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Review article: Aflatoxins as Tumor Promoters in poultry

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Abstract:*Mycotoxins are toxins that produced from the fungi Aspergillus are concept to provoke cancer, aflatoxin tumour promoter was once used to browse PubMed's abstracts, thereby 44 papers have been fetched .while 951 from key phrases aflatoxin cancer in which 20 only where selected. 57papers had been used as sources of information.*
\From observations of posted facts our readings revealed that aflatoxin may additionally affect greater than one part of the body both molecularly and pathogenically in human and animal. Here aflatoxicosis in poultry speed up immunosuppression and intolerance and disturb the metabolism at all.

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I. Definition and main features promoting the pathogenicity

Mycotoxins are secondary metabolites(Adekoya et al., 2019; Ben Taheur, Kouidhi, Al Qurashi, Ben Salah-Abbes, & Chaieb, 2019; Devi & Sashidhar, 2019; Gotthardt et al., 2019; Ingenbleek et al., 2019; Omotayo, Omotayo, Mwanza, & Babalola, 2019; Sossah et al., 2019; Tolosa, Rodriguez-Carrasco, Ferrer, & Manes, 2019; Weng, Zhang, Chen, & Hu, 2019; Yao et al., 2019)

Toxicity in human :

Aflatoxin is considered to be a highly toxic toxin, and many studies have indicated that exposure to high doses of poison (>6000mg) of the poison leads to acute toxicity and has a fatal effect, while exposure to small doses for multiple periods leads to the poison. Chronic toxicity is called a poisoning condition that occurs with this poison Aflatoxicosis. The target organ of this poison is the liver, where the poison affects the liver in a massive way and causes a defect in fat and protein metabolites and deposits fat in the liver, which leads to lubrication and then damages liver cells and eventually fibrosis and cancer. In addition to being a carcinogen, it also has an effect on embryos and is transmitted through breast milk and cow's milk.* Foods known to contain aflatoxin toxins:

The preferred foods for the growth of mushrooms that secrete this poison are:

Peanuts - peanut butter - nuts such as (pistachios - walnuts - almonds - corn - wheat - rice - barley wheat - oil seeds - legumes)which are exerted by several for instance Fusarium, Aspergillus, prncillium ….(Ben Taheur et al., 2019; Cobo-Diaz, Baroncelli, Le Floch, & Picot, 2019; Devi & Sashidhar, 2019; Gotthardt et al., 2019; Mongalo, Dikhoba, Soyingbe, & Makhafola, 2018; Omotayo et al., 2019; Sabino et al., 2019; Sossah et al., 2019; Sudharshana, Venkatesh, Nayana, Manjunath, & Mohana, 2019; Weng et al., 2019). Mycotoxins are highly toxic metabolite and life threaten to both human and animal as it affect mainly liver and initiate tumor and other toxigenic impacts (Aupanun et al., 2019; Diaz de Leon-Martinez et al., 2019; Ji, Zhang, Zheng, & Yao, 2019; Kadawathagedara, de Lauzon-Guillain, & Botton, 2018; Li et al., 2019; Omotayo et al., 2019; Schulz, Pohlmann, Dietrich, Martlbauer, & Elssner, 2019; Tolosa et al., 2019; Yan, Shi, You, Li, & He, 2019; Zhang, Li, Xu, Pan, & Sun, 2019). Between all, AFB1 Fif 1is the highly dangerous mycotoxin, Chemical Names of it are ;AFLATOXIN B1; 1162-65-8; Aflatoxin B; NSC 529592; HSDB 3453; PubChemCID:186907, Molecular Formula:C17H12O6 and Molecular Weight:312.277 g/mol (NCBI, 2019)

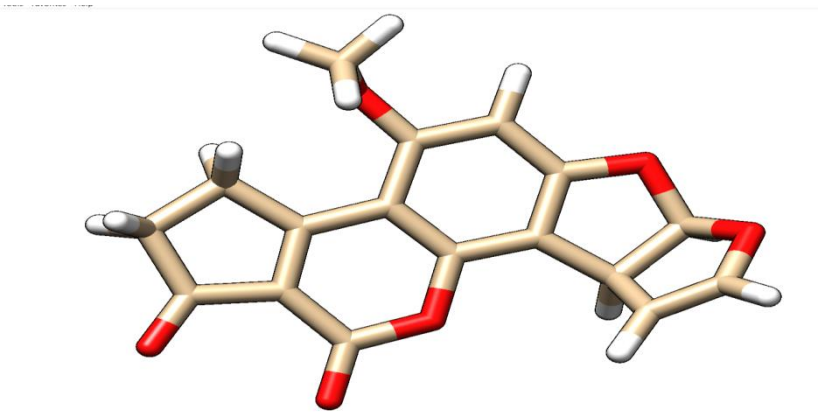

Figure 1 AflatoxinB1 imageproduced by Chimera software .

However many other aflatoxins are available in natureBetween them , T-2 toxin, citrinin CTN, patulin PAT, aflatoxin B1 AFB1 and ochratoxin A (OTA)(Schulze et al., 2015).
(look at fig .2) and considered a risk factor for different maladies(Bovard et al., 2018; Dhanasekaran, Nault, Roberts, & Zucman-Rossi, 2019; Furlan, Konc, & Bren, 2018; Le Pape et al., 2019; Lien, Wang, Pan, & Ling, 2019; Mahale et al., 2019; Masiello, Somma, Ghionna, Logrieco, & Moretti, 2019; Rauf, Wajid, Hussain, Ather, & Ali, 2019; Rawla, Sunkara, Muralidharan, & Raj, 2018; Walker & White, 2001). Aflatoxin toxins (B1- E2- G1 - G2).The b1 marking is the most toxic and affecting the liver, where prothrombin is reduced and the blood clotting period is longer. Akratoxin toxins and their strong effect on the kidneys where they raise urine acid in blood, leading to visceral gout and blood clotting process and delaying sexual maturity.Triacothesin toxins cause anorexia and refusal to feed. Zilaralineone toxins have a similar effect to estrogen where they lead to custom swelling, ovaries and slot Complex. T2 toxins cause lesions in the blood clotting process and have distinct symptoms in the mouth, beak angle and throat, resulting in non-consumption of fodder with neurological symptoms. Citrine toxins cause increased water consumption, causing kidney enlargement and fading color. Moniliforminmonliformin toxins cause facial congestion and abdominal ascites. Fumonisins B1 toxins cause fumonicin swell swells in the internal viscera (liver, kidneys, glandular stomach and cane). Rubratoxinrupratoxin toxins cause bleeding in several places with the atrophy of the Fabrecius gland. Patulinalpatolin toxins cause developmental delays, as well as reduced calcium content in the body with the appearance of deformed eggs. Cyclopiazonic Acid acid toxins cause a decrease in fertility, especially in cocks.

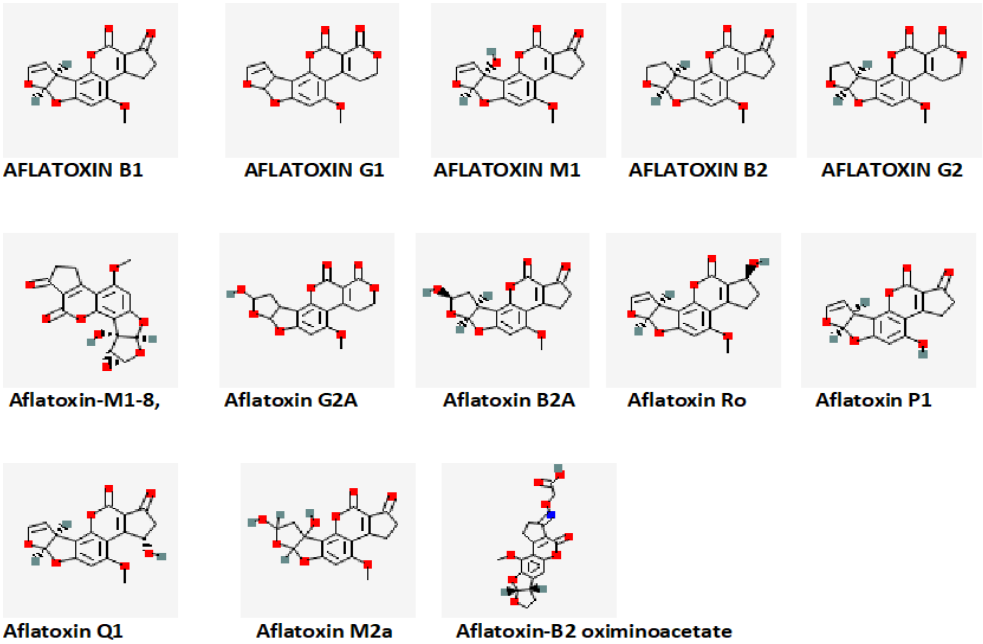

Figure2. Aflatoxins

AFB1 which is activated by liver enzymes to aflatoxin-8,9-exo-epoxide (AFBO) which interact with subcellular structural proteins and nucleaic acid and responsible for toxic and carcinogenic effect(Diaz, Murcia, Cepeda, & Boermans, 2010).

Aflatoxin and cancer in poultry

Poultry is affected by two main conditions: either fungal diseases or mycotoxicosismycotoxicosis produces chemical compounds called (metabolites and by-products) and these compounds have many beneficial and harmful effects, including:

A: Antibiotic (antimicrobial, and antioxidants).
B: The other destructive parallel activity is: acute and chronic toxins of plants or animals as well as human.

Most mycotoxins are metabolites and by-products. For , however, fungi does not need these compounds to complete their life cycle and reproduction. There are many varieties of mycotoxins, each with its own chemical composition and in general compositions and chemical varieties of fungal toxins are specific to a particular type of fungi and it can be said that there is one type of fungus that produces a variety of fungal poisons. For example, there are only two types of aspergillus that produce Aflatoxins toxins and types of
Few fusarium mushrooms produce a class of mycotoxins called Fumonisinsfumonizines and types of nationality of penicillinium and aspergillus can produce Ochratoxin toxins.

The origin of the fungal infection is the cultivation of crops that are not resistant to these , such as the poor types of corn, soy and others, which are the most important sources of fodder for poultry where the fungus grows on these crops during cultivation and also after harvesting them from the ground, the fungus releases enzymes that analyze or break down nutrients in the crop such as protein and fat and produce fungal toxins as a by-product of the metabolism, feeding on protein, losing its nutritional feed value.

These also grow during the storage of fodder in silos and during transport and import from abroad in ships where the duration of transportation and storage then when the feed reaches the farm or amber where the method of storage is an important factor in the growth of these by storing in places exposed to the sun and heat or put it in a place of high humidity or poor ventilation and also when putting feed on the ground directly or placed near water sources and also when providing the chicks and chickens for feed wet with water.

The danger of fungal toxins on the health of birds and the rate of production where the injury of fungal toxins is represented in two pictures first sharp image, which results from the consumption of birds for a high concentration of toxins, leads to wasting, loss of appetite, loss of feathers and yellowing of the face, and secondly the chronic image, which is when eating the bird may contain small amounts Of the toxins for a long time it causes many problems including in the municipality this chick takes it through feed so it is used on the gut in the first causes ulcers in the mouth and causes the oesophagusand the vesicle is filled with blood and then it comes down in the stomach and the inner layer that lining the stomach keeps intermittent as we talked about the topic of « how to diagnose diseases of poultry (third topic) > and then come down on the intestines and destroy it and cause severe diarrhoea, and of course trespassing on the liver because it is the center of detoxification, leading to liver failure, and also go to the kidney to get out of the body through it and cause kidney failure.

And always eliminate the big chick fire so you are surprised that his health is good and died and caused the low rate of food conversion and the low rate of consumption of fodder and the rate of weight gain and the low rate of egg production in white chicken and increase the rate of breakage in the eggs and the heterogeneity of the herd where there are big chicks and chicks Small and decreased immunity of birds become easier to receive infections with different microbes and less resistant to environmental effects such as heat stress and cause toxic effects in the liver causing yellow disease, enlarged liver and change of color to congestion or to yellow color as a result of increased presence of fat cells And according to the amount of mycotoxins in ration.

The impact on poultry industry

The underlying activities of tumour initiating by AFB1 is thought to belong to the indispensable role of post-translational amendment in specific histone phosphorylation H3 in manner of cancer, hereby two Zhu et al. (2017) located that Ser10 (p-H3S10) and Ser28 (p-H3S28) have been both expressed in AFB1 hepatic cancer-derived mobile line And has contributed that to DNA injury then hepatic cancer. Which is number 2 of dying etiological factors overworld
Fungi causes losses in stored grains and reduces their nutritional value

Symptoms begin depending on the concentration, quality and chemical composition of the poison, where the symptoms vary. Small animals and birds are more affected than birds and adult animals.Low weight, lack of weight gain, reduced food conversion factor and increased non-saleable animal is the most obvious observation. in poultry The rise of the daily dead and the low production of eggs and its weight and notice that the wall of the vesicles is thick and notices sores with the inner layer of the ganglet and the glandular stomach.

Low hatching and fertilization.Extreme or very low temperatures help increase the toxic
Low levels of vitamins increase the toxic effect of fungi and fungal toxins.

The most important symptoms of exposure to fungal toxins are; Symptoms of anemia (general pallor and lethargy), Dehydration, Enlarging and lubricating the liver as well as the rest of the organs, Failure of vaccinations and exposure to various diseases due to immunosuppression processes, Atrophy of the fabrichus gland, the thyme gland and the immune system in general, Avila and Accra toxins cause the fragility of the capillaries and thus rupture them , Avila and Accra toxins cause a reduction in the level of calcium in blood plasma and change the level of calcium, phosphorus and vitamin D, resulting in broken bones and necrosis, especially the head of the femur and the fragility of the egg cortex,

Aflatoxin B1 (AFB1) is secondary metabolite of Aspergillusflavus and is the most potent hepatocarcinogen in mammals andbelong Group 1 carcinogen. both dietary and occupational exposure to AFB1 cause the problem, AFB1 measures in the serum by enzyme-linked immunosorbent assay with specific biomarker (Viegas et al., 2016). It well reported that Aflatoxin B1 (AFB1) could lead to Alpha-lipoic acid (alpha-LA) was evaluated in this study for liver oxidative damage and inflammatory responses in Birds, in same study alpha-LA were found to reduce AFB1 side effects through inhibiting the proinflammatory mediators IL6 and NF-KB and minimise levels of nitric oxide synthase(Ma et al., 2015).

AFB1 also effect turkey farms and resulted in huge economic losesas these birds do not have the ability to destroy AFB1 , therefore AFB1 can be the source of turkey hepatic transcriptome(Monson et al., 2014).Cancer studies have been revealed that inhaled or ingested AFB1 is a major source of hepatocarcinoma and respiratory cancers between people exposed to direct contam such as poultry farms workers and in animals (Viegas et al., 2012).

P450 is a drug metabolising enzyme that been regulated upon Hepatitis B virus X protein which is is a key regulator of (Niu et al., 2013). Ducks are most sensitive birds to AFB1 as they have 4 types of Cytochrome P450 enzymes (CYP), which are capable of bio activate AFB1 into highly active epoxide responsible for carcinogenic and hepatic disorders (Diaz et al., 2010). Bintvihok and Kositcharoenkul (2006) were demonstrated that experimentally addedcalcium to the ration of poultry for 28days in form of calcium propionate at 0.25 and 0.5 % , are enough to minimise the levels of AFB1 in liver and muscles tissue by which gamma glutamyltransferase (gamma-GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are measured as an indicator of presence of AFB1 in treated broilers.In china AFB1 of ducks are correlated with human Hepatocellular carcinoma as it diagnosed in 85% bof studied samples and confirmed by molecular examination, tested livers showed a proliferation of bile duct, Thus AFBI considerd a predisposing factor to hepatic tumorsof ducks (Duflot et al., 1995) also Cova et al. (1994) have been referred to same

II. Conclusion.

In spite of the wide availability of mycotoxins in animal food but the impact are seen between poultry rather than other species of animals (Robens & Richard, 1992).

Thus AFT recognised as a food carcinogenic products thereby care should be taken to protect both human and animals life through following the right path of security methods such as continuous lab diagnosis and regular check of food and enhance store conditions (Linsell, 1979)

Bio activation of AFB1 to tumourpromoter depend on conversion into epoxide, the latter converted carbonium ion at C-2 that bind nucleophilicregions of DNA, and act as alkylating agent.(Shank, 1977), the different stages that take part into AFB1 conversion into carcinogen are illustrated in Fig.3

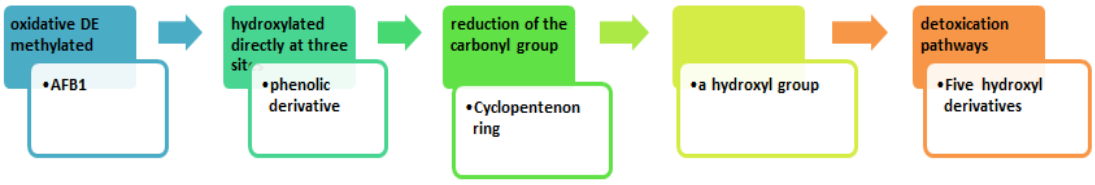

Figure3 A simplified mechanism of AFB1 metabolism into carcinogenic factor

Mechanism of AFB1 in Cancer

The underlying activities of tumour initiating by AFB1 is thought to belong to the indispensable role of post-translational amendment in specific histone phosphorylation H3 in manner of cancer, hereby two Zhu et al. (2017) located that Ser10 (p-H3S10) and Ser28 (p-H3S28) have been both expressed in AFB1 hepatic cancer-derived mobile line And has contributed that to DNA injury then hepatic cancer. Which is number 2 of dying

etiological factors overworld (Enriquez-Cortina et al., 2017). AFB1 are believed to negatively regulated Ras-association domain household 10 two RASSF10 in hepatoma cell line leading to anti-apoptotic two impact and enhancing tumour boom whereas overexpression of RASSF10 enhance programmed mobilephone demise (apoptosis) of most cancers cells and regulate cancer(Wang et al., 2016),

Thereby alter 161 genes pathway as tested by Schulze et al. (2015). On the different hand Y. J. Zhang et al. (2009) did not confirm any evidence of between AFB1 and The Hint1 protein, a member of the histidine triad (HIT) family methylation, two two which is a most cancers suppressor.

Taken together, our readings counseled that common genetic variants in AFB1 may additionally have an impact on DNA of by and large liver cells promotion with the aid of unique mechanisms as proven in fig 4.

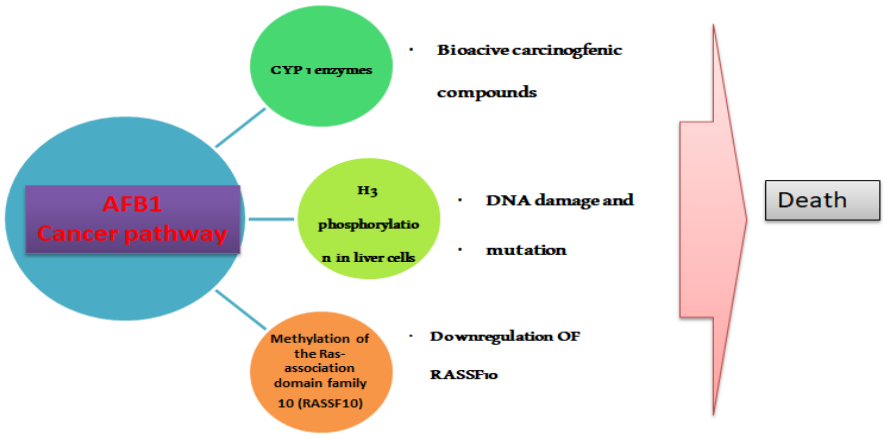

Figure4 Modes of action of AFB1 to initiate cancer

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