EPFL

FOOD CHEMISTRY

Chapter 8 : Toxic components

8.1 INTRODUCTION

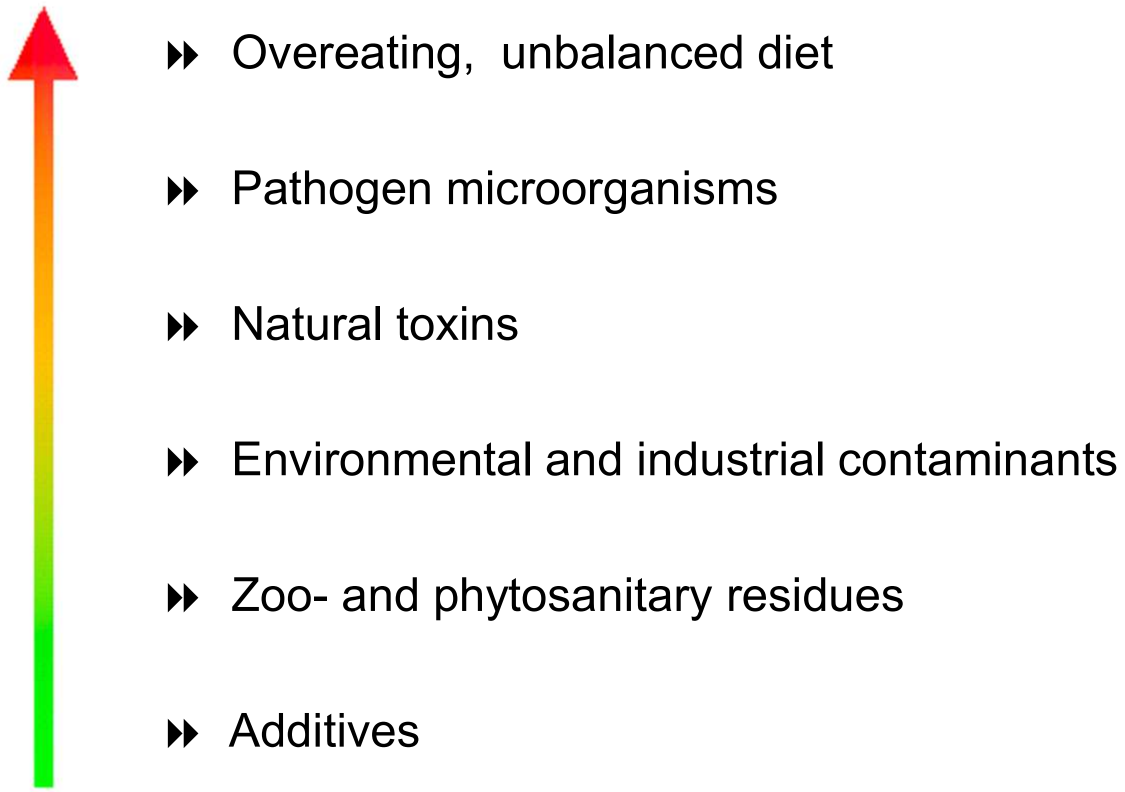
Recent examples of mass intoxications due to foods

Date	***Place***	***Food***	***Toxicant***	***Victims****
1930	Detroit (USA)	Bootlegged tonic	o-Cresyl-phosphate	16’000
1910 - 1945	Toyama (J)	Water, fish, rice	Cadmium	> 700
1956 - 1968	Minamata (J)	Water, fish	Methyl mercury	>10’000
1956	Turkey	Wheat	Hexachlorobenzene	4’000
1959	Morocco	Cooking oil	o-Cresyl-phosphate	10’000
1965	Niigata (J)	Water, fish	Mercury	>500
1972	Irak	Wheat	Methyl mercury	>5’000
1981	Spain	Cooking oil	Annilides ?	>10’000
1998 - 2005	Kenya	Alcohol	Methanol	>2’000
1998	Italy	Wine	Methanol	>2’000
2004	Kenya	Corn	Aflatoxins	>200
2011	Germany	Bean sprouts	Verotoxin	>900

* Death or permanently strongly impaired

8.1 INTRODUCTION

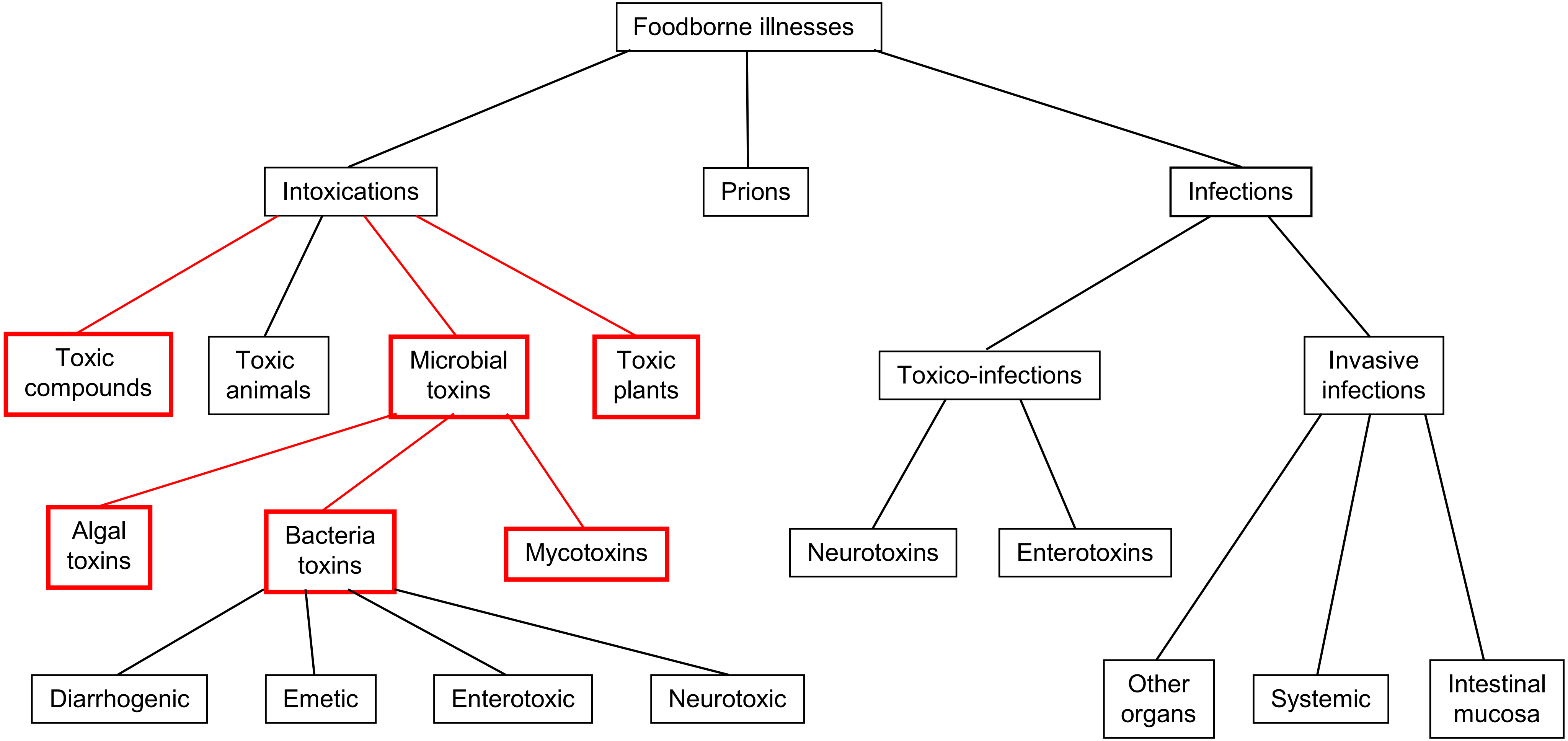
WHO classification of hazards due to foods



- Overeating, unbalanced diet
- Pathogen microorganisms
- Natural toxins
- Environmental and industrial contaminants
- Zoo- and phytosanitary residues
- Additives

8.1 INTRODUCTION

Origin of hazards due to foods



Foodborne illnesses

Intoxications

Prions

Infections

Toxic compounds

Toxic animals

Microbial toxins

Toxic plants

Toxico-infections

Invasive infections

Algal toxins

Bacteria toxins

Mycotoxins

Neurotoxins

Enterotoxins

Diarrhogenic

Emetic

Enterotoxic

Neurotoxic

Other organs

Systemic

Intestinal mucosa

8.1 INTRODUCTION

Toxicological terms

Acute toxicity	Adverse effects of a substance which result from a single exposure.
Chronic toxicity	Toxic effects on an organism continuously or repeatedly exposed to a given substance.
Median lethal dose (LD_{50})	Dose required to kill half of the members of a tested population.
NOAEL	No observed adverse effect level : the highest amount of a substance at which no adverse effect is found in test animals .
Acceptable daily intake	Measure of the amount of a substance that can be ingested on a daily basis over a lifetime without an appreciable health risk. Usually, ADI = NOAEL / (10 * 10)

8.2 HEAVY METALS

Occurrence of trace metal elements

Heavy metals are members of a loosely-defined subset of elements that exhibit metallic properties. It mainly includes the transition metals, some metalloids, lanthanides, and actinides. They are also called « Trace metal elements » according to their abundance.

Elements	***Cr***	***Fe***	***Co***	***Ni***	***Cu***	***Zn***	***As***	***Cd***	***Hg***	***Pb***
Continental crust	88	42’000	19	45	35	69	3.4	0.10	0.02	15
Oceanic crust	317	70’000	45	144	81	78	1.5	0.13	0.02	0.9

Values in mg/kg

8.2 HEAVY METALS

Natural and anthropogenic metals emissions (1980)

Element	***Continental dust***	***Volcanic dust***	***Industry***	***Fuel combustion***	***Interference factor (%)***
Al	35’650	13’250	4’000	3’200	15
Fe	19’000	8’775	7’500	3’200	40
Cr	50	8.4	65	29	160
Ni	20	8.3	60	38	350
Cu	10	9.3	220	43	1350
Cd	0.25	0.04	4	1.5	1900
Zn	25	11	700	140	2350
As	2.5	0.3	62	16	2800
Hg	0.03	0.01	5	6	27500
Pb	5	0.9	1’600	430	34600

Values in MTons/year

IF = 100 * anthropogenic/natural emissions

8.2 HEAVY METALS

Acute toxicity of trace metal elements

Acute poisoning due to heavy metals in foods is very rare. One exception : the thallium poisoning due to Tl_2SO_4 that was once used as a rodenticide (LD_{50} = 25 mg/kg for rats). Due to numerous accidents, this product has been banned.

In a group of the periodic table, toxicity increases with atomic number :

IA : Na < K < Rb < Cs
IIA : Mg < Ca < Sr < Ba
IB : Cu < Ag < Au
IIB : Zn < Cd < Hg
IIIA : Al < Ga < In < Tl

The common most toxic elements belong to the 6th period (Hg, Tl, Pb).

8.2 HEAVY METALS

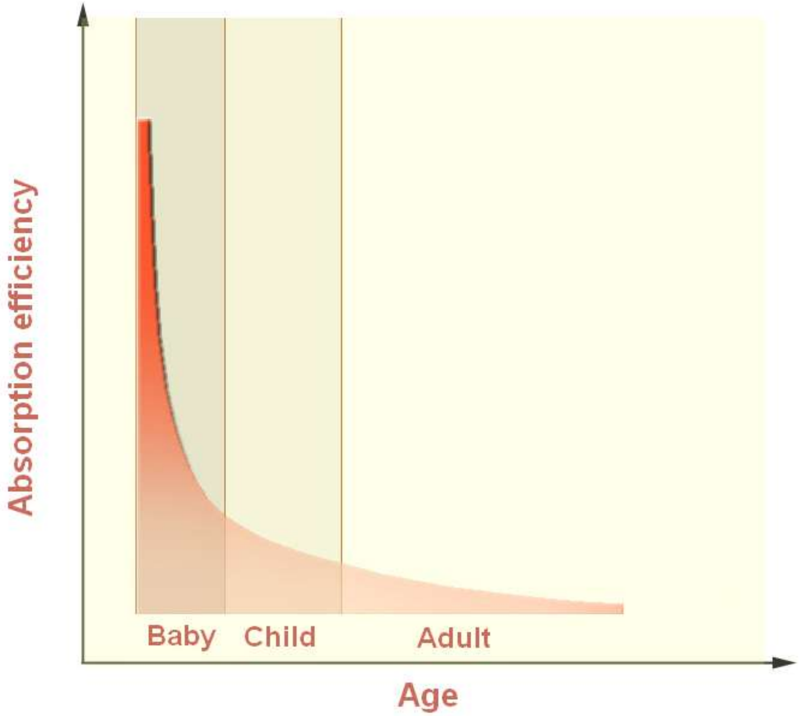
Chronic toxicity of trace metal elements

Various biochemical effect :

- Complexation with SH groups of proteins or nucleophilic groups of nucleic acids or other molecules.
- Perturbation of the catalytic effect of other elements in enzymatic reactions.
- Perturbation of the electrolyte concentrations in gastro-intestinal tract, in renal or neural systems.

Effects can be either local or systemic.

Toxicity is heavily dependant on age, due to maturation of detoxification mechanisms.



8.2 HEAVY METALS

Toxic effects of various elements

Organ	***Effect***	***Elements***
Skin	Dermatitis, eczema	Ni Cr As Be Pt V Sb
Mucosae	Inflammation, nasal perforation	Cr As Sb
Lungs	Emphysema, bronchitis	As Cr Ni
GI - tract	Diarrhea, cramps, ulcers	Sb Pb Tl Hg
Liver	Functional perturbations	Sb As Bi Cr Cu Se Cd
Kidneys	Functional perturbations	Pb Cd U Hg Bi
Nervous system	Neuropathies, sensory and motor pertubations	As Pb Mn Hg Tl Sn Se Au

Carcinogenicity is not taken into account !

8.2 HEAVY METALS

Biochemistry of lead

Burton’s line

Lead in the body

10% uptake from GI-tract (> 50% in babies)
95% sequestered in bones as $Pb_3(PO_4)_2$
Half-life : 20 – 30 years

Main targets

Inhibition of amino-levulinic acid dehydrogenase (ALAD) and ferrochelatase, enzymes involved in the synthesis of hemoproteins.
Inhibition of *N*-methyl *D*-aspartate receptors, thus impairing neurotransmission.

Main effects

Abdominal pains (« lead colics »)
Neurological disorders (memory impairement, mental retardation in children)
Anemia
Motor problems (loss of coordination, numbness and tingling in the extremities)
Hyperketonury (« saturnian gout »)

8.2 HEAVY METALS

Sources of lead in food and beverages

Wine	Corroded lead caps
Canned food	Tin-lead welding
Dishware	Lead salts paint
Fishes, mushrooms	Bio-accumulation
Lead-lined vessels	When producing low pH products, lead is oxydized and dissolved (wine, vinegar, cider – « Devonshire colic »)

Roman lead water pipe with taps

Bethooven died from chronic saturnism, due to his love of Rhine wine sweetened with $Pb(CH_3COO)_2$

8.2 HEAVY METALS

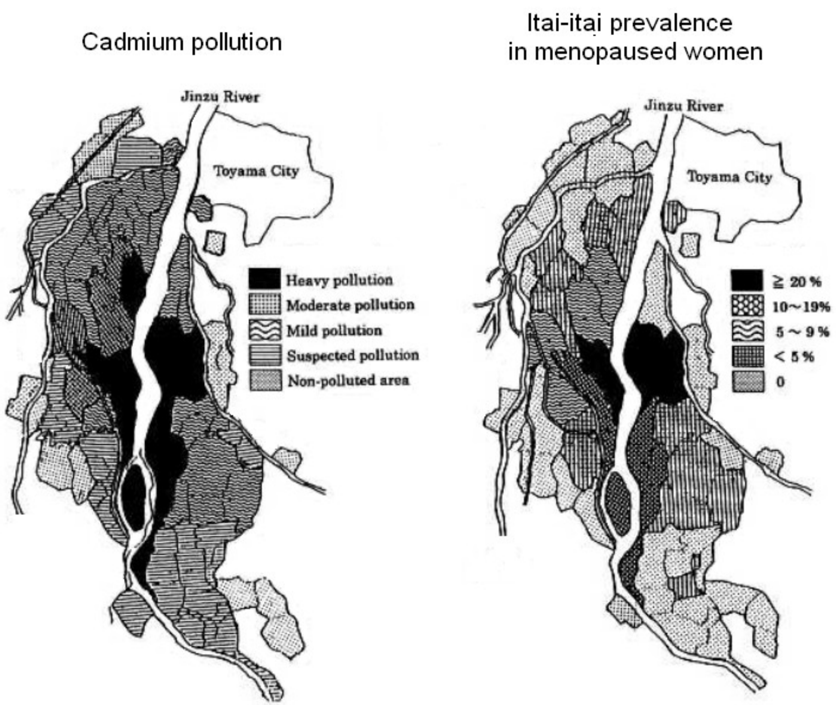
Biochemistry of cadmium

Cadmium in the body

Cd has no known biological function in higher organisms
6% uptake from GI-tract (increases with diets low in proteins and calcium)
Half-life : > 20 years

Accumulation route

Induces the formation of a metallothionein complex in the liver. After release in the circulation, Cd is absorbed in the proximal tubules of the kidneys.



Main effects of chronic intoxication

Anemia
Severe loss of bone minerals, fractures
Severe pains in the joints and spine.

8.2 HEAVY METALS

Sources of cadmium in food and beverages

British study (2000)
Values in mg/kg

Offal	0.07
Potatoes	0.03
Cereals	0.02
Fish	0.02
Vegetables	0.008
Meat	0.007
Milk	0.001

Mushrooms are very efficient Cd concentrators, especicially the genera *Agaricus*, *Macrolepiota* and *Lepista*

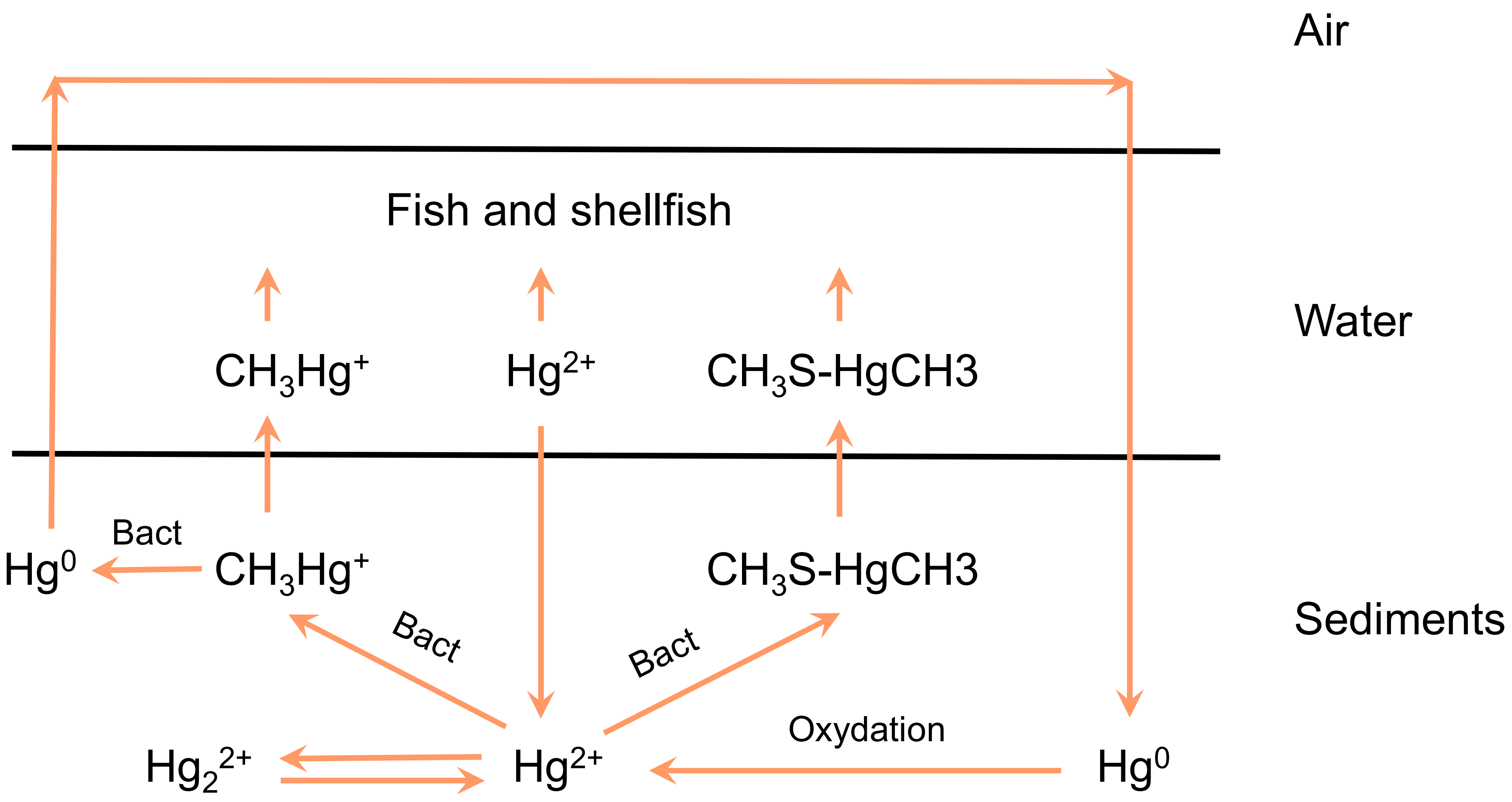
Concentrations : 0.2 – 30 mg/kg !

Provisional Weekly Tolerance Intake : 7 µg/kg BW

In developed countries, intake 10 – 20 µg/day

8.2 HEAVY METALS

The speciation of mercury



8.2 HEAVY METALS

Mercury toxicity

Uptake : 7% for inorganic, 100% for organic

LD_{50} (rat, mg/kg)

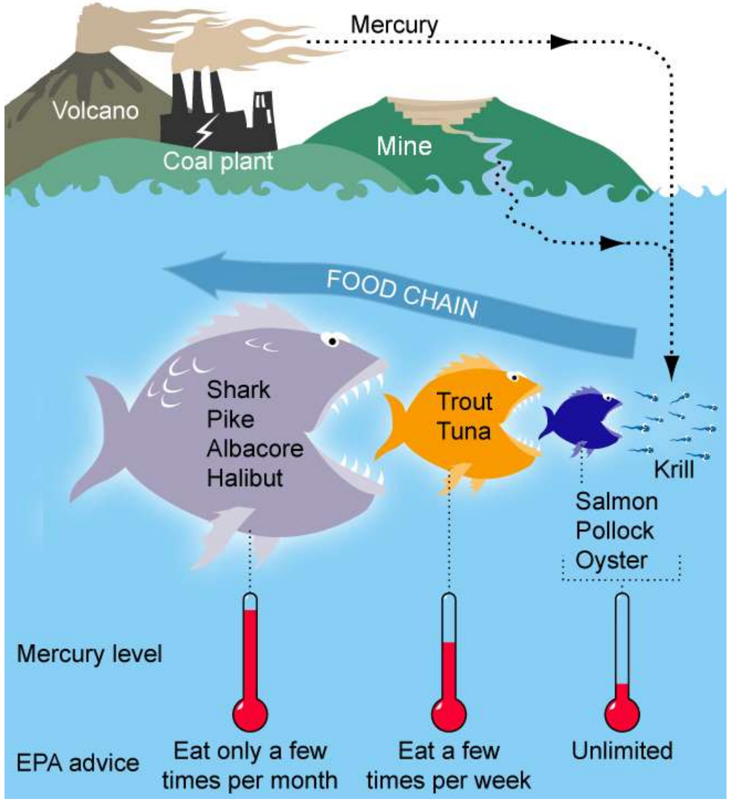
Hg^+	210
Hg^{2+}	37
$Me\text{-}Hg^+$	10
$Et\text{-}Hg^+$	40
$Phe\text{-}Hg^+$	60

Distribution : Liver and kidneys for inorganic
All tissues, mainly brain for organic

Effects of mercury :

Inorganic	kidney failure
Organic	neurotoxin

Main sources : fish, shellfish



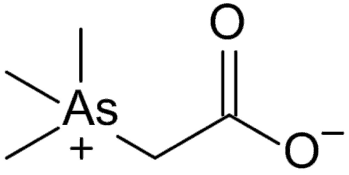
8.2 HEAVY METALS

Arsenic toxicity

Inorganic arsenic is metabolised through methylation, and the products are eliminated. In humans, the methylation products are $(CH_3)_2AsOH$ (dimethylarsinous acid) and $(CH_3)_2As(O)OH$ (dimethylarsinic acid).

Chronic exposition to As leads to cancers and probably type II diabetes. WHO has set a limit of 10 µg/l in water, which is exceeded in more than 70 countries, affecting over 137 million people.

Argentinia



Arsenobetaine is found in fish and shellfish (nearly non-toxic).

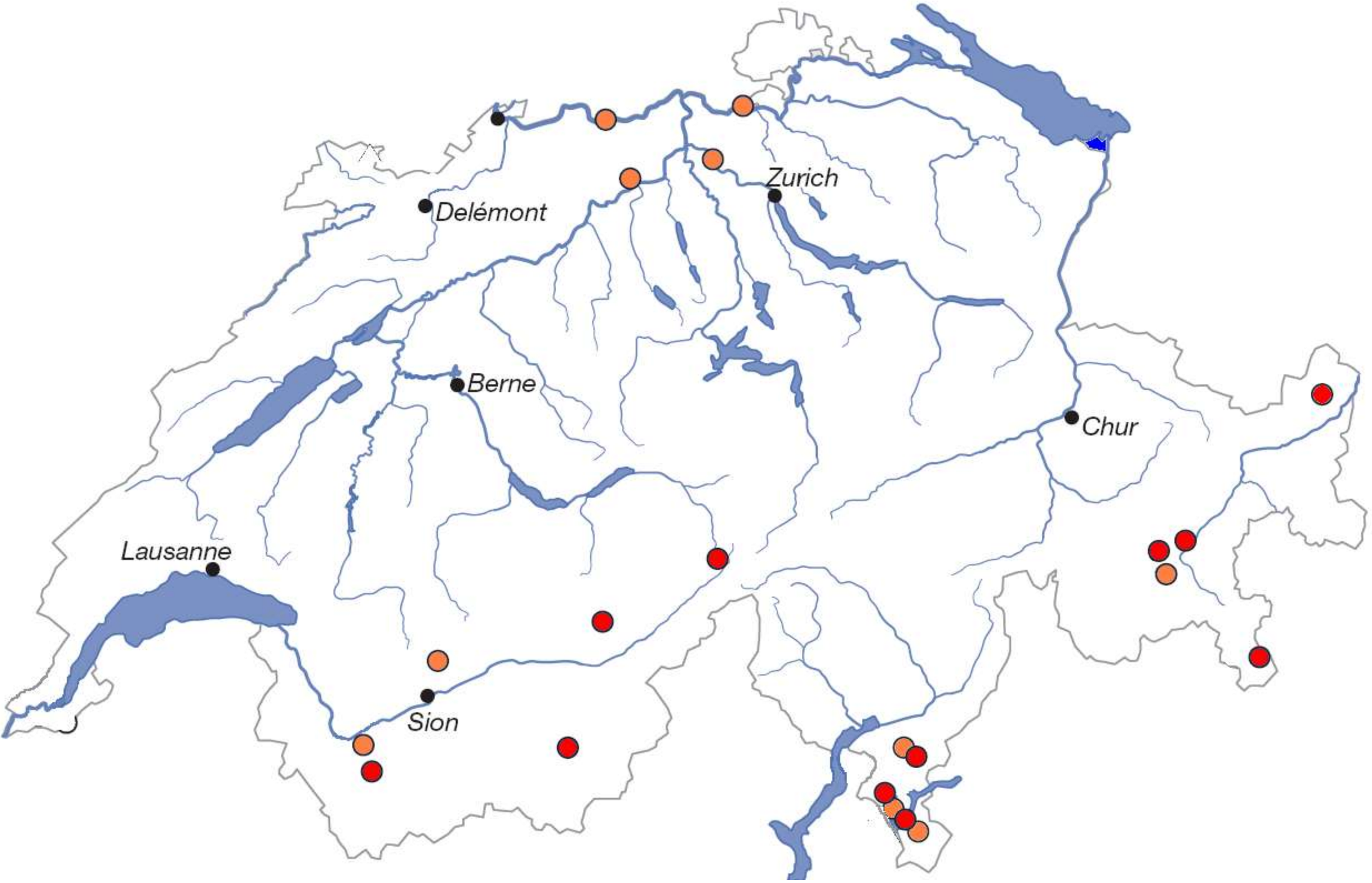
8.2 HEAVY METALS

Arsenic in swiss drinking waters

Water of mineral and hot springs from the Northeast of Switzerland comes from deep layers of granite and gneiss from the range of the Black Forest.

The Alps present arsenic sulphide deposits and crystalline silicate rocks rich in arsenic.

In the Sottoceneri, contaminated waters come from moraines and unconsolidated sediments from reservoirs upstream in the watershed.

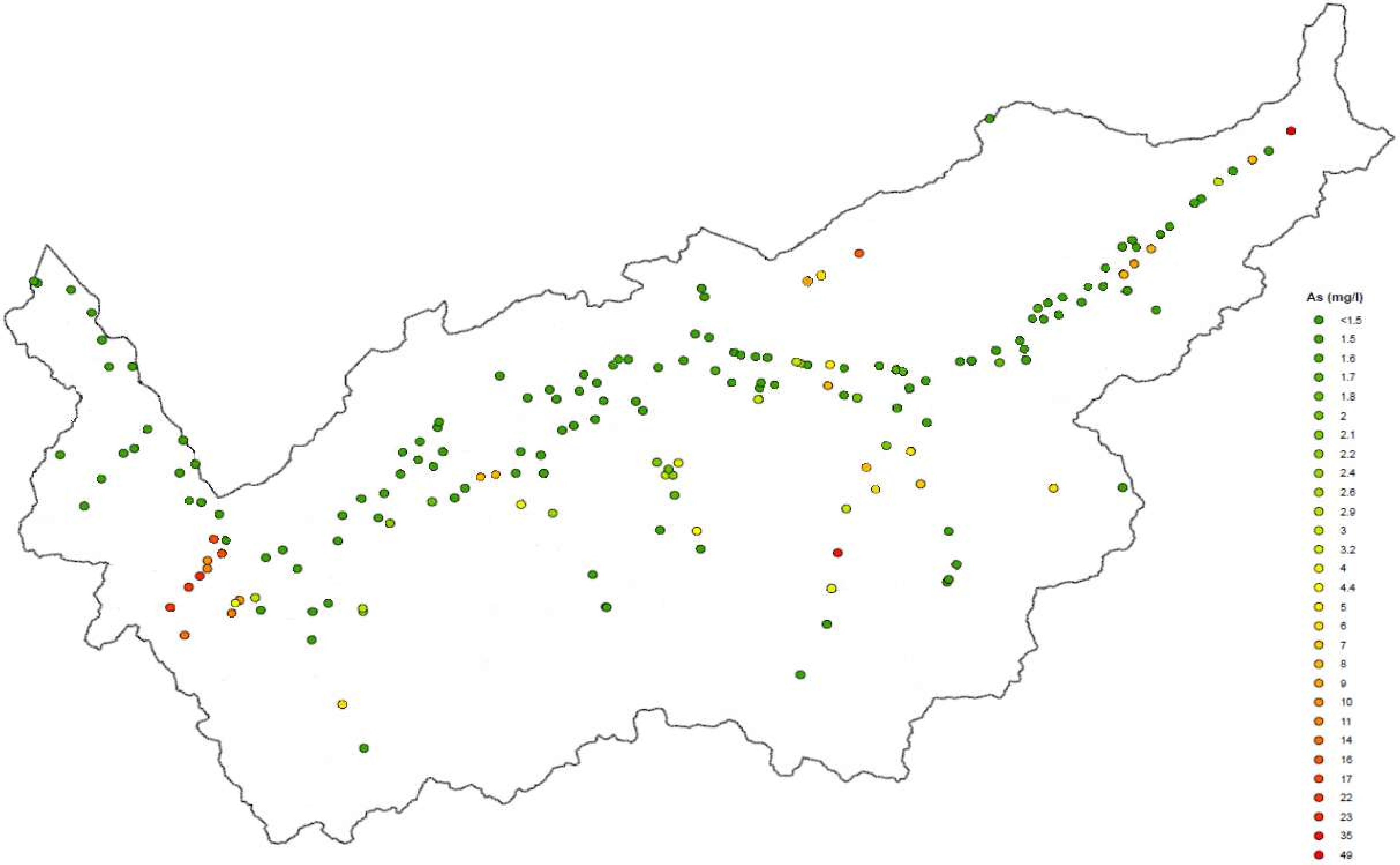


● Mineral and thermal wells : up to 3’000 µg/l

● Contaminated groundwater (10 – 300 µg/l)

8.2 HEAVY METALS

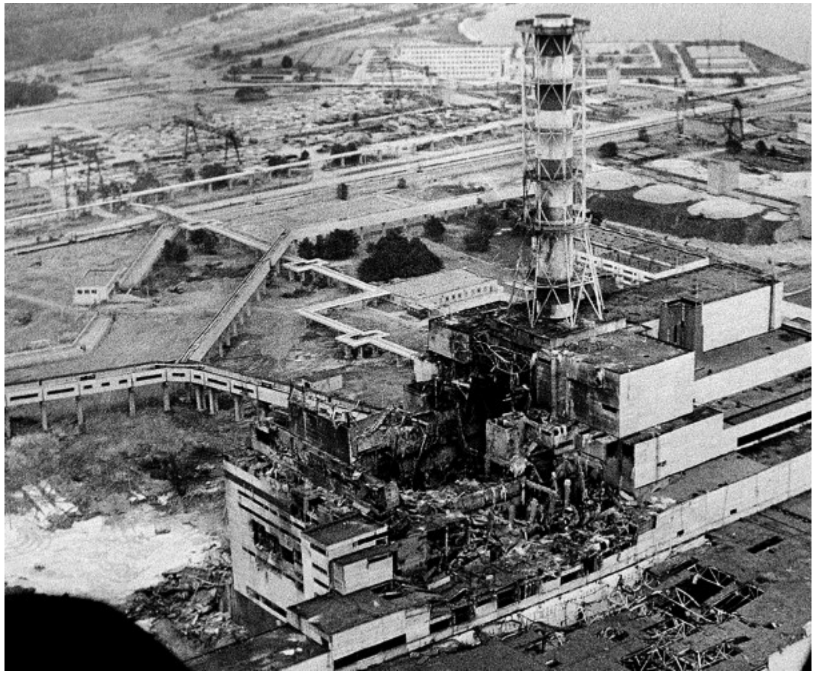
Arsenic in the canton of Valais



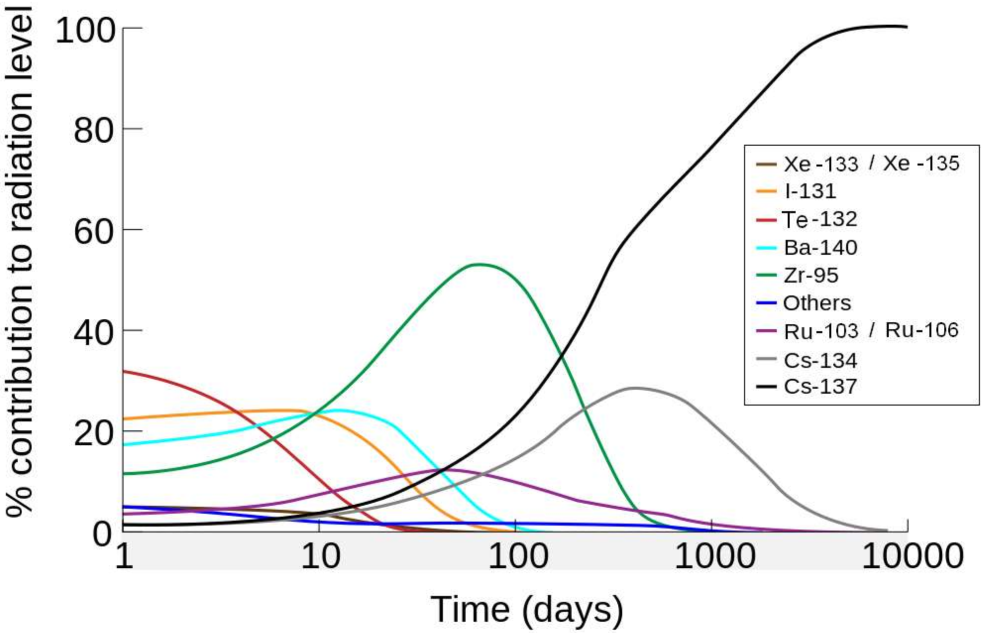
8.3 RADIOACTIVE ELEMENTS

The Chernobyl disaster

The Chernobyl disaster was a catastrophic nuclear accident that occurred on april 26th, 1986 at the Lenin Nuclear Power Plant in Chernobyl, Ukraine



View of the reactor No 4
after explosion



Radioactive isotopes released

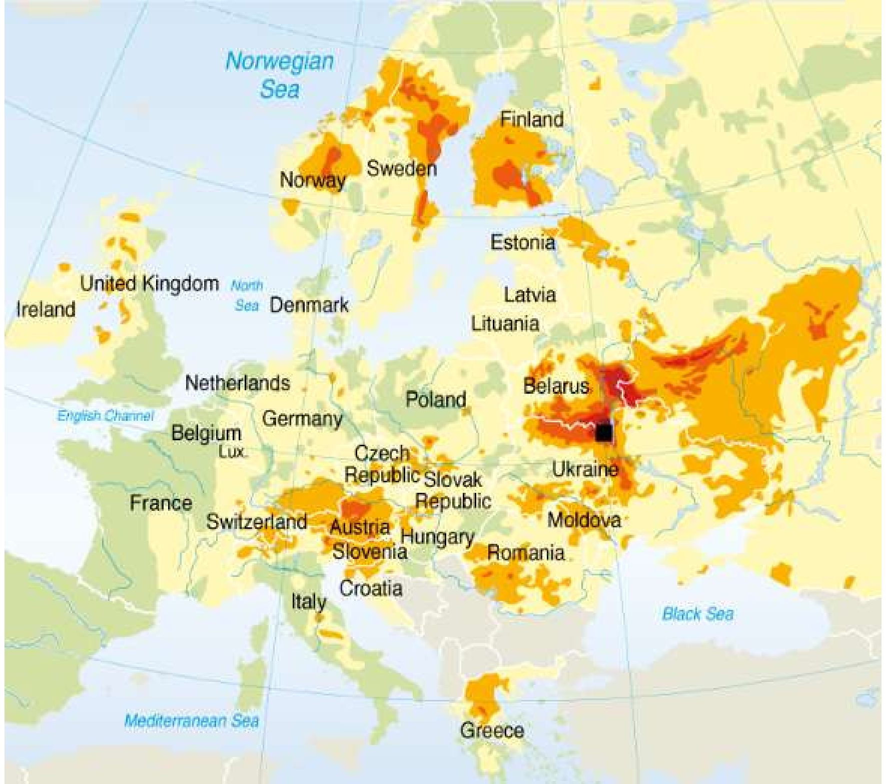
8.3 RADIOACTIVE ELEMENTS

Radioactivity released by the Chernobyl disaster

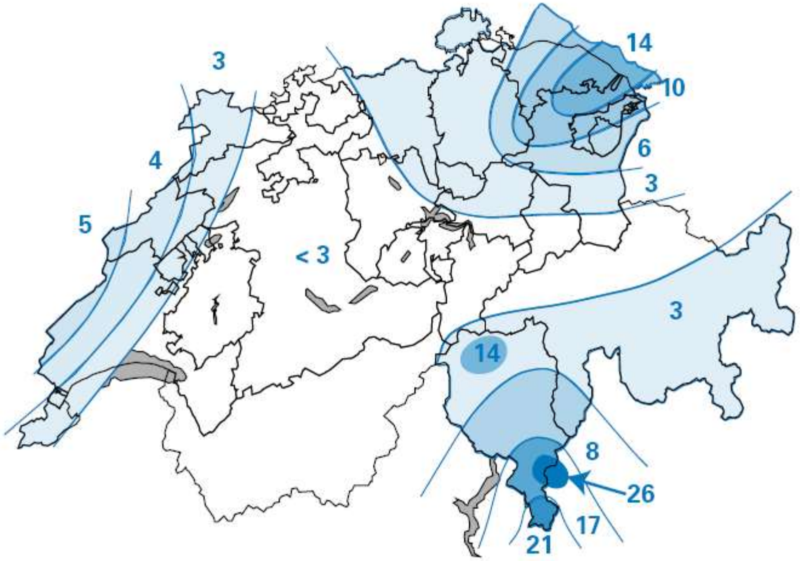
Type of element	Element	Half-life	Estimated activity released (x 10^{15} Bq)
Inert gas	^{133}Xe	5.3 d	6 290
Volatile elements	^{131}I	8 d	630-1740
	^{134}Cs	2,2 y	18-44
	^{137}Cs	30,2 y	37-90
	^{132}Te	78 h	400-1000
Semi-volatile elements	^{103}Ru	39,6 d	170
	^{106}Ru	1 y	59
Non-volatile elements	^{90}Sr	28 y	8,1
	^{140}Ba	12,8 d	180
Refractory elements	^{95}Zr	64 d	155
	^{141}Ce	33 d	144
	^{144}Ce	285 d	137
	^{239}Np	2,4 d	1440
	^{241}Pu	13,2 y	5,9
	^{242} Cm	163 d	~ 0,9

8.3 RADIOACTIVE ELEMENTS

The Chernobyl fallout



Contamination in Europe



^{137}Cs deposition in Switzerland (in kBq/m^2)

8.3 RADIOACTIVE ELEMENTS
Mushrooms contamination after the Chernobyl catastrophe

^{137}Cs uptake increases with :
- low exchangeable potassium concentration
- low clay contents
- low pH values

Large species variability. Some high absorbing mushrooms :

Hydnum repandum

Laccaria laccata

Xerocomus badius

Cantharella lutescens

8.4 INDUSTRIAL CONTAMINANTS

Some selected examples

Polychlorinated dibenzodioxins (Dioxins)

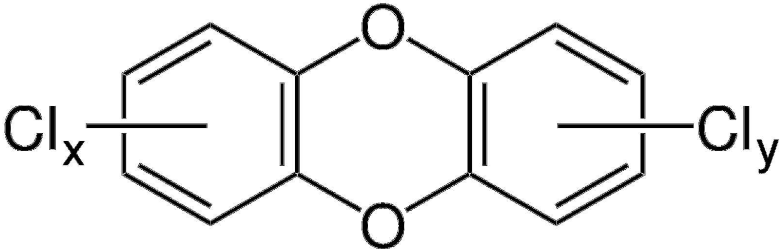
Polychlorobiphenyls (PCB’s)

Persistent organic pollutants (POP’s)

- Polybrominated diphenyl ethers
- Bisphenol A

8.4 INDUSTRIAL CONTAMINANTS

Polychlorinated dibenzodioxins



Low concentrations of dioxins existed in nature prior to industrialization due to natural combustion and geological processes.

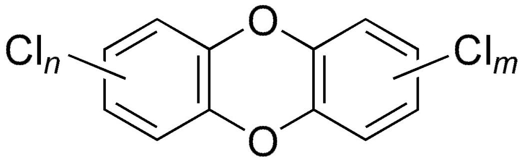
At present time :

- Combustion sources, e.g. municipal waste incinerators
- Metal smelting
- Chemical manufacturing sources (Seveso, Agent Orange)
- Environmental reservoirs

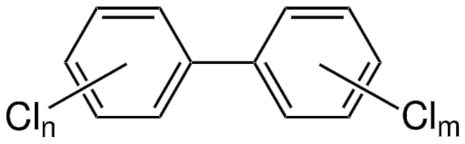
Dioxins bioaccumulate in fatty tissues, so even small exposures may eventually reach dangerous levels. Dioxins are carcinogens, and interfere with reproduction, sexual development, immune system).

8.4 INDUSTRIAL CONTAMINANTS

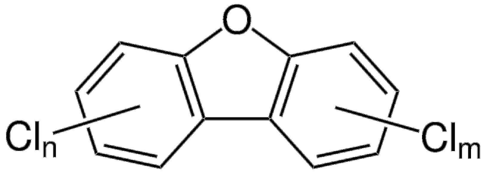
Toxicity of poly-chloro dioxins and related compounds



PC - dibenzodioxins



PC -biphenyls



PC - dibenzofurans

Toxicity equivalent :

$$TEQ = \sum_{i=1}^{n} C_i * TEF_i$$

Examples of toxic equivalent factors (TEF) :

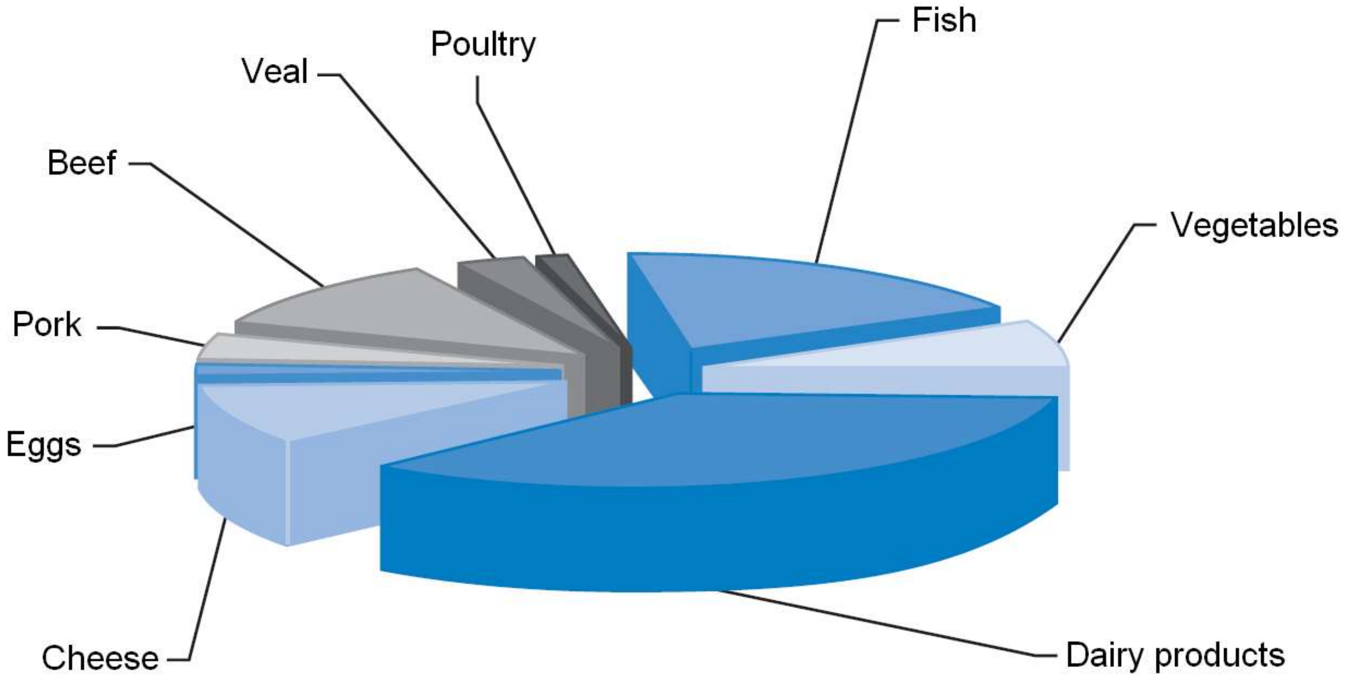
2,3,7,8-TCDD	1
1,2,3,6,7,8-HCDD	0.1
OCDD	0.0003

3,3',4,4',5-PCB	0.1
3,3',4,4',5,5'-PCB	0.03
2,3,3',4,4'-PCB	0.00003

2,3,4,7,8-PCDF	0.3
2,3,7,8-TCDF	0.1
OCDF	0.003

8.4 INDUSTRIAL CONTAMINANTS

Dioxins in foods

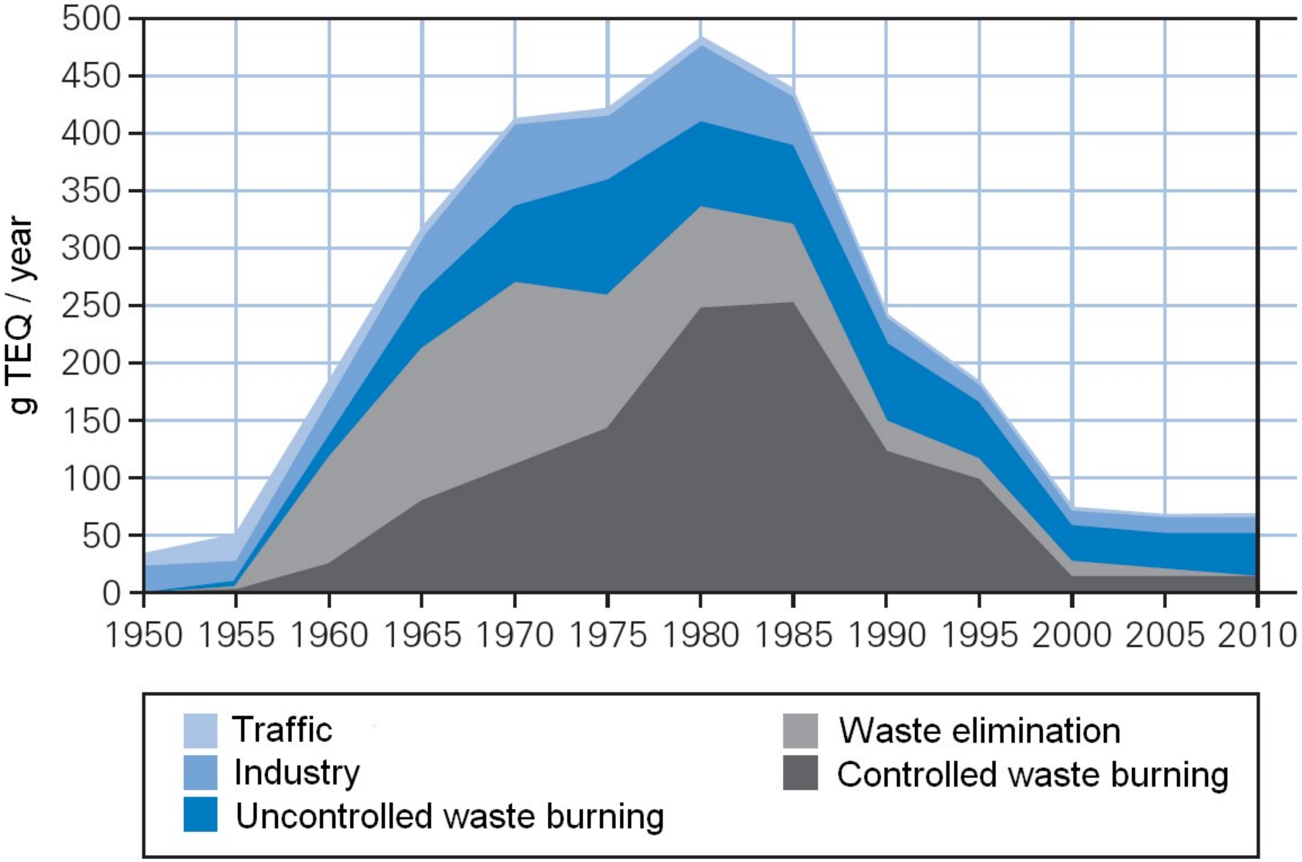


Provisory monthly tolerable intake (WHO) : 70 pg/kg BW

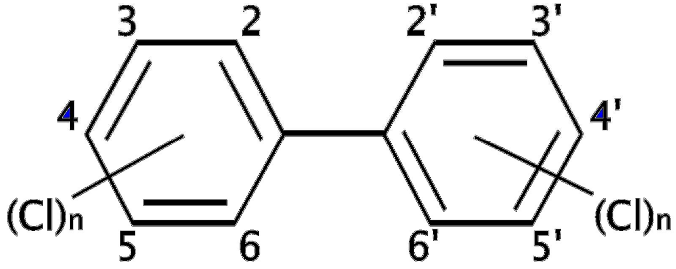
Mean swiss monthly intake : 60 pg/kg BW !

8.4 INDUSTRIAL CONTAMINANTS

Dioxins contamination in Switzerland



8.4 INDUSTRIAL CONTAMINANTS
Nomenclature of polychlorinated biphenyl (PCB's)



Group of 209 CONGENERS with general formula $C_{12}H_{10-x}Cl_x$

Example : most chlorinated PCB is 2,2',3,3',4,4',5,5',6,6' decachloro-biphenyle

UIPAC nomenclature

For each congener, one choses the first name among the possible names, classifying them according to the number of Cl atoms, in the following order: 2, 2 ', 3, 3, 4, 4 ', 5, 5', 6, 6 ‘ (note that 2,3' is equivalent to 3,2').

Each congener is denoted by its number in the list :
2-Chlorobiphenyl is Nr 1
3,4,4',5-Tetrachlorobiphenyl is Nr 81
Decachlorobiphenyl is Nr 209

8.4 INDUSTRIAL CONTAMINANTS

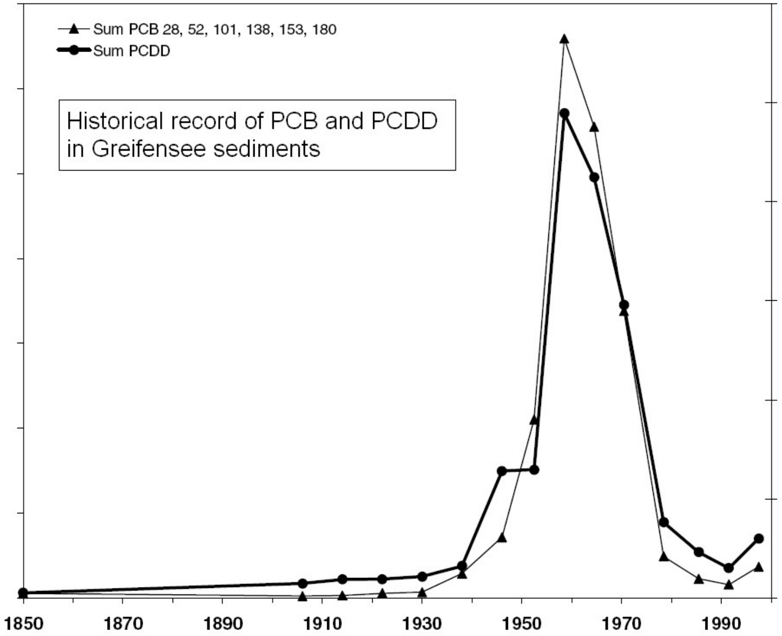
History of PCB's

PCBs were widely used as dielectric and coolant fluids, as additives in numerous industrial products.

Most PCBs are probable carcinogens, endocrine disrupters and / or enzyme inducers might disrupt metabolism.

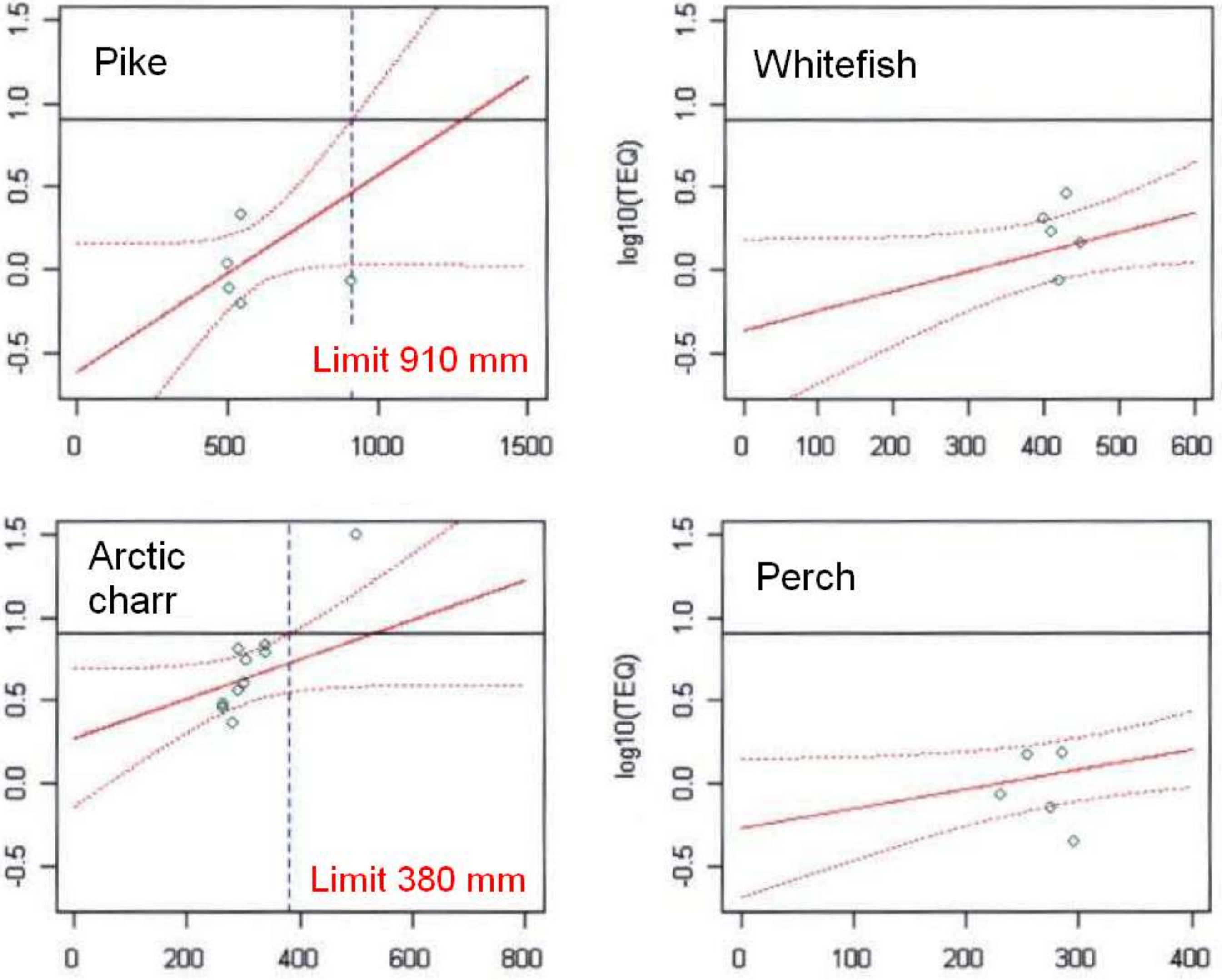
In 1973, the use of PCB's was banned
in "open" or "dissipative" sources.
Definitive ban on PCB's : 1987

1999 Eggs and poultry scandal in Belgium
2007 PCB's in Rhône fishes
2008 Irish pork crisis
2008 Ban on lemanic arctic charrs
2010 PCB's in german eggs



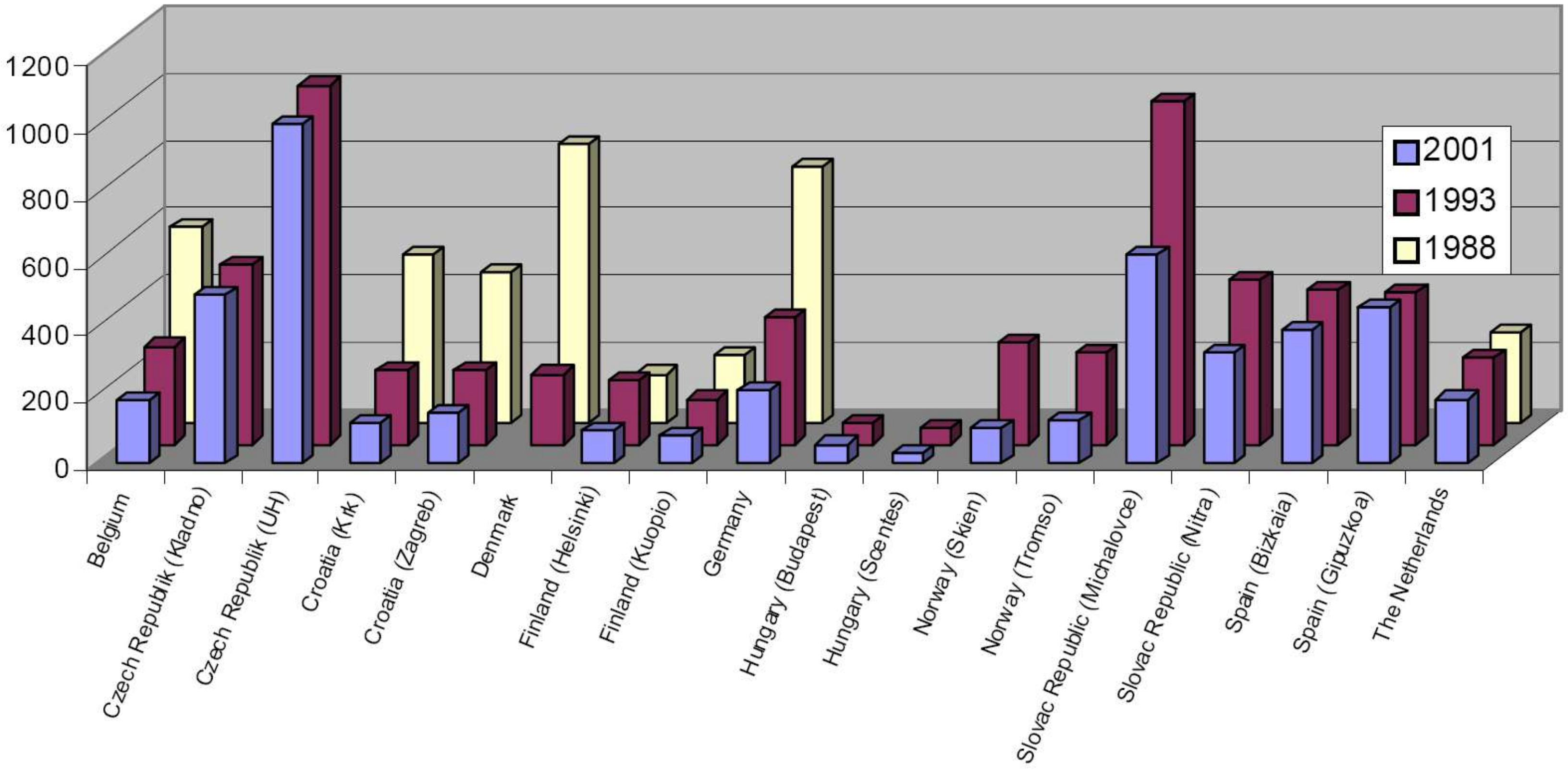
8.4 INDUSTRIAL CONTAMINANTS

Ban on arctic charrs in the Leman lake due to PCB's



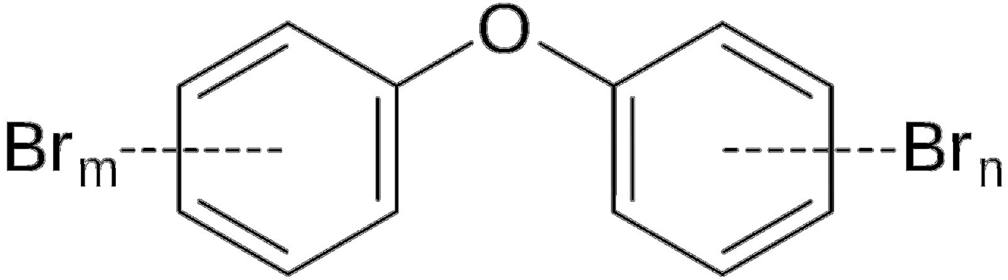
8.4 INDUSTRIAL CONTAMINANTS

PCB in human milk (ng/g fat)



8.4 INDUSTRIAL CONTAMINANTS

Polybrominated diphenyl ethers



Flame retardants

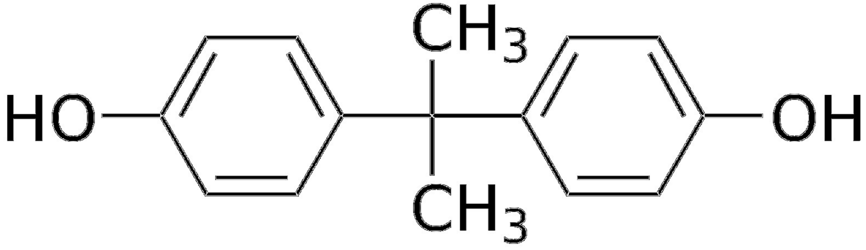
PBDE’s presents liver toxicity, thyroid toxicity, and neurodevelopmental toxicity (NOAEL 5 mg/kg for 8-BDE and 2 mg/kg for 5-BDE).

Very lipophilic : bioaccumulate along the food chain.Found in meat, fatty fishes, milk.

Low vapor pressure : easily transported over long distances. The amount of PBDEs increased in Arctic over the past ten years.

8.4 INDUSTRIAL CONTAMINANTS

Bisphenol A



Used to make polycarbonate plastic and epoxy resins

Found on the lid of canned foods.

Bisphenol A is an endocrine disruptor, which can mimic the body's own hormones and may lead to negative health effects.

Even at levels of 0.025 µg/kg/day in mice and rats, Bisphenol A induces permanent changes to genital tract, and in breast tissue that predispose cells to hormones and carcinogens.

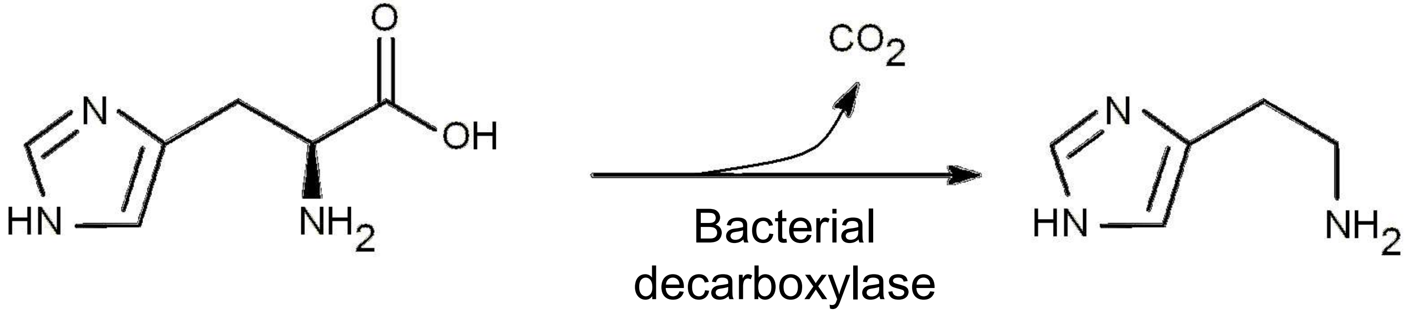
8.5 CROP CONTROL CONTAMINANTS

Major phytosanitary groups

Herbicides	weedkillers, used to kill unwanted plants
Fungicides	used to kill or inhibit fungi or fungal spores
Insecticides	used against insects (including ovicides and larvicides)
Molluscicides	used to control gastropods like slugs and snails
Nematicides	used to kill parasitic nematodes
Acaricides	used to kill acarines, which includes ticks and mites
Rodenticides	used to kill rodents
Growth regulators	- onset of flowering (fruit trees) - prevent germination of potatoes - fight against folding in cereals

8.6 TRANSFORMATION COMPOUNDS
Biogenic amines

« Scombroid fish poisonning »



Histidine

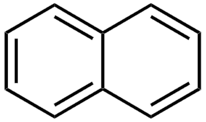
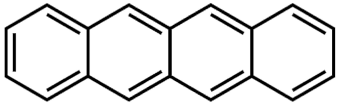
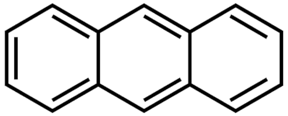
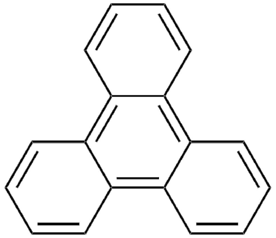
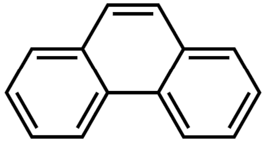
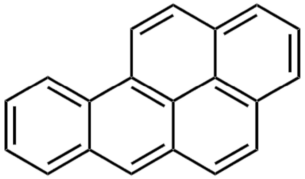
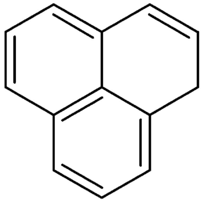
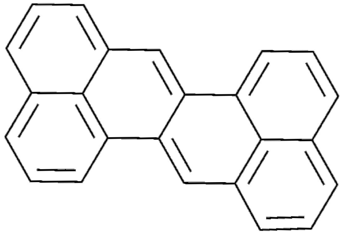
Histamine

Produced by the bacterial proliferation in fishes rich in histidine (tuna, mackerel, sardine, anchovies), due to poor sanitary conditions.

At doses > 200 mg, symptoms consist of skin flushing, severe headache, oral burning, abdominal cramps, diarrhea, palpitations and tachycardia.

8.6 TRANSFORMATION COMPOUNDS

Structures of polyaromatic hydrocarbons (PAH's)

Naphtalene		Tetracene	
Anthracene		Triphenylene	
Phenanthrene		Benzopyrene	
Phenalene		Zethrene	

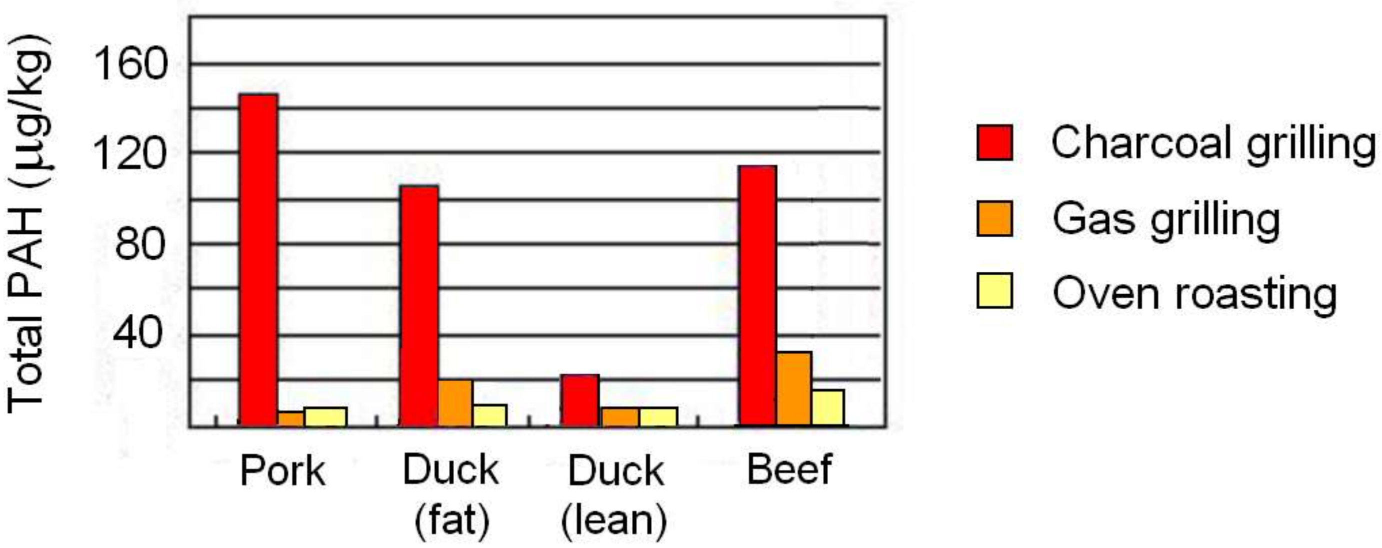
8.6 TRANSFORMATION COMPOUNDS

Occurrence of PAH's

Over 100 PAHs are present in the environment as pollutants. PAHs are formed during processing of crude oil and incomplete burning of organic substances. They are ubiquitous in the environment, being present in air, soil, water and food.

The main source of exposure to PAH's is food, which contributes to more than 90% of total exposure.

Sources : beer, whisky (and not irish whiskey!), smoked meat, barbecued meat.



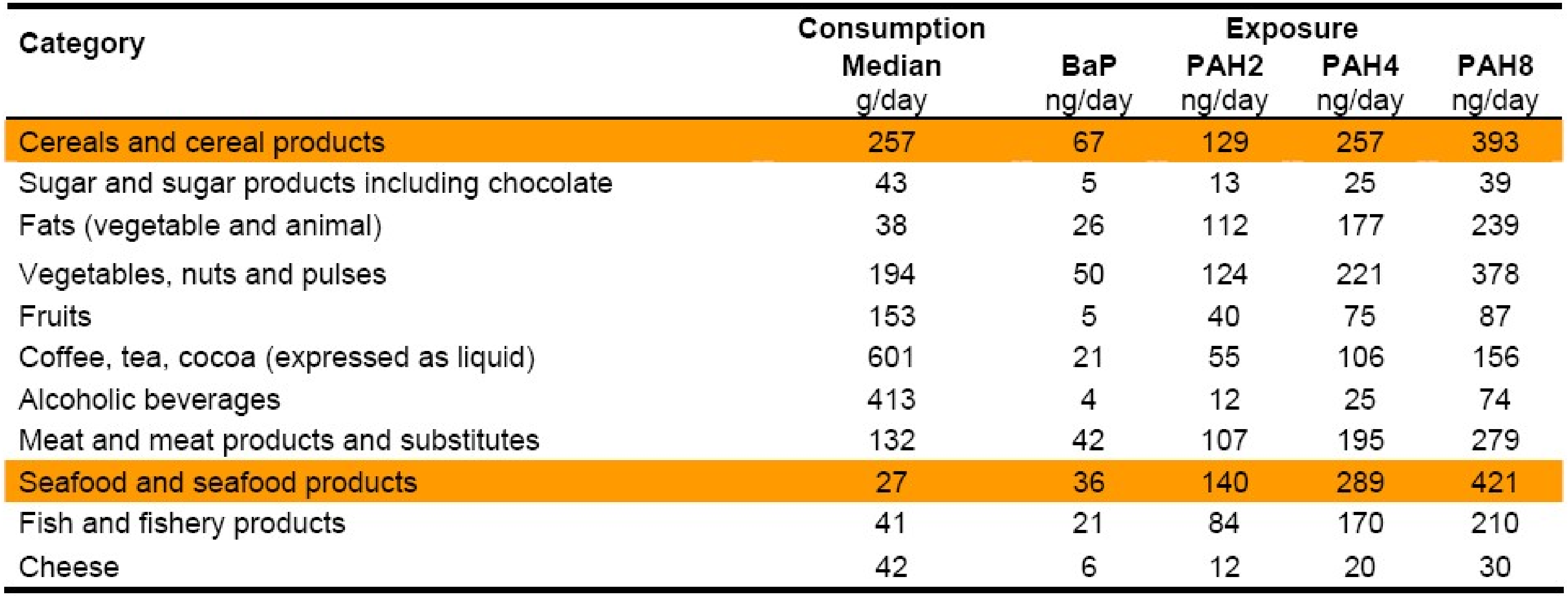
8.6 TRANSFORMATION COMPOUNDS

Toxicity of PAH’s

PAH	***Toxicity***	***Carcinogenicity***	***Mutagenicity***
Naphtalene	Moderate	Suspected	
Acenaphtene	Moderate		Animals
Fluorene	Low		Animals
Phenanthrene	Moderate		Animals
Antracene	Moderate		Animals
Fluoranthene	Moderate	Suspected	Man
Pyrene	Moderate	Suspected	Man
Benzo(a)anthracene	High	High	Man
Chrysene		High	Man
Benzo(b)fluoranthene		High	Animals
Benzo(k)fluoranthene		High	Animals
Benzo(a)pyrene	High	High	Man
Benzo(e)pyrene		Suspected	Man
Dibenzo(a,h)anthracene	High	High	Man

8.6 TRANSFORMATION COMPOUNDS

European exposure to PAH's in food

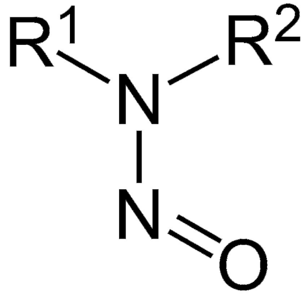


Category	Consumption		Exposure		
	Median g/day	**BaP** ng/day	**PAH2** ng/day	**PAH4** ng/day	**PAH8** ng/day
Cereals and cereal products	257	67	129	257	393
Sugar and sugar products including chocolate	43	5	13	25	39
Fats (vegetable and animal)	38	26	112	177	239
Vegetables, nuts and pulses	194	50	124	221	378
Fruits	153	5	40	75	87
Coffee, tea, cocoa (expressed as liquid)	601	21	55	106	156
Alcoholic beverages	413	4	12	25	74
Meat and meat products and substitutes	132	42	107	195	279
Seafood and seafood products	27	36	140	289	421
Fish and fishery products	41	21	84	170	210
Cheese	42	6	12	20	30

Bap	Benzo(a)pyrene
PAH2	BaP + Chrysene
PAH4	PAH2 + Benzo(a)anthracene + Benzo(b)fluoranthene
PAH8	PAH4 + Benzo(k)fluoranthene + Benzo(ghi)perylene + Dibenzo(a,h)anthracene + Indeno(1,2,3-cd)pyrene

8.6 TRANSFORMATION COMPOUNDS

Nitrosamines



In foods, nitrosamines are produced from nitrites and secondary amines, which often occur in the form of proteins.

Their formation can occur only under acidic conditions and / or high temperatures, as in frying :

$$HNO_2 + H^+ \rightleftharpoons H_2O + NO^+$$

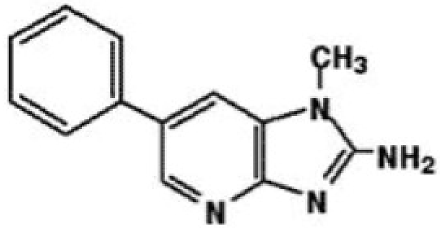
$$NO^+ + R_2NH \rightleftharpoons R_2N\text{-}NO + H^+$$

Main sources : beer, fish, fish byproducts, and meat preserved with nitrite pickling salt.

⚠ Curing of meat is very important to prevent botulism.

8.6 TRANSFORMATION COMPOUNDS

Heterocyclic amines

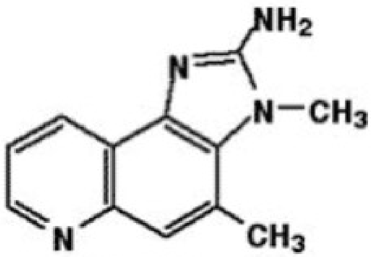


PhIP

2-amino-1-methyl-6-phenylimidazo-[4,5-*b*]pyridine

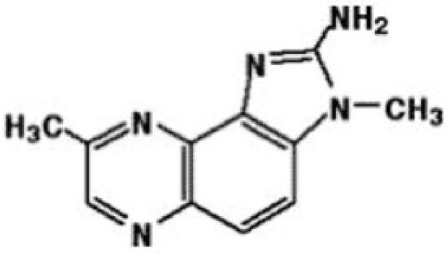
IQ

2-amino-3-methylimidazo-[4,5-*f*]quinoline



MeIQ

2-amino-3,4-dimethylimidazo-[4,5-*f*]quinoline



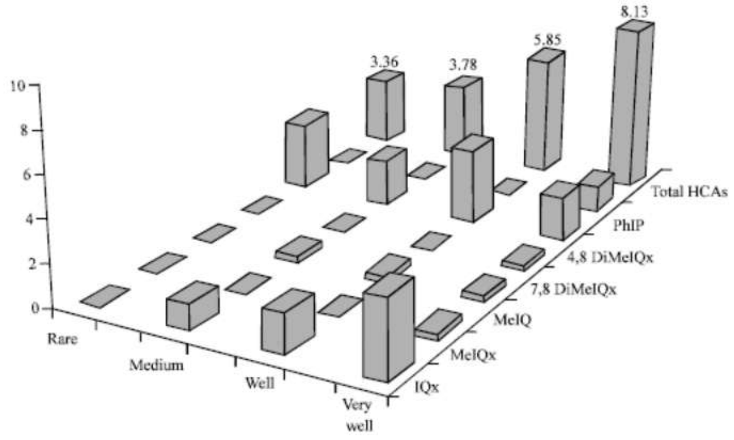
MeIQx

2-amino-3,8-dimethylimidazo-[4,5-*f*]quinoxaline

Produced in cooked meat and cooked fish.

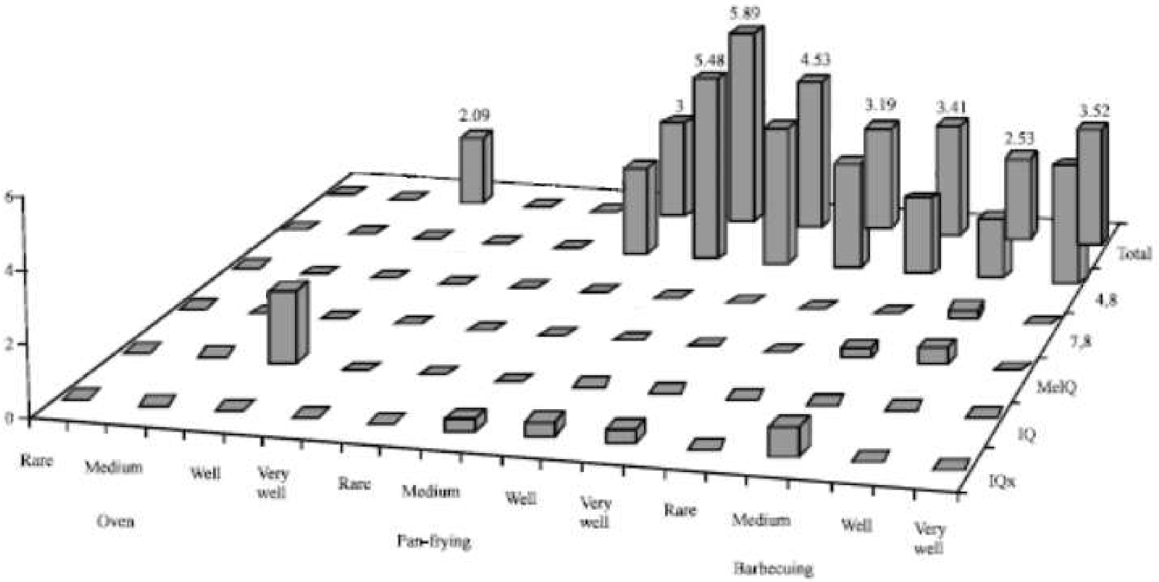
According to IARC, IQ is probable carcinogen (group 2A), whereas PhIP, MeIQ and MeIQx are possible carcinogens (group 2B). Recent results (2005) suggest that these compounds are involved in colon cancer.

8.6 TRANSFORMATION COMPOUNDS
Occurrence of heterocyclic amines



HCA's in cooked chicken chops (ng / g)

HCA's in cooked fish fillets (ng / g)



8.7 NATURAL TOXINS

Classification

Toxin types	***Examples***	
Bacterial toxins	Enterotoxins	Hemolysins
	Shigatoxin	Verotoxin
	Botulinum toxin	Clostridium toxin
	Listeriolysin	Lipopolysaccharide
Mycotoxins	Aflatoxins	Citrinin
	Ergotamin	Fumonisin
	Ochratoxin	Patulin
	Deoxynivalenol	
Fungal toxins	Amatoxin	Phallotoxins
	Ibotenic acid	Muscimol
Indirect toxins	Saxitoxin	Tetrodotoxin
	Palytoxin	Yessotoxin

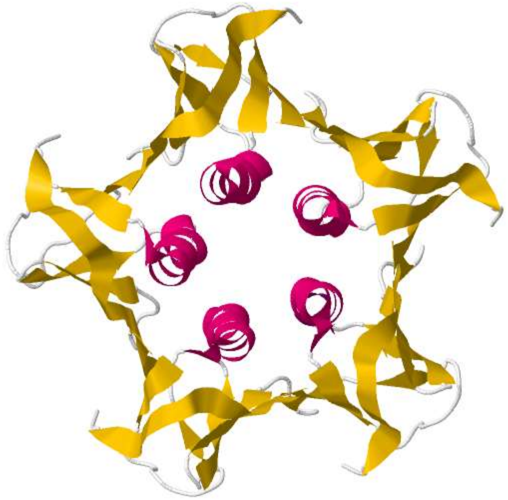
8.7 NATURAL TOXINS

Verotoxin

Toxin produced by enterohemorrhagic *Escherichia coli* strains, mainly O157:H7 and O104:H4 (but also strains O26, O45, O103, O111, O121, and O145).

The "O" in the serological classification identifies the cell wall lipopolysaccharide antigen, and the "H" identifies the flagella antigen.

Cattle and swine do not carry specific receptors and may harbor toxigenic bacteria without ill effects.

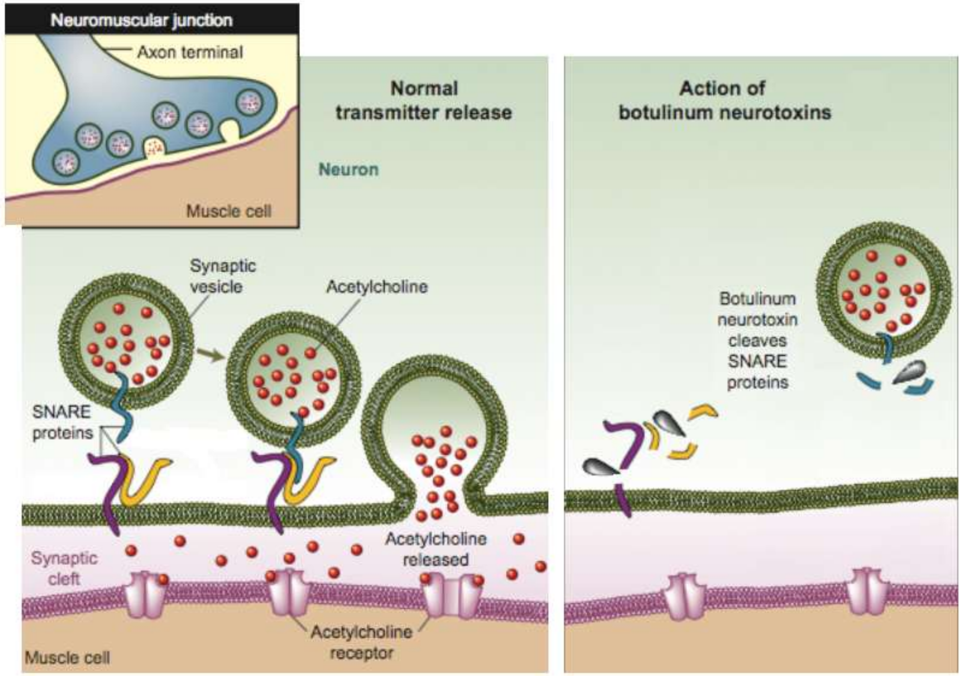


β subunit

Toxin binds on the lining of the blood vessels via its β subunit, and the α subunit interacts with the ribosomes bringing a halt to protein synthesis, leading to the death of the cell. The vascular endothelium has to continually renew itself, so this killing of cells leads to a breakdown of the lining and to hemorrhage. The toxin is effective against small blood vessels, such as found in the digestive tract, the kidney, and lungs, but not against large vessels such as the arteries or major veins. Destroying these structures leads to development of the often deadly *hemolytic uremic syndrome (HUS)*.

8.7 NATURAL TOXINS

Botulinum toxins



Toxins produced by *Clostridium botulinum*, which is thermolabile and resistant to acids and digestive juices.

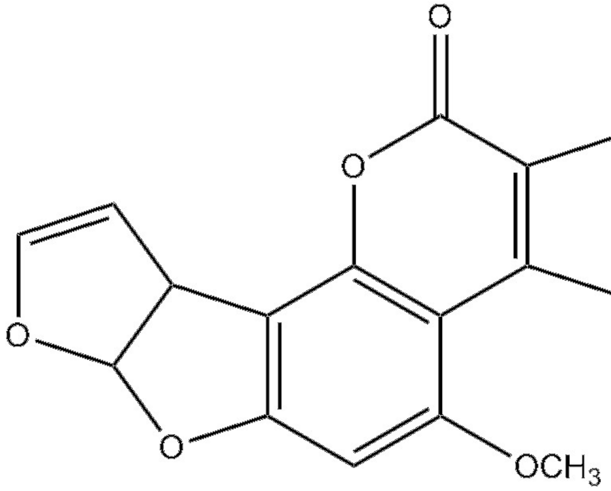
Seven types (A to G). Human botulism is associated to types A, B, E and F. LD_{50} for BoT/A is < 50 ng/kg (most potent neurotoxin known).

C. Botulinum are anaerobic bacteria, which can be found in sausages and meat products, and in cheese.

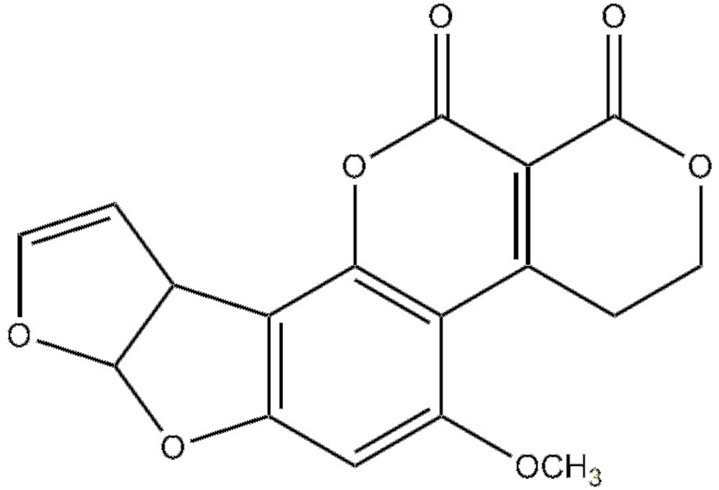
Botulism begins with gastrointestinal troubles, double vision, nystagmus and dry mouth. There is then a progressive weakness of the extremities and respiratory muscles. The patient eventually dies of suffocation.

8.7 NATURAL TOXINS

Aflatoxins



AFB1



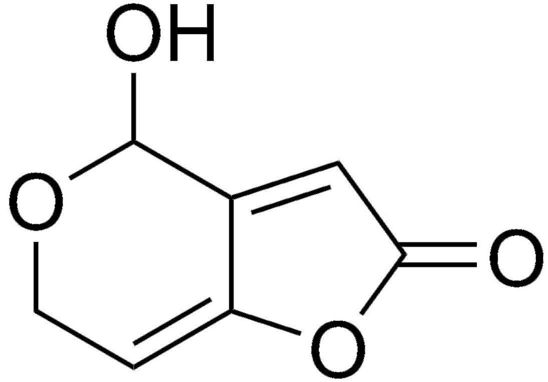
AFG1

Aflatoxins are produced by fungi (*Aspergillus spp*.) that grow on stored seeds in hot and humid atmosphere. They are among the most carcinogenic substances known and were discovered in 1960 in England.

Numerous food products may contain aflatoxins : maize, cereals, nuts, figs, cocoa, coffee, soybeans, etc. In cattle, aflatoxin B1 is metabolized in aflatoxin M1, which is excreted in milk.

8.7 NATURAL TOXINS

Patulin

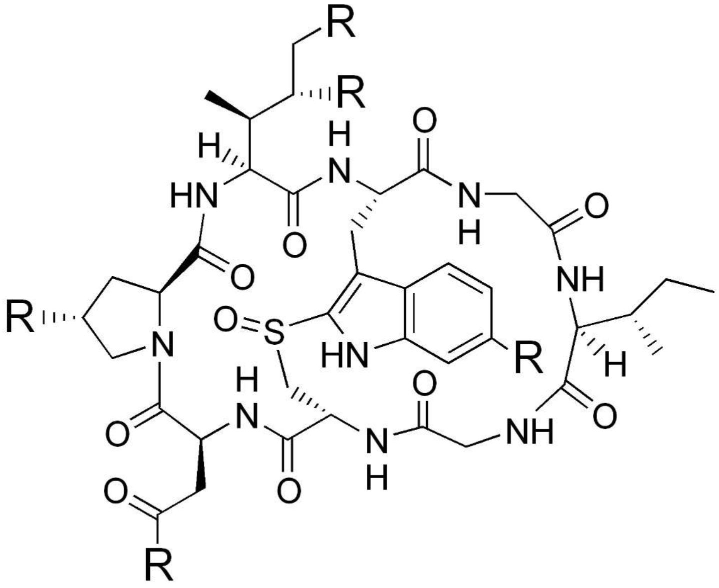


Patulin is produced by several molds (*Aspergillus and Penicillium spp.*) and is commonly found in rotting apples. Numerous studies have shown that it is genotoxic.

In EU, the limit is set to 50 µg/kg in apple juice and cider, to 25 µg/kg in solid apple products and to 10 µg/kg in products for infants and young children.

8.7 NATURAL TOXINS

Amatoxins

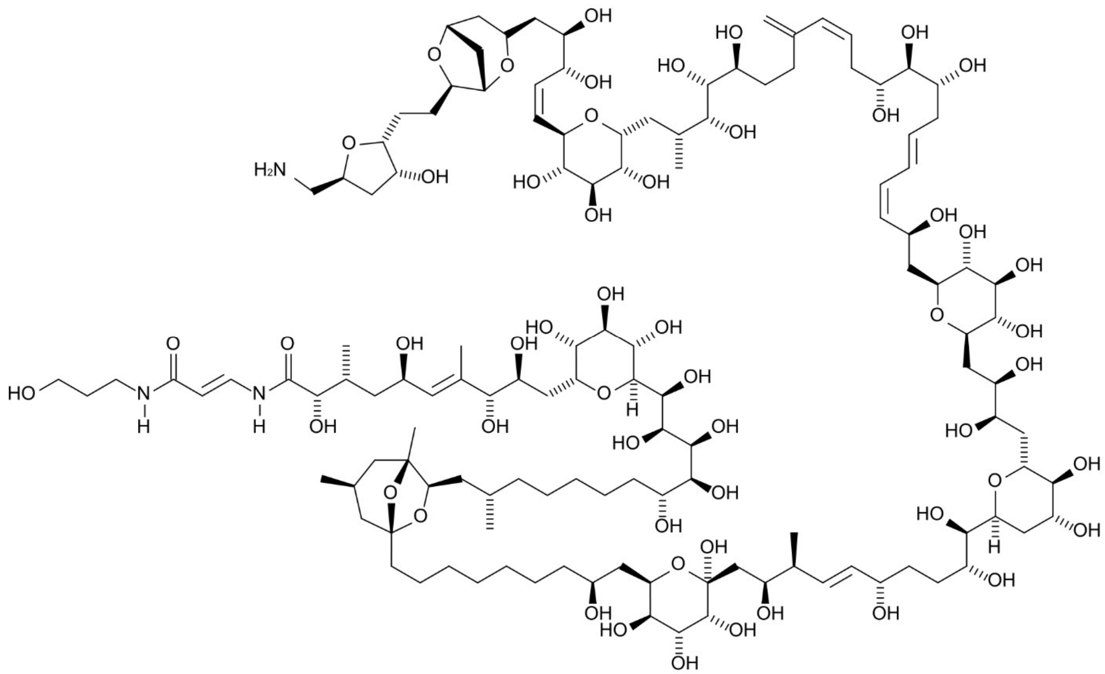


Amatoxins are a group of at least eight toxic compounds found in several genera of poisonous mushrooms, most notably *Amanita phalloides.*

Major toxic mechanism is the inhibition of RNA polymerase, which stops protein synthesis and the cell dies. Estimated minimum lethal dose is 0.1 mg/kg. The most severe effects are hepatitis and nephropathy (hepatorenal syndrome).

8.7 NATURAL TOXINS

Palytoxin



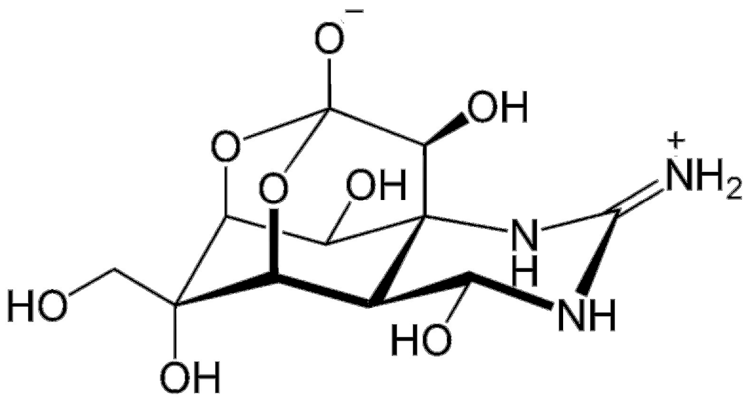
Synthesized in 1994 by Yoshito Kishi & al. This feat is still considered today to be the greatest synthetic accomplishment ever (the "Everest of stereosynthesis").
64 asymmetric carbons,
7 double bond isomers.
2^{71} combinations
(2'361'183'241'434'822'606'848)

Palytoxin is one of the most toxic non-peptide substances known, produced by dinoflagellate *Ostreopis siamensis.* It binds to the sodium pumps of the cells of every vertebrate and create a channel where ions can diffuse freely in and out, thereby destroying the ion gradient of the cell. Death occurs due to heart failure.

Several intoxications have been reported after consumption of contaminated fish and seafood.

8.7 NATURAL TOXINS

Tetrodotoxin (TTX)



TTX is a potent neurotoxin with no known antidote. The bacteria associated with TTX production are *Vibrio* species which live in association with several animal, including Fugu fish.

Tetrodotoxin binds to the sodium channels of cells (mainly the contractile cells of the muscles), thereby inhibiting their contraction. Death occurs due to paralysis of the diaphragm and respiratory failure.

From 1974 through 1983, there were 646 reported cases of pufferfish poisoning in Japan, with 179 fatalities.

8.8 ADVERSE NATURAL COMPOUNDS

Classification

Protease inhibitors

Hemagglutinins

Goitrogens

Cyanogenic glucosides

Lathyrogens

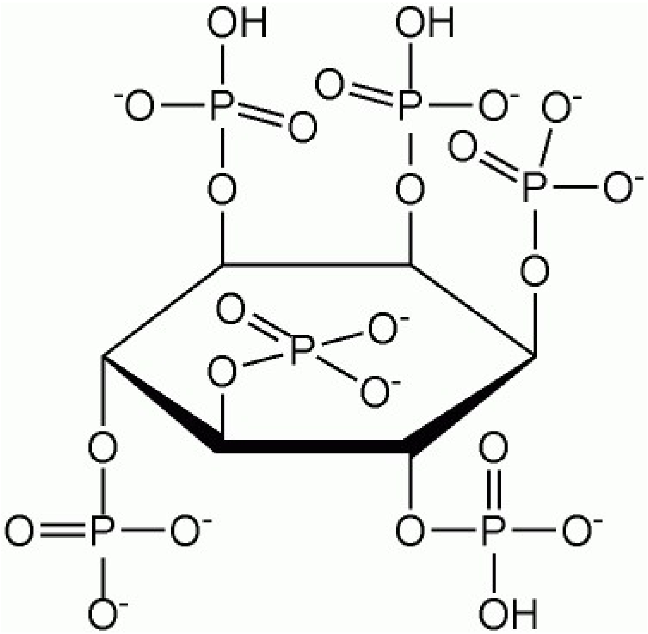
Various

8.8 ADVERSE NATURAL COMPOUNDS

Phytic acid

Phytic acid is found within the hulls of nuts, seeds, and grains.

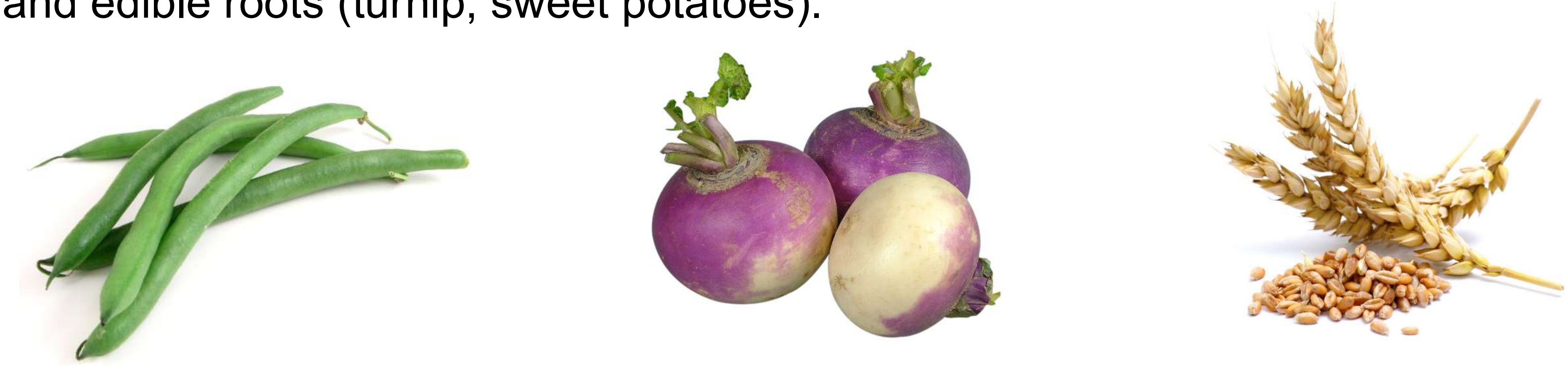
It has a strong binding affinity to calcium, iron, and zinc, forming insoluble precipitate



8.8 ADVERSE NATURAL COMPOUNDS

Protease inhibitors

Protease inhibitors are found mainly in legumes (beans, soybean…), cereals and edible roots (turnip, sweet potatoes).



They are proteins (MW = 7-20 kDa, 80-200 a.a.), with a high contents in cystein, providing numerous disulfur bridges. This feature makes them not very sensitive to heat or acidity.

Nutritional value of raw legumes is diminished as compared to cooked legumes, due to partial denaturation of protease inhibitors.

8.8 ADVERSE NATURAL COMPOUNDS

Hemagglutinins (lectins)

Leucoagglutinin

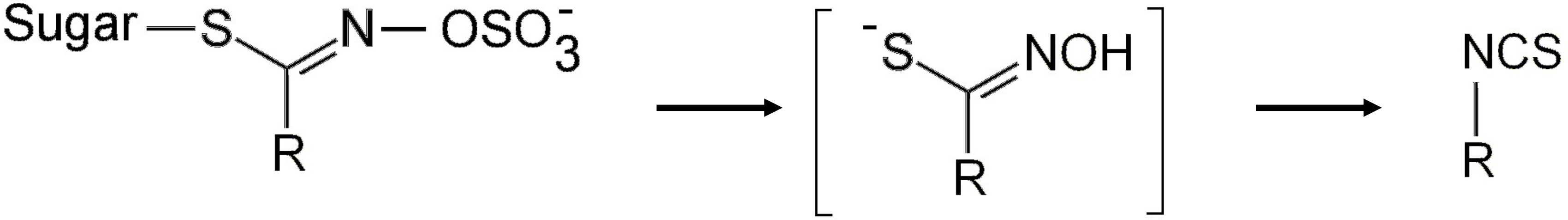
Symbol	***Name***	***Source***
ConA	Concanavallin	Jack beans
LCH	Lentil lectin	Lentils
RCA	Ricin (5-20 beans are fatal!)	Castor beans
AIL	Jacalin	Jack fruit
LeA	Leucoagglutinin	Fava bean
SNA	Elderberry lectin	Elderberries

Foods with high concentrations of lectins, such as beans, cereal grains, seeds, and nuts, may be harmful if consumed in excess in uncooked form. Adverse effects may include nutritional deficiencies, and immune (allergic) reactions. Highly toxic lectins prevent protein synthesis. It also agglutinates red blood cells.

8.8 ADVERSE NATURAL COMPOUNDS

Goitrogens

Goitrogens are substances that suppress the function of the thyroid gland by interfering with iodine uptake, causing an enlargement of the thyroid, i.e., a goitre.



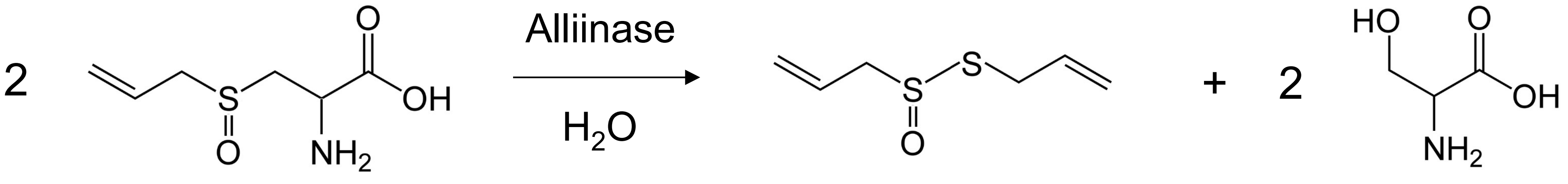
Glucosinolates

Isothiocyanates

Glucosinolates occur as secondary metabolites of almost all *Brassicaceae* (cabbage, radish, mustard, etc), but also in *Euphorbiaceae*.

Allyl isothiocyanate serves the plant as a defense against herbivores; since it is harmful to the plant itself, it is stored in the harmless form of the glucosinolate, separate from the myrosinase enzyme. When an animal chews the plant, the allyl isothiocyanate is released, repelling the animal.

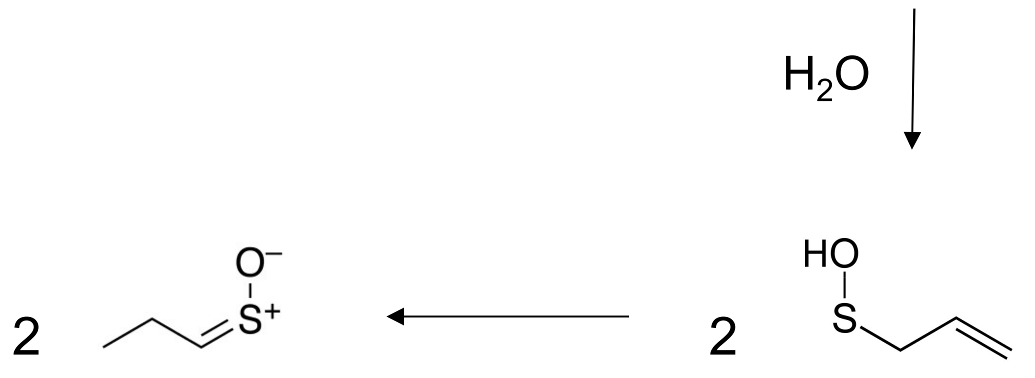
8.8 ADVERSE NATURAL COMPOUNDS
Pungency of garlic and onions



Alliin
(Allyl cystein oxyde)

Allicin
(Thiosulfinate)

Serine

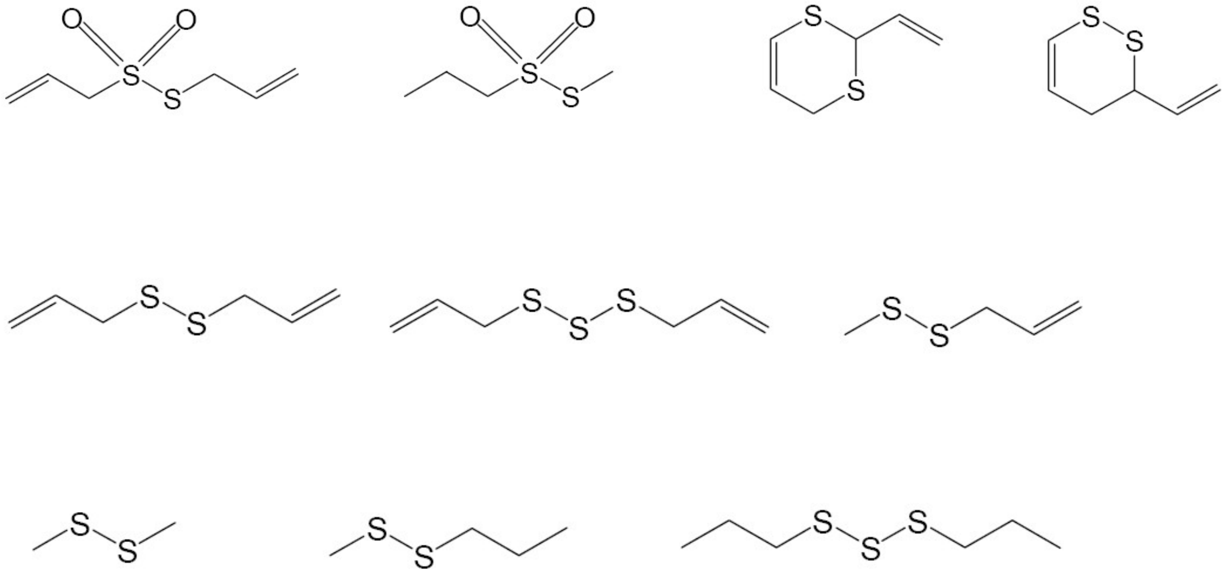


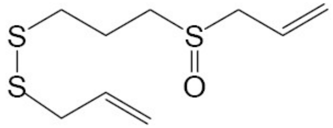
Propanethial-S-oxide
(Lachrymator)

Propenesulfenic acid

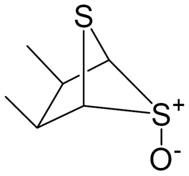
8.8 ADVERSE NATURAL COMPOUNDS

Odours of Allium species





Ajoene

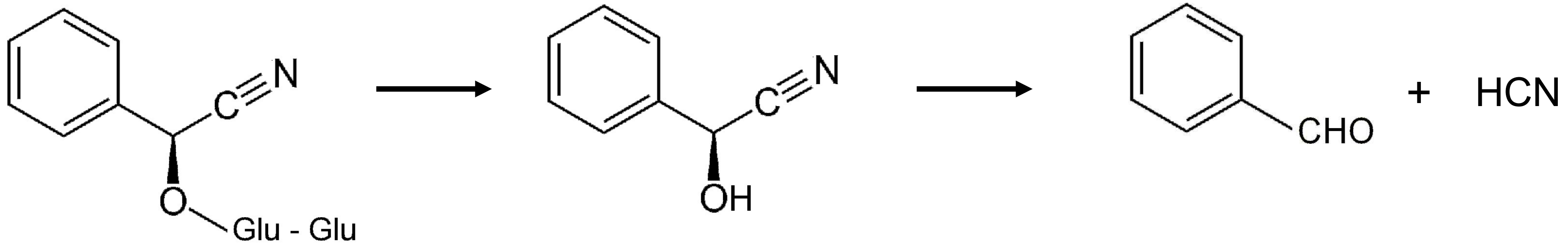


Zwiebelane

8.8 ADVERSE NATURAL COMPOUNDS

Cyanogenic glucosides

Cyanogenenic glucosides are found in *Prunus* seeds (amygdalin), cassava, lima bean (linamarin), sorghum (dhurrin)



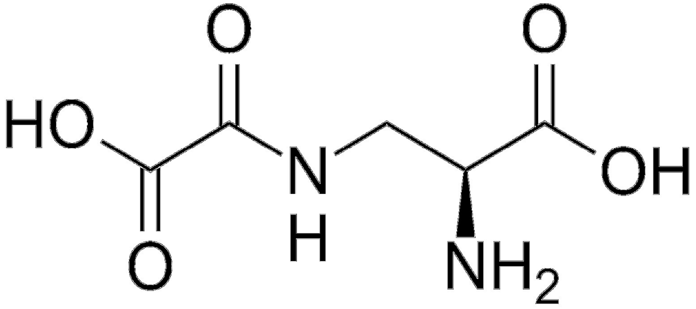
Amygdalin *Benzaldehyde*

The gastric juice alone is unable to release hydrogen cyanide. It is therefore necessary to keep the cells intact (glucosidase is extracellular) and to heat the product to inhibit this enzyme.

«Konzo» is an african paralytic disease associated with almost exclusive consumption of insufficiently processed bitter (cyanide-rich) cassava as a famine food.

8.8 ADVERSE NATURAL COMPOUNDS

Lathyrogens



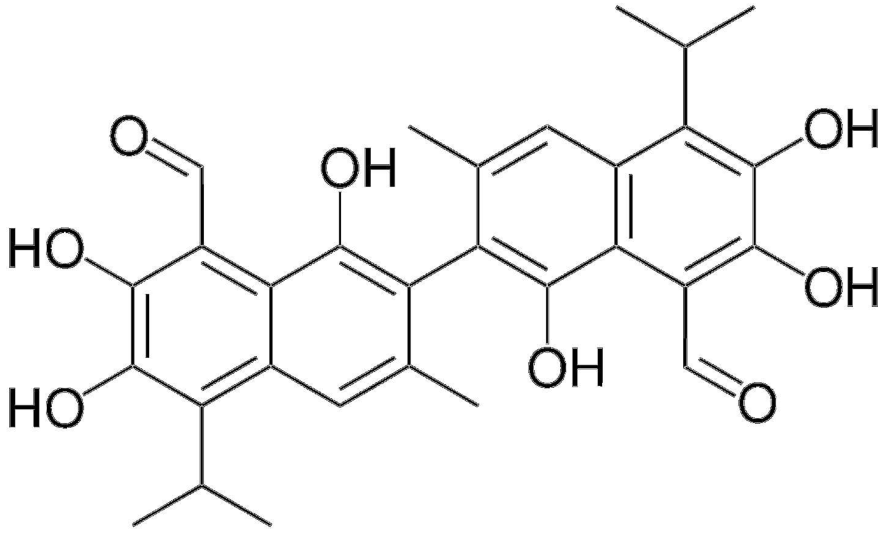
Oxalyldiaminopropionic acid (ODAP)

Lathyrism is a neurological disease caused by eating legumes of the genus *Lathyrus* containing the toxin ODAP. It is characterized by lack of strength in or inability to move the lower limbs. A unique symptom of lathyrism is the emaciation of the buttocks.

This disease is prevalent in some areas of Bangladesh, Ethiopia, India and Nepal. For an unknown reason, it affects more men than women.

8.8 ADVERSE NATURAL COMPOUNDS

Gossypol



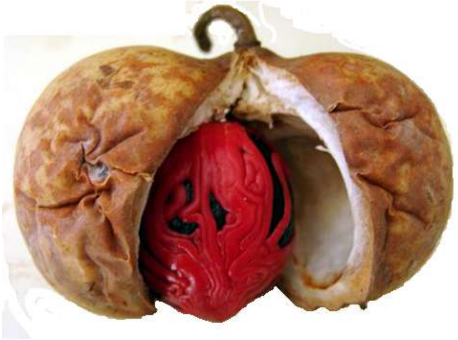
Present in cottonseed. Induces masculine sterility, fatigue, muscle weakness, and at its most extreme, paralysis.

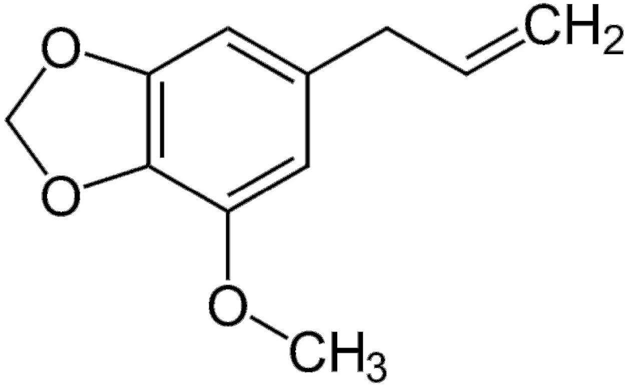
Cotton plants produce two times the amount of cotton seed as they do actual cotton.

Oil must be refined to eliminate gossypol.

8.8 ADVERSE NATURAL COMPOUNDS

Myristicin

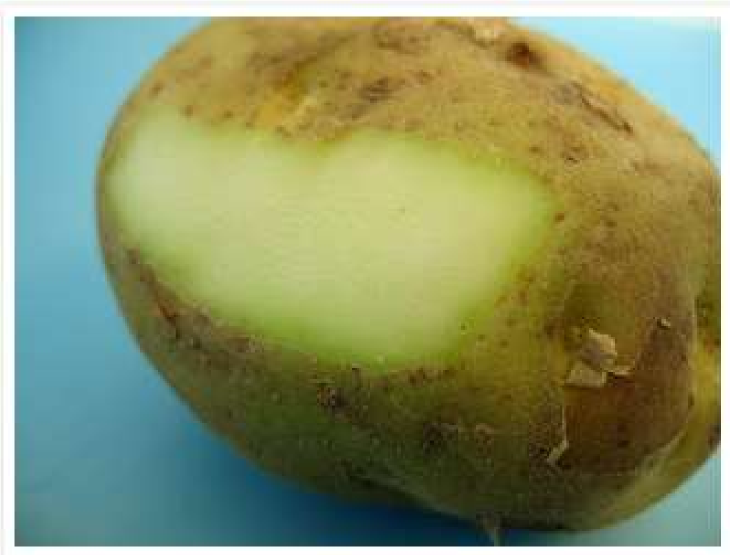


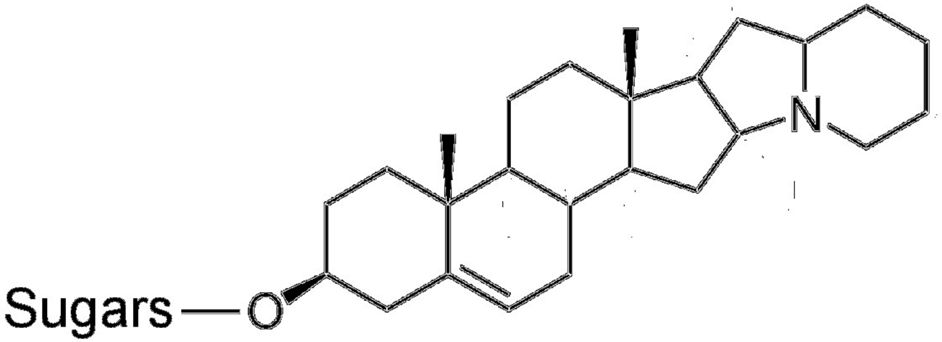


Nutmeg can cause intoxications, characterized by nausea, vomiting, dizziness, anxiety, headache, hallucinations (prison drug).

8.8 ADVERSE NATURAL COMPOUNDS

Solanin





Doses of 200-400 mg of solanin can be fatal for a human. A “green potato” can contain up to 300 mg of solanin !

Solanin is a glycoalkaloid found in *Solanaceae* family, causing gastrointestinal and neurological disorders, as well as cardiac dysrhythmia. When potatoes are exposed to light, they turn green and increase glycoalkaloid production. Most of the solanine develops in and close to the skin.

8.9 ENDOCRINE DISRUPTORS

History of their discovery

R. Carson

~ 1960 : Clover and alfalfa disrupt the reproduction of ruminants

1962 : Silent Spring, from Rachel Carson
Health of wildlife is affected by pesticides

~ 1980 : Micro-pollutants are responsible for adverse effects in birds and fish

1991 : Winspread Conference, organized by Theo Colborn
First appearance of the term "endocrine disruptor"

2012 : More than 3,000 articles published to date

T. Colborn

8.9 ENDOCRINE DISRUPTORS
Definition

An endocrine disrupter is a substance

- exogenous
- altering the functions of the endocrine system
- inducing adverse effects on health
  - of an intact organism
  - of its descendants
  - in (sub) populations.