SECTION 1
INTRODUCTION TO FOOD CONTAMINANTS AS FOOD HAZARD

PART 1

This lesson will focus on general knowledge about food contaminants. Where possible, we will present the impacts on human health when they are identified. This lesson has been split in small video capsules. The first will focus on naturally occurring contaminants.

FOOD CONTAMINANTS

Definition of the *Codex Alimentarius*

"Any substance not intentionally added to food, which is present in such food as a result of the production (including operations carried out in crop husbandry, animal husbandry and veterinary medicine), manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food or as a result of environmental contamination."

Codex Alimentarius

According to the Codex Alimentarius, food contaminants are defined as: Any substance not intentionally added to food, which is present in such food as a result of the production (including operations carried out in crop husbandry, animal husbandry and veterinary medicine), manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food or as a result of environmental contamination. The term does not include insect fragments, rodent hairs and other extraneous matter.

This definition provides several insights: the first is the notion of the non intentional nature of food contaminants. So because of this, you have to make the difference between food contaminants and intentional adulterants, which are related to food fraud cases.

The second is the notion of the wide spread nature of possible food contamination with a possible introduction at any point of the food production chain.

The third is that this definition may help us differentiate food contaminants depending on their point of introduction into the food chain. We would be able therefore to distinguish contaminants introduced as a result of environmental sources, from those related to human activities such as the indirect introduction of residues of veterinary drugs used to treat food producing animals, as part of animal husbandry practices, as an example.

PROPOSED CLASSIFICATION

Naturally occuring contaminants:

- Chemicals that are naturally produced by living organisms.
  - Plants (Glycoalkaloids, phenolic coumpounds, etc..)
  - Fungi (Mycotoxins)
  - Algae (Phycotoxins)
  - Animals (Venoms, various toxins)
  - Bacteria (see microbiological hazard)
- These toxins are not harmful to the organisms themselves.
- They may be toxic to other creatures, including humans, when eaten.

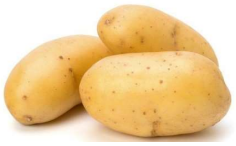
Food contaminants are classified based on two main criteria The first one is how they enter in the food production chain and the second when they enter the food chain. If contaminants come from external sources, they are called primary contaminants. On the contrary, if they are produced *in situ*, meaning in the food products themselves, they are called secondary contaminants.

The first category that we will review in thus course will focus on what is known as “Naturally occurring contaminants”. This category contains contaminants produced under specific conditions by living organisms: fungi, leading to mycotoxins, or algae, leading to phycotoxins. The production of some these contaminants may be influenced by human activities, which can contribute to an increase of their availability and occurrence in food products. These toxins are generally not harmful to the plants or crops themselves. They may be on the other hand toxic to other creatures, including humans, when the crop is

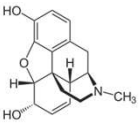
consumed as food or feed.

PHYTOTOXINS

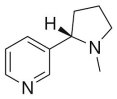
Naturally occurring contaminants



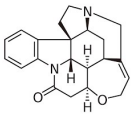
- Glycoalkaloids
  - Produced by *Solanaceae* (potatoes)
  - Unlikely that human consume fatal doses
- Toxic phenolic coumpounds (tannins, flavonoids, etc…)
- Cyanogenic coumpounds
- Lectins
- Goitrogens
- Toxic mushrooms



Morphine



Nicotine



Strychnine

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Among Naturally occurring contaminants, the first type of molecules that we will review are phytotoxins not to be confused with Phycotoxins. Phytotoxins are poisonous substances produced by plant or plant pathogens with a bioactive property, meaning showing both useful and harmful effects in human beings and animals.

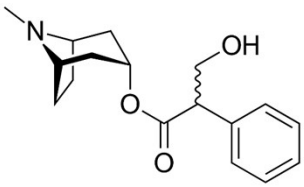
They have great diversity in their composition, occurrence, mode of action and lethal effects. They belong to diverse classes of compounds such as toxic alkaloids, phenolics, terpenoid, glycoside, polyacetates and sometimes combinations of all these classes.

The biological activity of a phytotoxin can be measured in a number of ways depending on the chemical nature and the apparent effect. Some of these compounds are used by humans, seeking their possible biological effects, such as Morphine and its anesthetic / pain management effect.

Finally, **although mushroom poisons** are definitely fungal metabolites, that can cause disease and death in humans and other animals, they are considered as phytotoxins instead of mycotoxins. The distinction between a mycotoxin and a mushroom poison is based not only on the size of the producing fungus, but also on the way humans are exposed to them. Exposure to mycotoxins is unintentional as a result of the metabolism of microscopic fungal organisms. Consuming mushrooms (which are not microscopic fungi), is intentional.

PHYTOTOXINS

Naturally occurring contaminants



Atropine

Tropane alkaloids caused Ugandan food aid outbreaks

By Joe Whitworth on November 1, 2019

International investigations have found two outbreaks of illness in Uganda were likely caused by food aid contaminated with tropane alkaloids.

Outbreaks caused by phytotoxins are rare compared to others Naturally occurring contaminants but as these molecules are not frequently monitored, they could be incriminated in more cases than are actually reported. For example in 2019 in Uganda, a case was reported where 5 people died and more than 300 were sick as a result of an incident attributed to exposure to a culprit phytotoxin called atropine.

This is a good example of showcasing the difficulty to classify phytotoxins such as atropine. On the one hand they are substances with possible medicinal applications. On the other hand they may be a very strong poison that can be found in plants like belladonna or nightshade.

Phytotoxins has been investigated only for a limited number of compounds, for instance in the case of strongly toxic glycoalkaloids produced from potato (*Solanum tuberosum*) or

Solanine. Phytotoxins are not subjected to widespread set of regulatory provisions at very few exceptions like Solanine.

MYCOTOXINS

Naturally occuring contaminants

- Mycotoxins: Mycotoxins are toxic chemical products formed by fungi that can grow on crops in the field or after harvest.
  - Small molecules (< 1000 Da)
  - Produced as secondary metabolites
  - Not biodegradable
  - Resistant to heat and freezing
  - Resistant to food processing (no elimination)
- There are now more than 300 known mycotoxins of widely different chemical structures and differing modes of action.

The second kind of naturally occurring contaminants reviewed in this course are mycotoxins which are among the most studied food contaminants in general.

The name mycotoxin was introduced in 1962 just after a large scale animal health crisis occurred, in the UK close to London. During this crisis approximately 100,000 poultry died. The disease was linked to a peanut meal contaminated with secondary metabolites from *Aspergillus flavus* (aflatoxins). At that point, scientists became aware of the possibility that mold metabolites can be deadly.

All mycotoxins are low-molecular-weight natural products (i.e., small molecules) produced as secondary metabolites by filamentous fungi. These metabolites constitute a chemically heterogeneous group. The only reason why they are all regrouped together is because they can all cause disease and death in human beings and other animals.

About 300 to 400 compounds are now recognized as mycotoxins classified in different groups composed by chemically related metabolites. Approximately a dozen groups regularly receive attention as threats to human and animal health.

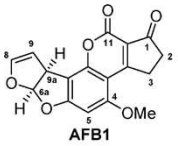
While all mycotoxins are of fungal origin, not all toxic compounds produced by fungi can be called mycotoxins. The target and the concentration of the metabolite are both important. Fungal products that are mainly toxic to bacteria (such as penicillin) are usually called antibiotics. Other low-molecular-weight fungal metabolites such as ethanol, that are toxic only in high concentrations, are not considered mycotoxins

MYCOTOXINS

Naturally occuring contaminants

Common mycotoxins include

- Aflatoxins (produced by *Aspergillus flavus* and *A. parasiticus*)



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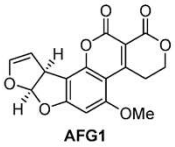

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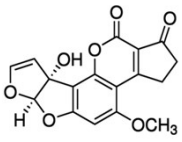

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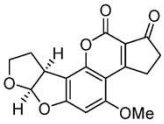

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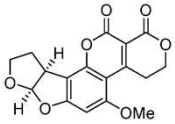

AFG2

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Even if there are more than 300 mycotoxins, only a few of them are regulated. Among those, Aflatoxins are probably the most known mycotoxins and are widely monitored

There are more than 20 known aflatoxins but the four major aflatoxins are called B1, B2, G1, and G2 based on their fluorescence under UV light (blue or green) and relative chromatographic mobility during thin-layer chromatography. Aflatoxin B1 is the most potent natural carcinogen known and is usually the major aflatoxin produced by toxigenic strains. It is also the most studied substance. The level of toxicity associated with aflatoxin varies with the types.

Aflatoxins are produced by many strains of *Aspergillus flavus* and *Aspergillus parasiticus* which are common fungi, occurring in agricultural products. Other Aspergillus strains are also aflatoxin-producing species, but they are encountered less frequently

Aflatoxins specifically target one organ: the liver. Early symptoms of hepatotoxicity caused by aflatoxins comprise fever, malaise and anorexia followed with abdominal pain, vomiting, and hepatitis; however, cases of acute poisoning are exceptional and rare. Despite continued control measures, aflatoxin continue to be a major threat to food and agricultural commodities.

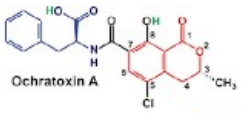
The *Codex Alimentarius* Commission adopted a limit of 10 to 15 microgram/kg for total aflatoxins depending on the food commodity.

MYCOTOXINS

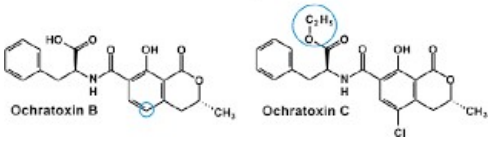
Naturally occuring contaminants

Common mycotoxins include

- Ochratoxin A (*Aspergillus ochraceus*)



From Koszegi and Poór (2017)



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Among the most potent and problematic mycotoxins, ochratoxin A is also another candidate

There are three types of ochratoxins, namely A, B, and C. Specifically, OTA is known to be the most common and important Ochratoxin with significance to human and animal health. Ochratoxin A was discovered as a metabolite of Aspergillus ochraceus in 1965 and was quickly recognized as a potent nephrotoxin but may also present hepatotoxic, teratogenic and immunotoxic effects to several animal species.

Members of the ochratoxin family of compounds have been identified as metabolites of many different species of Aspergillus, including *Aspergillus alliaceus, Aspergillus auricomus, Aspergillus carbonarius, Aspergillus glaucus, Aspergillus melleus*, and *Aspergillus niger*. Although some early reports implicated several *Penicillium* species, it is now thought that

Penicillium verrucosum, a common contaminant of barley, to be the only confirmed ochratoxin producer in this genus.

OTA was found to be one of the most common contaminants of food like cereals, coffee, wine, dried fruits and nuts, and meat products.

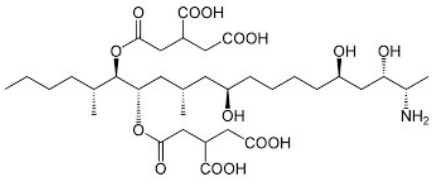
A maximum limit of 5 µg/kg was set by the Codex General Standard for Contaminants and Toxins in Food and Feed, for wheat, barley and rye.

MYCOTOXINS

Naturally occuring contaminants

Common mycotoxins include

- Fumonisins
- Trichothecenes such as deoxynivalenol
- Zearalenone



Fumonisin B1

Several other mycotoxins, like Fumonisins and Deoxynivalenol, which is also known as Vomitoxin, are also on the list of Codex Standards.

Fumonisins are carcinogenic mycotoxins first isolated in 1988 and are found ubiquitously in maize and maize-products. International consensus has resulted in Maximum Limits being set for fumonisins by the *Codex Alimentarius* Commission. These were set at 4000 µg/kg for raw maize and at 2000 µg/kg for maize flour and maize meal. The MLs are intended to be applied to maize in local or international trade and are intended to be health protective for the respective populations consuming these products.

Deoxynivalenol was first isolated in the 1970s, in connection with vomiting and other adverse gastrointestinal effects in Japan and in the United States. In fact, DON (as it is called) should be included in a broader group of mycotoxins, called trichothecenes. Other

trichothecenes like Nivalenol also present strong health impacts.

The *Codex Alimentarius* Commission managed DON by setting maximum levels for its presence in cereal based foods for infants and young children, in wheat, maize and barley intended for further processing, in semolina or flakes derived from wheat, maize or barley. Compared with other mycotoxins such as aflatoxins, relatively fewer food regulators around the world have already set Maximum Limits for DON in food, or are considering to do so. These includes regulators in Canada, the US and the EU.

Both fumonisins and DON are mycotoxins produced by Fusarium species including *Fusarium oxysporum, F. culmorum, F. roseum,* and *F. graminearum* but they are not the only ones.

Another Fusarium mycotoxin to mention is, Zearalenone, which is also a mycotoxin with important health impacts. Occurrence of ZEA has been reported in cereal crops and foodstuffs from many regions of the world including Europe, Asia and Africa. Due to high levels of possible contamination, ZEA is regulated through Maximum Levels, in over 15 countries including a few Asian countries like South Korea, Thailand, China.

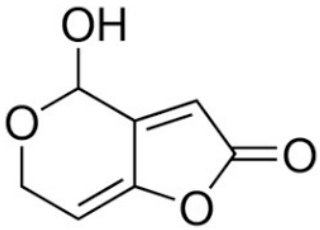
Other fusarium toxins like fusaproliferin (FUS), beauvericin (BEA), enniatins (ENNs), and moniliformin (MON) also present health impacts but are less studied.

MYCOTOXINS

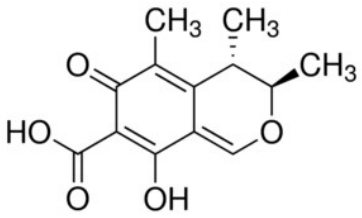
Naturally occuring contaminants

Common mycotoxins include

- Ergot alkaloids (*Claviceps*),
- Patulin (*Penicillium* and *Byssochlamys*),
- Citrinin (*Penicillium citrinum*)



Patulin



Citrinin

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Among other mycotoxins of interest, Ergot alkaloids are produced as a toxic cocktail by Claviceps, which are common pathogens of various grass species. The ingestion of these ergots, has been associated with diseases since the antiquity. The human disease acquired by eating cereals infected with ergot sclerotia, usually in the form of bread made from contaminated flour, is called ergotism or St. Anthony's fire. Human ergotism was common in Europe during the Middle Ages.

Patulin is produced by many different molds but was first isolated as an antimicrobial active substance during the 1940s from *Penicillium patulum*. The same metabolite was also isolated from other species and given the names clavacin, claviformin, expansin, mycoin c, and penicidin. During the 1960s, patulin was reclassified as a mycotoxin as it became apparent that, in addition to its antibacterial, antiviral, and antiprotozoal activity, patulin was toxic to both plants and animals. Patulin is prevalent as a mycotoxin in Apple and apple

derived product. It is also regulated through a ML set at 50 Micrograms per Kg (ppb).

Citrinin was first isolated from *Penicillium citrinum* and was then identified in over a dozen species of Penicillium and several species of Aspergillus, including certain strains of *Penicillium camemberti* (used to produce cheese) and *Aspergillus oryzae* (used to produce sake, miso, and soy sauce). More recently, citrinin has also been isolated from *Monascus ruber* and *Monascus purpureus*, industrial species used to produce red pigments.

MYCOTOXINS

Naturally occuring contaminants

- The foods that can be affected include cereals, nuts, fruit and dried fruit, coffee, cocoa, spices, oilseeds and milk.



- Importance of environmental conditions
  - High humidity (over 70%)
  - High temperature (over 30 degrees)
  - Insect infestations, etc…

If we examine the foodstuffs that may be contaminated by mycotoxins, we identify a wide variety of crops. Specifically, cereals, grains, nuts, oilseeds, fruits, dried fruits, vegetables, cocoa and coffee beans, wine, beer, herbs, and spices are considered as major mycotoxin vectors since they are consumed by a large mass of population and also animals.

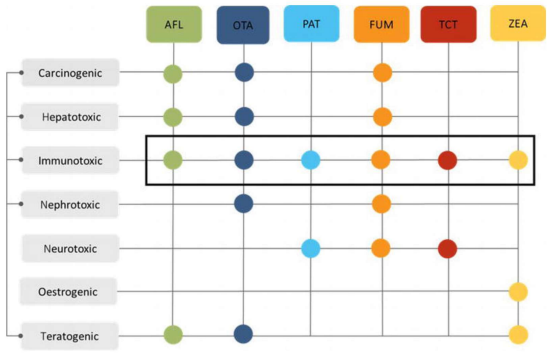
In general, mycotoxin exposure is more likely to occur in parts of the world where poor methods of food handling and storage are common, where malnutrition is a problem, and where few regulations exist to protect exposed populations. However, even in industrialized countries, specific subgroups may be vulnerable to mycotoxin exposure. In the United States, for example, Hispanic populations consume more corn products than the rest of the population and consequently may more exposed to mycotoxins found in corn and derived products.

Mycotoxins can be present in food in two ways: first as a result of mold growth as a pathogen to the plant plant in the field, second, growth may occur during storage. After plant materials are contaminated with mold spores from soil and air, they easily contaminate other food sources and production areas. Such cross contamination can even be found in laboratories, and even consumers' kitchen. Only certain species of mold may capable of mycotoxin synthesis; therefore, the presence of mold on or in food is not always indicative of mycotoxin presence. Nevertheless, moldy products are considered to be risky products and should be avoided. Storage conditions are crucial to prevent mycotoxin growth and should therefore be the focus of prevention approached applied by producers, especially through temperature and humidity control.

MYCOTOXINS

Naturally occuring contaminants

- Health impact: some target the kidney, liver, or immune system and some are carcinogenic.



From Cinar and Onbaşı (2019)

Diseases caused by mycotoxins are called Mycotoxicoses. They can be categorized as acute or chronic. Acute toxicity generally has a rapid onset and an obvious toxic response, while chronic toxicity is characterized by low-dose exposure over a long time period, resulting in diseases like cancers and other generally irreversible effects.

Almost certainly, the main human and animal health burden of mycotoxin exposure is related to chronic exposure (like cancer induction, kidney toxicity, immune suppression). However, the best-known mycotoxin episodes are manifestations of acute effects.

Health effects can be different from one mycotoxin to another but most of mycotoxins are immunotoxic.

SECTION 1
END OF PART 1

SECTION 1
INTRODUCTION TO FOOD CONTAMINANTS AS FOOD HAZARD

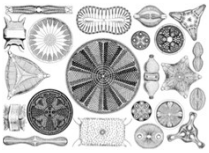
PART 2

In this part, we will continue examining naturally occurring contaminants in food – with the review of Phycotoxins

PHYCOTOXINS

Naturally occuring contaminants

- Phycotoxins (or shellfish toxins): produced by algae (dinoflagellates, cyanobacteria and diatoms,) in both temperate and tropical climate.
- About 100 species (among 5000) are known phycotoxin producers



Phycotoxins are also included in the category of naturally occurring contaminants. Like mycotoxins, Phycotoxins are natural metabolites but they are produced by **algae** instead of fungi.

Phycotoxins, more properly called “marine and freshwater toxins”, belong to many different groups of small or medium-sized compounds (between 300–3000 Da). Besides the chemical variability of the classes, each class group includes several compounds characterized by similar structures, which are either produced by algae or are secondary products of the primary algal toxin produced during metabolism by fish and shellfish.

The algae responsible for phycotoxin production and excretion belong to the cyanobacterium and dinoflagellate groups.

Among the thousands of microalgal species known in nature, about 100 produce natural toxins that can cause intoxication or even death in humans and animals. These find their way through the food chain and are subsequently consumed by humans, eliciting diseases or, in the most serious cases, death.

PHYCOTOXINS

Naturally occuring contaminants

Potential issues with

- bivalve shellfish such as clams, oysters, scallops, and mussels,
- other molluscan shellfish such as whelks, lobster and crab.



- Main phycotoxins are heat-stable (resistant to cooking), tastless and odorless

The risk posed by these contaminants is increased by accumulation and concentration of excreted toxins by different aquatic organisms, including feed-filtering bivalves (mussels, clams, oysters), shellfish, and herbivorous fish; these subsequently enter the food chain and cause toxicosis in species that consume contaminated products, for example predatory fish, marine mammals, birds, and humans. In all cases, toxic compounds are not produced by the shellfish or other high trophic species.

PHYCOTOXINS

Naturally occuring contaminants

Main phycotoxins: Ciguatoxins (CTXs)

- Various gastointestinal and neurological effects
- No antidotes
- The toxin is produced by *Gambierdiscus toxicus*, a type of dinoflagellate.
- Modification of the CTXs all along the food chain
- The bigger is the fish the higher is the level of toxin

For the control of phycotoxins, directives and regulatory measures were developed around the world.

Phycotoxins are classified on the basis of their poisoning symptoms. So you will find toxins causing ciguatera fish poisoning (itching, tingling, rash and other symptoms). Paralytic shellfish poisoning, diarrheric shellfish poisoning, etc...

However, additional syndromes exist; each type of poisoning is associated with a specific group of biotoxins.

Ciguatera Fish Poisoning is the most frequently reported seafood-toxin illness in the world. It causes substantial human health, social, and economic impacts. The illness produces a complex array of gastrointestinal, neurological, and cardiovascular symptoms, which may

last days, weeks, or even months.

Ciguatera Fish Poisoning is not due to the mishandling of fish and is not prevented by any particular storage, preparation, or cooking methods. The Ciguatoxins are tasteless, colorless, odorless, heat and acid stable, and stable for at least six months at commercial freezing temperatures.

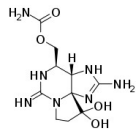
Ciguatoxins and their precursors are produced by microscopic algae known as dinoflagellates, in the genus, *Gambierdiscus*. They are transferred and metabolized through the food web, as *Gambierdiscus* cells are ingested by herbivorous fish, which are then consumed by piscivorous fish, both of which are then consumed by humans. It is believed that ciguatoxins are bioaccumulated and concentrated, such that fish higher in the food web tend to contain the highest ciguatoxin concentrations

PHYCOTOXINS

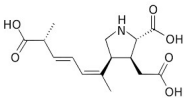
Naturally occuring contaminants

Other major phycotoxins:

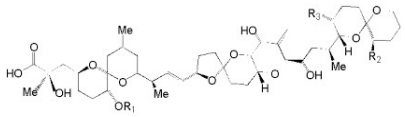
- Diarrhetic Shellfish Poison (DSP) (Including Okadaic acid) causing… Diarrhetic shellfish poisoning
- Saxitoxins causing Paralytic shellfish poisoning (PSP)
- Domoic acid causing Amnesic shellfish poisoning (ASP)



Saxitoxin



Domoic acid



Okadaic acid

In the 21st century, Diarrhetic shellfish poisoning has been the most prevalent poisoning related to marine biotoxins after Ciguatera fish poisoning. The major toxins related to this poisoning are Okadaic acid and dinophysitoxins. These compounds are potentially present in shellfish as a result of toxins metabolic pathways. Current legal limits are established for OA-group toxins by Codex and industrialized countries, and set at values varying from 160 to 200 µg OA-eq/kg for DSP toxins.

Paralytic shellfish poisoning is one of the most studied intoxications with serious symptoms in humans. PSP may be caused by exposure to Saxitoxin and other analogues, such as gonyautoxins (GTXs), neosaxitoxin (NeoSTX),etc.. There is at least 58 closely related compounds responsible for this poisoning. The main producers of these toxins are dinoflagellates found along the Atlantic and Pacific coast of both Northern and Southern hemispheres, but also in the Mediterranean Sea.

Beyond that, some cyanobacteria that may occur in fresh waters have been reported to produce PSP toxins. PSP is characterized by symptoms varying from nausea, vomiting, tingling of the mouth to paralysis, and in severe cases it can be life threatening. The European legislation has set a limit for PSP toxins (800 μg STX-eq/kg).

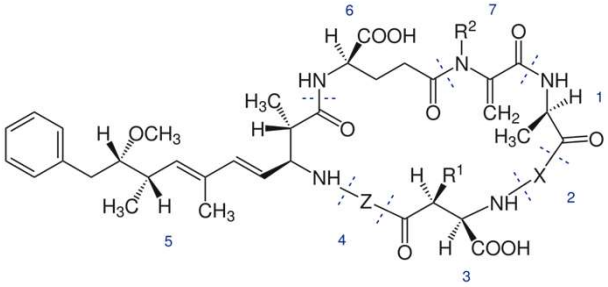
Finally, Amnesic shellfish poisoning is caused by DA which is a natural neurotoxin produced by red algae and diatom algal species.
It was isolated for the first time in 1958 from an algea called *Chondria armata*. Different analogues of DA have been reported since and they are heat stable, so cooking does not destroy the toxin. DA accumulates in filter-feeding shellfish by consuming DA-producing phytoplankton.

Outbreaks occur when populations of DA-producing organisms 'bloom' to a sufficiently high concentration to become dangerous to health. This is actually an issue as algal blooms are accelerating frequently worldwide. The CODEX Committee on Fish and Fishery Products set a maximum limit at 20 ppm for DA and its analogues in mollusk flesh for international trade.

PHYCOTOXINS

Naturally occuring contaminants

Fresh water toxins: Microcystin



Chemical structure of Microcystin

From *NASA Earth Observatory*

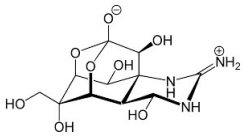
One last category of phycotoxins in related to cyanobacteria production in fresh water leading to the secretion of microcystins and other related toxins. They are called blue green algae toxins, These toxic substances are found in fresh water reservoirs and fresh water fish, particularly during algal bloom seasons. The most potent toxin is now as MicroCystin LR – although over 80 toxic variants have been reported.

ANIMAL TOXINS

Naturally occuring contaminants

Animal toxins:

- Poisoning after eating an animal is almost always linked to bacterial poisoning (see microbiological hazards)
- Few venomous animal are eaten
  - Scorpions
  - Snake
  - Porcupine fish (Tetrodotoxin)
- Removal of poisonous glands and avoidance of toxic tissues



Tetrodotoxin

So far, we talked about plant, fungi and algae toxins but animal toxins should also be included in this category even if few venomous animals are eaten. Most of the time, the removal of the poisonous glands is sufficient. Every year you may however find a small number of cases of food poisoning due to animal toxins because of particular food diets. For example the consumption of porcupine fish is not rare in some pacific islands. In the same way, fugu is considered as a gourmet meal in Japan.

To the best of our knowledge, there are currently no regulations regarding animal toxins in the main international regulations (Codex, Europe or United States).

ALLERGENS

Naturally occuring contaminants

- Cause the abnormal response of the immune system to otherwise harmless foods
- Mostly proteins

Vegetal allergens

Animal allergens

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Finally, we are not sure that we should qualify allergens as contaminants, because they are ingredients that may have a detrimental health effects for a small proposition of human population that may present hypersensitivity to these ingredients. It is estimated that up 6% of consumers may present such conditions for certain food categories.

The term food allergy is used to describe an adverse immune response to foods. Although an allergy could be triggered by virtually any food, “major allergens” responsible for most significant reactions include peanut, tree nuts, wheat, soy among others for vegetal allergens and milk, egg, shellfish and fish for animal allergens. Allergies to additives and preservatives are generally uncommon. Food allergy rates vary by age, local diet, and many other factors.

The Codex Alimentarius has set up a standard for the labelling of several food allergens.

However, the European Union, the United States and several others countries have developed their own list of priority allergens, each with their own specificity. For example, Canada, Europe but also Australia and New Zealand put mustard in the list of priority allergens while the US did not.

Gluten and sulfites are also on this list despite the fact they are not real food allergens.

SECTION 1
END OF PART 2

SECTION 1
INTRODUCTION TO FOOD CONTAMINANTS AS FOOD HAZARD

PART 3

In this part of the course, I will present several categories of food contaminants, namely agrochemicals, environmental contaminants and food-processing-induced chemicals.

PROPOSED CLASSIFICATION

Agrochemicals:

contaminants present in foodstuffs as trace or derivatives thereof from agrochemical uses

- Pesticides
- Veterinary drugs

- They are present as residues in foodstuffs as trace or derivatives thereof from agrochemical uses

- They can be potential Persistent Organic Pollutants (POPs)

Agrochemicals are the various chemical products that are used in agriculture. In most cases, the term agrochemical refers to the broad range of pesticides and include synthetic fertilizers, hormones, and other chemical growth agents.

Typically, agrochemicals are toxic and may pose significant environmental risks, particularly in the event of accidental spills. As a result, in many countries, the use of agrochemicals has become highly regulated and government-issued permits for purchase and use of approved agrichemicals may be required. For example, excessive use of fertilizers has led to the contamination of groundwater with nitrate, a chemical compound that in large concentrations may be poisonous to humans and animals.

In addition, the leaching from the soil of agrochemicals into streams, lakes, and other surface waters can increase the growth of algae, which can have an adverse effect on the

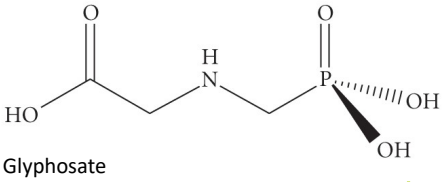
life-cycle of fish and other aquatic animals.

All of these compounds are generally detected and quantified by LC or GC coupled to MS.

PESTICIDES

A pesticide is a chemical substance designed to be effective against pests. The common terminology refers to plant protection products. They are applied:

- to keep plants healthy, and
- to prevent them from being destroyed by disease and infestation.



Glyphosate

The first type of agrochemical is pesticides. A Pesticide is a chemical substance designed to be effective against pests.

The common terminology refers to plant protection products. Plant protection products are mainly applied on crops to keep them healthy and to prevent them from being destroyed by disease and infestation. They include herbicides, fungicides, insecticides, acaricides, plant growth regulators and repellents. However, this terminology (pesticide) also covers products such as biocides, which are intended for non-plant uses to control pests and disease carriers such as insects, rats and mice.

Exposure of the general population to these molecules most commonly occurs through consumption of treated food sources or being in close contact to areas treated with pesticides such as farms or lawns. Other exposure sources are related to occupational

activities, such as pesticide spraying in farming practices.

Most food competent authorities regulate the use of pesticides through imposing a compulsory registration of their active substances. This registration includes the demonstration of safety and the determination of conditions of use and what we consider to be Maximal residues levels. This level is defined as a key risk management measure ensuring the safety of consumers and workers, but also to minimize the application of pesticides to the minimum amounts that would ensure their effectiveness.

In order to prevent a high level of inconsistency in pesticide management, and in an attempt to harmonize food regulatory measures, the Codex Alimentarius Commission has developed a set of Maximal Residue Levels for a number of pesticides through its Codex Committee on Pesticide Residues (CCPR), which relies upon the assessment of safety of these substances developed by the Joint FAO/WHO Expert Meeting on Pesticide Residues.

VETERINARY DRUGS

A veterinary drug (also animal drug) refers to a drug intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in animals

They are applied:

- to keep animals healthy, like antibiotics, and
- to enhance animal growth

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The second main type of agrochemical is Veterinary drugs. They have been a key element in increasing the production of animal-derived foods. These are administered to animals to prevent and treat infections, promote growth, or otherwise improve animal health, particularly for those animals maybe be raise in confinement, meaning that are in close contact over long periods of time. Like for pesticides, residues of veterinary drugs may pose health risks when consumed through food.

Veterinary Drugs are an essential component of animal husbandry and modern food production practices, but their residues can persist in animal-derived foods and present potential food safety risks. Some of these substances have been banned after the discovery of severe health impacts.

To minimize these risks, national authorities establish strict controls for the authorization,

labeling, and use of veterinary drugs in food-producing animals, and they conduct surveillance programs to detect unsafe drug residues in animal-derived foods.

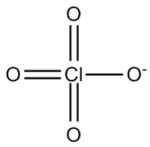
The approach to evaluate the safety of food containing veterinary drug residues is similar to the safety assessment applied to food additives but is complicated by metabolic and dispositional processes that take place in the target animal.

PROPOSED CLASSIFICATION

Environmental contaminants:

Chemicals that accidentally or deliberately enter the environment, often, but not always, as a result of human activities.

- Persistent Organic Pollutants (POPs)
  - Dioxins and furans, Polychlorinated biphenyls (PCBs), Polybrominated Diphenyl Ethers (PBDEs), Perfluorinated chemicals (PFCs),
- Perchlorate
- Heavy metals
- Naturally occurring contaminants



Perchlorate

Staying at the beginning of the food production chain, let us review environmental contaminants. They are chemicals that accidentally or deliberately enter the environment, often, but not always, as a result of human activities.

Some of these contaminants may have been manufactured for industrial use and because they are very stable, they do not break down easily. If released into the environment, these contaminants may enter the food chain.

A wide variety of environmental contaminants have been detected in foods. These range from metals and "ionic" species like perchlorate to organic (or carbon-based) substances, including the so-called "persistent organic pollutants". Other environmental contaminants are naturally occurring chemicals, but industrial activity may increase their mobility or increase the amount available to circulate in the environment, allowing them to enter the

food chain at higher levels than would otherwise occur. This is the case for heavy metals or metaloids.

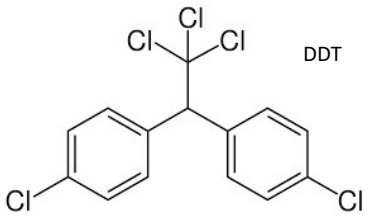
All of the molecules presented on this slide have impacts on human health.

PERSISTENT ORGANIC POLLUTANTS

Persistent organic pollutants (POPs) are organic compounds that are resistant to environmental degradation through chemical, biological, and photolytic processes = “forever chemicals”.

- Dichlorodiphenyltrichloroethane DDT (banned since the 70s)
- Lindane (banned since 2009)

Impact on human health on the long term.



DDT

The most important Environmental contaminants are Persistent organic pollutants (or POPs). They are chemicals of global concern due to their potential for long-range transport, persistence in the environment, ability to bio-magnify and bio-accumulate in ecosystems, as well as their significant negative effects on human health and environment.

The list of POPs is available on the site of the Stockholm Convention. This list was updated several times to include new POPs.

Many POPs were widely used during the boom in industrial production after World War II, when thousands of synthetic chemicals were introduced into commercial use.

There are in fact two subgroups of POPs.

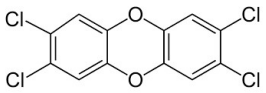
and the first one is “Intentionally produced chemicals”. Many of these chemicals proved

beneficial in pest and disease control, crop production, and industry. These same chemicals, however, have had unforeseen effects on human health and environment. Examples include DDT, once used as pesticide, which is still used to control mosquitoes that carry malaria in some parts of the world. DDT Persists in the environment, even after decades its use was stopped in most part of the world.

PERSISTENT ORGANIC POLLUTANTS

Dioxins and dioxin-like compounds

- Several subgroups:
  - Polychlorinated dibenzo-p-dioxins (PCDDs), or simply dioxins
  - Polychlorinated dibenzofurans (PCDFs), or furans
- And their cousins:
  - Polychlorinated biphenyls (PCBs)
  - Polybrominated Diphenyl Ethers (PBDEs)
- By-products of industrial process
- Different toxicities and health impact



2,3,7,8-Tetrachlorodibenzo-P-dioxin
or TCDD

The second subgroup is “unintentionally produced chemicals” that result from some industrial processes and from combustion.

Actually, this subgroup is also divided in several subgroups. Among those POPs, you can find dioxins and dioxin-like compounds, like furans. There are 210 different dioxins and furans.

All dioxins have the same basic chemical "skeleton". Exposure to dioxins and furans has been associated with a wide range of adverse health effects in laboratory animals and humans.

The type and occurrence of these effects typically depend on the level and duration of exposure but the most toxic congener is TCDD, which is presented on right part of the slide.

TCDD is used as a baseline to evaluate the toxicity of all dioxins and dioxin-like compounds. Indeed, “toxic equivalency factors” have been established to compare the toxicities of individual PCDDs, PCDFs and PCBs relative and the toxic equivalent factor of TCDD is 1.

Dioxins are mainly by-products of industrial processes, including smelting, chlorine bleaching of paper pulp and the manufacturing of some herbicides and pesticides, but can also result from natural processes, such as volcanic eruptions and forest fires.

In terms of dioxin release into the environment, uncontrolled waste incinerators are often the worst culprits, due to incomplete burning.

Dioxins and dioxins-like compounds are found throughout the world in the environment. The highest levels of these compounds are found in some soils, sediments and food, especially dairy products, meat, fish and shellfish, as they are lipophilic. Very low levels are found in plants, water and air.

PCBs are also organic chlorine compounds. There are 209 congeners of PCBs and 12 of them are dioxin-like compounds du to their chemical structure. They are generally considered as contributors to overall dioxin toxicity. PBDEs are bromine analogs of PCBs with similar applications and environmental concerns.

These compounds are not regulated everywhere. For example, the Codex Alimentarius Commission has not setup any maximum limits so far. However, Europe has set up some maximum limits for a number of food commodities. It should be noted that these compounds are under surveillance by several regulatory agencies. To finish on dioxins and dioxin-like compounds, these molecules are detected and quantified by LC or GC-MS.

HEAVY METALS

"Heavy metals" refers to any metallic element with a high density (more than 5g/cm^3) and is toxic at low concentration.

- Mercury (Hg): muscle weakness, neurobiological symptoms
- Lead (Pb): several symptoms, including coma and death
- Arsenic (As) : Abdominal symptoms, including cancer
- Cadmium (Cd)
- Antimony (Sb)
- Tin (Sn)
- Etc…

Another important type of environmental pollutant are Heavy metals. The term heavy metal refers to any metallic chemical element that has a relatively high density and is toxic or poisonous at low concentrations.

Examples of heavy metals include mercury, lead, arsenic, cadmium, but also antimony, tin, chromium, thallium and many others.

They are toxic, persistent in the environment, as they are not biodegradable, and can be bioaccumulated, but they are not POPs because they are not organic.

In fact, most of them are known to be potential carcinogens. Various adverse health hazards are known due to long term and continuous exposure to heavy metals.

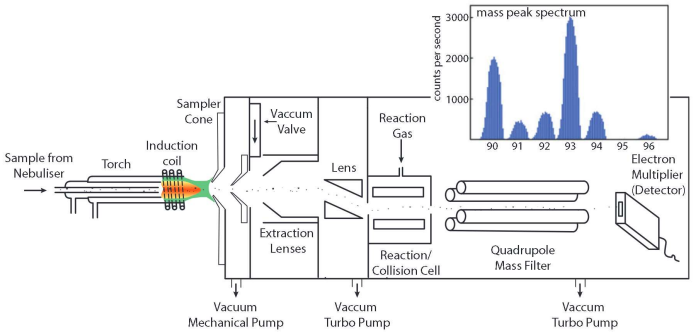
Besides, the acute toxicity of Heavy metals have been demonstrated all along the human history as heavy metals are historically linked with adulteration, like Lead in wine, Copper in

pickles, Aluminum in bread, Use of red lead as colorant, all leading to food poisoning.

Natural sources of heavy metals include weathering of metal-bearing rocks and volcanic eruptions, while anthropogenic sources include mining and various industrial and agricultural activities. Mining and industrial processing for extraction of mineral resources and their subsequent applications for industrial, agricultural, and economic development has led to an increase in the environment of such compounds.

HEAVY METALS

Reference method for detection in food: **Inductively coupled plasma mass spectrometry (ICP-MS)**



Schönbächler (2016)

Many regulatory agencies (including the Codex Alimentarius Commission) issued some Maximal Limits to manage risks associated heavy metals are toxic at ppb levels.

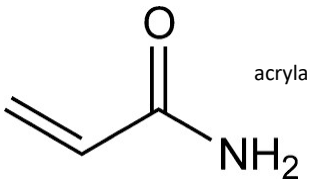
The levels of lead should be as low as possibly achievable, as it was identified that there was no safe value of exposure to lead – the smallest amount would have an impact on the IQ of humans.

Unlike the other molecules presented here, heavy metals are detected using Inductively coupled plasma mass spectrometry (ICP-MS), as a method of choice.

PROPOSED CLASSIFICATION

Food-Processing-Induced Chemicals:

- Produced during food processing
  - From naturally occurring components
  - From components intentionally used
- Most of them are unevitable



acrylamide

Benzene

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The last category of chemical contaminants is called food-processing-induced chemicals. Contaminants coming from packaging are included in this category.

Unwanted chemicals can be formed in certain foods during processing as a result of reactions between compounds that are natural components of the food. In some cases an undesirable chemical may be formed as a result of a food additive being intentionally added to food and reacting with another compound in the food.

When foods are heat-processed (baked, deep-fried, etc.), there are reactions that occur between components of the food, resulting in the desired flavour, appearance and texture of the food. However, some of these reactions can lead to the production of undesirable compounds. Similarly, certain storage or processing conditions may allow reactions to occur that otherwise would not, this is the case for Benzene which is the result of the

reaction between ascorbic acid – or vitamin C and the presence of an additive based on benzoates at higher temperatures.

Removing the precursor, such as the replacement of Benzoates with Sorbates as preservatives, would eliminate such occurrence.

In many cases, the presence of processing-induced chemicals in food cannot be avoided. However, understanding the processes by which these products are formed can allow us to optimize or adjust food preparation methods, formulae or processes, thereby reducing or eliminating the formation of such chemicals.

For this reason, most of the time there is no limitation for this compounds, but regulatory agencies issued guidelines and established mitigation measures to avoid the production of such compounds.

FOOD CONTAMINANTS

Sources of contamination all along the food chain:

- During the primary production (Water, soils, staff, etc..)
- During the transformation (Equipment, staff, etc..)
- During the storage (Container, packaging, etc..)
- During the consumer's handling (Consumer, water, cooking material, etc..)

To conclude this part of the program, a food contaminant is a term that regroup more than 1000 different molecules, covering a large variety of chemical structures. Some of them cannot be avoided, some of them are natural while others are the result of human activities.

One key point is that they can be introduced in food products all along the food chain, during the production, the processing, even during storage and transport of food products.

However, one needs to remember that most of food contaminants can be introduced at a specific point of entry in the food chain.

FOOD CONTAMINANTS

Principles regarding the food and feed contaminants

Potential impacts of food contaminants:

- Impact on human health (and/or animal health).
- Impact on food and feed quality.
- Environmental impact.

Control of the contamination levels through:

- Good Agricultural Practice (GAP), and
- Good Manufacturing Practice (GMP) following an appropriate risk assessment.

Overall, food contaminants may have impacts on the long term, like the development of cancers, or may present acute toxicity, like food poisoning, allergic reaction or even death. More importantly, they can also have impacts we have not foreseen like for several POPs.

Finally, Food contaminants are not regulated as an homogenous group. Some of them are prohibited in foodstuffs, some of them are controlled through the setup of maximal limits and finally others are simply mitigated though guidance documentation.

Being able to analyse the contaminant and detect its presence is a key measure that supports the verification of compliance and the validation of the adopted mitigation approaches.

Analytical methods are an important arsenal used by food regulators as part of their

conformity assessment programs, but also for surveillance and monitoring activities, which are a key requirement to support risk management of contaminants in food.

SECTION 1

END OF PART 3