Aflatoxin B_1

Introduction:

Aflatoxins : Secondary metabolic compounds are carcinogenic and toxic revert to group of Difuranocoumarine and produced by a group of fungi most important : *A.flavus* which produces aflatoxin B1 , B2 and *A.parasiticus* produces B1,B2,G1,G2 and from fungus that produces aflatoxin B1 but less efficiently: *A.niger* , *A,wentii* , *A.rubber* and some Species of *penicillium* such as *: P.citrinum* , *P.frequentans, P.puberulum*

Aflatoxin B1: is a potent Hepatotoxic ,hepatocarcinogenic mycotoxin ,and mutagenic,teratogenic,produced by the fungi ***Aspergillus flavus*** and ***Aspergillus parasiticus .*** Causes aflatoxicosis and liver disease

Aspergillus growth and Aflatoxin B1 production is dependant upon the **temperature**, **humidity**, **host plant type**, and **the strain of fungus**; high humidity usually required for growth

Aspergillus spp. *grow on plants and crops from tropical and subtropical areas:* corn , wheat, maize, Brazil nuts, pecans…etc.

Chemical and physical properties:

1_aflatoxins are white or colorless crystalline substances

2_They fluoresce under UV radiation

3_freely soluble in moderately polar solvents such as chloroform.

4_dissolve in water to the extent of 10-20 mg/litre.

5_Very heat-stable and not easily degraded

6_The lactone ring makes them susceptible to alkaline hydrolysis

Metabolism:

Both metabolized and unmetabolized aflatoxin is excreted mostly in urine. It is also excreted in milk, stool,and saliva (which may be swallowed and re-enter the GI tract)

Mechanism of Action:

1_ AFB1 is oxidized by CYT P450 in the liver into AFB1-8,9-epoxide which is the major metabolite that exerts hepatotoxic effects

2_ The 8,9 epoxide is neutralized by conjugation in the liver with GSH (glutathione) by glutathione-S-transferase,

GSH has many roles in membrane maintenance and stability as well as reducing oxidative stress. Its reduction further enhances the damage to critical cellular components (DNA, lipids, proteins) by the 8,9 epoxides

3_ The 8,9 epoxide binds preferentially to mitochondrial DNA hindering ATP production and FAD/NAD-linked enzymatic functions. The result is reduced mitochondrial function and increased prevalence of mitochondrial directed apoptosis

4_One of the most serious effects of the AFB1-8,9-epoxide metabolite is it reacts with amino acids in DNA and forms an **adduct**.

5_ This adduct is fairly resistant to DNA repair processes and thus this gene mutation may cause carcinoma of the liver.

6_However, the liver can detoxify AFB1 by oxidizing it to other metabolites such as AFQ1 which has very little cancer-causing potential. These are usually excreted in urine with little effect on the body.

BIOLOGICAL EFFECTS:

Aflatoxins are also recognized as teratogenic,mutagenic, carcinogenic agents, immunosuppressants,and potent inhibitors of protein synthesis.

1_The binding of the epoxide with proteins may:

*Inhibit the protein from performing its enzymatic functions

*Create a reservoir of the toxin in proteins, prolonging exposure

2_Immunological Suppression

Using animal models, AFB1 has been shown to impair normal immune function either by reducing phagocytic activity or reduce T cell number and function.

3_Nutritional Interference:

It interferes in nutrient modification such as Vitamin A or D in animal models.

4_Aflatoxicosis when taken in high concentrations characterized by:

vomiting, abdominal pain, pulmonary edema,convulsions, coma and death with cerebral edema and fatty conditions of the liver, kidneys and heart

5_hepatocellular carcinoma

6_Lipid accumulation in the liver due to decreased lipid transport and reduced oxidation

7_Symptoms of liver failure occur with acute aflatoxicosis:

_Jaundice

_ascites (fluid build up)

_portal hypertension

necrosis of the liver

for most species the **LD50** value ranges from 0.5 to 10 mg/kg of body weight.

The factors that influence the toxicity of aflatoxin:

Environmental factors,exposure level,duration of exposure ,age,health,nutrional status of diet

Methods for Detection and Quantification of Aflatoxin

1. enzyme linked immunosorbent assay (ELISA).
2. Electrochemicals techniques
3. Chromatography:
   - Liquid chromatography
   - Thin-Layer Chromatography (TLC)
   - High Performance Liquid Chromatography (HPLC)
   - Electrokinetics
4. Fluorescence
5. Ultra violet absorption
6. Spectrometry

Treatment:

Inactivation of toxin **before ingestion**:

1_Synergistic combination of gamma radiation and hydrogen peroxide degrades the toxin

2_Treatment of corn with ammonia

3_NaHSO3 soak for corn also shows beneficial results

4_Dichlorvos inhibits aflatoxin B1 biosynthesis

After ingestion

Treatment with antibiotics or other drugs has little effect .