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Mycotoxins in broiler production

Micotoxinas na produção de frangos de corte

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ABSTRACT

The occurrence of mycotoxins has become a problem to be discussed, due to its harmfulness to humans and animal's health, and may be an obstacle to the poultry economy. Mycotoxins are toxic metabolites produced by certain species of fungi and may contaminate food. Aflatoxins are mainly produced by *Aspergillus flavus* and *Aspergillus parasiticus*, and B1, B2, G1 and G2 are its best known types. Fumonisin, with its B1, B2 or B3 types, are produced by *Fusarium*, while ochratoxin A is produced by *Penicillium* and *Aspergillus*. The main trichothecenes mycotoxins are T-2 toxin, deoxynivalenol and diacetoxyscirpenol. Zearalenone, produced by different species of *Fusarium* fungi affects chickens only when they are exposed to extremely high levels of contamination. Generally, immunosuppression, hepatotoxicity and nephrotoxicity as a decrease in performance and production gains are the most observed effects. There are several laboratory methods that can be used for the determination of mycotoxins. In order to control the contamination, it is necessary to adopt proper farming practices which prevent fungi growth. Once grains and feed are contaminated, biological, physical and/or chemical decontamination methods may be employed, although the physical process with adsorbents mixed to the feed is more widely used. Due to the importance of mycotoxins to poultry production, it is necessary to adopt measures to prevent contamination, and also develop a control and an anti-fungal growth and toxin production program by reviewing the critical points favorable to the emergence of toxin-producing fungi.
KEYWORDS: aflatoxin, fumonisins, ochratoxins, trichothecenes, zearalenone.

RESUMO

A ocorrência de micotoxinas tornou-se um problema a ser discutido, pois representa riscos à saúde dos animais e humanos, podendo constituir um obstáculo à economia avícola. Micotoxinas são metabólitos tóxicos produzidos por algumas espécies de fungose podem contaminar os alimentos. Aflatoxinas são majoritariamente produzidas por *Aspergillus flavus* e *Aspergillus parasiticus*, sendo B1, B2, G1 e G2 os tipos mais conhecidos. Fumonisinas são do tipo B1, B2 e B3, e produzidas pelo gênero *Fusarium*, enquanto a ocratoxina A é produzida por fungos da espécie *Penicillium* e *Aspergillus*. As principais micotoxinas dos tricotecenos são toxina T-2, deoxynivalenol e diacetoxyscirpenol. A zearalenona, produzida por diferentes espécies de fungos do gênero *Fusarium*, afeta os frangos apenas quando estes são expostos a níveis extremamente altos de contaminação. De modo geral, são observados efeitos imunossupressores, hepatotóxicos e nefrotóxicos, com queda no desempenho e nos ganhos de produção. Vários são os métodos laboratoriais que podem ser utilizados para a determinação de micotoxinas. Para o controle da contaminação, é necessário adoção de práticas agrícolas correta, com vistas à prevenção do crescimento de fungos. Após a contaminação de grãos e rações, métodos de descontaminação, biológicos, físicos e/ou químicos podem ser empregados, embora o processo físico com adsorventes misturados às rações seja o mais utilizado. Pela importância que as micotoxinas representam à produção de frangos, é necessário adotar medidas que previnam a contaminação e desenvolver programas de controle e combate ao desenvolvimento fúngico e produção de toxinas, revendo os pontos críticos propícios ao aparecimento dos fungos geradores das toxinas.
PALAVRAS-CHAVE: aflatoxina, fumonisinas, ocratoxinas, tricotecenos, zearalenona.

INTRODUCTION

World production of poultry meat in 2016, according to the ABPA (2015), was 116 million tons, with Brazil accounting for 13.146 million tons produced, which corresponds to almost 16% of the total poultry

meat production chain. In this way, Brazil demonstrates its production potential and importance as food supplier for both home and foreign market. What contributes to this reality is the fact that Brazil finds in agriculture one of the strongest bases of economy, which ensures continuous supply of inputs based on grains, mainly corn and soybeans, important ingredients in poultry feed (LEINONEN & KYRIAZAKIS 2016).

Since the Brazilian poultry industry is becoming increasingly widespread in the world market and trying to adapt to market requirements, the purchase of ingredients with high standard of nutritional quality must be considered in the manufacture of broilers feed. For this reason, the occurrence of mycotoxins in feed has become a problem to be discussed, as it represents a serious risk to the health of animals and humans and could be a considerable obstacle to the poultry economy (DRASTIG et al. 2016).

The biggest damage caused by mycotoxins to livestock is due to the effect of low concentrations of toxins in feed, it is not enough to induce a easily identified clinical condition, but capable of changing the animal performance, productivity and profitability of production. Such loss occurs, for example, in weight gain, and it is determined by a reduction in protein synthesis rate and changes in energy metabolism (KUBENA et al. 2001, ARAVIND et al. 2003), compromising the immune system of animals and making them vulnerable to infectious diseases (LOPES et al. 2006).

The scientific literature has shown several techniques that can be used as helper methods to prevent or decrease the damage caused by mycotoxins. However, there is a need to consider the initial level of contamination and the type of technique to be employed, aiming to use the most appropriate procedure for each situation (CARÃO et al. 2014). It was aimed, with this literature review, to clarify the problems caused in broilers due to the development of toxin-producing fungi, emphasizing the methods of detection, fight against fungal growth and ways to mitigate and/or inhibit the action of mycotoxins.

DEVELOPMENT

Definition of mycotoxins

Mycotoxins are toxic metabolites produced by some species of filamentous fungi and may contaminate food for human and animal consumption. About 400 different mycotoxins have been identified, which differ greatly in size and structural shapes (IAMANAKA et al. 2010).

In tropical and subtropical climates, such as seen in Brazil, the fungal development finds favorable conditions of humidity and temperature (DILKIN 2002). However, the occurrence of mycotoxins is not only a problem from developing countries. Agribusiness in many countries is affected, and this may interfere with or even prohibit exportation, reducing animal and agricultural production (LEUNG et al. 2006).

The production of mycotoxins depends on fungal growth and may occur at any stage of the plant growth, harvest, or storage of food. However, fungal growth and mycotoxins are not synonymous, since not all fungi species produce toxins. The non-detection of signs of fungus presence does not indicate the absence of mycotoxins, since this may remain after elimination of the fungus or thermal treatment situations in which the fungus may have been deleted, but the toxin persists due to their thermotolerance (ZHU et al. 2016).

The contamination by a mycotoxin may occur indirectly and directly. Indirect contamination occurs when toxins in food remain even after the destruction of fungi. On the other hand, direct contamination occurs when the ingredient or the feed becomes contaminated by a toxigenic fungi, with subsequent formation of mycotoxins (FRISVAD & SAMSON 1991, IAMANAKA et al. 2010).

Analyses carried out in the 90s showed almost half of all commodities produced in the world, especially staple foods, was in some way contaminated by mycotoxins (BHAT & MILLER 1991). In developing countries the problem is even more serious. Where as good quality products are usually exported, those commodities of inferior quality, with higher mycotoxins levels than those permitted in importing countries are sold and consumed internally, with obvious risks to human and animal health (DAWSON 1991).

Interaction between mycotoxins and broiler immunity

With the consumption of contaminated food, cells of the intestinal mucosa, which possesses both components of innate as specific immunity may be exposed to large concentrations of these toxins (PRELUSKY et al. 1996). As described by BOUHET & OSWALD (2005), the function performed by the physical barrier of the intestinal epithelium is achieved by trans-epithelial electrical resistance that exists in the cell monolayer. Some toxins may affect this trans-epithelial electrical resistance in the intestinal mucosa. MCLAUGHLIN et al. (2004) explained this can happen due to the decrease in the amount of proteins found in the cell junctions.

On the other hand, cells of the intestinal mucosa which make this innate physical protection are

comprised of a constantly renewed tissue to maintain the integrity of the epithelium, which occurs from the proliferation of differentiated cells from the crypt, which differentiate and move along, being eliminated by extrusion at the height of intestinal villi. It is also known that mucus production has an important function as a lubricant and protective barrier of this epithelium, and when the intestinal mucosa is challenged, there is an increase in the number of these cells in the intestine, with increased mucus production. The influence of toxic fungal metabolites in mucosal immunity can greatly affect the animal performance, as the induction of immunity is very important to ensure protection against various pathogens which typically invade these surfaces (STREATFIELD 2006).

The administration of oral vaccines is a very practical and economical route of animal immunization; however, when mycotoxins interfere with the immune response, the result of vaccination may be affected. Several changes observed in the scientific literature show that mycotoxins alter the immune response of animals, may interfere with the vaccine response and make the animals susceptible to nonspecific infections, which animals have not been vaccinated against (GERTNER et al. 2008).

Mycotoxins affecting broiler production

Aflatoxins

The term aflatoxin was created based on the name of its main producer (*Aflavus*). The main known aflatoxins are B1, B2, G1 and G2, with an established classification based on their fluorescence under ultraviolet light (B¼ blue, green G ¼) and mobility for thin layer chromatography. They are mainly produced by *Aspergillus flavus* and *Aspergillus parasiticus*. However, recently, the species *Aspergillus nomius*, *Aspergillus bombycis*, *Aspergillus pseudotamari* and *Aspergillus ochraceoroseus* have also proved to be aflatoxigenic (MOSS & LONG 2002).

Aflatoxins are secondary metabolites associated with toxicity caused by food in animals and are reported to be hepatotoxic, mutagenic, immunosuppressive and neoplastic (FERREIRA et al. 2006). They are responsible for major hazards in commercial poultry health and livestock production, mainly due to financial losses resulting from the decrease in animal weight gain (CARÃO et al. 2014).

The high susceptibility of young birds to intoxication by aflatoxins compared to older birds has been demonstrated by MARIANI (1998), who found that birds intoxicated in the first two weeks of life have not recovered body weight after 42 days, although the toxic stimulus had been removed. The response is directly related to the level of comfort of the birds, in other words, higher stresslevels require fewer amount of toxins for changing the performance of animals (DOERR et al. 1983).

The signs of intoxication by aflatoxins mainly depend on its concentration in the feed, the type of aflatoxin and the time of ingestion (OGIDO et al. 2004), being characterized by immunosuppression and bone abnormalities, bleeding, depigmentation and changes in liver function (ROSA et al. 2001, MIAZZO et al. 2005, TESSARI et al. 2010). In research performed by TESSARI et al. (2005), there was a reduction in total protein serum in broilers fed diets containing 200 µg of AFB1/kg for 20 days.

Fumonisin

Fumonisins (B1, B2 and B3) belong to a large group of mycotoxins produced by *Fusarium* fungi, natural contaminant of cereals, especially corn and its by-products. The occurrence of fumonisin B1 in food produced in Brazil have been described by several researchers, reaching nearly 90% of positivity, with levels up to 300 mg/kg feed. The fumonisin B1 is the most abundant metabolite of this group of mycotoxins, representing about 70% in naturally contaminated food (RODRIGUEZ-AMAYA & SABINO 2002). Fumonisins produced by *F. moniliforme* and *F. proliferatum*, are a family of mycotoxins can contaminate food, especially composed by corn (LINO et al. 2004).

In avian species, they are associated mainly with performance reduction and also severe immunosuppression, affecting cells and organs of the immune system (GERTNER et al. 2008), besides affliction of liver function in broilers (TESSARI et al. 2010). According to LEUNG et al. (2003), the reduction in sphingolipid biosynthesis caused by fumonisins may alter the electrical regulation of epithelial cells. Fumonisins are also described as blocking of the mitotic cycle phases of epithelial cells, decreasing its proliferation (BOUHET et al. 2004).

Fumonisin induces hyperplasia of epithelial cells in the intestinal mucosa of chickens (BROWN et al. 1992) and also affects cytokine production by intestinal cells, which play a fundamental role in the recruitment of inflammatory cells to defense the intestinal mucosa (OSWALD et al. 2003).

Ochratoxins

Ochratoxin A (OTA) produced by fungi of the species *Penicillium* and *Aspergillus* naturally occurs throughout the world in various plant products, such as barley, coffee beans, cocoa beans, and nuts. It has been also detected in products made of cereals, wine, beer, grape juice and animal origin (NOGUEIRA &

OLIVEIRA 2006).

In a study performed by GUPTA et al. (2008), it was observed OTA produces nephrotoxic and hepatotoxic effects and may cause immunosuppression in broilers. It can also cause serious pathological changes in chicks, making the chickens fed foods contaminated with ochratoxin more susceptible to *Salmonella* infection. Even though this mycotoxin is extremely harmful to the birds, fortunately there is little contamination in poultry feed in Brazil (SANTURIO 2000).

GARCIA et al. (2003) concluded that broilers exposed to ochratoxin diet showed lower body weight, reduction in food intake, reduction in the levels of plasmatic proteins, albumins and globulins, with or without the use of adsorbents. They also found an increase in blood uric acid level, necrosis of renal tubular cells and hepatocytes, bile duct hyperplasia and increase in the diameter of proventricular glands.

Trichothecenes

The main trichothecene mycotoxins are T-2 toxin, deoxynivalenol (DON) and diacetoxyscirpenol (DAS). All of them are produced by several species of *Fusarium* fungi, at temperatures below 15 °C (SANTURIO 2000).

T-2 toxin was shown to be, *in vitro*, toxic for chicken's macrophages, inhibiting their phagocytic capacity (KIDD et al. 1995). It may also form peroxides from lipids, resulting in a decrease of the concentration of vitamins in birds (HOEHLER & MARQUARDT 1996). T-2 and DAS mycotoxins, at levels around 1 ppm in the feed, produced oral lesions in broilers, what may result in lack of appetite, with consequent decrease in feed intake (HOERR et al. 1982). Low doses of Deoxynivalenol (DON) interfere with the differentiation of enterocytes (KASUGA et al. 1998).

ANTONISSEN et al. (2014) found broilers experimentally infected with *Clostridium perfringens*, when fed diet containing 3,000 to 4,000 mg/kg DON, presented duodenum with lower electrical transepithelial resistance and lower villi height, suggesting disruption of the barrier and damage to the epithelium gut, which may lead to increased permeability and reduced absorption of proteins.

BURDITT et al. (1983) observed its most significant toxic effects with the level of 4 ppm, where the birds showed low feed intake, delay in growth, changes in the blood parameters and neurotoxicity. Liver lesions were found in chickens that received T-2 in the diet (GARCIA et al. 2003). DÄNICKE et al. (2007) noted lower feed intake in broilers when fed diets containing corn contaminated by DON.

Zearalenone

Zearalenone (ZEA) is a mycotoxin produced by various species of *Fusarium*, especially *Fusarium graminearum* and *Fusarium culmorum*, main agents involved in its formation (ZINEDINE et al. 2007). Except for extremely high levels of contamination, chickens are not affected by the ingestion of ZEA (LEE et al. 1985). Broilers were intoxicated with levels of 800 ppm of ZEA, and showed no changes in performance, however, a decrease in the number of white blood cells was observed, hypertrophy of some oviducts and comb shrinkage (CHI et al. 1980). The ZEA can also be hepatotoxic, and change some serum parameters (ZINEDINE et al. 2007).

Although the ZEA does not affect the performance of the chickens in natural contamination, it should be noted health authorities in some importing countries are on alert as the ZEA residues in chicken meat, as this mycotoxin, in certain concentrations, may induce an anabolic effect in humans and other mammals (SANTURIO 2000) and tumor development due to chronic exposure (YU et al. 2005).

Methods for detection of mycotoxins

The monitoring of mycotoxins in foods is important to public health, and consists of the adoption of technological measures to reduce exposure of food at risk for these toxins (MAZIERO & BERSOT 2010). There are several laboratory methods that can be used for the determination of mycotoxins, and they are extremely specific and precise. These include: thin layer chromatography (TLC), high-performance liquid chromatography (HPLC) and gas chromatography (GC); and immunological methods, such as enzyme linked immunosorbent assay (ELISA), biosensors and colorimetric enzyme immunoassay of sequential injection (AMARAL & MACHINSKI 2006).

The HPLC is highly efficient, but the high cost restricts its deployment in the laboratory routine. In high-performance liquid chromatography, normal phase or reverse phase columns are used for separation and purification of the toxin, depending on the polarity. With this technique, it is not necessary to clean the sample and various mycotoxins can be simultaneously analyzed. Research using this method was published for *Fusarium* toxins analysis (HARTMANN et al. 2008, SENYUVA et al. 2008). For aflatoxins, studies are not common, since the methods using HPLC with fluorescence detection are well established.

For some mycotoxins, such as fumonisins, derivatization is necessary with a specific reagent due to the absence of a chromophore. The use of natural fluorescence of some mycotoxins such as aflatoxins,

ochratoxin A and citrinin, enables a high specificity and sensitivity, with various methods already established by the AOAC, among others (CIGIĆ & PROSEN 2009). Gas chromatography is used only for volatile and thermally stable analytes. Immunochemical methods are promising alternatives for detection of toxins, engaging biological specificity and the reliability of chemical procedures (FUJII et al. 2004).

Fighting fungal growth and food decontamination

The adoption of good agricultural practices is the first and most important way of controlling the contamination of mycotoxins in foods, since it prevents fungal growth. Contamination of grains by mycotoxins may be a serious problem that can happen not only through inadequate storage conditions, but earlier, as in the fields during the pre-harvest period. For this reason, the use of good agricultural practices and the choice of genotypes of plants more resistant to storage fungi contamination are excellent alternatives (IAMANAKA et al. 2010).

They are also essential procedures to decrease the moisture of harvested grain and storage according to internationally recommended standards. Therefore, it has been used as a preventive method of inhibiting fungal growth in stored grains (SMITH & HAMILTON 1970). IAMANAKA et al. (2010) described some necessary agricultural procedures:

- Adjust the harvesting equipment to work properly, producing the lowest mechanical damage;
- Immediate harvest of the product at maturity;
- Drying the product to safe moisture levels as soon as possible; and
- Cleaning oil seeds and grains, to remove organic matter and damaged seeds, and pay attention to storage areas, that should be clean, free of insects and rodents and protected from climatic influences.

After contamination of grains and feed, different methods of decontamination can be used, including biological, physical and/or chemical procedures. According to EMAN (2000), the ideal decontamination process must be easy to apply, economical, should not lead to the formation of compounds which retain toxicity, or change the nutritional properties and palatability of grains and feed. The degree of decontamination depends on the used method and the toxicity that remains in the sample to be treated (SORIANO & DRAGACCI 2004). The decontamination by biological agents, which began in the 1960s, has been using microorganisms, as fermentation processes, started in the 1980s, employ the use of yeast (BATA & LÁSZTITY 1999).

In recent years, compounds present in plant extracts have also been used, since the biological agent compete with the fungus by the ecological niche in the plant or food (BACON et al. 2001). Some extracts inhibit fungal growth and transgenics increase the plants' resistance to fungi and insects (DUVICK 2001).

The effectiveness of the method depends on the physical milling and manufacturing to which grains are subjected, since many mycotoxins are inside the grain, and removal of the germ and / or pericarp eliminates a large amount of toxin. This, however, is a preliminary process of decontamination. The dry or wet milling may reduce the mycotoxin content in food (SORIANO & DRAGACCI 2004). In dry milling, an increase in the concentration of mycotoxins occurs in the pericarp. In wet milling, toxins migrate to the aqueous solution, reducing its concentration in the grain (EMAN 2000). The use of elevated temperatures is also an alternative for the removal of toxins, but the time and temperature used in the process should be considered (SEEFELDER et al. 2003). Processes such as grain flocculation and extrusion can also reduce the content of toxins (KIM et al. 2003). Adsorbent materials, with capacity to bind mycotoxins and immobilize them in the gastrointestinal tract of animals, reducing the bioavailability of the toxin, are widely used. Another physical method is the use of radiation.

For the chemical form of partial decontamination, water and sodium bisulfite solution, sodium chloride and / or ammonium hydroxide washing is used, although, in this process, toxins must be not totally eliminated (SORIANO & DRAGACCI 2004).The physical and chemical methods have the disadvantage of not being totally effective and may result in loss of nutrients and generate high costs, making many studies report the best solution in the future will be decontamination by biodegradation.

Adsorbents in feed of use for broiler

Research has been directed to the use of natural or synthetic adsorbents, to reduce the effects of the ingestion of food contaminated by mycotoxins, since they adhere to mycotoxin and prevent its absorption by the gastrointestinal tract, making it inert and non-toxic to animals (LOPES et al. 2009). There are other feed decontamination processes, but the physical process with adsorbents mixed to the feed is the most used nowadays (SEKIYAMA et al. 2006).

Activated carbon can be used as adsorbent in feed, however, KUBENA (1995) found no relevant results. The most successful in adsorbing mycotoxins substances, when added to feed, are those of volcanic origin: aluminosilicate and montmorillonites (SANTURIO et al. 1999). The sodium calcium aluminosilicate

compounds, at a concentration of 0.5% in the feed, have shown significant result in reducing the adverse effects of aflatoxin in poultry. Several studies have also shown that sodium bentonite is a good adsorbent for aflatoxins in poultry, as much as sodium calcium aluminosilicate compounds (MALLMANN et al. 2007, LOPES et al 2009). LOPES et al. (2006) observed, in treatments containing 3 mg/kg^{-1} of aflatoxins, the adsorbent promoted better performance, with 0.3% of bentonite showing better results.

CONCLUSION

Many studies have been conducted on the nutrition of broilers, in order to reach lower costs of production with more efficiency. Thus, search for prevention of possible attacks the immune system of these animals, with consequent optimization of its performance and production has been stimulated. It emphasizes the importance of studying mycotoxins in broiler production chain, taking care from harvesting grain to be manufactured until the feeding of animals. The methods for evaluation of food and daily observations of the animals are essential for investigation of intoxication by mycotoxins. Decontamination processes used in food have variable efficacy and assisting preventing or reducing the damage caused by mycotoxins. Among these processes, the use of adsorbents has been shown to be a safe, easily accessible and effective method to reduce or even avoid the deleterious effects in poultry. However, the adsorbents should not cause nutritional or palatability changes and not to stimulate the production of toxins by fungi in animal feed, in order to be safely applied without inhibiting the consumption by the birds. It is indispensable to consider the initial level of contamination and the type of technique to be employed, in order to make the most appropriate choice. Because of the importance that mycotoxins pose to poultry production, it is necessary to adapt to the field, to factory and farm feed, measures to prevent contamination, such as developing control programs to combat fungal growth and toxin production, reviewing the actual critical points favorable to the appearance of toxin-producing fungi.

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