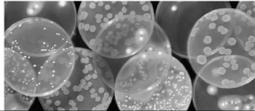
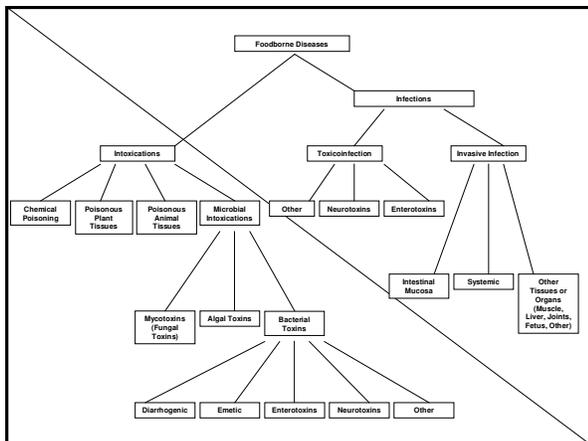


FOOD AND TOXICITY: Natural Toxins

Hazards in food

- Physical: glass, stone, metal, wood, etc
- Chemical:
 - natural toxins
 - residues
 - metals
 - toxins formed during food processing
- Microbiological: pathogenic microorganisms (bacteria, viruses, parasites, etc)





Natural Toxins

- They are naturally present in plants & animals.
- The long term ingestion of natural toxins in commonly eaten foods → the risks to human health?
- Usually, natural toxins are not acutely toxic, except in a few cases in animals.
- Most of the natural toxins, particularly those occurring in plant-derived foods, induce adverse effects only after chronic ingestion or by allergic reactions.

Risks of toxins in food

- General toxicity (instant death or illness)
- Carcinogenic
- Mutagenic
- Teratogenic
- Endocrine disrupters (hormones)
- Microbial pathogens

Natural Toxins in Foods

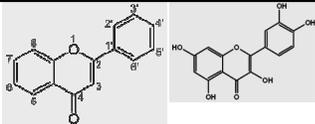
- **Endogenous toxins of plant origin**
 - Toxic phenolic substances: flavonoids, tannins, coumarin, safrole, and myristicin
 - Cyanogenic glycosides
 - Glucosinolates
 - Acetylcholinesterase inhibitors
 - Biogenic amines
 - Central stimulants
- **Natural contaminants**
 - Mixing of edible plants with toxic plants
 - Contamination resulting from intake of toxic substances by animals
 - Microbial toxins

Endogenous toxins of plant origin

Flavonoids

- A class of plant pigments that are widely present in human food, are the flavonoids.
- These pigments are polyhydroxy-2-phenylbenzo- γ -pyrone derivatives, occurring as aglycones, glycosides and methyl ethers. A group of yellow pigments that occurs abundantly is the flavones.
- Examples are nobiletin, tangeretin (in citrus fruits) and 3, 3', 4', 5, 6, 7, 8-heptamethoxyflavone (in grapefruit).





Flavonoids

- The flavones are generally located in the oil vesicles of the fruit peel. Flavones are apolar, and therefore readily soluble in the oil.
- They can be found in the juice after pressing the peel.
- The flavones group has been extensively investigated for mutagenicity.
- A well-known mutagenic representative is quercetin, occurring, for example, in cereal crops. Quercetin is the only flavonoid shown to be carcinogenic in mammals after oral administration.



Tannins

- Tannins are a heterogeneous group of broadly distributed substances of plant origin.
- Two types of tannins can be distinguished on the basis of degradation behavior and botanical distribution, namely hydrolyzable tannins and condensed tannins.
- The *hydrolyzable* tannins are gallic, digallic, and ellagic acid esters of glucose or quinic acid.
- An example of this group is tannic acid, also known as gallotannic acid, gallotannin, or simply tannin. Tannic acid has been reported to cause acute liver injury, i.e., liver necrosis and fatty liver.



Tannins

- The *condensed* tannins are flavonoids. They are polymers of leucoanthocyanidins.
- Tannins occur in many tropical fruits, including mango, dates, and persimmons.
- The contribution of the tannins in tea, coffee, and cocoa to the total tannin intake by humans is of particular importance. Tea has the highest tannin content.
- Other important sources of tannins are grapes, grape juice, and wines.
- A person may easily ingest 1 g or more tannins per day.



Safrole, coumarin, myristicin

- *Coumarin* widely occurs in a number of natural flavorings, including cassis, lavender, and lovage. These flavorings are extensively used in sweets and liquors. Traces of coumarin occur in citrus oils and some edible fruits.
- *Safrole* has been shown to cause liver tumors in rats. It is found in the oil of saffras and in black peppers.
- Both coumarin and safrole are still allowed for food use in the European Community. They are prohibited in the US though, as they have been found to cause liver damage in rats.

Safrole, coumarin, myristicin

- *Myristicin* is found in spices and herbs such as nutmeg, mace, black pepper, carrot, parsley, celery, and dill.
- It has been suggested that myristicin contributes to the toxicity of nutmeg. After nutmeg abuse, tachycardia, failing salivation, and excitation of the central nervous system have been reported. Nutmeg has been abused as a narcotic.



Cyanogenic glycosides

- Cyanogenic glycosides are glycosides from which cyanide is formed by the activity of hydrolytic enzymes. They are widely spread in higher plants.
- Can be found in food plants like cassava, lima beans and the seed of some fruits (e.g. peaches) → cyanide content.
- Fresh cassava cortex produces cyanide in quantities ranging from 1.0 to more than 60.0 mg per 100 g, depending on several conditions, including variety, source, time of harvest and field conditions.
- Damaged roots can contain even more cyanide, i.e., 245 g per 100 g.

Cyanogenic glycosides

Table 2.1 Cyanogenic glycosides in edible plants

Glycosides	Aglycone	Sugar	Food found
Amygdalin	D-mandelonitrile	Gentiobiose	Almonds, apple, apricot, cherry, peach, pear, plum, quince
Dhurrin	L-p-hydroxymandelonitrile	D-glucose	Sorghums, kaffir corns
Linamarin	α-hydroxyisobutyronitrile	D-glucose	Lima beans, flax seed, cassava or manioc
Lotoaustralin	α-hydroxy-α-methylbutyronitrile	D-glucose	Same as linamarin: cassava
Prunasin	D-mandelonitrile	D-glucose	Same as amygdalin
Sambunigrin	L-mandelonitrile	D-glucose	Legumes, elderberry
Vicianin	D-mandelonitrile	Vicianose	Common vetch, and other vicias

Jansenn, Put & Nout (1997)

Cyanogenic glycosides

Table 2.2 Hydrogen cyanide contents of some foodstuffs

Food	HCN (mg/100 g)
Lima beans	210–310
Almonds	250
Sorghum sp.	250
Cassava	110
Peas	2.3
Beans	2.0
Chick peas	0.8

Jansenn, Put & Nout (1997)

Cyanogenic glycosides

- It can be fatal if those foods are eaten raw or prepared improperly.
- Consumption of cassava may lead to goiter, as the cyanide formed can be metabolized to thiocyanate by the enzyme rhodanase.
- Peeling, washing in running water, and cooking or fermenting can inactivate the enzymes & remove and volatilize the cyanide.

Goitrogens (Glucosinolates)



- Glucosinolates are a particular group of substances, occurring in cruciferous plants, such as cabbage and turnips. They can be considered as natural toxins, but also as antinutritives.
- Presents in many commonly consumed plants, such as cabbage, cauliflower, brussel sprouts, broccoli, kale, turnip, radish, oil seed meals.
- Inhibit the uptake of iodine by the thyroid → iodine deficiency.
- Concerning toxicity and antinutritive activity, the hydrolysis products are the active agents, not the glucosinolates themselves.



Goitrogens (Glucosinolates)

- Hydrolysis of glucosinolates results in the formation of isothiocyanates and nitriles.
- The enzyme becomes available for catalysis when cells are damaged on cutting or chewing.
- Several isothiocyanates have been shown to be embryotoxic in rats, while *in vitro* studies have proved a number of them to be cytotoxic and mutagenic.
- Further, several nitriles have been identified as precursors of N-nitroso compounds.

Lathyrogens

- It is found in legumes such as chickpeas and vetch, are derivatives of amino acids that act as metabolic antagonists of glutamic acid, a neurotransmitter in the brain.
- When foods containing these chemicals are eaten in large amounts by humans or other animals, they cause a crippling paralysis of the lower limbs and may result in death.
- Lathyrism is primarily a problem in some areas of India.

Acetylcholinesterase inhibitors

- Acetylcholinesterase inhibitors have been detected in several edible fruits and vegetables.
- Their active components are alkaloids.
- In potato, eggplant and tomato — members of the Solanaceae family — the principal alkaloids have been identified.
- The most potent inhibitors are found in potatoes, and of these the most active component is the glycoalkaloid solanine.
- Oral administration of solanine results primarily in gastrointestinal and neurological symptoms.

Acetylcholinesterase inhibitors



- The solanine concentration of potato tubers varies with the degree of maturity at harvest, rate of nitrogen fertilization, storage conditions, variety, and greening by exposure to light.
- Commercial potatoes contain 2 to 15 mg of solanine per 100 g fresh weight.
- Greening of potatoes may increase the solanine content to 80 to 100 mg per 100 g.
- Most of the alkaloid is concentrated in the skin.
- Sprouts may contain lethal amounts of solanine.
- Peeling will remove most of solanine

Acetylcholinesterase inhibitors

- Since potatoes also contain other glycoalkaloids, namely chaconine and tomatine, with biological properties similar to solanine, the symptoms seen in potato poisoning may be due to combined actions of the alkaloids.
- Solanine is heat stable and insoluble in water. Hence, toxic potatoes cannot be rendered harmless by cooking.
- It is generally accepted that 20 mg solanine per 100 g fresh weight is the upper safety limit.

Biogenic amines

- Low molecular weight organic bases, which pose biological activity.
- Naturally present in animals, plants and microorganisms.
- Sources: fermented foods, vegetables, meats
- Mainly caused by the enzymatic decarboxylation of amino acids by microorganism origin.
- High concentration in fish and cheese.

Biogenic amines

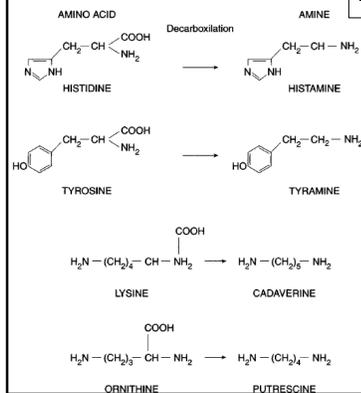
Table 2.3 Biogenic amine content of some fruits and vegetables (mg per 100 g fresh weight)

Amines	Avocado	Banana pulp	Eggplant	Orange	Red plum	Tomato (ripe)	Potato
	Dopamine	0.4-0.5	66-70		0.1		
Epinephrine		<.25					
Norepinephrine		10.8					0.01-0.02
Serotonin	1.0	2.5-8.0	0.2		1.0	1.2	
Tyramine	2.3	6.5-9.4	0.3	1.0	0.6	0.4	0.1

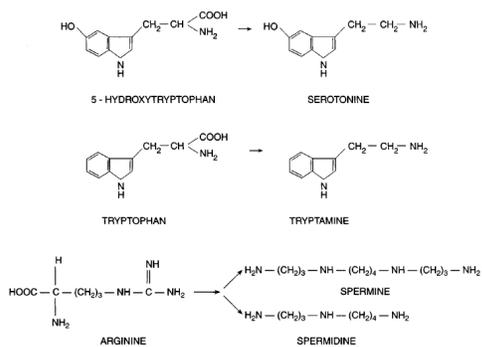
Amines	Pineapple			Plantain					
	Date	Fig	Pawpaw	Green	Ripe	Juice	Green	Ripe	Cooked
Dopamine	<.08	<.02	0.1-0.2						
Epinephrine	<.08	<.02					0.2	0.25	
Norepinephrine	<.08	<.02							
Serotonin	0.9	1.3	0.1-0.2	5.0-6.0	2.0	2.5-3.5	2.0-6.0	4.0-10	4.7

Jansenn, Put & Nout (1997)

Biogenic amines



Biogenic amines



Biogenic amines

Factors influencing the formation of biogenic amines:

- Microorganisms:
Amine-producing bacteria - (enterococci, lactobacilli, enterobacteriaceae, pediococci)
- pH
- Temperature
- Salt concentration (cheese)
- The availability of free amino acids
- The level of starter culture (cheese)

Biogenic amines

- Legal upper limit (Silla-Santos, 1996):
 - histamine: 100 mg/kg food
 - tyramine: 100-800 mg/kg food
 - phenylethylamine: 30 mg/kg food
- 1000 mg/kg amine (based on histamine intoxication & amine concentration in food) is dangerous for human health.
- The toxicity dose of BA depends on the individual sensitivity and characteristic.

Biogenic amines

- (+) - cell proliferation
 - regulation of nucleic acid function
 - protein synthesis
- (-) - histamine intoxication
 - nausea
 - respiratory distress
 - hot flushes
 - heart palpitation
 - headache
 - hypertension & hypotension



Mushroom Toxins

- Caused by the high content of amatoxins in mushrooms.
- Mushrooms identified as containing amatoxin toxins are the species *Amanita bisporigera*, *A. temifolia*, *A. ocreata*, *A. suballiacea*, *Galerina autumnalis*, and *Lepiota brunneolilacea*.



Mushroom Toxins

- There are four categories of mushroom toxins:
 1. Neurotoxins
Cause neurological symptoms such as profuse sweating, hallucinations, depression, spastic colon, excitement, convulsions, and coma.
 2. Protoplasmic poisons
Cause generalized destruction of cells, which is followed by organ failure.

Mushroom Toxins

3. Gastrointestinal irritants
Produce rapid, transient nausea, abdominal cramping, vomiting, and diarrhea.
4. Disulfiram-like toxins
Disulfiram-like toxins are usually nontoxic and produce no symptoms. However, if alcohol is consumed within 72 hours after eating them, they may produce vomiting, nausea, headache, flushing, and cardiovascular disturbances.

Mushroom Toxins

- The first symptoms of mushroom poisoning occur within 6–24 hours after ingestion of the mushrooms (phase one).
- Phase two, also called the gastrointestinal phase, involves severe vomiting and abdominal cramps, nausea, and watery diarrhea.
- Phase three lasts about 12–24 hours and is characterized by improved clinical symptoms; however, it is also the beginning of liver necrosis.

Mushroom Toxins

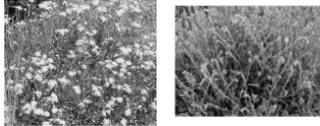
- Phase four (the last phase), results in hepatic failure, encephalopathy, internal bleeding, and, often, acute renal failure. Internal bleeding is usually observed and may cause complications and death.
- Patients usually die within 5–20 days after ingestion of the mushrooms.

Natural Contaminants

- Natural contaminants can also originate from biological systems different from those in which they occur.
- There are three important sources:
 - Raw materials of plant origin can become contaminated if they are mixed with toxic non-nutritive plant species.
 - Raw materials of animal origin, mainly fish and milk, can also become contaminated if the animal has ingested toxic substances of natural origin.
 - Contaminants of natural origin can be the products of microorganisms.

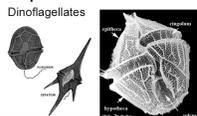
Mixing of edible plants with toxic plants

- Several intoxications have been reported following the consumption of contaminated cereals.
- The causative agents are pyrrolizidine alkaloids, produced by the genera *Senecio*, *Crotalaria* and *Heliotropium*.
- Pyrrolizidine alkaloids can be the cause of acute liver damage and vein lesions. These substances may also contribute to the liver cancer incidence in humans.



Contamination resulting from the intake of toxic substances by animals: **Natural toxins in aquatic organisms**

- Paralytic shellfish poisoning (PSP) is attributed to the consumption of shellfish that have become contaminated with a toxin or group of toxins from the ingestion of toxic plankton, in particular toxic dinoflagellates.
- The shellfish involved are pelecypods, a family of mollusks, including mussels and clams.
- The dinoflagellates produce a complex mixture of toxins. One of the components has been identified as **saxitoxin**.



Contamination resulting from the intake of toxic substances by animals: **Natural toxins in aquatic organisms**

- Shellfish poisoning symptoms include tingling and burning in face, lips, tongue, and ultimately the whole body, and parathesia followed by numbness, general motor incoordination, confusion, and headache.
- These symptoms develop within 30 minutes after ingestion. Death, preceded by respiratory paralysis, occurs within 12 hours.
- The chance of contamination and poisoning is highest during a so-called red tide (dinoflagellate bloom) → although the bloom may also be yellowish, brownish, greenish, and bluish in color. The red color is probably due to the xanthophyll peridinin.

- Red Tide



Contamination resulting from the intake of toxic substances by animals: **Natural toxins in aquatic organisms**

- The high toxicity of the paralytic shellfish poisons, intoxication rarely occurs.
- This is largely due to strict regulations set by many countries and the awareness in coastal areas of the risks associated with eating shellfish during red tides.
- Although ordinary cooking destroys up to 70% of the toxin(s) and pan-frying destroys even more, there may be sufficient toxin left in the mollusks to cause serious poisoning.

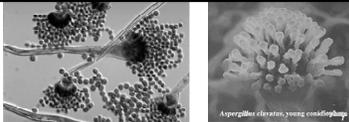
Microbial Toxin: Mycotoxin

- Mycotoxins are secondary metabolites of fungi which can induce acute as well as chronic toxic effects (i.e., carcinogenicity, mutagenicity, teratogenicity, and estrogenic effects) in animals and man.
- Currently, a few hundred mycotoxins are known, often produced by the genera *Aspergillus*, *Penicillium*, and *Fusarium*.
- Toxic syndromes resulting from the intake of mycotoxins by man and animals are known as **mycotoxicoses**.

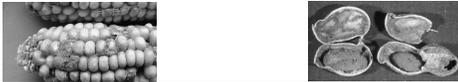
Microbial Toxin: Mycotoxin

- Mycotoxin contamination of food and feed highly depends on the environmental conditions that lead to mold growth and toxin production.
- The detectable presence of live molds in food, therefore, does not automatically indicate that mycotoxins have been formed.
- On the other hand, the absence of viable molds in foods does not necessarily mean there are no mycotoxins. The latter could have been formed at an earlier stage prior to food processing.
- Because of their chemical stability, several mycotoxins persist during food processing, while the molds are killed.

Aflatoxins



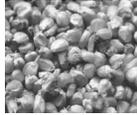
- Aflatoxins are the most important mycotoxins, which is produced by certain species of *Aspergillus* (*A. flavus* and *A. parasiticus*), which develop at high temperatures and humidity levels.
- Aflatoxins are carcinogenic substances and may be present in a large number of foods. This toxin can cause cancer, cirrhosis of the liver.
- For substances of this type there is no threshold below which no harmful effect is observed.



Aflatoxins



- The most common commodities contaminated are tree nuts, peanuts, and corn and cottonseed oil.
- The major aflatoxins of concern are B1, B2, G1, and G2 → usually found together in various proportions. Aflatoxin B is usually predominant, and it is the most toxic and carcinogenic.
- TLC method can detect aflatoxins.



Aflatoxins

- The aflatoxins B1, B2 fluoresce blue and G1, G2 fluoresce green when viewed under a microscope.
- A major metabolic product of aflatoxin B1 is aflatoxin M (usually excreted in the milk of dairy cattle that have consumed aflatoxin-contaminated feed).
- LD₅₀ ranges from 0.5 to 10 mg/kg body weight (any species of animals)

What are some of the regulations guiding the levels of toxins in food?

- Commission Regulation (EC) No 466/2001 of 8 March 2001
Setting maximum levels of certain contaminants in foodstuffs.
- USFDA
- CODEX STAN 193-1995 (Rev.1-1997)
How to establish the maximum limit of toxins or contaminants in foods.
