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Abstracts

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STUDIES ON FUMONISIN B1 IN RABBITS
Saad, A.E.*, Hammad, A.M.** and Tantawy, A.A.***
** Mycology Dept., Animal Health Research Institute, Dokki.

ABSTRACT
The present study was carried out to investigate the effect of fumonisin B1 (FB1) contaminated feed on the immune response of rabbits to inactivated rabbit pasteurellosis-vaccine as well as the pathological changes induced by this toxin in the internal organs of intoxicated rabbits. Feeding of rabbits on FB1 2.29 and 1 ppm contaminated feed induced immunosuppressive effect on the humoral immunity of these rabbits and consequently lowered their resistance to subsequent challenge with virulent Pasteurella multocida organism. The immunosuppressive effect was evidenced by lower antibody titers measured by indirect haemagglutination test (IHT) in rabbits which received FB1 and vaccinated in comparison with the antibody titre reported in control-fed and vaccinated rabbits. This effect was dose-dependent where, rabbits fed on FB1 2.29 ppm showed lower antibody titers than those fed on FB1 1ppm. Moreover, high mortalities which reached 80 and 40 % were reported in the vaccinated challenged rabbits fed on FB1 in a dose of 2.29 and 1 ppm respectively while the deaths in the vaccinated and unvaccinated control fed rabbits were 10 and 100 % respectively.

The pathological pictures in rabbits fed on FB1 1ppm and 2.29 ppm were nearly similar. However, the severity of the lesions was more in rabbits fed on higher dose of FB1 than those recorded in rabbits fed on low dose. Severe congestion and enlargement of the liver and kidneys, softening of the brain, together with edematous lungs and small sized spleen were the main gross lesions in both groups. Histopathologically, the recorded lesions were mainly in the kidneys and liver followed by the lungs, brain, spleen and heart. The most consistent hepatorenal lesions were represented by degeneration and necrosis with lymphocytic infiltration. The lungs showed severe congestion and inflammatory edema, particularly in rabbits which were fed on FB1 2.29 ppm. The brain showed congestion, perivascular cuffing, focal hemorrhages and cerebral encephalomalacia. Moreover, cardiac hyalnosis and splenic necrosis were noticed only in rabbits which were fed on higher dose.
INTRODUCTION

Fumonisins are mycotoxins produced by certain fusarium moulds principally *Fusarium moniliforme*, a world wide corn contaminant. It is already well known that fumonisins are associated with various animal toxicosis and carcinomas including equine leukencephalomalacia, porcine pulmonary edema, hepatotoxicosis, hepato-carcinomas and nephrotoxicosis in addition to their immunosuppressive effects. Among fumonisin isomers fumonisin B1 (FB1) is a predominant molecular form and a major toxicant (Segvic and Pepeljnjak, 2001). The different toxic effects of FB1 were evaluated in many species of animals and poultry. Adult rabbits, intravenously injected with FB1 in different doses, were anorectic and showed liver lesions in the form of mild necrosis, hepatic vacuolation and bile stasis (Gumprecht et al., 1995). Pregnant rabbits dosed FB1 died. They showed focal hemorrhages and malacia in the cerebellum with a marked degeneration of the renal tubular epithelium and hepatocytes (Bucci et al., 1996). Erythroid depletion and myeloid hyperplasia followed feeding of rabbits on FB1-contaminated feed (Mariscal et al., 1997). Moreover, hepatorenal lesions were recorded after FB1 intoxication in pregnant rabbits and fetuses (Kovacs et al., 2003).

The immunosuppressive effect of FB1 was detected in poultry by Javed et al. (1995) who reported impaired anti-ND haemagglutination inhibition antibodies associated with a decrease in the total serum globulin in broiler chicks, fed on FB1-contaminated diet. A decrease in the weight of the bursa Fabricius was detected in turkeys, fed on FB1-contaminated ration (Leitgeb et al., 2000). Also, Li et al. (2000) found that the turkey poults fed on diet containing FB1 showed a lower antibody response to ND vaccine. However, no studies have been carried on the immunosuppressive effect of FB1 in rabbits. So this investigation was planned to determine the effects of FB1-contaminated feed on the immune response of the rabbits to the inactivated rabbit pasteurellosis-vaccine and the associated lesions in the different body organs of the rabbits intoxicated with two doses of FB1 (1 and 2.29 ppm).
MATERIAL AND METHODS

1- Rabbit pasteurellosis vaccine and challenge:

Commercial formalized polyvalent rabbit pasteurellosis vaccine and virulent *P. multocida*, used in challenge, were obtained from the Vet. Serum and Vaccine Research Institute, Abbasia, Cairo.

2- Assay of feed:

To ensure the absence of FB1 mycotoxin, the control feed was assayed fluorometrically using the method described by Hansen (1993).

3- Preparation of fumonisin B1 mycotoxin:

*Fusarium moniliforme* was isolated and identified from local commercial diet of rabbits according to Booth (1977). FB1 was produced by the isolated *Fusarium moniliforme* according to the method described by Wyllie and Morehouse (1978). Then, the produced toxin was measured using VICAM fluorometric method of Hansen (1993).

4- Animals and experimental design:

Sixty white New Zealand rabbits (2 months old) were divided into six equal groups (1-6). Groups (1-4) were used to study the effect of FB1 on the immune response to rabbit pasteurellosis-vaccine. While groups (5 & 6) were used to study the pathological changes associated with this toxicity (table 1). Groups (1&5) received FB1 2.29 ppm contaminated feed (Laborde et al., 1997). While groups (2&6) were fed on FB1, 1 ppm contaminated feed (Mariscal et al., 1997). Groups (3&4) were fed on a control feed, without toxin. Feeding of rabbits on FB1-contaminated diet was continued for one month. During the 2\textsuperscript{nd} and 4\textsuperscript{th} weeks, post receiving the contaminated feed, rabbits of groups (1-3) were vaccinated with formalized rabbit pasteurellosis-vaccine subcutaneously (1 ml/rabbit). After 4 weeks, after the last vaccination, rabbits of groups (1-4) were challenged by intranasal (i/n) instillation of 0.25 ml of broth culture of virulent *P. multocida* strain containing $2 \times 10^{10}$ CFU/ml according to Borkowska et al. (1996). The challenged rabbits were observed for two weeks and the mortalities, signs and lesions were recorded. Reisolation of *P. multocida* from the internal organs (heart blood, liver and spleen) of the dead challenged rabbits was tried.

5- Blood samples:
Blood samples were collected from the marginal ear-veins of the individual rabbits in groups (1-4) before vaccination, beside one week, 2 weeks and 3 weeks post the last vaccination and at challenge. The blood was allowed to clot and sera were separated and inactivated at 56°C for 30 minutes and frozen at -20°C until tested serologically.

6- Assay for humoral immunity:

Indirect haemaggultination test (IHT), described by Carter and Rappy (1962), was used for the measurement of the serum antibody levels for *P. multocida*.

7- Tissue specimens:

Small tissue specimens from different internal organs including the liver, lungs, kidneys, heart, spleen, brain and intestines of the sacrificed rabbits in groups (5 & 6) were collected after four weeks of feeding of the contaminated food. Moreover similar samples were taken form the dead rabbits in groups (1-4) after challenge. These specimens were immediately fixed in 10 % neutral buffered formalin. After proper fixation, the specimens were dehydrated in alcohol, cleared in xylol, embedded and casted in paraffin. Five microns thick paraffin sections were prepared and stained with hematoxylin and eosin stain for microscopical examination according to Drury and Wallington (1986).

### RESULTS

Table (2) shows the mean antibody titers, measured by the IHT, in the experimental rabbits fed on the contaminated feed with FB1 in doses of 2.9 and 1 ppm as well as the unvaccinated and vaccinated control rabbits. It is clear that lower humoral antibody titers were detected in the FB1 exposed rabbits (groups 1&2) as well as the unvaccinated control fed rabbits (group 4) in comparison to the higher antibody titers, detected in the vaccinated rabbits fed on normal ration (group3).

The results of challenge test, in the experimental rabbits, are indicated in table (3). Higher mortalities were recorded in groups (1,2 &4) in percentages of 80, 40 and 100 % respectively. While 10 % deaths were encountered in group (3). Higher recovery rates of *P. multocida*, from the dead challenged rabbits, were obtained from groups (1,2 & 4) in percentages of 87.5, 75 and 100 % respectively. While no *P. multocida* was recovered (0%) from the challenged rabbit of group (3) which died.

**Pathological findings:**

**Gross findings:**
Group (6): The liver was enlarged, congested and showed minute white foci on its surface. The gallbladder was distended with bile. The kidneys were swollen, pale, soft and their cut surface showed dark red medulla. The examined lungs were edematous and showed emphysematous and reddish areas. The spleen was smaller in size and dark brownish-red in color. Softening of the brain and congestion of the cerebral blood vessels were seen. Moreover, severe congestion of the blood vessels and capillaries of the intestine and myocardium were also noticed.

Group (5): Nearly similar gross lesions, as in group 6, were noticed in this group, however the picture was more severe.

Groups (1 & 2): The lesions were similar to those of groups (5 & 6) with severe congestion of the visceral blood vessels, enlargement of the internal organs and presence of multiple minute grayish white areas in the liver besides pneumonic foci in the lungs.

Group (3 & 4): There were no characteristic gross lesions in the examined rabbit which died in group (3), while in group (4), a characteristic macroscopic picture of fibrinous pneumonia with severe hydrothorax were noticed in addition to congestion and enlargement of the internal organs.

Microscopic findings:

Kidneys:

Group (6): Multiple focal degenerative changes, in the form of cloudy swelling and vacuolar degeneration of the renal epithelium were prevalent. Congestion of the renal blood vessels, intertubular blood capillaries and glomerular tufts with perivascular lymphocytic aggregations were seen. Focal intertubular hemorrhages and perivascular edema with lymphocytic aggregations, mostly around the glomeruli, were observed.

Group (5): Lesions, similar to those of group (6), were encountered besides recent thrombosis and coagulative necrosis of the renal epithelium were seen (Fig. 1). Shrinkage and even necrosis of the glomerular tufts with cystic dilatation of the renal tubules and flattening of their lining epithelium were found (Fig. 2). Severe medullary congestion of the intertubular blood capillaries with desquamation and necrosis of the renal epithelium were found. Moreover, proliferation of the
interstitial tissues with leucocytic infiltration, mostly lymphocytes, were observed (Fig. 3).

Liver:

Group (6): Congestion of the hepatic sinusoids, central and portal veins with activation of the Kupffer's cells and vacuolation of the hepatocytes were prevalent. Moreover, perivascular edema and mononuclear cellular aggregations mostly lymphocytes, were seen in the portal areas (Fig. 4).

Group (5): Severe congestion of the central veins and sinusoids with presence of focal hemorrhages were found (Fig. 5). Thrombosis of the portal vessels with hyperplasia of the bile ductal epithelium and periductal lymphocytic infiltration were noticed (Fig. 6). Multiple coagulative necrosis of hepatocytes were prominent (Fig. 7). Moreover, fibrous connective tissue proliferation, surrounding numerous non-functional bile ductules in the portal areas, was detected in some examined livers.

Lungs:

Group (6): Severe congestion of the pulmonary blood vessels and interalveolar capillaries was seen. Inflammatory edema, represented by pale eosinophilic homogenous material infiltrated with mononuclears, mainly lymphocytes, was detected (Fig. 8). Moreover, hyperplasia of the bronchial epithelium, peribronchial lymphocytic infiltration and multiple large areas of compensatory alveolar emphysema were found.

Group (5): The lesions were similar to those of group (6), however, extensive leucocytic infiltration with severe pulmonary edema involving large areas of the pulmonary tissues were observed.

Brain:

Group (6): Congestion of the cerebral blood vessels and meningeal capillaries with aggregations of few lymphocytes around some capillaries were found.

Group (5): The lesions were similar to those of group (6) besides, vacuolation of the cerebral tissues was seen (Fig. 9). Focal cerebral hemorrhages together with neural degeneration, neurophagia and gliosis were also noticed (Fig. 10).

Heart:
Group (6): The myocardium showed congestion of the intermuscular blood vessels and capillaries.

Group (5): Severe congestion of the myocardial blood vessels and focal hyalinization of cardiac muscle fibers were encountered (Fig. 11).

Intestine:

Group (6): Catarrhal enteritis characterized by activation of the goblet cells and hyperplasia of the mucosal lining epithelium with presence of bluish mucous exudates, mixed with cellular debris in the lumen, was noticed. Moreover, leucocytic infiltration of both the mucosa and submucosa, mainly with lymphocytes was also found.

Group (5): The lesions were similar to those described for group (6).

Spleen:

Group (6): Congestion of the splenic blood vessels and sinusoids with excessive deposition of brown granules of hemosiderin were noticed. The walls of the splenic blood vessels were thickened due to perivascular edema. Lymphoid depletion was seen in the white pulp (Fig. 12).

Group (5): Severe depletion of the lymphoid tissues of the white pulp and excessive hemosiderosis were detected. Moreover, multiple areas of necrosis in the splenic lymphoid tissues, were also noticed.

Groups (1 & 2):

The microscopic examination of the internal organs of rabbits in groups (1&2) revealed nearly similar findings like the non-challenged groups (5&6). However, characteristic fibrinous pneumonia evidenced by severe congestion of the pulmonary blood vessels with presence of eosinophilic network of fibrin threads mixed with mononuclears, mostly lymphocytes in the lumens of alveoli, were detected in the examined lungs.

Groups (3 & 4):

No abnormal microscopical changes were seen in the examined organs of dead rabbit in the group (3). However, fibrinous pneumonia with severe congestion and leucocytic infiltration of the internal organs, mainly liver and kidneys were encountered in group (4).
Although *Fusarium moniliforme*, which produces FB1, is a widely corn contaminating fungus there is a few available information about the effect of FB1 in rabbits. This stimulated us to carry out the present investigation as a trial to demonstrate both the immunosuppressive effect of FB1 and the lesions induced by this toxin in rabbits. The immunosuppressive effect was studied in rabbits fed on contaminated diet with FB1 (2.29 and 1 ppm), and vaccinated with inactivated rabbit pasteurellosis vaccine. The FB1 showed an adverse effect on the humoral immunity of rabbits, fed on FB1 contaminated feed. The antibody titers, measured by the IHT, were considerably higher in the control (normally) fed and vaccinated rabbits (group 3) when compared with those of the FB1-exposed rabbits (groups 1 and 2) as well as the normally fed and unvaccinated rabbits (group 4). This adverse effect began from the 2nd week post-vaccination and was dose-dependent where rabbits of group (1) showed lower antibody titers when compared with those of group (2). This suppressed antibody-titer could be attributed to a hepatorenal toxic effect of FB1 which was confirmed by the histopathological changes observed in the present study where degeneration and necrosis were found in the examined liver and kidneys. This opinion gets along with the idea that the hepatotoxic effect of FB1 inhibits protein-synthesis and subsequently inhibits the antibody production. Also the renal damage followed by a loss of large amounts of immunoglobulins through the impaired kidneys lead to hypoproteinaemia and decrease in the levels of the circulating immunoglobulins. Moreover, similar hepatotoxic and renal toxic effects of FB1 were previously reported in rabbits by Gumpercht et al. (1995), Bucci et al. (1996) and Kovacs et al. (2003) and in chicken by Brown et al. (1992) and in ducks by Bailly et al. (2001) and in turkey poults by Ledoux et al. (1996). The immunosuppressive effect of FB1 could be explained by its effect on the spleen where lymphoid depletion and necrosis were noticed in the microscopic examination of the spleen. Our results are partially in agreement with Javed et al. (1995) and Li et al. (2000) who reported impaired and lower antibody response to ND vaccine in chicks and turkey poults fed on FB1- contaminated feed, and with Wafaa et al. (2000) who recorded adverse effect of aflatoxin B1 (AFB1) on the humoral and cellular immunity in AFB1 exposed rabbits and vaccinated with inactivated rabbit pasteurellosis vaccine.
The challenge test reflected the immunological status and resistance of the treated rabbits. It is clear that, rabbits failed to develop a high antibody titers in groups 1 and 2 (FB1 exposed) or in group 4 (control fed and unvaccinated). The mortality rates were 100, 80 and 40% in groups (4, 1 & 2) respectively. At challenge, the mean antibody titers were 64, 24 and 4 in groups (2,1 & 4) respectively. The normally fed and vaccinated rabbits (group 3) showed a low mortality (10%) and a high antibody titer (the mean antibody titer was 1024) at challenge. Our results are partially in agreement with those reported by Wafaa et al. (2000) who reported 21% deaths in the control-fed vaccinated rabbits in comparison with 43% mortality in AFB1 intoxicated vaccinated rabbits.

The rate of isolation of \( P.\ multocida \), from the rabbits which died after challenge, was higher (100%) in the control fed and unvaccinated rabbits, (group 4) in comparison with the other experimental groups (groups 1-3). Rabbits fed on FB1 (2.29 ppm) contaminated feed, showed 87.5% isolation of \( P.\ multocida \) compared with 75% isolation from rabbits which received FB1 (1ppm) contaminated feed. These findings are in concurrence with Wafaa et al. (2000).

In the present study, the lower antibody titer or vaccination failure, detected in rabbits fed on FB1 contaminated feed, could give a reason for the outbreaks of pasteurellosis which occurred in rabbitries adequately vaccinated with efficient inactivated \( P.\ multocida \) vaccines. Moreover, the consumption of feed contaminated with FB1 will increase the susceptibility of the immunized rabbits not only to pasteurellosis but also for other infectious diseases. Similar studies by Pier and Heldstone (1970) and Batra et al. (1991) showed a vaccination failure and a decreased resistance to \( P.\ multocida \) and other infectious diseases in birds exposed to AFB1.

According to the results of the pathological examination of the internal organs of rabbits intoxicated with FB1, it was clear that, FB1 caused a variety of lesions in the various organs, particularly the liver and kidneys followed by the lungs, brain, heart and spleen. The severity of these lesions was increased with increasing the dose.

Regarding the effect of FB1 on the renal tissue of rabbits, the microscopic examination of the kidneys revealed renal congestion and intertubular hemorrhages. These vascular changes reflected the effect of toxin on the blood vessel-walls depending on the base that FB1 interferes with the synthesis of complex glycol-sphingolipid which resulted in disturbance of the endothelial cell-permeability. Moreover, in the present work, degeneration
Fig. 1, group (5): Kidney showing extensive coagulative necrosis of the renal epithelium. H & E, X200

Fig. 2, group (5): Kidney showing cystic dilatation of some renal tubules with leucocytic infiltration in the interstitial tissues and shrunken necrotic glomerular tufts. H & E, X200

Fig. 3, group (5): Kidney showing proliferation of the interstitial connective tissue and leucocytic infiltration. H & E, X200

Fig. 4, group (6): Liver showing congestion of the portal vessels with perivascular lymphocytic aggregations. H & E, X200
Fig. 5, group (5) : Liver showing focal hemorrhages. H & E, X200

Fig. 6, group (5) : Liver showing thrombosis of blood vessel and hyperplasia of the bile ductal epithelium. H & E, X200

Fig. 7, group (5) : Liver showing focal coagulative necrosis of hepatocytes. H & E, X200

Fig. 8, group (6) : Lung showing pulmonary edema with round cells infiltration, mostly lymphocytes. H & E, X200
Fig. 9, group (5): Brain showing vacuolation of the cerebral tissues. H&E, X200.

Fig. 10, group (5): Brain showing focal gliosis. H&E, X200.

Fig. 11, group (5): Myocardium showing hyalinization of some muscle fibers. H&E, X200.

Fig. 12, group (6): Spleen showing slight depletion of the lymphoid tissues of the white pulp H&E stain X200.
**Table (1):** Rabbit groups, number and treatments.

<table>
<thead>
<tr>
<th>Group</th>
<th>No of rabbits</th>
<th>Type of treatment</th>
<th>challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>Fed on FB1 contaminated feed (2.29 ppm) and vaccinated</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>Fed on FB1 contaminated feed (1 ppm) and vaccinated</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>Normal ration and vaccinated</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>Normal ration and unvaccinated</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>Fed on FB1 contaminated feed (2.29 ppm) and used for histopathology</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>Fed on FB1 contaminated feed (1 ppm) and used for histopathology</td>
<td>-</td>
</tr>
</tbody>
</table>

**Table (2):** Rabbit groups, treatments and mean antibody titre.

<table>
<thead>
<tr>
<th>Group</th>
<th>Type of treatment</th>
<th>Mean antibody titre *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>FB1 (2.29ppm) contaminated ration and vaccinated</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Fed on FB1 (1ppm) contaminated ration and vaccinated</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Normal ration and vaccinated</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Normal ration and unvaccinated</td>
<td>5</td>
</tr>
</tbody>
</table>

*Measured by indirect haemagglutination test (IHT)*
Table (3): Rabbit groups, treatments, titers, dead to challenged rabbits, mortalities and reisolation of *P. multocida*.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Titers at challenge*</th>
<th>No of dead/ No of challenge</th>
<th>Mortality %</th>
<th>P. multocida reisolation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FB1 (2.20 ppm) contaminated ration and vaccinated</td>
<td>24</td>
<td>8/10</td>
<td>80</td>
<td>7/8</td>
</tr>
<tr>
<td>2</td>
<td>FB1 (1 ppm) contaminated ration and vaccinated</td>
<td>64</td>
<td>4/10</td>
<td>40</td>
<td>3/4</td>
</tr>
<tr>
<td>3</td>
<td>Normal ration and vaccinated</td>
<td>1024</td>
<td>1/10</td>
<td>10</td>
<td>0/10</td>
</tr>
<tr>
<td>4</td>
<td>Normal ration and unvaccinated</td>
<td>4</td>
<td>10/10</td>
<td>100</td>
<td>10/10</td>
</tr>
</tbody>
</table>

*Mean antibody titer at the time challenge*
REFERENCES


and necrosis of the renal tubular epithelium and glomerular tufts were also observed mainly in group (2). This effect of FB1 was induced either by the accumulation of the toxin itself or its metabolites in the renal tissues or to acceleration of the programmed cell death in the kidneys induced by FB1 (Tolleson et al., 1996). Similar results were mentioned by Bucci et al. (1998) and Kovacs et al. (2003) in rabbits. In addition to the previously recorded renal lesions, focal interstitial fibrosis and cystic dilatation of some renal tubules were seen in the kidneys of some rabbits, fed on FB1 (2.29 ppm).

The hepatotoxic effect of FB1 was characterized by congestion and vacuolation of the hepatocytes at a low dose (1 ppm), while in larger dose (2.29 ppm), caused more severe focal hemorrhages and coagulative necrosis. These alterations were closely correlated with an increase in sphinganine concentration in the hepatic tissue, caused by FB1 (Voss et al., 1998). Similar hepatic lesions were also reported by Gumpercht et al. (1995), Bucci et al. (1996) and Kovacs et al. (2003) in rabbits, Ledoux et al. (1992) in broilers and Bondy et al. (1997) in mice. Moreover, proliferation of the bile ductal epithelium with lymphocytic infiltration in the portal areas, were recorded in our examined liver of rabbits exposed to 2.29 ppm FB1 (group 5). These changes could be attributed to the irritant effect of the toxin during its excretion through the bile ducts. These results are in harmony with those described by Gumpercht et al. (1995) in rabbits, Gelderblom et al. (1991) in rats; Ledoux et al. (1992) in broilers and Weibking et al. (1993) in turkey pouls.

The pulmonary lesions induced by FB1, were prominent particularly in group 5 (larger dose) where severe pulmonary edema, extensive leucocytic infiltration with large areas of compensatory alveolar emphysema were detected. These microscopic changes are in accordance with those recorded by Colvin et al. (1993) in the lungs of pigs.

The neurotoxic effect of FB1, in our examined rabbits, was characterized by congestion and perivascular cuffing in the brain of rabbits in groups (5 & 6) in addition to focal cerebral hemorrhages and encephalomalacia in group 5, (2.29 ppm of FB1). These microscopic lesions are completely in agreement with Bucci et al. (1996) and partially in agreement with Ficken et al. (1993) who recorded only encephalomalacia in turkey poults intoxicated with FB1.

In the present study, the histopathological examination of the spleen of rabbits, intoxicated with FB1, revealed its immunosuppressive effect. This effect was more prominent in group 5, (larger dose) where severe depletion and necrosis of the lymphoid
tissues of the splenic white pulp were found. The effect of FB1 on the lymphoid tissues could be explained by those mentioned by Martinova (1998) who reported that, FB1 disrupts the balance between the different subpopulations of lymphocytes, inhibits DNA-synthesis in lymphocytes and suppressed the immune response to T-dependent antigens.

Concerning the cardiac lesions, induced by FB1, congestion and focal myocardial hyalinosis were observed in rabbits fed on FB1 (2.29 ppm). These lesions are in a partial agreement with those of Gelderblom et al. (1988) who reported myocardial necrosis in the intoxicated rats with FB1. Moreover, our histopathological examination of the intestine of the intoxicated rabbits cleared that FB1 showed an irritant effect on the intestinal mucosa that was represented by development of catarrhal enteritis.

Regarding the necropsy and microscopic findings in the rabbits which died after challenge, the lesions were similar in groups (5&6) in addition to the lesions of acute pasteurellosis which characterized by fibrinous pneumonia.

From this study, it could be concluded that FB1 induced an immuno-suppressive effect and lesions, primarily in the liver and kidneys, followed by the lungs and brain. Consequently, the contamination of the feed with FB1 or by Fusarium moniliforme which is the main mould producer of FB1 must be taken in consideration as a problem in rabbit industry and extra-prophylactic measures should be introduced for the removal of FB1 from the rations. This could be done through the application of adsorbent agent technology by using commercially hydrated sodium calcium aluminosilicate and Egyptian montmorillonite which had an excellent capability to adsorb the toxin (Aly et al., 2004), or by the addition of nutritionally inert adsorbents like esterified glucomannan to decrease the toxicity in animals (Bursian et al., 2004).


دراسات على الفيومونزين بـ 1 في الأراين

أحمد علي محمد سعد 1، عبد الرحمن حداد 2، وأحمد عبد الحكيم طلطاوي 3

1 قسم الأمراض الدوائية كليية الطب البيطري بمستشفى جامعة القاهرة، فرع بيها.
2 قسم الطب، بمستشفى الأمراض الطبية، جامعة القاهرة، فرع بيها.
3 قسم الفيزيولوجيا كليية الطب البيطري بمستشفى جامعة القاهرة، فرع بيها.

أجريت هذه الدراسة لإظهار مدى تأثير العلف الملوث بالفيومونزين بـ 1 على الاستجابة المناعية للأرانب لمصابة بلقاع الباستريلا ملتوسيدا الميثاب وتلك التغيرات البالغة في الأعضاء الداخليّة التي أحدثت هذه السم في الأرانب المريضة. وقد أدت تغذية الأرانب على علف ملوث بالفيومونزين بـ 1، بتركيز 0.249 جزء في المليون إلى أحداث تأثير مثبت للمناعة المصلية لهذه الأرانب وبناءً عليه تقليل المقاومة لتحدي ميكروب الباستريلا ملتوسيدا الضار.

وقد وضح التأثير المثبت للمناعة بقلة مستوى الأجسام المضادة التي تم قياسها باختبار التلالان المناعي الدموي الغير مباشر في الأرانب المغذاة بالفيومونزين بـ 1، وتم الحصول عليها بالم Latter ≥ 0.249 جزء في المليون. وحولت على ذلك سجل نسبة نفوذ عالية 100% و 100% في الأرانب المغذاه وتعبرت الى عودة التحديد والمقاومة على جرعة 0.249 جزء في المليون. بينما كانت نسبة النفوذ في الأرانب الضابطة المحصنة أو الفيومونزين بـ 1 (100% على التوالي).

أما بالنسبة للتغيرات البيولوجية المسجلة في الأرانب المغذاه بالفيومونزين بـ 1 (0.249 جزء في المليون) فنلاحظ ان الصور المرضية مماثلة للتي ثبتت. إن كانت شدة التغيرات المرضية أكبر في الأرانب المغذاه على الجرعة الأعلى من الفيومونزين عليها في الجرعة الأقل. وتأثير الفيومونزين على تضخم الكبد والكلى تكمن الداعم مع استجابة التراجت والدهان عيني في المجموعتين. ان حجم الطحال تبين بالبحث المحوري أن التغيرات المرضية تركزت أساسا في الكلى والكبد ثم الرئتين والدماغ والدمار والعضو، وتلك التغيرات المرضية الثانية في الكلى والكبد عبارة عن تغيرات مستدامه وتكمن مع تراكم للخلايا الليفية، كما شهد احتقان لليمغامات الجديدة. كما سجل بالبحث احتقان وجمبات للخلايا الإلتهابية حول الأعاجية الدموية مع وجود انتفاضات وتلّين والدمام علاوة على ذلك لوحظ تغيرات زجاجية حادة بالكبد وتتكسر بالدمار في الأرانب المغذاه على الجرعة الأعلى.