1.3, 16)***	***0.82 (ND, 3.5)***	***43 (ND, 60)***	***ND (ND, 5.2)***	***1.3 (ND, 3.3)***	***7.1 (ND, 734)***	***6.2 (ND, 11)***	***0.11 (ND, 0.24)***
Bread	1.2	<1.5	6.9	2.8	1.3	46	<0.50	1.3	74	6.2	0.24
Pasta (dry)	<0.10	<1.5	1.0	1.3	0.82	18	<0.50	<0.50	7.1	<0.90	<0.10
Buns	2.8	2.1	9.8	5.1	<2.5	61	5.2	1.9	734	11	0.19
Breakfast cereals	<1.0	<1.0	24	16	<2.5	43	<3.0	<1.0	3.9	6.4	<0.10
Flour	0.26	<1.5	4.7	3.0	3.5	<10	3.6	3.3	<1.0	<0.90	0.11
Milk and dairy products	***ND***	***ND (ND, 9.3)***	***3.1 (ND, 5.4)***	***ND (ND, 31)***	***ND***	***126 (19, 173)***	***ND***	***3.9 (ND, 24)***	***49 (6.8, 166)***	***ND***	***ND (ND, 0.72)***
Milk	<0.10	<1.5	<0.50	<0.50	<0.50	19	<0.50	<0.50	17	<0.90	<0.02
Hard cheese	<3.0	<3.0	3.3	<5.0	<7.5	173	<10	1.5	81	<5.0	0.72
Cheese spreads	<3.0	<3.0	3.0	<5.0	<7.5	128	<10	24	166	<5.0	<0.10
Norwegian brown cheese	<3.0	9.3	5.4	31	<7.5	124	<10	6.3	6.8	<5.0	<0.10
Meat and meat products	***ND (ND, 20)***	***ND***	***0.47 (ND, 12)***	***0.55 (ND, 5.8)***	***ND (ND, 78)***	***ND (ND, 117)***	***ND***	***ND (ND, 29)***	***47 (3.0, 275)***	***ND (ND, 13)***	***0.24 (ND, 3.2)***
Minced meat	<1.5	<1.5	12	2.9	78	64	<5.0	19	41	<2.0	0.19
Chicken fillet	<0.10	<1.5	<0.50	<0.50	1.6	<10	<0.50	<0.50	4.0	<0.90	<0.10
Sausages	18	<3.0	<1.5	5.2	<7.5	<25	<10	<3.0	275	6.8	2.1
Hamburgers	<1.5	<1.5	2.7	<2.0	<4.0	<15	<5.0	<1.5	52	13	0.17
Sliced salami	20	<3.5	4.2	5.8	Interference	117	<10	29	153	<5.0	0.29
Liver paté	<3.0	<3.0	<1.5	<5.0	11	<25	<10	18	16	<2.0	3.2
Sliced ham	<8.0	<8.0	<4.0	<12	<20	<70	<25	<8.0	3.0	<0.90	<0.10
Sliced turkey	<0.10	<1.5	0.93	1.1	<0.5	15	<0.50	<0.50	76	<0.90	0.88
Fish and fish products	***ND (ND, 0.53)***	***ND***	***0.72 (ND, 3.2)***	***0.78 (ND, 12)***	***ND (ND, 32)***	***ND (ND, 35)***	***ND (ND, 30)***	***ND (ND, 14)***	***38 (2.0, 55)***	***1.7 (ND, 3.7)***	***1.2 (ND, 7.3)***
Fish balls	0.41	<1.5	0.52	0.78	<0.50	<10	<0.50	<0.50	6.5	1.7	7.3
Fish pudding	0.53	<1.5	0.72	3.0	<0.50	<10	<0.50	<0.50	38	3.7	1.3
Mackerel fillet in tomato sauce (canned)	<3.0	<3.0	3.2	12	<7.5	35	<10	14	55	<5.0	1.2
Caviar spread, cod roe	<3.0	<3.0	1.7	<5.0	32	<25	30	<3.0	2.0	<2.0	0.42
Frozen fish packed in plastic	<1.0	<1.0	<0.50	<1.5	4.0	10	<3.0	12	54	2.6	<0.10
Fats	***ND***	***ND***	***ND***	***ND***	***ND***	***221 (118, 323)***	***ND***	***14 (ND, 27)***	***7.5 (ND, 15)***	***ND***	***ND***
Margarine	<8.0	<8.0	<4.0	<12	<20	323	<25	27	<8.0	<6.0	<0.10
Butter	<8.0	<8.0	<4.0	<12	<20	118	<25	<8.0	15	<6.0	<0.10
Fruits and vegetables	***2.6 (0.30, 4.9)***	***ND***	***ND***	***0.46 (ND, 0.92)***	***ND***	***4.8 (ND, 9.5)***	***ND***	***ND***	***3.5 (2.9, 4.0)***	***1.8 (ND, 3.6)***	***0.19 (ND, 0.38)***
Jam	4.9	<1.5	<0.50	0.92	<0.50	9.5	<0.50	<0.50	4.0	3.6	0.38
Frozen vegetables packed in plastic	0.30	<1.5	<0.50	<0.50	<0.50	<10	<0.50	<0.50	2.9	<0.60	<0.10
Ready to eat	***1.6***	***1.75 (1.7, 1.8)***	***4.1 (2.7, 5.4)***	***3.6 (2.9, 4.2)***	***2.9 (ND, 5.7)***	***136 (37, 235)***	***ND***	***4.2 (3.1, 5.2)***	***70 (45, 94)***	***5.1 (5.0, 5.1)***	***5.8 (2.9, 8.7)***
Frozen pizza	1.6	1.7	2.7	2.9	<2.5	37	<3.0	5.2	45	5.1	2.9
Canned dinners	1.6	1.8	5.4	4.2	5.7	235	<3.0	3.1	94	5.0	8.7
Snacks	***0.75 (ND, 1.5)***	***ND***	***6.9 (6.2, 7.7)***	***3.6 (ND, 7.1)***	***ND***	***66 (56, 76)***	***ND***	***6.8 (5.7, 7.9)***	***225 (88, 362)***	***9.9 (9.7, 10)***	***ND***
Chocolate spreads	1.5	<3.0	7.7	7.1	<7.5	56	<10	7.9	362	9.7	<0.10
Biscuits	<3.0	<3.0	6.2	<5.0	<7.5	76	<10	5.7	88	10	<0.10
Beverages	***ND (ND, 0.060)***	***0.040 (ND, 0.070)***	***0.18 (0.060, 0.88)***	***0.41 (0.34, 0.95)***	***ND (ND, 0.19)***	***0.66 (0.17, 0.74)***	***ND (ND, 0.070)***	***0.040 (ND, 0.12)***	***ND (ND, 3.2)***	***ND***	***ND (ND, 0.37)***
Soft drinks (plastic bottle)	<0.025	0.067	0.059	0.35	<0.030	0.67	<0.040	0.024	3.2	<0.60	<0.020
Soft drinks (cans)	<0.025	0.051	0.28	0.95	<0.030	0.74	<0.040	0.059	<0.80	<0.60	0.37
Bottled water	<0.025	0.037	0.079	0.34	<0.030	0.17	<0.040	<0.020	<0.80	<0.60	<0.020
Juice	0.060	<0.025	0.88	0.46	0.19	0.65	0.073	0.12	<0.80	<0.60	<0.020
Condiments	***ND***	***ND***	***1.5 (0.79, 2.2)***	***0.60 (ND, 1.2)***	***ND***	***17 (ND, 33)***	***ND***	***8.8 (ND, 18)***	***12 (9.4, 14)***	***0.43 (ND, 0.86)***	***2.7 (ND, 5.4)***
Mayonnaise	<8.0	<8.0	2.2	<12	<20	<70	<25	18	14	<6.0	<0.10
Canned tomatoes	<0.10	<1.5	0.79	1.2	<0.50	33	<0.50	<0.50	9.4	0.86	5.4
Whole egg	***<1.5***	***<1.5***	***<1.0***	***<2.0***	***<4.0***	***<15***	***<5.0***	***<1.5***	***<1.0***	***<1.3***	*1.2*

ND = not detected.

Norway

1. **Phthalates and BPA were found in all foods and beverages**
2. **BPA was found in 54% of samples**

Sakhi et al., 2014

Contamination of drinking water by xenoestrogens.

- Plastic or glass bottles
- Bottle caps
- Transport pipelines
- Disinfection agents
- The bottling process itself
- Environmental pollution of water sources

Country	Samples	Outcome (ng/l EEQ)	Source
Italy	Mineral water	0.03 – 23.1 Mean: 9.5	Pinto & Reali, 2009
	Tap water	Average: 15.0	
Germany	Bottled water	2.64 – 75.2 (60%) Mean: 18.0	Wagner & Oehlmann, 2009
Spain	Bottled water	79.3 % (Mean: 0.113)	Real et al., 2015
Finland	Bottled water	Nil (n= 10)	Omoruyi and Pohjanvirta, 2015
	Mineral water	Nil (n=10)	
	Tap water	Nil (n= 24)	
Nigeria	Sachet water	0.79 – 44.0 (31%)	Omoruyi et al., 2014

- Waste-water treatment plants (WWTPs) are also, potential sources of human exposure to EDCs

Finland	Nigeria
WWTPs are present and in use	No working WWTPs (Daily Trust, 2014)
Waste collection are centralized	waste collection are decentralized

Table 1 Characterisation of sampled wastewater treatment plants (WWTPs) and the detected estrogenic activity

Label in this article	Country	Location/WWTR name	Composition of wastewater	Plant capacity (thousands of m^3/d)	Capacity population equivalent (thousands)	Type of secondary (and tertiary if applied) treatment	Detected EEQ (ng/L)
WWTP A1	Italy	Roma nord ACEA	Dom. Ind. Rain	354	780	biological, not specified, final disinfection step	12.2
WWTP A2	Czech Rep.	Not displayed	Dom. Ind. Rain	>200	>500	AS, DN, N, CHP	2.1
WWTP A3	Czech Rep.	Not displayed	Dom. Ind. Rain	>100	>500	AS, DN, N, CHP	1.3
WWTP A4	Finland	Helsinki	Dom. Ind. probably Rain	30[a]	825[a]	AS, DN, N, CHP	<0.5
WWTP A5	Germany	Bremen	Dom. Ind. Rain	94	1 000	AS, D/N, CHP	<0.5
WWTP A6	Germany	Klärwerk Gut Marienhof	Dom. Ind. Rain	493	1 500	AS, DN, N, CHP	<0.5
WWTP A7	Ireland	Dublin		400	1 900	AS (sequencing batch reactor) with DN/N, UV Light Treatment	<0.5
WWTP A8	Netherlands	Harnaschpolder	Dom. Ind. Rain	150	1 400	AS, DN/N, BP	<0.5
WWTP A9	Netherlands	Rotterdam Dokhaven	Mainly Dom.	117	500	AS, D/N - SHARON® and ANAMMOX®, CHP	<0.5
WWTP A10	Switzerland	Zürich Werdhölzli	Dom. Ind. Rain		640	AS, DN, N, BP, CHP	<0.5
WWTP B1	Slovenia	Ljubljana	Dom. (62 %), Ind. (11 %), Rain (21 %)	103	360	AS not further specified	4.1
WWTP B2	Czech Rep.	Not displayed	Dom. Ind. Rain	52	170	AS, DN, N, CHP	1.7
WWTP B3	Lithuania	Kaunas		82	370	AS, DN/N, CHP	1.0
WWTP B4	Netherlands	Venlo		71[b]		AS, DN/N, BP	0.9
WWTP B5	Netherlands	Almere	Dom., Hospital, no Rain		330	not specified	0.6
WWTP B6	Austria	Wiener Neustadt - Sud	Dom. (90 %), Paper Ind.	37	260	AS, DN/N, P removal not specified,	0.5
WWTP B7	Austria	AWV Hall i. Tirol-Fritzens	Dom. Ind. (Rain was not further specified)	16	120	AS not further specified	<0.5
WWTP B8	Belgium	Deurne	Waste water from Antwerp	50[a]	325	AS not further specified	<0.5
WWTP B9	Finland	Espoo	Dom. Ind. Rain not specified	110	250	AS, DN, N, P removal not specified	<0.5
WWTP B10	Netherlands	Amstelveen	Dom.		125	AS not further specified	<0.5 ∇
WWTP B11	Netherlands	Nieuwgraaf	Dom. Ind. (30-40 %), Hospital		395	AS not further specified	<0.5 ∇
WWTP B12	Netherlands	Garmerwold (Noorderzijlvest)	Dom.		300	AS, DN/N - SHARON®, P removal not specified	<0.5
WWTP B13	Netherlands	Zaandam Oost	Dom. Urban runoff, Ind. Craft Industry		150	AS, DN/N, P removal not specified	<0.5
WWTP B14	Lithuania	Klaipedo vanduo	Dom. Ind. (Rain was not further specified)	95	200[a]	AS, DN/N, P removal not specified	<0.5
WWTP B15	Lithuania	Panevezys regional	Dom. Ind. Rain	70		not specified	<0.5
WWTP C1	Cyprus	Larnaka	Dom.	6	27.5	AS, no DN, N and P removal not specified, sand filtration, chlorination	3.6
WWTP C2	Spain	Ulldecona		1.6	13.5	not specified	3.3
WWTP C3	Czech Rep.	Not displayed	Dom. Rain	3	15	AS, N, DN, CHP	1.2
WWTP C4	Austria	Eisenstadt eisbachtal		12[b]	42[b]	AS, DN/N not specified, CHP	<0.5
WWTP C5	Austria	Feldkirchen		6.6	50	AS, N, DN, BP	<0.5
WWTP C6	Belgium	Hasselt	Dom.	12	65	AS, (DN/N and P removal not specified)	<0.5
WWTP C7	Cyprus	Limassol	Dom. Ind.	15	70	AS, N, DN, no BP (CHP not specified), sand filtration, chlorination	<0.5
WWTP C8	Czech Rep.	Not displayed	Dom. Rain	19	75	AS, N, DN, CHP	<0.5
WWTP C9	Ireland	Oberstown			80	cyclic AS, N, DN, CHP	<0.5
WWTP C10	Netherlands	Leek (Noorderzijlvest)	Dom.		34	not specified	<0.5 ∇
WWTP C11	Netherlands	Simpelveld	Dom., Health Care Unit		20.5	not specified	<0.5
WWTP C12	Netherlands	Winterswijk	Dom. Ind. (30-40 %). Hospital		83.5	not specified	<0.5
WWTP C13	Spain	Tortosa		10	46.8	not specified	<0.5
WWTP C14	Switzerland	Affoltern a.A.	Dom. Ind. Rain		14	AS, DN/N not specified, CHP	<0.5

Jarošová et al., 2014

Table 1 (continued)

Label in this article	Country	Location/WWTR name	Composition of wastewater	Plant capacity (thousands of m^3/d)	Capacity population equivalent (thousands)	Type of secondary (and tertiary if applied) treatment	Detected EEQ (ng/L)
WWTP D1	Czech Rep.	Not displayed	Dom. Ind. no Rain	0.3	2.5	AS, N, DN, CHP	1.9
WWTP D2	Germany	AZV Hungerbachtal			7[a]	AS not further specified	0.8
WWTP D3	Hungary	Alattyán	Mainly Dom.		0.25	not specified	0.8
WWTP D4	Switzerland	Wenslingen	Dom. Rain		0.7	AS (DN/N and P removal not specified)	0.6
WWTP D5	Czech Rep.	Not displayed	Dom. Ind. no Rain	0.7	5	AS, N, DN, CHP	<0.5
WWTP D6	Finland	Nummi-Pusula		1[b]	6[a]	Fe coag., As (no DN/N)	<0.5
WWTP D7	Spain	Godall		0.15	0.9	not specified	<0.5
WWTP D8	Switzerland	Konolfingen	Dom. Ind. Rain		7.9	AS, CHP (DN/N not specified)	<0.5
WWTP D9	Switzerland	Seuzach	Dom. Rain	4	6.5	AS, CHP (DN/N not specified)	<0.5 ∇
WWTP E1	Belgium	Agristo	Food industry (potato products)				3.4
WWTP E2	Belgium	TWZ Evergem	Tank cleaning and various ind. activities				1.8
WWTP E3	Belgium	Bayer Antwerpen	Chemical industry (e.g. pesticide production)				1.2
WWTP E4	Belgium	3M	Different industrial branches				0.8
WWTP E5	Belgium	Janssen Pharmaceuticals	Pharmaceutical industry				0.6
WWTP E6	Austria	WV Hofsteig	Dom. (25 %). Ind. (75 %) (Metal, food, textile)	138	216	AS not further specified	<0.5
WWTP E7	Belgium	Ajjinomoto Omnichem	Herbal extracts, polyphenols production				<0.5 ∇
WWTP E8	Belgium	Ardo	Food industry (frozen vegetable)				<0.5
WWTP E9	Belgium	Colortex	Textile industry (dyeing)				<0.5 ∇
WWTP E10	Belgium	EOC Oudenaarde	Chemical industry (e.g. adhesives, surfactants)				<0.5
WWTP E11	Belgium	Tack Oostrozebeke	Tank cleaning and various industrial activities				<0.5 ∇
WWTP E12	Belgium	Taminco	Chemical industry (Amine company)				<0.5 ∇
WWTP F1	Hungary	Martfű	Dom. or soya or brewery production?	1			17.9
WWTP F2	Portugal	Parada				AS, DN, N, no BP	6.0
WWTP F3	Austria	AWV Region Feldkirch		380		AS not further specified	1.2
WWTP F4	Portugal	Viana do Castelo			90[a]	AS not further specified	0.7
WWTP F5	Greece	Thessaloniki (EELTH)	Dom. Ind. probably Rain				0.7
WWTP F6	Italy	Depuratore 'Jugendwerk Brebbia'					0.6
WWTP F7	Belgium	Geel				trickling filter, AS (INVENT®), sand filtration	<0.5
WWTP F8	Belgium	Ronse					<0.5
WWTP F9	Belgium	Waregem	Region with textile industry				<0.5 ∇
WWTP F10	Finland	Lohja					<0.5
WWTP F11	Finland	Mäntsälä					<0.5
WWTP F12	Finland	Vihti					<0.5
WWTP F13	Greece	Thessaloniki (EEL AINEIA)	Waste water from Thermaikos city				<0.5
WWTP F14	Belgium	Claerebout					<0.5
WWTP F15	Belgium	Shanks lokeren					<0.5

Dom. domestic, *Ind.* industrial, *AS* reservoirs with activated sludge, *DN* denitrification, *N* nitrification, *DN/N* biological treatment of nitrogen (not specified if N, DN or both are used), *BP* biological removal of phosphorus, *CHP* chemical precipitation of phosphorus

[a] Approximate number

[b] Average daily discharge or currently connected equivalent citizens and not maximal capacity of WWTP

∇ ∇ Cytotoxic/antiestrogenic samples (open and full symbols indicate less and more pronounced effects, respectively)

Jarošová et al., 2014

Two-year study (2011 and 2014) of influent and effluent samples from Viikinmäki WWTP

- The oestrogenic activity of influent samples were generally low (approximately 0.5 ng/l EEQ) throughout this period
- March (14.o ng/l EEQ) and August 2011 (7.8 ng/l EEQ)
- All treated effluent waters from the WWTP were none oestrogenic
- Influent and effluent samples from an equivalent household water purification plant were also none oestrogenic in an *in vitro* test system

Omoruyi and Pohjanvirta, 2015

Conclusion

- Commercially processed foods are potential sources of human exposure to genotoxic chemicals.
- These chemicals are often difficult to regulate/control, because they are formed in food as a result of food processing. However, appreciable progress has been made in Finland towards reducing the levels of these contaminants in commercial foodstuffs.
- In Nigeria, much still needs to be done, since the majority of food items (chin-chin, hamburger, suya and bean cake) investigated were proven to be mutagenic. The dissimilar mutagenic outcome in the two countries may largely be due to differences in processing techniques.

- Drinking-water sources (tap water, bottled still and mineral waters) and water from drinking- water treatment plants in Finland are not sources of concern, with respect to their oestrogenic potentials.

- Meanwhile, sachet-pure water samples from Nigeria, as well as packaging materials, could pose grave problems for consumers, because 31% of the samples were oestrogenic, of which 40% were attributed to FCMs.

- A 2-year study of both influent and effluent wastewater samples from Viikinmäki WWTP in Finland showed that the treatment process (activated sludge coupled with mechanical, chemical and biological purification) used in the treatment of wastewater is effective in removing oestrogenic chemicals. In Nigeria, there are no centralized WWTPs. This may impair proper waste treatment and also increases exposure to EDCs.

Thank you for your attention