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EFFECT OF FUMONISIN B1 ON HISTOLOGY OF SPLEEN OF BROILER CHICKEN *GALLUS GALLUS*

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ABSTRACT : The present results of our study showed exhibited severe damage in spleen tissue of chicken compare with the control including necrosis and decrease in the cell number along with vacuolation. A transverse section of the spleen tissue of the treatment group with toxin and *Petroselinum crispum* (1.5 g/kg%). The histological changes in the end grope, which is treated toxin with *Cinnamomum* (1.5g / kg%) shows bleeding and necrosis and in the transverse section of the spleen tissue.

Key words : Fumonisin, spleen, chicken.

INTRODUCTION

Fumonisin B was isolated in 1988 by Gelderblom *et al* (1988). It was chemically characterized by Bezuidenhout *et al* (1988) and shortly thereafter as 'macrofusine' by Laurent *et al* (1989a) from cultures of *Fusarium verticillioides* (Sacc.) Nirenberg (formerly known as *Fusarium moniliforme* Sheldon) (Marasas *et al*, 1979) as well as *Gibberella fujikuroi* (Leslie *et al*, 1996). The absolute stereochemical configuration of fumonisin B1.

The chemical structure of the fumonisins was first reported in 1988 (Fig. 1). For more information on the chemistry and analytical methods for fumonisins (Krska *et al*, 2007). Since then, more than 28 homologues have been discovered and more are likely to be found by Rheeder *et al* (2002) and Humpf and Voss (2004).

FB is the most common and, from a toxicological standpoint, the most thoroughly studied.

FB and FB4 are in order less prevalent and differ structurally from FB in the number and placement of hydroxyl groups on the molecule's hydrocarbon "backbone".

The structural similarity of fumonisins to the sphingoid bases sphinganine (Sa) and sphingosine (So) is critical to their ability to disrupt sphingolipid metabolism (Merrill *et al* (2001), Riley *et al* (2001) as discussed below.

When cooked under alkaline conditions (nixtamalization), as when maize is made into masa for tortillas and other foods (Bolger *et al*, 2001) and references therein), the tricarballylic acid (TCA) groups are cleaved, yielding a corresponding hydrolyzed FB (HFB 1), HFB 2, HFB etc. (also known as aminopolyols (Bouhet amd Olwald, 2007), which have been found in alkaline cooked products (Voss *et al,* 2006a).

Partially hydrolyzed fumonisins, that is, those lacking one TCA group, have also been found in the faeces of rats (Frank Ross, personal communication) and nonhuman primates (Shephard *et al*, 1994); while the mechanism of their formation is not well understood, it is likely carried out by gut microflora.

The health effects of partially or fully hydrolyzed fumonisins to agriculturally important species has not been established, but is likely not significant. This expectation is based on the low amounts of these compounds found in maize (Shephard *et al*, 1994) and their comparatively (relative to FB 3) low biological activity and toxicity *in vivo* (Gelderblom *et al*, 1996 and Howard *et al*, 2002).

Mycotoxins are secondary fungal metabolites associated with severe toxic effects to vertebrates. They are produced by many phytopathogenic and food spoilage fungi including the *Aspergillus*, *Penicillium*, *Fusarium*, and *Alternaria* species. Food and feed contamination with mycotoxins is a worldwide problem. Beside their toxic effects on other organ systems, mycotoxins are neurotoxins that can produce a wide spectrum of behavioral and cognitive changes, ataxia and convulsions.

Fumonisins are produced by *Fusarium verticillioides* (formerly = *F. moniliforme*), *F. proliferatum* and other

Fusarium species (Gelderblom *et al*, 1991; Bolger *et al*, 2001; Glenn, 2007). The most frequent and potent among them is fumonisin B1 (FB1). Fumonisin B1 which, is produced by the genus Fusarium, is the best known and most toxic of the Fusarium toxins (Manning, 2001). FB1 frequently occurs with FB2 and they are mainly produced by *F. verticillioides* and *F. proliferatum*, which occur predominately in maize. The toxicological and pathological effects of fumonisins have been extensively studied in laboratory animals; the liver and kidney are the major target organs but species-, strain- and sex-dependent differences in dose–response occur (Riley *et al*, 1996).

FB1 can also have adverse effects on the central nervous system in carp (*Cyprinus carpio*). FB1 is a hydrophilic molecule with low molecular weight (500 Da), which can pass through the blood brain barrier (BBB) of young individuals. The BBB is a structure that allows selective entry of oxygen and glucose into the brain and spinal cord while preventing the entry of a spectrum of large, potentially toxic molecules. Once FB1 reaches the brain, it produces edemas and cell degeneration (Kovaèiæ *et al*, 2009).

Further, fumonisins also have immunosuppressive effects in many species as it was found that FB1 reduces the amount of macrophages, inhibiting immunological function activity against pathogens and diminishing levels of antibodies. FB1 can therefore lead to increased vulnerability to infectious diseases (Mello and Placinta, 1999).

In all animal species analyzed, FB1 has been proven to be both hepatotoxic and nephrotoxic (Lyon, 2002; Tardieu *et al*, 2007). Therefore, our study was focused mainly to evaluate the histopathological findings due to Toxicological aspects of FB1 in cultured *O. niloticus*.

Mycotoxins are structurally diverse compounds produced by filamentous fungi that vary in their chemistry and biological effects (Sudakin, 2003). Among the various mycotoxins, aflatoxins (AFs), ochratoxin A (OTA), T-2, zearalenone (ZEN) and deoxynivalenol are often encountered in foodstuffs in different parts of the world. In nature, mycotoxins rarely occur as a single contaminant since many fungal species that produce mycotoxins grow and produce their toxic metabolites under similar conditions.

Furthermore, a typical animal diet is made up of several sources, each of which may be contaminated with a different mycotoxin or more than one mycotoxin. Thus, mixed feeds, made from foodstuffs contaminated with individual mycotoxins, may have all the mycotoxins present in different individual ingredients. The consumption of multiple mycotoxin contaminated diet may induce hematological, biochemical and liver physiological changes and growth depression in animals (Awad *et al*, 2006a) and thus the presence of mycotoxins in poultry feeds causes significant economic losses to animal industries (Awad *et al*, 2006b).

At present, the most potent dietary approach to prevent mycotoxicoses in poultry is the use of adsorbents (Surai and Dvorska, 2005).

In the last few years, most studies related to the alleviation of mycotoxicosis by the use of adsorbents are focused on aluminosilicates (mainly zeolites, hydrated sodium calcium aluminosilicates (HSCAS) and aluminosilicate-containing clays) and esterified glucomannan (EGM) derived from cell wall of Saccharomyces cerevisiae1026. Several studies have revealed aluminosilicates (Pasha *et al*, 2007; Gowda, 2008) and esterified glucomannan (Julia *et al*, 2007; Girish and Smith, 2008) have shown considerable promise in countering aflatoxins.

However, single mycotoxin adsorbent lack binding effects against multiple mycotoxins of practical importance (Edrington *et al*, 1997; Watts, 2003) reported that addition of HSCAS to diets containing multiple mycotoxins did not prevent the negative effects observed in poultry. Yiannikouris and Jouany (2002) revealed that EGM was not effective in counteracting the toxic effects of multiple mycotoxins. Huwig *et al* (2001) revealed the addition of different adsorbents to animal feed provided versatile tools of preventing mycotoxicosis. Therefore, the present trial was conducted to evaluate the effects of a compound mycotoxin adsorbent (CMA), the mixture of EGM and HSCAS on growth performance, hematological and serum biochemical parameters and liver morphology in broilers chickens exposed to mold contaminated feed.

Fumonisins are mycotoxins that are produced by several fungus species, especially *Fusarium verticillioides* and *Fusarium proliferatum*, which produce large amounts of these mycotoxins and are present in several places in the world as contaminants in corn plantations (Voss *et al*, 2007). Streit *et al* (2013) estimated that 50–63% of all grains produced for livestock feeding in the world are contaminated with fumonisins with a worldwide average of 0.914 mg/kg. In positive samples, the average level of fumonisins was 1.689 mg/kg, and the maximal level was approximately 77.502 mg/kg. Contamination with mycotoxins in grain plantations has attracted economic and scientific interest because these plantations are widely

used for livestock and human feeding.

Several countries have implemented laws that limit the maximal levels of fumonisins and other mycotoxins that are allowed in foods for human and animal consumption. The limits established by law are generally obtained by extrapolating experimental data and a revision of permissible levels may be necessary based on new data that become available (Voss *et al*, 1996). Fumonisins were isolated and chemically characterized for the first time in 1988. Since then, 28 analogs have been described.

Fumonisin B1 (FB1) is the most abundant analog representing 70–80% of the total amount. Fumonisin B2 (FB2) represents 15–25% and the remaining analogs occur in low amounts (Rheeder *et al*, 2002). Despite almost 30 years of research, the mechanism of action of fumonisins is not yet fully understood. Wang *et al* (1991) reported that FB1 is a potent inhibitor of ceramide synthase, a key enzyme in the de novo synthesis and turnover of complex sphingolipids, such as sphingomyelin and glycosphingolipids, which participates in the composition of cellular membranes.

In cells exposed to fumonisins, the synthesis of ceramide is reduced with a consequent decrease in the amount of sphingolipids and increase in their precursors, sphinganine and sphingosine. In addition to their structural role in cellular membranes, sphingolipids and their metabolic precursors participate in cellular signaling (Soriano *et al*, 2005). Thus, alterations caused by fumonisins in the metabolism of sphingolipids impact other metabolic pathways, thereby leading to alterations in development, morphology and cell survival (Merril *et al*, 1997).

The consumption of foods that are naturally contaminated with fumonisins is related to the development of porcine lung edema and equine leukoencephalomalacia (Waes *et al*, 2005), which is a disease characterized by necrosis of the brain hemispheres. In humans, epidemiological studies indicate a relationship between the ingestion of fumonisins and an increased incidence of defects in neural tubes (Kovaèiæ *et al*, 2009).

The intake of fumonisins may also be related to neurodegenerative diseases, such as multiple sclerosis, Alzheimer's disease and Parkinson's disease (Purzycki and Shain, 2010; Domijan, 2012). Several studies have been conducted with the objective of clarifying the mechanisms by which fumonisins induce toxicity in the nervous system (Bouhet and Oswald, 2007). However, until now, such studies have focused on the effects on the central nervous system and rarely investigated the effects on the peripheral nervous system.

Despite evidence that fumonisins affect the digestive system (Anderson *et al*, 2006), leading to alterations in intestinal absorption, increased susceptibility to infections, and alterations in the intestinal immune response, no study of which we are aware of has investigated the effect of these mycotoxins on the enteric nervous system, which is responsible for the intrinsic innervation of this system.

The enteric nervous system is the more complex portion of the peripheral nervous system. It is indispensable for maintaining homeostasis in the digestive system and an excellent model for the study of the nervous system as a whole (Jaskiewicz *et al*, 1987). Considering that exposure to neurotoxic substances during childhood can cause neurological problems later in development, the present study evaluated the effects of a fumonisin-contaminated diet (1 and 3 mg/kg fumonisin) on the myenteric plexus of the jejunum in developing rats.

Fumonisins, mycotoxins produced by *Fusarium moniliforme* and other Fusarium species are common contaminants of com. Although hepatic injury has been induced experimentally in all vertebrate species studied of Kellerman *et al* (1990), Haschek *et al* (992), Ledoux *et al* (1992), Voss *et al* (1993) and Harrison *et al* (1990), other target organs appear to be more species-specific. Ingestion of fumonisin-contaminated com has been associated with spontaneous outbreaks of equine leukoencephaIomalacia (Haschek *et al*, 1992) and acute pulmonary edema in pigs (Fincham *et al*, 1992 and Anfal *et al*, 2017). Other species-specific effects induced experimentally by fumonisin include renal injury in rats (Harrison *et al*, 1990). The genetic study of Spleen of chicken, which is treating with four substances which include Antitoxin (A) *Petroselinum crispum* (M), (D) and Treatment (T) which represent Fumonisin (fungal toxin).

MATERIALS AND METHODS

Experimental animals

Total of twenty chicken were used for this experiment. The chicken were kept for two weeks before commencement of fumonisin administration. This was in order to allow the chicken acclimatized to the environment. The chicken were given adequate feed (grower mash), water and kept under good ventilation.

Experimental design (chicks)

Twenty five, one-day-old broiler chicks (Faobrow CD) were obtained from a commercial hatchery, individually weight, wing-banded and housed in experiment room and continuous fluorescent lighting. The birds were randomly assigned to 5 treatment groups (5 birds/each). Control group feed without toxin addition,

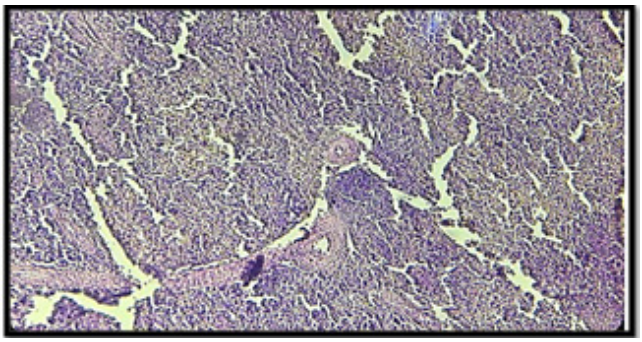

Fig. 1 : A transverse section of the spleen tissue of the control group shows the tissue in its natural form (Hematoxylin & Eosin 40X).

energy (Kcal/kg) according to feed factory (Ghadeirbabil)/ Babylon, Iraq.

Protocols : (1) Tissue processing and staining

At the end of eight weeks of oral administration of fumonisin to the chicken, except group I that received distil water only, they were humanely sacrificed by anesthetizing them in a suffocating chamber using chloroform. The thoracic regions of the chicken were dissected and the lungs were removed, and immediately fixed in formalin.

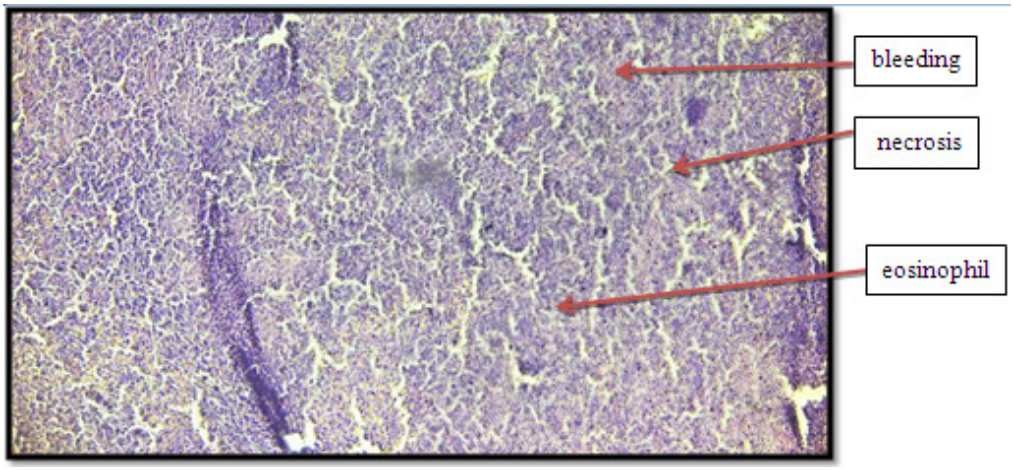

Fig. 2 : A transverse section of the spleen tissue of the treatment group shows necrosis, bleeding and eosinophil (Hematoxylin & Eosin 40X).

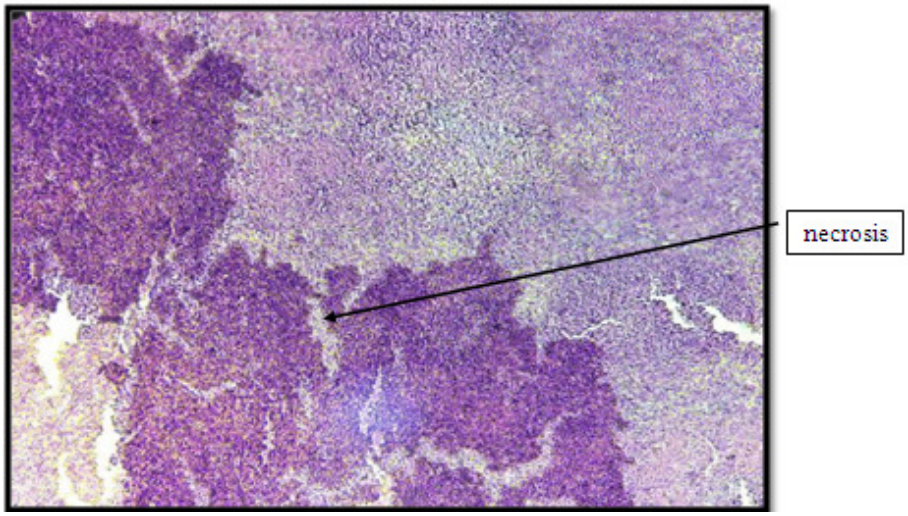

Fig. 3 : A transverse section of the spleen tissue of the treatment with antitoxin group shows necrosis (Hematoxylin & Eosin 40X).

(treatment1) fumonisin toxin (729 ppb) (treatment 2), fumonisin toxin with antitoxin (treatment 3), toxin with *Petroselinum crispum* (1.5 g/kg%) (treatment 4), toxin with *Cinnamomum* (1.5g / kg%) (treatment 5). Feed and water were provided for ad libitum consumption. Chicks were reared in individual wire cages for 30 days and fed a typical broiler with crude protein and metabolizable

After fixation, the lungs were transferred into an automatic processor where they went through a process of dehydration in ascending grades of alcohol (ethanol) 70%, 80%, 95% and absolute alcohol for 2 changes each. The tissues were then cleared in xylene and embedded in paraffin wax. Serial sections of 5 micron thick were obtained using a rotary microtome. The tissue sections

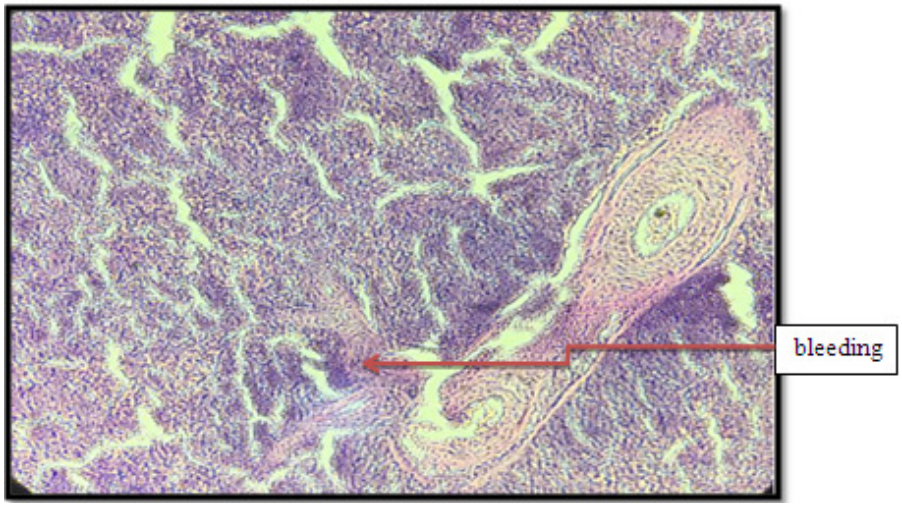

Fig. 4 : A transverse section of the spleen tissue of the treatment group with darsin shows bleeding (Hematoxylin & Eosin 40X).

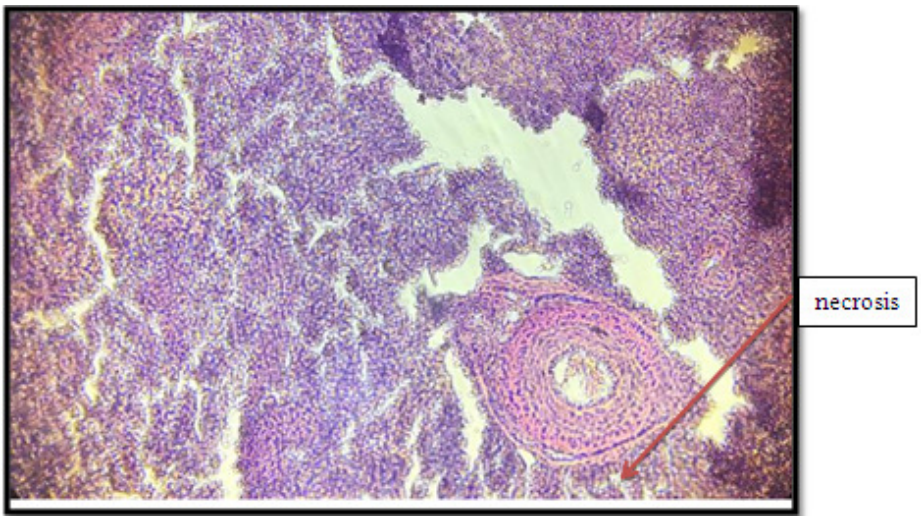

Fig. 5 : A transverse section of the spleen tissue of the treatment group with madanos shows necrosis (Hematoxylin & Eosin 40X).

were deparaffinised, hydrated and stained using the routine haematoxylin and eosin staining method (H&E).

The stained sections were examined under the light microscope fitted to a digital camera and lap top.

RESULTS

The results presented in Fig. 1 summarized the histological structure observed in spleen of adults chicken of the control group shows the tissue in its natural form. In Fig. 2 showed a transverse section of the spleen tissue of the treatment group shows necrosis, bleeding and eosinophil, while the result of group, which treated with with antitoxin group shows necrosis (Fig. 3). Fig. 4 a transverse section of the spleen tissue of the treatment group with darsin shows bleeding. The histological changes in the end group, which is treated in madanos showed necrosis in the transverse section of the spleen tissue (Fig. 5).

Spleen of chicken in control groups showed normal red and white pulp (Fig. 1).

The identified pathological changes were represented by hepatocytes vacuolation and cellular membrane damage (necrosis), nuclei grown in size; toxic injury and focal tissue necrosis in target organ, severe vacuolar degeneration of hepatocytes, biliary hyperplasia and mild vacuolar degeneration and apoptotic cells.

DISCUSSION

The present results exhibited severe damage in spleen tissue of chicken compare with the control including necrosis and decrease in the cell number along with vacuolation.

Similar results were recorded by Uguz *et al* (2003), who reported a significant increase in the cells after one week of 4-nonylphenol exposure. Hughes *et al* (2000) have shown NP-induced cell death.

Galembeck *et al* (1998), Hughes *et al* (2000), Uguz *et al* (2003) reported that the disappearance of the cell membranes could be due to the lytic activity of alkylphenols.

The presented data showed that birds treated with fumonisin B1 developed significant pathomorphological alterations mainly in the spleen.

The extensive apoptotic and necrotic changes in the spleen of chickens fed FB1-polluted crops disturb the performance, proliferation and activation of T and B lymphocytes and their antigenic response, resulting in the absence of plasma cells and antibody production (lack of ER structures).

Decreased spleen cell viability and mitogenic response caused by FB1 were reported by Keck and Bodine.

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