Mycotoxin Binder Review: An Effective Solution for Mycotoxin Contamination in the Poultry Industry.

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Abstract : *Mycotoxin contamination in poultry feed is a significant challenge in the poultry industry, with adverse effects on poultry health and productivity. Mycotoxins such as aflatoxin, ochratoxin, and zearalenone—produced by fungi like Aspergillus, Penicillium, and Fusarium—impact organ function and immune responses in poultry, leading to economic losses. Mycotoxin binders, including both inorganic (bentonite, zeolite) and organic (yeast cell wall components) types, play an essential role in mitigating these effects by adsorbing toxins in the digestive tract and preventing their absorption into the bloodstream. This review explores the types, mechanisms, and recent advancements in mycotoxin binder technology, evaluating their effectiveness in reducing mycotoxin impact on poultry health and feed safety. Additionally, it highlights the latest innovations in binder formulations designed to enhance binding specificity and efficacy across a broader spectrum of mycotoxins. These advancements offer promising potential to improve poultry production outcomes and contribute to food safety within the industry.*

Keywords: Poultry industry, mycotoxin, mycotoxin binders, aflatoxin, ochratoxin, zearalenone, bentonite, zeolite, yeast cell wall, feed safety, toxin adsorption.

1. Introduction

Mycotoxins are toxins produced by fungi. These substances are secondary metabolic products of fungi that can cause diseases and even death in animals and humans [1]. When mycotoxins enter the body, they can lead to decreased performance, loss of appetite, weight loss, weakened immunity, reproductive disorders, and residues in the products produced [2]. Mycotoxins are produced by over 200 species of fungi. Generally, fungi capable of producing mycotoxins belong to three genera: Aspergillus, Penicillium, and Fusarium. Aflatoxin, zearalenone, ochratoxin A, fumonisins, trichothecenes such as deoxynivalenol, and T-2 toxin are examples of mycotoxins that have detrimental effects on the health and productivity of poultry [3].

Each type of mycotoxin can affect the function of various organs (both in animals and humans), but each has a primary target organ, rendering the affected organ dysfunctional or damaged. For instance, aflatoxin inhibits RNA synthesis in liver cells, causing necrosis. Ochratoxin attacks the kidneys by interacting with Fe to form complex molecules that generate hydroxyl radicals, leading to lipid oxidation. T-2 toxin causes mouth lesions, resulting in loss of appetite in animals. Zearalenone affects the transcription in egg cells, disrupting reproduction. Fumonisin causes nerve cell damage and affects liver function [4].

Prevention and detoxification of mycotoxins in feed can be achieved through good management, physical, chemical, biological treatments, and the use of mycotoxin binders as toxin-binding agents. Adding mycotoxin binders to feed is an effective solution to reduce the intake of toxins in animals. The binders used are compounds with large molecular weights that act like chemical sponges, binding mycotoxins in the digestive tract of animals, which are then excreted through feces [5]; [6].

Materials used as mycotoxin binders can be both inorganic and organic. An example of an inorganic mycotoxin binder is clinoptilolite/zeolite. This type of aluminosilicate mineral not only binds toxins

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due to its absorptive capabilities but also offers advantages such as improved nutrient absorption, positive effects on gut microflora, and reduced negative impacts of mycotoxins. According to research, adding 2% clinoptilolite to the feed of laying hens can increase the average egg weight to 64.69 grams compared to the control of 63.73 grams, as well as enhance daily feed efficiency [7].

Organic mycotoxin binders are derived from microbes and plants, including various types of yeast and lactic acid bacteria. Microbes act as agents of mycotoxin biodegradation or biotransformation, thereby reducing their metabolic toxicity. Important components in this process include the cell walls of yeast, such as *Saccharomyces cerevisiae*, which contain glucans. Research has shown that glucan binders from yeast cell walls effectively combat aflatoxicosis in broiler chickens and improve feed efficiency and egg production compared to bentonite and spirulina mycotoxin binders [8].

This review aims to evaluate recent advancements in mycotoxin binder technologies as a solution to mycotoxin contamination in the poultry industry. Specifically, it examines the various types of mycotoxin binders, their mechanisms of action, and their effectiveness in mitigating the adverse effects of mycotoxins on poultry health and productivity. By summarizing recent research and innovations in mycotoxin binder development, this review provides insights into their role in enhancing the safety and performance of poultry feed, ultimately supporting the sustainability of the poultry industry.

2. Types of Mycotoxins

a. Aflatoxin

Aflatoxin is the most common mycotoxin found in corn, produced by *Aspergillus flavus* or *Aspergillus parasiticus*. These fungi often contaminate agricultural products, both food and feed [9]. Aflatoxin contamination occurs when the moisture content in corn is high, typically in humid environments with optimal humidity above 85% and temperatures between 4-40°C (optimal 25-32°C) with a moisture content of 18%. *Aspergillus* sp. fungi produce aflatoxin B1 (AFB1), aflatoxin B2 (AFB2), aflatoxin G1 (AFG1), aflatoxin G2 (AFG2), aflatoxin M1 (AFM1), and aflatoxin M2 (AFM2) [10]. AFB1 is the most toxic type of aflatoxin and is classified as a class I carcinogen [11]. The type of cancer caused by AFB1 is liver cancer that affects poultry. The mechanism of liver cancer due to aflatoxin is complex, involving mutations in cytochrome p53. Low doses of AFB1 (<60 ppb) in feed cause changes in liver color and size, reduce proventriculus weight, and cause hemorrhaging in the small intestine [12] [13].

b. Ochratoxin A

Ochratoxin A is a mycotoxin produced by several fungi species from the genera *Aspergillus* sp. and *Penicillium* sp.. Ochratoxin A-producing Aspergillus species include *A. ochraceus, A. carbonarius, A. niger, A. westerdijkiae, A. alliaceus, A. sclerotiorum, A. sulphureus, A. albertensis, A. auricomus, A. lacticoffeatus, A. sclerotioniger, A. fumigatus, A. versicolor, A. wentii, A. awamori, A. cretensis, A. flocculosus, A. pseudoelegans, A. roseoglobulosus, A. westerdijkiae, and A. affinis. Ochratoxin A-producing Penicillium species include P. verrucosum, P. nordicum, P. expansum, P. chrysogenum, P. glycyrrhizacola, and P. polonicum* [14]. These fungi are commonly found in wheat, corn, peanuts, and other crops [15]. Ochratoxin A contamination in livestock feed can affect metabolism, resulting in reduced production, reproduction, and the quality and safety of animal products [16]. Ochratoxin A is nephrotoxic, hepatotoxic, teratogenic, and immunotoxic, and causes oxidative stress at the cellular level, potentially leading to a disease known as ochratoxicosis [17] [18] [19].

Ochratoxin A concentrations of 2 ppm in feed cause symptoms of ochratoxicosis in poultry, including reduced body weight and egg production, diarrhea, kidney damage, and hematological changes. Studies have shown that feeding ochratoxin A at doses of 1-5 mg/kg leads to blood biochemical changes, including reduced cholesterol, total protein, albumin, globulin, potassium, and triglyceride levels, and increased uric acid, creatinine, and serum alkaline phosphatase (ALP) and gamma-glutamyl

transpeptidase (GGT) activities. High concentrations of ochratoxin A (4 ppm) can drastically increase mortality rates [20].

c. Zearalenone

Zearalenone is a mycotoxin primarily produced by fungi such as *Fusarium graminearum* and is commonly found in various grains like corn and wheat. As a result, zearalenone can significantly affect crop yields. Zearalenone has a resorcylic acid lactone structure, and various derivatives can be produced by altering its structure (typically through functional differences on carbons C1 and C6 in the lactone ring structure). Common derivatives include a/b-zearalenol (a/b-ZOL), a/b-zearalanol (a/b-ZAL), and zearalanone (ZAN) [21].

Structurally, zearalenone resembles natural estrogen, allowing it to bind to estrogen receptors in the body and disrupt reproductive hormones [22]. Zearalenone is metabolized in the liver by hydroxysteroid dehydrogenase enzymes into two isomeric metabolites, α-Zearalanol (α-ZAL) and α-Zearalenol (α-ZOL). These isomers can bind to estrogen receptors (E2) and increase estrogen levels (hyperestrogenism). Excessive levels of α-ZAL and α-ZOL in the blood can lead to uncontrolled cell proliferation, potentially triggering carcinogenic effects [23]. Zearalenone also induces genotoxicity, hepatotoxicity, immunotoxicity, and cytotoxicity through oxidative damage, endoplasmic reticulum stress, mitochondrial apoptosis, autophagy, and other pathways [24]; [25]; [26]; [27].

Zearalenone has been identified as a mycotoxin causing decreased livestock production in Indonesia [28]. Zearalenone concentrations of 5-20 ppm in feed can increase infertility rates in livestock by up to 80% [29]. Generally, zearalenone exhibits low acute toxicity to animals at low concentrations [30]. Poultry appears to be quite tolerant of ZEN, which may be explained by the high natural estrogen concentrations in their blood. Natural estrogen is considered to have a higher receptor affinity compared to Fusarium toxins [31].

d. Trichothecenes

Trichothecenes are sesquiterpenoid metabolites produced by several toxigenic fungal species, including *Fusarium* sp., *Myrothecium* sp., *Phomopsis* sp., *Stachybotrys* sp., *Trichoderma* sp., and *Trichothecium* sp. [32]. Trichothecenes are divided into four groups (types A-D), with types A and B being the main sources of natural contaminants in grains, both before and after harvest. The most common trichothecenes in food are type A: T-2 toxin (T-2), HT-2 toxin (HT-2), diacetoxyscirpenol (DAS); and type B: deoxynivalenol (DON) and nivalenol (NIV). Like most mycotoxins, trichothecenes are heat-stable and resistant to degradation during conventional food processing temperatures. When consumed, these mycotoxins can cause gastrointestinal bleeding and vomiting, and direct contact can cause dermatitis [33].

e. Deoxynivalenol

Deoxynivalenol is a trichothecene produced by Fusarium sp. [34]. Also known as vomitoxin, deoxynivalenol is a natural toxin produced in cereal grains infected by *Fusarium culmorum*, *Fusarium graminearum*, and closely related fungi, with common acetyl derivatives including nivalenol and fusarenon-X [35]; [36]; [37]; [38]. After consuming deoxynivalenol-contaminated feed, animals may exhibit symptoms such as vomiting, reduced appetite, diarrhea, and even death, resulting in significant losses in the livestock industry [39]. Low doses of deoxynivalenol can damage the intestinal barrier and immune system in humans and animals; high doses can cause severe diarrhea, vomiting, gastrointestinal inflammation, and immune suppression [40]. Deoxynivalenol also causes cytotoxicity by inhibiting related signaling pathways, inducing oxidative stress, autophagy, apoptosis, and other mechanisms [41]; [42].

f. Fumonisin

Fumonisin is a contaminant found in corn and grain products produced by *Fusarium verticillioides* (formerly *F. moniliforme*) and several other Fusarium species. The most common fumonisins are from the 'B series,' namely FB1, FB2, and FB3, which are frequently found in feed [43]. The presence of fumonisins at levels around the European Union's reference level of 1 mg/kg in feed shows harmful effects on poultry health. A concentration of 2 mg FB1/kg in feed correlates with liver residues, liver oxidative stress, immune system disorders, gut health issues, and increased aspartate aminotransferase activity (a marker of liver, kidney, muscle damage, and toxicity) [44]. In another study, the highest cumulative concentrations of fumonisin B were detected in the muscle and liver of chickens and turkeys when they were fed contaminated feed (contamination levels were 0.06 mg/kg and 0.10 mg/kg) [45].

3. History and Development of Mycotoxin Binders

The term "mycotoxicosis" was first used in 1952 in a study about animal diseases. However, the discovery of aflatoxin came after the death of 100,000 turkeys in England in 1960, marking the beginning of modern mycotoxin research. Over the next few years, laboratory and field experiments showed that many fungi causing food spoilage and plant diseases produced various toxic metabolites [46]. The discovery of mycotoxin binders is closely related to mid-20th-century research, where scientists began investigating the detrimental effects of mycotoxins in agriculture and livestock. Mycotoxins, secondary metabolite toxins produced by fungi such as Aspergillus, Fusarium, and Penicillium, were found to contaminate crops and pose risks to human and animal health [47].

The first mycotoxin binders were mainly natural clays, such as bentonite and zeolite, found to have absorbent properties capable of binding mycotoxins like aflatoxin. Bentonite clay has a high affinity for aflatoxin due to its unique layered structure, which allows it to trap and prevent the toxin from entering the bloodstream when ingested by animals. These initial discoveries laid the foundation for developing various mycotoxin binders, including modified clays, activated charcoal, yeast cell walls, and other absorbent compounds [48].

Several potential absorbent materials can be used as mycotoxin binders. These materials are generally classified into two categories: organic (cellulose, polysaccharides in yeast and bacterial cell walls such as glucomannan, peptidoglycan, and others) and inorganic (clay minerals like aluminosilicate, bentonite, zeolite, diatomite, and others) [49]. Some absorbent substances can be inorganic (silica-based): aluminosilicate, bentonite, montmorillonite, zeolite, hydrated sodium calcium aluminosilicate (HSCAS); organic such as: yeast cell walls, micronized fibers, activated carbon, enzymes, and bacteria; and polymers like: cholestyramine and polyvinylpyrrolidone. Various mycotoxin binders available in Indonesia are made from inorganic materials, organic materials, or a combination of both [50].

4. Impact of Mycotoxins on Animals

The main issue related to mycotoxin-contaminated livestock feed is not the cause of acute diseases, but the accumulation of low-concentration toxin consumption, which leads to metabolic disorders and affects livestock productivity [51]. The level of toxicity caused by mycotoxins in animals mainly depends on the type of mycotoxin, amount, duration of exposure, overall animal health, gender, age, breed, and other factors. The presence of even a single type of mycotoxin can be harmful to animals, and the presence of multiple types can be more toxic due to their synergy [52]; [53].

The toxic effects of these mycotoxins cause oxidative stress and increased formation of radicals due to malfunction of the antioxidant system, causing damage to DNA, proteins, and lipids [54]. Mycotoxins affect various organ systems, including the digestive system, liver, immune system, and reproductive system. Animals at the highest risk of mycotoxin infection are poultry and pigs, due to their feed primarily consisting of grains. The biggest challenge of mycotoxicosis in poultry is non-specific clinical

symptoms, which are similar to those caused by poor management, nutrition, and health, making diagnosis and appropriate action difficult [55].

In poultry cases, aflatoxin in layer hens reduces egg production and hatchability [56]. In broiler chickens, mycotoxins generally lead to decreased feed consumption, inadequate feed conversion, and reduced growth rates during the production cycle [57]. Poultry are more tolerant to zearalenone toxicity, but chronic exposure may affect fertility. Additionally, high levels of deoxynivalenol in poultry are known to affect growth rates, feed efficiency, and increase susceptibility to infectious diseases such as necrotic enterocolitis. However, mycotoxin levels below established guideline levels still negatively impact the metabolic, immune, and physiological aspects of animals [58].

5. Types of Mycotoxin Binders Used in the Poultry Industry

a. Clay Minerals

Clay minerals consist of hydrated silicates of aluminum, iron, and magnesium, which usually contain alkali and alkaline earth ions. The primary clay mineral is aluminosilicate. The basic structural unit of aluminosilicate consists of a combination of silica tetrahedral sheets and aluminum octahedral sheets. Aluminosilicates are more commonly used for aflatoxin adsorption, and their hydrophilic surfaces are less effective in adsorbing non-polar mycotoxins [59]. The beta-dicarbonyl system of aflatoxins allows the formation of coordination bonds with metal cations present in aluminosilicate clays. To enable aluminosilicates to absorb low-polarity mycotoxins, such as zearalenone, ochratoxin, and type A trichothecenes (T-2), organoaluminosilicates are created by modifying aluminosilicate cation exchange with organosilicates (typically quaternary alkylammonium ions) [60].

b. Bentonite (Montmorillonite)

Bentonite (montmorillonite) currently refers to clay with a layered microcrystalline structure with varying composition. Bentonite is often called smectite because it is the dominant clay mineral. The adsorption effectiveness of bentonite primarily depends on its montmorillonite content and exchangeable cations [61]; [62]. Bentonite contains gaps called interlayer spaces that have 80% of exchangeable cations compensating for negative charges occurring in the reticulate spaces. Due to this structure, its large surface area and high cation exchange capacity allow it to absorb organic substances with cation penetration and polar molecules [59].

Aflatoxin can react at various sites, primarily in the interlayer regions. In dry conditions, the primary bond between adsorbed AFB1 and smectite is ion-dipole interaction and coordination among exchangeable cations and carbonyl groups. In moist conditions, hydrogen bonds between carbonyl groups and the hydration shells of exchangeable water become the dominant binding force. These findings indicate that AFB1 binding on smectite interlayer surfaces involves chemical bonding mechanisms. Due to these characteristics, most bentonites have a greater ability to absorb aflatoxins (90-95%) than zearalenone and ochratoxin [63]; [64].

c. Zeolite

Zeolite has a structure containing crystalline substances with interconnected tetrahedral frameworks, each consisting of four oxygen atoms surrounding a cation [59]. This framework has large pores in the form of channels and "cages" that can accommodate water molecules and extra-framework cations from the alkali metal and/or alkaline earth groups, which can generally be exchanged without altering the crystal structure. The channel system of zeolites is formed by different combinations of tetrahedral rings, hence called molecular sieves. The wider the narrowest part of the channel, the larger the cations that can be accommodated within the structure [65]. The adsorption mechanism of zeolites is related to the interaction of AFB1 with Ca^{2+} on the zeolite surface. It showed that better FB1 adsorption by zeolites occurs at pH 3.0, indicating electrostatic interaction between anionic FB1 and the positively charged surface under acidic conditions [66].

d. Diatomite

Diatomite is a material derived from sediment formed by the accumulation of algae shells in lacustrine and marine environments. These fossils are formed from silica deposits in their structure, arranged in thin or thick layers, interspersed with clay lenses [59]. Diatomite is a very fine material with a porous structure, high surface area, and a microstructure mainly composed of amorphous silica, or opal and frustules. In addition to amorphous silica, other components may be associated, such as alumina, iron, calcium, magnesium, sodium, potassium, titanium, and others, in smaller proportions [67].

There are different terminologies used to describe these materials based on the impurities associated with diatomite. For example, if it contains a lot of clay, it is called diatomaceous earth; if associated with limestone, it is referred to as diatomaceous marl. The term diatom refers to single-celled aquatic algae belonging to the class of golden-brown algae. Diatomite is defined as nearly pure sedimentary deposits composed almost entirely of silica [59].

Diatomaceous earth is commonly used as an anti-caking agent during feed processing [68]. Due to its high silica content, diatomite has reduced mass and a honeycomb structure that results in high adsorption capacity. Its high permeability is due to the linkage of individual diatom particles and the fact that each diatom has very fine pores and channels that allow fluid flow [59]. The surface of diatomite is more hydrophilic, affecting zearalenone adsorption, which primarily occurs on hydrophobic surfaces. The most likely driving force connecting zearalenone and diatomite is hydrophobic bonding between siloxane groups on the diatomite surface and the partial positive charge of the zearalenone molecule, considering this as a physical adsorption process. Zearalenone adsorption on diatomite is limited by competition from less polar toxin molecules with stronger water molecules [69].

e. Activated Carbon

Activated carbon is a powder formed by the pyrolysis of various organic compounds and produced through an activation process aimed at developing a highly porous structure. Activated carbon is one of the most effective and non-toxic adsorbents for a wide range of drugs and toxic substances, such as mycotoxins. The adsorption properties of activated carbon depend on many factors, such as pore size, surface area, and the structure of the mycotoxins. Activated carbon is a relatively non-specific adsorbent, so essential nutrients can also be absorbed, especially if their concentration is higher than that of the mycotoxins [70]. The ability of activated carbon to adsorb fumonisin B1 in aqueous solution has been demonstrated in vitro, but it was ineffective in in vivo experiments. The affinity of aflatoxin for activated carbon is also very high, and the primary mechanism is likely hydrophobic binding. Activated carbon shows high affinity for all toxins, including deoxynivalenol, in in vitro tests. However, activated carbon has low specificity and, when analyzed in vivo, it becomes saturated by the food matrix [59].

f. Yeast

Yeast cells (*Saccharomyces cerevisiae*), with different components, including specific proteins and certain fractions to complete yeast cells, are used as mycotoxin binders. The most well-known are glucomannan and mannan-oligosaccharides. The cell wall or cell wall fractions offer many different and easily accessible adsorption sites, such as polysaccharides, proteins, and lipids. Due to the different properties of these adsorption sites, adsorption can occur through various mechanisms, sometimes simultaneously, such as hydrogen bonding, ionic or hydrophobic interactions. These bonds are relatively weak compared to covalent or ionic bonds, but if present in large numbers, these interactions can play a significant role. Hydrophobic interactions become more important as pH increases [71]; [72].

6. Conclusion

Mycotoxin contamination in poultry feed has serious impacts on livestock health and productivity. Mycotoxin binders offer a solution to this challenge by binding mycotoxins in the digestive tract of poultry, preventing toxin absorption into the body. Mycotoxin binders consist of inorganic materials, such as bentonite, zeolite, and diatomite, as well as organic materials like yeast cell walls, which have the ability to adsorb toxins. Over time, this technology continues to evolve with innovations that enhance effectiveness and broaden the adsorption spectrum for various types of mycotoxins. These innovations have the potential to improve livestock resilience to mycotoxins, ultimately supporting productivity and food safety in poultry.

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