# Mycotoxins



### Fungi.

- The study of fungi is called mycology; scientists who study fungi are called mycologists.
- Fungi are found virtually everywhere.
- Some fungi are harmful, some are beneficial.
- Fungi represent a diverse group of eukaryotic organisms that include yeasts, molds, and fleshy fungi (e.g., mushrooms).
- Fungi are the "garbage disposers" of nature.
- Fungi are not plants they are not photosynthetic.
- The toxins of the fungi called "MYCOTOXINS

### Mycotoxins

#### Introduction:

- Historical:
- Modern mycotoxicology was not developed until the discovery of aflatoxins in the early 1960s as the causative agent in the
- peanut meal causing the "Turkey X" disease that killed more than 10,000 turkeys fed with the contaminated meal.
- Because aflatoxins are a series of highly potent carcinogens produced by commonly occurring Aspergillus flavus and A. parasiticus, research has focused new attention on mycotoxins.

In the last 40 years, many new mycotoxins have been identified and characterized, and their biosynthetic origin in various fungi elucidated. It has been estimated that at least 25% of the world's agricultural product is contaminated with mycotoxins and certain diseases have been linked to ingestion of food and feed contaminated with mycotoxins.

### **Definition of Mycotoxins**

Mycotoxin: is a convenient broad term describing the toxic secondary metabolites produced by fungi. "Myco" means fungal (mold) and "toxin" represents poison.

- □ They include a great variety of <u>low molecular weight</u> <u>compounds</u> with diverse chemical structures and biological activities.
- ☐ Some mycotoxins could also be toxic to plants or other microorganisms; but these compounds are not classified as antibiotics of fungal origin.
- □ Like most microbial secondary metabolites, the benefit of mycotoxins for the fungi themselves is still not clearly defined

#### Cont....

- In considering the effects of mycotoxins on animals, it is important to distinguish between "mycotoxicosis" and "mycosis.":
- Mycotoxicosis is used to describe the action of mycotoxin(s) and is frequently mediated through a number of organs, notably the liver, kidney, lungs, and the nervous, endocrine, and immune systems.
- Mycosis" refers to a generalized invasion of living tissue(s) by growing fungi.

#### Cont.....

 Due to their various chemical structures, mycotoxins may exhibit a number of biological effects, including both acute and chronic toxic effects as well as carcinogenic, mutagenic, genotoxic, and immunotoxic effects.

 The interaction of mycotoxins with cellular macromolecules plays a dominant role in their toxic actions. Recent studies on the effect of mycotoxins on apoptosis have further revealed their mode of action at the cellular level

## Economic Impact of Mycotoxin Contamination

- The most noticeable negative economic impact of mycotoxins is an outright loss of crops and affected animals.
- Also, humans may encounter severe health hazard or high mortality rates in countries with less regulation or monitoring programs.

 Thus, the negative economic impact resulting from mycotoxin contamination is certainly very significant and estimated to be \$932 million annually

#### **Fungal Growth**

- **a. Field fungi**: fungi that attack plants that grow in the field) occurring *prior to harvest*) grow under special conditions. (*Fusarium*)
- b. Storage fungi: Storage fungi usually invade grain or seed during storage and are generally not present in large quantities before harvest in the field. The most common storage fungi are species of *Aspergillus and Penicillium*. Contamination occurs through spores contaminating the grain as it is going into storage from the harvest.

#### The development of fungi is influenced by the

- Moisture content of the stored grain
- Temperature
- Condition of the grain going into storage
- · Length of time the is grain stored and
- Amount of insect and mite activity in the grain

## PRODUCTION OF MYCOTOXINS BY TOXICOGENIC FUNGI

- Invasion by fungi and production of mycotoxins in produces can occur under favorable conditions in the field, at <u>harvest</u>, and during <u>processing</u>, <u>transportation</u> and <u>storage</u>
- Fungi that are frequently found in the field e.x : : A. flavus, Alternaria
- Species most likely introduced at harvest e.x : F. sporotrichioides, Stachybotrys atra,
- Most penicillia are storage fungi e.x : Penicillium citrinum P. citreoviride
- \*\*All of which are capable of producing mycotoxins in grains and foods.

\*\* It is apparent, most of the mycotoxin producing fungi belong to three genera: Aspergillus, Fusarium, and Penicillium. However, not all species in these genera are toxicogenic

#### Factors Affecting Mycotoxin Production

- Genetics and environmental and nutritional factors greatly affect the formation of mycotoxins.
- Depending on the susceptibility of the crop, geographic and seasonal factors, as well as cultivation, harvesting, storage, and transportation practices, mycotoxins are found worldwide.
- In the field, weather conditions, plant stress, invertebrate vectors, species and spore load of infective fungi, variations within plant and fungal species, and microbial competition all significantly affect mycotoxin production.

#### Con..

- Physical factors such as time of exposure, temperature during exposure, humidity, and extent of insect or other damage to the commodity prior to exposure determine mycotoxin contamination in the field or during storage.
- Chemical factors including the nutritional status of the crops or chemicals (such as <u>fungicides</u>) used in crop management could affect fungal populations, and consequently toxin production

## Characteristics of mycotoxin induced disease

- a. not transmitted among animals.
- b. Pharmaceutical treatment does not alter the pathway of disease.
- c. Mycotoxicosis most often presents as a uncertain, sub-acute or chronic condition

## Prevention of mycotoxin-induced disease

- a. Avoiding
- **b.** Diluting
- c. Cleaning
- d. Testing
- e. Drying
- f. Adding (organic acids will prevent mold growth)

#### Removal or Elimination of Mycotoxins.

- Since most of the mycotoxin burden in contaminated
- commodities is localized to a relatively <u>small number</u> or seeds or
- kernels removal of these contaminated seeds/kernels is effective in
- detoxifying the commodity.
- Methods currently used include:
  - (a) physical separation by:
    - identification and removal of damaged seed;
    - mechanical or electronic sorting;
    - flotation and density separation of damaged or contaminated seed;
    - physical screening and subsequent removal of damaged kernels by air blowing;
    - washing with water
    - use of specific gravity methods

All these methods have shown some effect for some mycotoxins, including DON, FmB, and AFB1

- (b) removal by filtration and adsorption onto filter pads, clays, activated charcoal, etc.,
- (c) removal of the mycotoxin by solvent extraction

#### Inactivation of Mycotoxins

When removal or elimination of mycotoxins is not possible, mycotoxins can be inactivated by:

- (a) physical methods such as thermal inactivation, photochemical or gamma irradiation,
- (b) chemical methods such a treatment of commodities with acids, alkalies, aldehydes, oxidizing agents, and gases like chlorine, sulfur dioxide, NaNO2, ozone and ammonia,
- (c) biological methods such as fermentations and enzymatic digestion that cause the breakdown of mycotoxins. The commercial application of some of these detoxifying mechanisms is not feasible because, in a number of cases, the methods will be limited by factors such as the toxicity of the detoxifying agent, nutritional or aesthetic losses of commodities during treatment, and the cost of the sophisticated treatment.

Although several detoxification methods have been established for aflatoxins, only the ammoniation process is an effective and practical method. Other chemicals such as ozone, chlorine, and bisulfite have been tested and some effect for

some mycotoxins was shown in it. Solvent extractions have been shown to be effective but are not economically feasible.

#### Removal of Mycotoxins During Food Processing.

 While cooking generally does not destroy mycotoxins, some mycotoxins can be detoxified or removed by certain kinds of food processing.

Mycotoxins heat stabile toxin

## Treatment of mycotoxin -induced disease

a. For most mycotoxins, there is no specific treatment or antidote

 b. Supplement with vitamins & selenium may be helpful, and provision of adequate high-quality protein

Mycotoxins in food & milk	Fungi	Effect on animals & human
<u>Aflatoxin</u>	Aspergillus flavus , Aspergillus parasiticus	liver disease, carcinogenic and teratogenic effects
<u>Trichothecenes</u>	Fusarium graminearum, Fusarium sporotrichioides	immunologic effects, hematological changes, digestive diorders, edema
<u>Zearalenone</u>	Fusarium graminearum	estrogenic effects, atrophy of ovaries and testicles, abortion
<u>Ochratoxin</u>	Aspergillus ochraceus, Penicillium verrucosum	nephrotoxicity, mild liver damage, immune suppression
Ergot alkaloid	Claviceps purpurea, Claviceps paspaspali	nervous or gangrenous syndromes
<u>Fumonisin</u>	Fusarium verticillioides, Fusarium proliferatum	Pulmonary edema, leukoencephalomalacia, nephrotoxicity, hepatotoxicity

#### A- Aflatoxin

#### 1. Sources:

Aspergillus flavus & A.paraciticus:

(الفول السوداني) Corn, peanuts

#### 2. Factor favoring production of aflatoxins:

- a. Temperature: 25-30 oc
- b. Grain moisture

#### A- Aflatoxin

3. Chemical characteristics

Exhibit intense blue or green fluorescence under UV.

: aflatoxins B1, B2, G1 and G2

also

: aflatoxin M1 is a metabolites of AFB1 found in animal urine, milk or tissues.

#### Mechanism of Toxicologic Damage:

Also called *steatosis*, fatty liver can be a temporary or longterm condition, which is not harmful itself, but may indicate some other type of problem. Left untreated, it can contribute to other illnesses. It is usually reversible once the cause of the problem is diagnosed and corrected. The liver is the organ responsible for changing fats eaten in the diet to types of fat that can be stored and used by the body. Triglycerides are one of the forms of fat stored by the body and used for energy and new cell formation. The break down of fats in the liver can be disrupted by alcoholism, malnutrition, pregnancy, or poisoning. In fatty liver, large droplets of fat, containing mostly triglycerides, collect within cells of the liver. The condition is generally not painful and may go unnoticed for a long period of time. In severe cases, the liver can increase to over three times its normal size and may be painful and tender



#### A- Aflatoxin

- The major effect of toxin :
- a. Loss of enzyme
- b. Lack of formation of lipid acceptor protein in liver
- c. Decreased cellulose digestion, volatile fatty acid formation & proteolysis (breakdown of proteins)
- d. Necrosis

## Toxicity & Diagnosis& Treatment & Prevention

- Toxicity in farm animals:
- a. Young animals are more susceptible than adult.

 b. Nutrition deficiency increase susceptibility

- The visual diagnosis:
- Clinical sign: decreased growth rate, reduced feed efficiency,,, mild anemia, and increased susceptibility to infectious disease.
- Treatment & Prevention
  - a. *Detoxification*: Hydrated sodium calcium aluminosilicate (HSCAS) can *absorb aflatoxins*
  - b. Supportive: Vitamin .E & selenium
  - c. Prevention
    - Mold inhibitor

#### **Trichothecenes (TCTCs)**

- Several species of Fusaria infect corn, wheat, barley, and rice.
- Under favorable conditions, they elaborate a number of different types of Mycotoxins.
- The effect of TCTC:

The TCTC mycotoxicoses affect many organs, including the gastrointestinal tract, hematopoietic, nervous, immune, hepatobiliary, and cardiovascular systems.

#### Mechanistically:

, inhibition of protein synthesis is one of the earlier events in manifestation of TCTC toxic effects and they act at different steps in the translation process. Inhibitory effects of these mycotoxins vary considerably with the chemical structure of the side chain.

#### **B- Zearalenone**

• 1. Sources: Fusarium roseum (F.graminearum): corn, wheat, barley, oats

- 2. Factor favoring production
  - **a.** High moisture 22% 25%
  - b. Alternating high and low temp. (7-21 oc)

#### B- Zearalenone con...

- 3. Mechanism of toxicological damage:
- a. initiating specific RNA synthesis
  - b. Function as a weak estrogen.

- 4. Toxicity:
- a. Swine are most susceptible
  - b. low for all effects except reproductive function.

#### 1.Source:

Claviceps purpurea:

barley, wheat & oats

2. Factor favoring:

Warm & humid

- 3. Mechanism of toxic:
- a. potent initiators of contraction in smooth muscle
- b. mimic the action of dopamine

#### 4. Clinical sign:

- a. necrosis of the feet, ears and tail
- b. increased temperature., pulse & respiration rate
- c. lactation does not occur
- d. hyper-excitability & tremors
- e. heat intolerance in cattle

#### 5. Treatment:

 a. animals should be provided with a warm, clean, stress-free environment

- b. Control secondary bacterial infection
- c. milk supplement



#### **D-Fumonisin**

Fumonisins (Fm): are a group of toxic metabolites produced primarily by *F. verticillioides*, *F. proliferatum* and other related species readily colonize corn all over the world.

More than 11 structurally related Fms (B1, B2, B3, B4, C1, C4, A1, A2, etc.), have been found since the discovery of FmB1.

Fumonisins are most frequently found in *corn*, corn-based foods, and other grains (such as sorghum and rice). The level of contamination varies considerably with different regions and year, ranging from negligible to more than 100 ppm; but is generally reported to be between 1 and 2 ppm

#### **Fumonisin**

#### **Toxicologic Effects:**

Fumonisin B1 is primarily a hepatotoxin and carcinogen in rats. Feeding culture material from *F. verticillioides* or pure FmB1 to rats resulted in cirrhosis and hepatic nodules, carcinoma. Kidney is also a target organ.

Mechanistically, Fms are inhibitors of ceramide synthase