Eurasian Journal
of Veterinary Sciences

www.eurasianjvetsci.org

INVITED REVIEW

Detoxification of aflatoxin in poultry feed: An update

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Received:12.07.2018, Accepted: 07.09.2018
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Kanatlı yemlerindeki aflatoksinlerin etkisizleştirilmesi: Bir güncelleme

Eurasian J Vet Sci, 2018, 34, 4, 204-227
DOI: 10.15312/EurasianJVetSci.2018.203

Öz

Bu meta-analitik çalışmada, kanatlı yemlerinde aflatoksinlerin etkisinin azaltılmasına yönelik yem katkı maddesi olarak adsorbanlar ve biyolojik ürünlerle gerçekleştirilen in vivo deneysel çalışmalar özetlendi. Toplam 42 farklı ülkede yürütülen 231 araştırma incelenerek ilk yazarın ülke adıyla listelendi ve sonuçları özet halinde sunuldu. Bu derleme, yem sektörü temsilcileri ve bilim insanlarına yapılan çalışmaların sonuçlarını sunmakta ve bölgesel sonuçlara dayalı olarak bütüncül değerlendirme için bir temel oluşturmaktadır. Araştırmalar çoğunlukla kanatlı türlerinden broyler civcivlerde (%85) ve nemli iklime sahip ülkeler ile o ülkelerden yem hammaddesi ithal edenlerde yoğunlaşmaktadır. Kanatlı yemlerinde aflatoksinlerin etkilerini azaltmak için çoğunlukla bentonitler (BENT) ve hidrate Na Ca aluminosilicat (HSCAS) gibi killer ile bunların maya (*Saccharomyces cerevisiae;* SCE) ve maya komponentleri (Esterified glucomannan; EGM) gibi biyolojik ürünler ile kombinasyonlarıyla gerçekleştirilmiştir. Üreticiler ve araştırıcılar için yeme aflatoksin bağlayıcı olarak katılan yem katkısının etkinliğini belirlemede en iyi yol, aflatoksin ve aflatoksin + bağlayıcı madde grubunu karşılaştırılarak elde edilen sonuçların performans, biyokimyasal-hematolojik, immunolojik ve makroskobik-histopatolojik verilerin hepsinin "bir bütün olarak" ele alınması ve değerlendirilmesidir. Üreticiler ve araştırıcılar denemelerin bütününe ulaşıp koruyucu maddenin pratikte kullanılabilirliğini değerlendirmek için makale başlıklarını, ortak yazarları ve/veya makalenin materyal ve metodunu takip edebilirler. Pratikteki uygulamalar için deneysel koşullar altında olumlu etkiler gösteren yem katkılarından mucizeler beklemek yerine aslında hasat ve depolama koşullarını optimize ederek aflatoksin kontaminasyonunun sınırlandırılmasına odaklanmak gerekir.

Anahtar kelimeler: Aflatoksin, etkisizleştirme, kanatlı, yem

Abstract

In this meta-analytical study, in vivo experimental studies with adsorbents and biological products as feed additives for inactivation of aflatoxin (AF) in poultry feeds are summarized. Totally, 231 researches carried out in 42 different countries were examined and listed with the first author's country name and presented their results in summary. This review presents the results of the experiments for nutritionists in the feed industry and scientists and provides a basis for total evaluation on the basis of regional results. The studies have been performed mostly in broilers (85%) among poultry species; and mostly in humid countries and/or the countries which import feedstuffs from them. Experiments to reduce negative effects of AF in poultry feed have been mainly performed with clays such as bentonites (BENT) and hydrated Na Ca aluminosilicate (HSCAS) single or in combination with biological matters such as yeast (*Saccharomyces cerevisiae;* SCE) and yeast derivates (Esterified glucomannan; EGM). The best way for producers and researchers, it is preferable to evaluate the preventive efficacy of feed additives as total in terms of performance, biochemical-hematological, immunological and gross and histo-pathological parameters, comparing AF group with AF plus feed additive groups. Scientists can assess the preventive efficacy and practical usability of feed additives in more detail by following the titles of articles, associate authors and/or materials and methods of related articles. In fact, for application in practice, focus on limiting AF contamination by optimizing harvesting and storage conditions should be stressed instead of expecting miracles from feed additives which have shown positive effects under experimental conditions.

Keywords: Aflatoxin, detoxification, poultry, feed

Introduction

Aflatoxins (AF) are a major concern in poultry production and public health because of serious economic losses and health problems. AF in poultry feed cause listlessness, anorexia with lowered growth rate, poor feed utilization, decreased egg production and increased mortality (Miazzo et al 2000). Anaemia (Oguz et al 2000a), reduction of immune function (Gabal and Azzam 1998, Oguz et al 2003), hepatotoxicosis, hemorrhage (Ortatatli and Oğuz 2001), teratogenesis, carcinogenesis and mutagenesis are also associated with aflatoxicosis. The toxicity of AF in poultry has been widely investigated by determining their teratogenic (Sur and Celik 2003), carcinogenic, mutagenic and growth inhibitory (Oguz and Kurtoglu 2000) effects. The biochemical-hematological (Basmacioglu et al 2005), immunological (Qureshi et al 1998), gross and histopathological (Ortatatli and Oğuz 2001) toxic effects of AF have also been well described.

The problem of aflatoxicosis is not so easy to solve and requires constant attention throughout the entire process of grain harvest, shipping, storage, feed manufacturing, and its formulation. Utilization of AF-contaminated (AF-CT) raw materials presents a major problem. Detoxification as well as routine AF analysis of feed ingredients is an important step in a control program at field level. Preventing of mould growth and AF contamination in feed and feedstuffs is very important but when contamination cannot be prevented, decontamination of AF is needed before using these materials. Producers, researchers and governments aim to develop effective prevention management and decontamination technologies to limit toxic effects of AF.

Physical, chemical and biological strategies are essential to counteract the level of contamination of AF in foods and feeds. Practical and cost-effective methods of detoxifying AF-CT feed are in great demand. Besides of the preventive management, approaches have been employed including physical, chemical and biological treatments to detoxify AF in contaminated feeds and feedstuffs. An approach to the problem has been to use non-nutritive and inert adsorbents in the diet to bind AF and reduce the absorption of AF from the gastrointestinal tract.

Since the early 1990s, experiments with adsorbents such zeolites (ZEO) and aluminosilicates have proven successful, but high inclusion rates and possible potential interactions with feed nutrients are causes for concern (Dwyer et al 1997, Phillips 1999, Rosa et al 2001). Also, possible dioxin contamination may be a risk factor for using of natural clays in case of forest and trash fire near their source (Abad et al 2002, Fiedler 2002, Trckova et al 2004, Arikan et al 2009).

Possible solutions

Some studies suggested that the best approach for decontamination would be biological degradation such as yeast and yeast components which could allow removal of AF under mild conditions, without using harmful chemicals or causing appreciable losses in nutritive value and palatability (Bata and Lasztity 1999). A successful detoxification process must be economical and capable of eliminating all traces of toxin without leaving harmful residues without impairing the nutritional quality of the commodity (Bailey et al 1998, Kubena et al 1998, Parlat et al 1999). As a result, researchers have directed efforts towards finding effective means of biological degradation of AF.

Many pellet binding products and flowing agents (clay minerals) or feed materials (yeast and their derivatives) with the claim of mycotoxin (MYC) binding and or detoxification have been used in animal feeds worldwide. However, regulations for MYC binders and deactivators have not been implemented in many parts of the world for various reasons.

This negates the guarantee on the safety and efficacy of the product to the user. Therefore it is important to have guidelines in place which prove safety and efficacy of such additives under different in vitro and in vivo conditions (Murugesan et al 2015).

The European Commission established a new group of technological feed additives for the reduction of MYCs in feed to overcome this unsatisfactory legal situation. In 2010, the European Food Safety Authority (EFSA) published guidelines with stringent requirements, e. g. the binding capacity must be demonstrated; MYC degradation products must be safe for target animals and consumers; minimum 3 in vivo studies with significant efficacy at the lowest recommended dose; relevant biomarkers of each individual MYC have to be used to demonstrate the efficacy of the product, for the evaluation of MYC deactivating products (EFSA 2010, Murugesan et al 2015).

Most studies have used greater concentrations of AF than are likely to be found under field conditions. The AF concentrations in these experiments ranged from 2 to 5 ppm (Kubena et al 1990, Stanley et al 1993, Kiran et al 1998, Kubena et al 1998, Ibrahim et al 2000, Miazzo et al 2000, Oguz et al 2000a, Rosa et al 2001), because these high concentrations were expected to elicit the toxic effects of AF and also any effects of the feed additive would be easily seen in a shorter experimental period.

The in vivo experimental trials performed by using adsorbents and biological products as feed additive in poultry are briefly given below. A total of 231 studies (in vivo and in poultry species only) were examined and are listed for 42 countries according to the first author's institute.

Countries and researches

Argentina

• Miazzo et al (2000) supplemented synthetic ZEO (1%) to AF-CT (2.5 ppm) broiler diet and ZEO significantly reduced the adverse effects of AF on performance and reduced the incidence and/or severity of hepatic histopathology lesions caused by AF.

• Miazzo et al (2005) incorporated Na BENT (SB; 0.3%) to AF-CT (2.5 ppm) broiler diet and SB provided significant improvements in liver histopathology and biochemistry.

• Magnoli et al (2008) added natural BENT (0.3%) to AF-CT (30-135 ppb) broiler diet and BENT reduced severity of hepatic damages associated with aflatoxicosis.

• Magnoli et al (2011) added SB (0.3%) and monensin (55 ppm) into AF-CT (100 ppb) broiler diet. Histopathology indicated that SB was effective in reducing the severity of hepatic changes associated with aflatoxicosis. Also the decrease of its capacity in the existence of monensin was observed.

• Pizzolitto et al (2013) incorporated SCE to AF-CT (1.2 ppm) broiler diet and drinking water for 28 d. The addition of SCE to drinking water and to the diets contaminated with AFB1, showed a positive preventive effect on the relative weight of the liver, histopathology, performance and biochemical parameters.

• Magnoli et al (2017) added yeast (P. kudriavzevii) (0.1%) to AFB1-CT (100 ppb) broiler diet for 21 d. Native P. kudriavzevii addition in broiler diets containing AF was shown to be effective in ameliorating the adverse effects of AF on production.

Australia

• Bryden (2012) reviewed MYC contamination in the feed supply chain, with implications for animal productivity and feed security; with numerous (260) related references.

Austria

• Lee et al (2012) supplemented mycofix select (2. 27 g/kg) into AF-CT (1, 1.5 and 2 ppm) laying hens' feed for 6 weeks. Results indicate that AF deactivating compound can ameliorate some of the negative effects.

• Murugesan et al (2015) reviewed prevalence and effects of MYCs on poultry health and performance, and recent development in MYC counteracting strategies, with related 174 references.

• Vekiru et al (2015) incorporated different BENTs and ZEOs (0.5%) into AF-CT (2 ppm) broiler feed for 21 d. The results indicated that tested ZEO was ineffective in AFB1 binding, while most of the tested Ca- or Na-BENTs were effective. Moreover, cis-BENTs were more effective than the tested trans-BENT. Even among the good binders there were differences in in vivo efficacy indicating that in vitro testing alone is not adequate for evaluation of adsorbents.

Belgium

• Schwarzer and Baecke (2009) reviewed inactivators for MYCs (based on botanicals, yeast and clay-minerals) on animal performance.

• Kolosova and Stroka (2011) reviewed the substances for reduction of the contamination of feed by MYCs with related articles.

Brazil

• Santurio et al (1999) added SB (0.25 and 0.5%) to AF-CT (3 ppm) broiler diet and SB partially reduced the effects AF on broiler chickens when included at 0.5% in the diet.

• Rosa et al (2001) supplemented SB (0.3%) to AF-CT (5 ppm) broiler diet and SB in the diets significantly improved the adverse effects of AF on performance, biochemistry and gross and histopathology of liver.

• Santin et al (2003) incorporated Saccharomyces cerevisiae (SCE; 0.2%) to the broiler diet and SCE did not improve the suppressive effects of AF on performance and immunity.

• Batina et al (2005) added sodic montmorillonite (MNT; 0.25 and 0.5%) to AF-CT (5 ppm) broiler diet and addition of 0.5% level MNT provided partial improvements in the biochemical changes associated with AF.

• Franciscato et al (2006) supplemented sodic MNT (0.25 and 0.5%) to AF-CT (3 ppm) broiler diet, addition of 0.5% sodic MNT significantly improved the biochemical parameters.

• Santin et al (2006) added YCW (0.1%) into AF-CT (250 and 500 ppb) broiler diet, and YCW was found to be effective in preventing the negative effects of AF on performance.

• Siloto et al (2011) supplemented glucan derived from YCW (0.2%) into AF-CT (1 ppm) layer hens' diet, and YCW partially ameliorated the detrimental effects of AF on performance and egg quality.

• Uttpatel et al (2011) incorporated EGM (0.1%) into AF-CT (500 and 750 ppb) broiler breeders' diet. Body weight of the breeders, egg weight, and specific weight of eggs, hatchability and chick quality were not affected by the levels of AF and adsorbent present in the diet.

• Rosa et al (2012) added EGM (0.1%) to AF-CT (500, 750 and 1000 ppb) broiler diet; the addition of up to 750 ppb AF and adsorbent in the breeder diets during eight weeks did not affect the performance or blood parameters of their progeny.

• Neff et al (2013) supplemented hydrated Na calcium aluminosilicate (HSCAS; 0.5%) to AF-CT (2.5 ppm) broiler diet for 21 d. AF residues were lower in livers and kidneys of birds fed AFB1 plus HSCAS when compared with birds fed AFB1 alone. The decrease in the bioavailability of AFB1 caused by the HSCAS reduced AF residues in liver and kidney, but not enough to completely prevent the toxic effects of AFB1 in broilers.

• Carao et al (2014) reviewed the physical and chemical methods of detoxification of AF and reduction of fungal contamination on poultry productive chain, with 38 references.

• Eckhardt et al (2014) added Brazilian Ca-MNT (2.5 and 5 g/kg) into AF-CT (3 ppm) broiler diet for 42 d. Dietary Ca-MNT positively affected parameters such as weight of liver, heart and gizzard and partially reduced the toxic effects of AF in broilers when included at levels of 2.5 and 5 g/kg in the diet.

• Bovo et al (2015) supplemented fermentation residue containing SCE (1%) into AF-CT (2 ppm) broiler diet for 42 d. Feed additives reduced the adverse effects of AF on performance parameters; and severity of histological changes in liver and kidney caused by AF while partially ameliorated the changes on relative liver and kidney weights.

• Oliveira et al (2015) incorporated anti-MYC additives based on SCE (0.2%) to AFB1-CT (1 ppm) broiler diet for 21 d. The addition of two different kinds of SCE (0.2%) could reverse such effects. These are the first data reported from Brazil anti-MYC additives with preliminary isothermal analysis. Since beneficial characteristics of YCW in animal industry are strain dependent, this study suggests two new promising alternatives to ameliorate AF problem.

• Sakamoto et al (2017) supplemented silymarin (0.05%) to AFB1-CT (1.5 ppm) feed for 60 days in quail. The concentrations of silymarin evaluated in this study were not able to mitigate the negative effect of AF on the metabolism and performance of laying quail.

Bulgaria

• Valchev et al (2017) supplemented Mycotox NG (0.5 g/kg) to AFB1-CT (0.2 and 0.4 ppm) feed from 7 to 42 days of age in turkeys. The supplementation of Mycotox NG reduced and prevented some of deleterious effects of AF on production traits, antibody titers and relative weights of visceral organs.

Cameroon

• Kana et al (2009) supplemented plant charcoal from Canarium schweinfurthii (charcoal A) and maize cob (charcoal B) at doses of 0.2; 0.4 and 0.6 % to AF-CT (22 ppb) broiler diet. The addition of 0.20% of charcoal A and 0.60% of maize charcoal was effective in absorbing AF and promoting growth performance of broilers.

China

• Shi et al (2009) added MNT (0.3%) and MNT nanocomposite (0.3%) to AF-CT (110 ppb) broiler diet; MNT nanocomposite significantly reduced the effects of AF on performance and biochemistry.

• Juan-juan et al (2010) added yeast cell extracts, HSCAS and a mixture of yeast product; HSCAS at the levels of 1.5% into AF-CT (100 ppb) broiler diet and HSCAS effectively prevented the toxic effects of AF on performance and biochemistry.

• Che et al (2011) supplemented EGM (0.05%), HSCAS (0.2%) and a kind of adsorbent (CMA) into AF-CT broiler. Addition of 0.05% EGM and 0.2% HSCAS partially alleviated the adverse effects of AF; 0.1% CMA ameliorated the adverse effects.

• Guan et al (2011) reviewed the microbial strategies to control AF in food and feed with 111 related references.

• Liu et al (2011) added EGM (0.05%), HSCAS (0.2%) and compound MYC adsorbent (CMA; 0.1%) to AF-CT (450 ppb) broiler diet. The addition of EGM, HSCAS or CMA prevented some adverse effects of MYCs to varying extents, with CMA being the most effective adsorbent treatment.

• Liu et al (2012) reviewed the advanced research on the MYC removing with related references.

• Fan et al (2013) added B. subtilisANSB060 to AF-CT (90 ppb) broiler diet for 42 d. The addition of B. subtilis provided protective effects on growth performance and meat quality while reducing the amount of AF residues in the livers of broilers fed naturally moldy peanut meal.

• Zhu (2013) supplemented wood vinegar (0.5, 1 and 2%) into AF-CT (40 ppb) broiler feed for 42 d. Wood vinegar could reduce or substantially eliminate the adverse effects from AFB1 on growth performance and tissue damage.

• Zou et al (2013) supplemented probiotic (0.5%) into AF-CT (400 ppb) broiler diet for 30 d. The results showed that adding 0.15% feed additive in broiler diets could significantly relieve the negative effect of AFB1 on chicken's production performance and nutrient metabolic rates. It could be concluded that the probiotic was able to degrade AFB1 and improve animal production.

• Chen et al added (2014a) supplemented Na-selenite (0.2, 0.4 and 0.6 ppm) to AFB1-CT (0.3 ppm) broiler feed for 21 d. The results indicate that Na selenite in diet can protect chicken from AFB1-induced impairment of humoral immune function by reducing bursal histopathological lesions and percentages of apoptotic bursal cells.

• Yu et al (2015) added Na-selenite (0.4 ppm) into AF-CT (300 ppb) broiler diet for 21 d. These results suggested that Na-selenite supplied in the diet could effectively inhibit AFB1- induced apoptosis and cell cycle blockage in renal cells of broiler.

• Ji et al (2016) reviewed biological degradation of MYCs with 103 related articles.

• Liu et al (2017a) supplemented LAB (3 x 1010 cfu/kg) to AFB1-CT (40 ppb) broiler diet for 35d. LAB is effective in the detoxification of AF by modulating toxin metabolism and activating the GSH pathway in animals.

• Liu at al. (2017b) added fermented and unfermented with Cellulosimicrobium funkei cottonseed meal (108 cfu/kg) to AF-CT (16 and 96 ppb) duck diet for 2 wk. Fermentation of AF-CT feed materials by C. funkei offers a new strategy to reduce the negative effects of aflatoxicosis in ducklings.

• Liu et al (2017c) supplemented Na selenite (0.4 ppm) to AFB1-CT (600 ppb) broiler diet for 21 d. Dietary supplementation of 0.4 ppm Se in the form of Na selenite could protect the cecal tonsils from the histological lesions and suppression of the mucosal humoral response provoked by 600 ppb AFB1.

• Muhammad et al (2017) added curcumin (150, 300 and 450 ppm) to AFB1-CT (5 ppm) feed from 1 to 28 d in broilers. The administration of curcumin partially ameliorated the increase in liver weight and decrease in body weight in a dose-dependent manner. However, curcumin treatment inhibited CYP2A6 at mRNA and protein levels in AFB1 treated broiler in a dose-dependent manner.

• Rajput et al (2017) supplemented grape seed (250 and 500 ppm) to AFB-CT (1 ppm) broiler diet for 28 d. The supplementation of grape seed in both levels to contaminated diet reduced AFB1 residue in the liver and significantly mitigated the negative effects of AFB1.

• Zhang et al (2017) added B. subtilis ANSB060 to AF-CT (22.44 ppb) feed for 42 d in ducks. The supplementation of B. subtilis ANSB060 into AF-CT diets moderately increased the average daily gain of ducks, significantly improved antioxidant enzyme activities, and reduced AF accumulation in duck liver.

• Fang et al (2018) incorporated Se (600 ppb) to AFB1-CT (400 ppb) broiler feed from 1 to 21 d of age. Se restored the parameters to be close to those in the control group and Se promoted cell cycle recovery from the AFB1-induced G2/M phase arrest by the molecular regulation of ATM pathway in the jejunum of broilers.

• Liu et al (2018a) added LAB (4x1010 cfu/kg) and Smectite (0.3%) to AFB1-CT (40 μg/kg) broiler feed from 1 to 42 d of age. The inclusion of the LAB strains selected in this study improved the growth performance, nutrient digestibility, and the hematological and biochemical parameters, and most parameters reached the levels of the diets without AFB1 contamination and the physical adsorbent smectite.

• Liu et al (2018b) incorporated LAB (1.5x1010cfu/kg) and HSCAS) (0.3%) to AFB1-CT (40 ppb) from 1 to 21 d of age in broiler chickens. The LAB and HSCAS increased the digestibility of dry matter, crude protein, crude fat, and digestible energy by 4.0–15.0%, and improved immune function by modulating the relative weights of immune organs, lymphocyte percentages, and immunoglobulin contents. Additionally, residual AFB1 in serum and organs in LAB treatment was lower than HSCAS.

Colombia

• Diaz et al (2009) added some feed additives (containing aluminosilicate and phytogenic substances) to AF-CT (250 and 500 ppb) turkey diet and used feed supplements partially diminished the negative effects of AF on performance and immunology by the supplements.

Croatia

• Peraica et al (2002) reviewed prevention of MYC production and methods of decontamination including adsorbents, with related 68 references.

Cuba

• Rivera and Farias (2005) reviewed clinoptilolite (CLI) -surfactant composites as a drug support and their mechanism, with related 52 references.

Czechia

• Trckova et al (2004) reviewed kaolin, BENT and ZEOs, their binding properties and their usage as feed supplements for animals, with related 108 references.

Denmark

• Shetty and Jespersen (2006) reviewed SCE and LAB for decontamination of MYCs. The authors also noted the binding mechanism of them, with related 84 references.

Egypt

• Matari (2001) incorporated SB (0.5 and 1%) into AF-CT broiler diet and SB significantly restored the adverse effects of AF.

• Eshak et al (2010) added SCE (0.5, 1, 2, 2.5%) to AF-CT (0.5 ppm) quail diet and addition of SCE to quail diets suppressed the aflatoxicosis in quail tissues leading to improvement of growth performances and enhancement of expression levels of neural and gonadal genes. .

• Ellakany et al (2011) supplemented HSCAS (0.50%), SCE (0.25%) and EGM (0.25%) into AF-CT broiler diet. While HSCAS significantly improved performance, biochemical and immunological parameters when compared with AF group; EGM significantly improved performance, but there was no effect on other parameters. SCE had no effect on any of the parameters tested when compared with broilers fed AF.

• Attia et al (2013) added mannanoligosaccharide (MOS), HSCAS and L. acidophilus (2 g/kg) to AF-CT (200 ppb) broiler diet for 21 d. Lactobcillus was most effective in reversing the adverse effects of AF on growth and FCR and on the percentage, functions and morphology of the liver. HSCAS also improved the economic traits of broilers but was less effective than Lactobacillus and more effective than MOS.

• El-Ghany et al (2013) incorporated HSCAS (0.5%), turmeric powder (80 ppm) into AF-CT (2.5 ppm) broiler diet for 5 weeks. Both HSCAS and turmeric powder treatment induced significant amelioration of the measured organs body weights ratio, humoral immune response to Newcastle Disease and biochemical parameters in aflatoxicated chickens. In conclusion, addition of HSCAS and or turmeric powder can be considered an integrated approach for the control of aflatoxicosis in broiler chickens.

• El-Deep et al (2016) added glutathione (0.5 ppm) to AFB1-CT (1 ppm) feed from 28 to 50 weeks in laying hens. Addition of glutathione to AF-CT diet could make significant improvements of most of measurements including egg quality, semen quality, fertility, antioxidant status, immune status against NDV.

• Salem et al (2018) supplemented Nutritox (Biological MYC binder; 0.1%) to AFB1-CT (250 ppb) broiler feed for 42 d of age. The supplementation of Nutritox significantly reduced AF levels in the liver and counteracted the negative effects of AFB1 on performance, biochemical and histopathological parameters.

France

• Guerre (2000) reviewed the physical and chemical methods used for inactivation of MYCs. The adsorbents including aluminosilicates were also explained in detail, with the results of related 128references.

• Jouany (2007) reviewed the methods for preventing, decontaminating and minimizing the toxicity of MYCs including aluminosilicates and yeast derivatives, with related 165 references.

• Jard et al (2011) reviewed MYC reduction methods in food and feed: from prevention in the field to detoxification by adsorption or transformation; with related 241 references.

Germany

• Danicke (2002) reviewed prevention and/or control of MYCs in poultry feed; results of the researches in detail, with related 128 references.

Greece

• Pappas et al (2014) added BENT (1%) into AF-CT (20 ppb) broiler diet for 42 d. The study revealed that the examined BENTs may maintain optimum broiler performance when AF levels present in the diet do not exceed EU limits.

• Pappas et al (2016) supplemented different BENTs (0.5% and 1%) to AF-CT (100 ppb) broiler diet for 42 d. The study revealed that binder composition and presence or not of multiple toxins may be important factors for optimum broiler performance under mycotoxicosis.

Hungary

• Bata and Laztity (1999) reviewed physical and chemical methods and biological adsorbents recommended for detoxification of MYC-contaminated feed. The present state of research in this field and the perspectives of such procedures were also discussed, with 42 related references.

India

• Jindal et al (1994) added ACH (200 ppm) to AF-CT (0.5 ppm) broiler diet; the results showed that ACH provided protection of broilers against harmful effects of AF on performance and biochemistry.
• Raju and Devegowda (2000) incorporated EGM (0.1%) into AF-CT (300 ppb) broiler diet; additionof EGM significantly decreased the detrimental effects of AF on performance parameters, biochemistry and organ morphology.
• Girish and Devegowda (2004) added EGM (0.1%) and HSCAS (1%) to AF-CT (2 ppm) broiler diet and both adsorbents provided significant improvements in performance and relative organ weights associated with aflatoxicosis.
• Gowda et al (2008) added turmeric powder (0.5%) and HSCAS (0.5%) to AF-CT (1 ppm) broiler diet and the adsorbents demonstrated protective action in the deleterious effect of AF on performance, biochemistry, antioxidant functions and histopathology.
• Sawarkar et al (2011) supplemented Toxiroak Gold (0.1%) to AF-CT (100 ppb) broiler diet; herbomineral toxin binder feed supplement provided amelioration of aflatoxicosis in broilers.
• Srikanth et al (2011) added ACH (0.4%) and yeast culture (0.1%) into AF-CT (1ppm) broiler diet; the combination of ACH and yeast culture was more effective incounteracting the combined toxicity of AF and T-2 toxin compared to the ACH alone.
• Gowda et al (2013) reviewed recent advances for control, counteraction and amelioration of potential AF in animal feeds with the results of 38 related references.
• Dhanapal et al (2014) also added citrus fruit oil (2.5 g/kg) into AF-CT (1 ppm) broiler diet for 35 d. The results showed that supplementation had a moderate effect on post treatment growth performance, relative organ weight, and biochemical parameters. It is suggested that citrus fruit oil as a feed additive causes partial amelioration of aflatoxicosis.
• Patil et al (2014) reviewed mycotoxicosis and its control in poultry with the results of 86 related references.
• Aravind and Churchill (2015) supplemented EGM (0.1%) to AF-CT (1 ppm) broiler diet for 6 weeks. The addition of EGM significantly counteracted the ill effects of AF on weight gain and feed consumption. The reduction in feed efficiency due to AF was restored to normal by EGM supplementation.
• Kumar et al (2013) incorporated citrus fruit oil (2.5 g/kg) into AF-CT (1 ppm) broiler diet for 35 d. The addition of citrus oil to AF-CT diet moderately decreased the magnitude and severity of lesions (hydropic degeneration and bile duct hyperplasia) in the liver.
• Mamta et al (2015) added methionine (0.05 and 0.1%) into AF-CT (250 ppb) broiler feed for 42 d. Supplementation of 0.1% methionine to the AF-CT diet had pronounced ameliorative effect on performance of the birds.
• Sharma et al (2015) added methionine (0.05 and 0.1%) into AF-CT (250 ppb) broiler feed for 42 d. Supplementation of 0.1% methionine to the AF-CT diet had pronounced ameliorative effect on performance of the birds.
• Tingting et al (2015) Na-selenite (0.2, 0, and 0.6 ppm) to AF-CT (300 ppb) broiler diet for 21 d. It was indicated that Na-selenite in the diets could exert protective effects against AFB1-induced damage on the red blood cells, and the transport capacity and immune adherence function of erythrocyte could be maintained.
• Lakkawar et al (2017) added diatomaceous earth (DAE; 0.2%) to AF-CT (0.5 and 1 ppm) feed for 35 d in broilers. The supplementation of DAE to AF-mixed feed revealed significant improvement characterized by decreased severity of lesions in lymphoid organs. Addition of 0.2% DAE in feed can be effectively used to reduce the the histotoxic effects of AF on lymphoid organs in broiler chicken.
• Raja et al (2017) supplemented Curcuma longa (1%) to AFB1-CT (1 ppm) broiler diet for 42 d. AF causes a marked oxidative stress in comparison to control, which was partially reversed by the supplementation of the C. longa (1%) in the feed. However, C. longa significantly improved the antioxidant status in induced aflatoxicosis and partially protected against the cytotoxic effects of AFB1 in broiler chickens.
• Wade and Sapcota (2017) incorporated EGM (0.025%, 0.5% and 0.1%) to AFB1-CT (300 ppb) feed for 42 d in broiler chickens. The feed efficiency was inferior in the AF-alone fed group; however, when EGM was supplemented there was significant, though partial improvement. Dietary EGM reduced cost of feeding. Among the various treatments, 0.1% of EGM addition gave the best results.

Indonesia

• Sjamsul et al (1990) supplemented ACH (1.5 and 3%) to AF-CT (150 ppb) duck dietand addition of charcoal alleviated the detrimental effects of AF on gross and histopathology of the livers of ducks. 3% ACH was found to be more effective.
• Istiqomah et al (2017) added LAB (Lactobacillus plantarum G7) (1%), Methionine (0.8 and 1. 2%) to AF-CT (2. 71 and 32. 39 ppb) broiler feed for 35 day of age. AF in feed for 35 days period did not significantly affect the body weight gain and feed conversion.
• Karimy et al (2017) added Lactobacillus plantarum G7 (1% w/w), methionine (0.8% w/w) to AF-CT (57. 18 ppb) feed for 1 to 34 d in broilers. The doses of additive in each treatment were insufficient to reduce adverse effect of AF on erythrocyte profile and histopathology. The LAB dose for binding AF (57. 18%) sho-

uld be evaluated and the dose for methionine should be reduced for chronic treatment of aflatoxicosis.

Iran

• Modirsanei et al (2004) added SCE (0.5%) and natural ZEO (0.75%) to AF-CT (1 ppm) broiler diet; addition of 0.75% ZEO did not reduce any of the adverse effects, whereas supplemention of SC moderately ameliorated the effects in respect of performance and biochemistry.

• Safameher et al (2004) administrated ammonia to AF-CT (1 ppm) broiler diet and they provided significant improvements in performance and hematology by treating ammonia in contaminated feed.

• Abousadi et al (2007) incorporated SB (0.5%), SCE (0.2%), HSCAS (0.5%), ammonia (0.5%), formycine (0.1%), and toxiban (0.1%) into AF-CT (125 ppb) broiler diet. Generally addition of the compounds made an improvement against negative effects of AFB1 on performance and biochemistry in broiler chickens. Formycine was recognized to be the best additive in this respect.

• Modirsanei et al (2008) added diatomaceous earth (30 ppm) to AF-CT (1 ppm) broiler diet; the added adsorbent alleviated the negative effects of AF in performance and biochemistry associated with aflatoxicosis.

• Safameher (2008) supplemented CLI (2%) to AF-CT broiler diet to ameliorate the toxic effect ofAF (0.5 ppm) and CLI provided significant improvements against AF toxicity in performance, biochemistry and liver histopathology.

• Ghahri et al (2009) added EGM (0.1%), SB (0.5%) and humic acid (0.2-1%) to AF-CT broiler dietto ameliorate the toxic effect of AF (254 ppb) against humoral immunity. The addition of EGM, SB and humic acid to the AF-CT diet ameliorated the negative effects of AF on ND antibody titers, but humic acid proved to be more effective in the amelioration of the detrimental effect of AF on humoral immunity against ND.

• Kamalzadeh et al (2009) added yeast GM (0.5, 1 and 1.5%) to AF-CT (184 ppb) broiler diet and yeast GM significantly decreased the negative effects of AF on performance. 1% GM was found more effective than other concentrations.

• Kermanshahi et al (2009) supplemented SB (0.5 and 1%) to AF-CT (0.5 and 1 ppm) broiler diet and SB significantly improved the effects of AF on performance and biochemistry.

• Manafi et al (2009) added high-grade SB (1%) to AF-CT (500 ppb) broiler diet and SB reduced the toxicity of AF on some parameters.

• Shabani et al (2010) incorporated nanoZEO (0.25-1%) into AF-CT (500 ppb) broiler diet; nanoZEO significantly reduced the toxic effects of AF in performance and biochemistry.

• Manafi (2011; 2012) added BENT (0.5; 0.75 and 1%), Spirulina platensis (0.1%) and EG (0.2%) to AF-CT (300, 400 and 500 ppb) broiler breeders diet. Among the binders, EG showed better protection against AF in terms of biochemical and immunological parameters, fertility and hatchability.

• Mogadam and Azizpour (2011) added yeast GM (0.05 and 0.1%) and SB (1.5 and 3%) to AF-CT (250 ppb) broiler diet. The addition of yeast GM and SB, individually and in combination to the AF-containing diet, ameliorated the adverse effects of AF. But 0.1% yeast GM supplementation to the contaminated diet with AF proved to be much more effective in the amelioration of the adverse effect of AF on performance and humeral immunity against ND.

• Rangsaz and Ahangaran (2011) incorporated ethanolic turmeric extract (0.05%) to AF-CT (3 ppm) broiler diet. The results suggested that turmeric extract (Curcuma longa) provided protection against the negative effects of AF on performance of broiler chickens.

• Kaki et al (2012) added ZEO (3 g/kg) and mycosorb (1 g/kg) to AF-CT (0.5 and 1 ppm) broiler feed for 6 weeks. The addition of mycosorb and ZEO to the AF-CT diet significantly recovered the adverse effect of AF on performance and biochemical-hematological values of broilers. The protective effect of mycosorb was higher than that of ZEO against the toxic effects of AF.

• Kasmani et al (2012) incorporated Bacillus probiotic (108 CFU/ml) and mill-bound-TX (2.5 g/kg) to AF-CT (2.5 ppm) Japanese quail diet for 49 d. The results verified its AFB1-binding activity in quails with regard to performance, serum biochemistry, and immune responses.

• Khadem et al (2012) supplemented yeast (0.5%), ZEO (1.5%) and active charcoal (1.5%), alone or in combination into AF-CT (200 ppb) broiler diet. Results indicated that the mixtures of the tested absorbents were more effective in reducing symptoms of AF toxicity in growing broilers.

• Gholami-Ahangaran and Jahromi (2013) added nanosilver (2500 ppm) to AF-CT (3 ppm) broiler feed for 28 d. Feed additive completely restored the adverse effects of AF on performance parameters. These improvements showed the ability of nanocid to diminish the inhibitory effects of AF.

• Sherefat et al (2013) added SB (0.5%) into AF-CT (1 ppm) broiler cockerel's diet for 42 d. The results showed that SB partially diminished the adverse effects of dietary AFB1 on performance and organ weights in broiler cockerels.

• Manafi et al (2014a) supplemented rosemary (500 ppm) into AFB1-CT (600 ppb) broiler feed for 6 weeks d. The rosemary could essence have partially restored the negative impacts of AF on performance and antibody titers in broilers.

• Manafi et al (2014b) added thyme essence (500 ppm) to AFB1-CT (600 ppb) broiler feed for 42 d. The inclusion of thyme essence have showed an improved data and addition of Thyme essence to AF-fed groups could partially alleviate the adverse effects of AF in the diet. The antibody titers of broilers fed AF were significantly increased and incorporation of thyme essence could partially restore the negative impact of AF in commercial broilers.

• Sadeghi et al (2014) incorporated savory essential oil (500 ppm/dry matter) into AF-CT (0.5 ppm) broiler diet for 42 d. The addition of savory reduced the adverse effects of AF on growth performance and provided slight positive effect on serum biochemistry and humoral immune responses in broilers exposed AF.

• Azizpour and Mogadam (2015) supplemented EGM (0.05 and 0.1%) and SB (1.5 and 3%) into AF-CT (250 ppb) broiler diet for 42 d. The addition of YG and SB to the AF-CT diet partially reduced the negative effects of AF. The 0.1% EGM supplementation to the AF-CT feed significantly prevented the pathological effect of AF on serum biochemical parameters and liver, and was found to be more effective than other treatments.

• Gholami-Ahangaran et al (2016) added Turmeric (5 ppm), Mycoad (25 ppm) to AF-CT (3 ppm) feed for 28 days in broilers. The study showed that turmeric may provide protection against the toxic effects of AF on liver and kidney.

• Jahanian et al (2017) incorporated Silymarin (500 and 1000 ppm) to AF-CT (0.5 and 2 ppm) feed from 7 to 42 d of age in broilers. Feeding silymarin at the level of 1000 ppm increased villi height and villi height-to-crypt depth ratio in aflatoxicated birds. Dietary inclusion of silymarin could improve performance by suppressing ileal bacteria and enhancing absorptive surface area in AF-challenged broiler chicks.

• Mohaghegh et al (2017) supplemented EGM (0.05% and 0.1%), to AF-CT (480 ppb) diet for 42 days in broiler chickens. Results indicated that supplementing EGM particularly at 0.1% level efficiently reversed the adverse effects of AF on broiler chickens.

• Rasouli-Hiq et al (2017) added Nigella sativa seeds (0.5, 1 and 1.5%) to AF-CT (2.5 ppm) feed from 7 to 25 d of age in quail. This study revealed that N. sativa as a biological detoxifier could relatively attenuate the negative effects of AFB1 in quails.

• Barati et al (2018) incorporated Toxeat (0.1%), Lactobacillus (0.1%), B. subtilis JQ618 (0.1%), YCW (0.1%), HSCAS (1.5%) to AF-CT (1 ppm) broiler diet from 7 to 42 d of age. It is concluded that a prebiotics and probiotics mixture is suitable for improving immune function and serum biochemical parameters as an effect of feeding AF-CT diet.

• Saki et al (2018) supplemented mycosorb (0.25%) into AF-CT (1 ppm) broiler diet from 1 to 42 d of age. The study demonstrated that mycosorb was effective in alleviating the adverse effects of dietary AF on performance and some biochemical values in broilers.

Iraq

• Ibrahim et al (2000) added SB (0.2, 0.4 and 0.6%) to AF-CT (2.5 ppm) broiler diet and the addition of SB was significantly effective in ameliorating deleterious effect of AF on humoral immunity. SB also improved the adverse effects of AF on performance and hematology (Ibrahim et al 1998) and carry-over of AF from feed to eggs (Ibrahim and Al-Jubory 2001).

• Ali (2004) supplemented vitamin E, poultry star, levamisole, acetic acid into drinking water of broilers with AF-CT (8 ppb) for 25 d. Using vitamin E with selenium and poultry star were reduced the effect of AF on immune response and protect the lymphoid organs. Whereas, levamisole and acetic acid were act in less degree as compared with vitamin E and poultry star.

• Al-Daraji (2012) added licorice extract (LE; 150 ppm) into AF-CT (2 ppm) broiler diet for 7 weeks. The simultaneous addition of LE to the AF-CT diet improved the negative effects of AF on carcass traits and provided great improvement in AF toxicity on broiler performance.

• Shareef and Omar (2012) incorporated synertox (0.5 ml/L) to AF-CT (2.5 ppm) broiler feed for 42 d. Synertox was effective in counteracting the negative effect of AF on relative bursal weight, thymus and spleen relative weights. A significant restoring of ND antibody titre to those of control group was recorded by addition of Synertox to the drinking water of broilers in compared with the AF fed group. It could be concluded that Synertox could be used in counteracting the negative effects of AF on health and performance of broiler chicks.

• Makki and Abed (2016) supplemented SCE (2%), Fructo-oligosaccharide (0.25%) to AF-CT (100 ppb) broiler feed for 35d. The supplementation of SCE and fructo-oligosaccharide had beneficial effects on broilers health and can minimize the effect of AF on broiler performance and immunity. .

• Al-Zuhariy and Hassan (2017) incorporated Ganoderma lucidum (CL; 0.2%), Andrographolide (AP; 0.2%), Turmeric curcuma (CM; 0.2%) to AF-CT (46. 768 and 48. 661 ppb) broiler diet for 45 d. The study showed that the role of GL, AP and CM in reducing the negative effects of AF by decreasing oxidative stress and immunosuppression in broiler chickens.

• Ulaiwi (2017) added probiotic (5×1012 CFU /kg), vitamin E and Se (80 mg and 1. 6 mg as 0.5ml/L) to drinking water. Broilers were fed AF-CT (0.8 ppm) diet for 35 d. The study confirmed the protective role of probiotic on body weight and histopathological changes, while vitamin E and selenium had a protective role on leukocyte count.

Italy

• Rizzi et al (1998) added EGM (0.11%) to the layer diet and EGM provided significant improvements in the detrimental effects of AF.

• Galvano et al (2001) reviewed dietary strategies to counteract the toxic effects of MYCs; feed additives and binding agents were discussed in detail, with the results of 113 related references.

• Rizzi et al (2003) supplemented CLI (2%) to AF-CT (2.5 ppm) layer diet and CLI provided no improvements in egg quality.

• Tedesco et al (2005) added silymarin-phospholipid complex (600 ppm BW) to AF-CT (800 ppb) broiler diet; they provided significant improvements in performance parameters by adding feed additive.

• Zaghini et al (2005) incorporated MOS (0.11%) to AF-CT (2.5 pmm) layer diet and MOS decreased the gastrointestinal absorption of AF and its level in tissues.

Korea

• Kim et al (2003) added soybean paste (doen-jang; 0.5, 1 and 5%) into AF-CT (500 ppb) layer diet and the addition of 5% soybean paste significantly reduced the negative effects of AF on performance, biochemistry, gross and histopathology of liver, egg production and accumulation of AF in hens' eggs.

Mexico

• Mendez-Albores et al (2007) treated AF-CT (110 ppb) duck feed with citric acid (1N for 15 min, 3ml/g feed) and citric acid significantly ameliorated negative effects of AF on mutagenity,

carcinogenity and toxicity in respect of performance, biochemistry and pathology.
• Mendieta et al (2018) added YCW (0.15%), to AFB1-CT (350 ppb) diet for 21 days in broiler chicks. The addition of YCW can be an alternative to counterage the negative effect of low doses of AFB1 in broilers diets.

Nepal
• Karn (2013) added N. sativa seed (2%) to AF-CT (30 ppb/d) duckling feed for 2 weeks. From the obtained results, it can be concluded that the addition of N. sativa as a feed additive in poultry diet products the hepatotoxicity induced by AF on biochemical and histopathological parameters.

Nigeria
• Lala et al (2015) incorporated nano-clay adsorbent (2.5 g/kg) into AF-CT (60, 110 ppb) turkey diet for 84 d. Dietary supplementation with clay adsorbents regardless of contamination levels of AF showed improved packed cell volume and hemoglobin count when compared with turkeys fed AF-CT diet containing no adsorbent.
• Ologhobo et al (2015) added MNT, HSCAS and SB (2 g/kg) into AF-CT (2 ppm) broiler feed for 8 weeks. No significant preventive effects were observed. AF binding agents should be rigorously tested paying particular attention to their effectiveness and safety.

Pakistan
• Musaddeq et al (2000) supplemented Myco-Ad, Sorbatox and Mycofix-Plus to AF-CT (8 and 60 ppb) broiler diet and the adsorbents recovered the negative effects of AF on performance of chicks.
• Hashmi et al (2006) added yeast sludge (1%; 0.26% mannan oligosaccharide) to AF-CT (100, 200 and 300 ppb) broiler diet and 1% yeast sludge act as toxin binder effectively at 100 and 200 ppb AF, but its efficiency was reduced at 300 ppb AF level; higher levels of yeast sludge effectively improved the aflatoxicosis condition.
• Pasha et al (2007) supplemented SB (0.5 and 1%), SB+gention violet, SB+acetic acid, Sorbatox and Klinofeed to AF-CT (100 ppb) broiler diet. Addition of indigenous 0.5% SB gave overall better results than the market products and provided significant improvements in performance, organ weight and immunology.
• Mahmood et al (2011) reviewed the comparative evaluation of different techniques for AF detoxification in poultry feed and its effect on broiler performance, with 93 related references.
• Khan and Zahoor (2014) incorporated magnetic carbon at five levels (0.2-0.5%), into AF-CT (200 ppb) broiler diet for 42 d. The prepared adsorbent was efficient for the detoxification of AFB1 in gastrointestinal tract in terms of biochemical, organ lesions and performance.
• Ditta et al (2016) supplemented sonicated yeast sludge fractions (YCW and Cell Solubles) with commercial glucomannan to AFB1-CT (100, 200 and 300 ppb) broiler feed from 8 to 28 d of age. The toxin binders showed significant effect on feed intake, weight gain, feed conversion ratio (FCR), relative liver weight, serum albumin, cholesterol and serum minerals while non-significant effect was observed on dressing percentage and serum phosphorus.
• Gul et al (2017) incorporated Na BENT (1.5%, 2% and 2.5%) to AF-CT (170 ppb) feed from 34 to 38 weeks of age in laying hens. The addition of 2% Na BENT showed better feed and protein utilizations leading an increased egg production and reduced eggs defects in layer hens.
• Alhidary et al (2017) reviewed anti-AF activities of milk thistle (Silybum marianum) in broilers with related 54 articles.
• Arafat and Khan (2017) supplemented humic acid (0.1% and 0.3%) to AFB1-CT (100 ppb) diet feed for 42 days in broilers. Humic acid was effective in diminishing the adverse effects caused by AF on body weight of broilers and also showed protective effects against liver damage and some of the hematological and serum biochemical changes associated with AF toxicity. The supplementation of humic acid also enhanced the humoral immunity by counteracting the AF contamination.
• Bhatti et al (2017) added BENT (0.37% and 0.75%) to AFB1-CT (0.1, 0.2 and 0.6 ppm) feed for 42 days in broiler chickens. The results here suggested that dietary addition of BENT could help ameliorate AFB1-mediated immune toxicities.
• Khan et al (2017) added distilled yeast sludge (0.5%, 1% and 2%) to AFB1-CT (136 ppb) diet for 42 days in laying hens. Almost all parameters were normal compared to control group with the addition of 2% yeast sludge, while 1% yeast sludge partially ameliorated the immunotoxic effects of AF.
• Mahmood et al (2017) supplemented ACH (5%), kaolin (5%), Vit E (200 mg), Se (1 mg), HSCAS (2.5 gm) to AFB1-CT (0.5 ppm) quail diet for 42 d. HSCAS, Vitamin E and Se were found as better detoxifying agent among the toxin binders used in this study. This study reports the success of commercially available toxin binders as chemical detoxification agent for the quails, an emerging protein source in thickly populated developing countries.
• Zafar et al (2017) added iron oxide/carbon nanocomposite (0.2%, 0.3%, 0.4% and %0.5) to AFB1-CT (200 ppb) broiler diet for 42 d. It was found that adsorbent at dose of 0.3% was highly effective in detoxifying AFB1 in gastrointestinal tract of poultry birds with no harmful effects. The high doses 0.4% and %0.5 showed slight variation in tested parameters. No negative symptoms associated with the use of ACH as previously reported were observed for the adsorbent under study.

Poland
• Kolacz et al (2004) reviewed the use of synthetic aluminosilicates in decontamination of MYCs including AF. They also noted the characteristics of aluminosilicate and its decontaminating effect, with 43 related references (Kołaczet al 2004).

Saudi Arabia
• Teleb et al (2004) supplemented kaolin and ACH (0.5%) to AF-CT (30 ppb) broiler diet and two adsorbents alleviated the toxic effects of AF on performance but did not reduce the histopathological changes associated with aflatoxicosis.

Serbia

• Zekovic et al (2005) reviewed the use of natural and modified glucans to promote health and control diseases including their immunomodulator effects and MYC adsorption ability, with245 related references.

Slovak Republic

• Iveta et al (2000) incorporated CLI and cephalite (0.5%) to AF-treated (0.5 ppm BW) broilers; long term oral administration of two sorbents caused an increase in CD3+ cells in lamina of duodenum. AF did not change the number of CD3+ lymphocytes significantly.

• Skalicka and Korenekova (2016) added Na humate (1 g/10 g feed mixture) to AFB1-CT (25 µg/kg of BW) broiler feed from 28 to 56 d. The results showed that Na humate has a positive effect on the growth of broilers; and it could have been a suitable natural supplement for growing broilers against the adverse effects of AF.

South Africa

• Rensburg (2005) added humic acid (0.35%) into AF-CT (1 and 2 ppm) broiler diet; partial improvements in performance, hematology and biochemistry were found.

• Rensburg et al (2006) also supplemented humic acid (0.35%) and dried brewer yeast (0.35%) to AF-CT (1 and 2 ppm) broiler diet; they provided significant improvements by humic acid in performance, biochemistry and hematology. Humic acid was found to be much more effective than brewer yeast.

• Dos Anjos et al (2015) added BENT (0.75%), diatomaceous earth (0.75%) and turmeric (0.37%) into AF-CT (2 ppm) broiler diet for 21 d. Feed additives partially alleviated the adverse effects of AF on performance, organ weights and biochemical parameters.

• Adebo et al (2017) reviewed microbial degradation of AF with related 92 articles.

Spain

• Marquez and Hernandez (1995) incorporated two Mexican aluminosilicates (Atapulgita and Fuller earth) at the levels of 0.5 and 1% to AF-CT (200 ppb) broiler diet and the results showed that both aluminosilicates were as efficient as the commercial material in protecting chicks against AF toxicity on performance and gross and histopathology.

• Ramos et al (1997) reviewed nonnutritive adsorbent compounds used for prevention of toxic effects of MYCs, with 111 related references.

• Denli et al (2009) supplemented AflaDetox (1, 2 and 5%) AF-CT (1 ppm) broiler diet; the addition of Afla Detox prevented all toxic effects on performance and serum biochemistry and reduced the accumulation of AFB1 residues in the livers.

• Vila-Donat et al (2018) reviewed MYC adsorbing agents, with an emphasis on their multi-binding capacity, for animal feed decontamination, with 116 related references.

Switzerland

• Huwig et al (2001) reviewed nonnutritive clay-based adsorbents used in poultry feed and their respective mechanism of adsorption. They also listed the adsorption capacity of compounds commonly used, with 73 related references.

Thailand

• Banlunara et al (2005) added EGM (0.05 and 0.1%) to AF-CT (100 ppb) duck diet; supplementation of EGM effectively reduced AFB1-induced hepatic injury in ducklings.

• Bintvihok and Kositcharoenkul (2006) added Ca propionate (0.25 and 0.5%) to AF-CT (100 ppb) broiler diet; addition of Ca propionate appeared to be effective in reducing toxicity of AF on performance and hepatic enzyme activities in broilers.

• Bintvihok (2010) reported that using EGM (0.05% and 0.1%) to AF-CT (60 and 120 ppb) duck diet and EGM provided significant improvements in performance, histopathology and leg deformity caused by AF. The addition of 0.05% EGM also recovered the adverse effects of AF (100ppb) on serum biochemistry and in ducklings.

• Suksombat et al (2011) added SCE (2x107 CFU/g) into AF-CT (250 ppb) broiler feed for 42 d. It is indicated in the present study that supplementation of either commercial or bovine yeasts had beneficial effects on performance of broiler chickens intoxicated with AF in terms of performance and biochemical parameters.

• Tengjaroenkul et al (2016) supplemented Thai BENT (0.2%), HSCAS (0.1%) to AF-CT (70.4 ppb) feed from 7 to 42 d in ducks. Supplementation of 0.1% HSCAS or with 0.2% BENT reduced the adverse effects on all parameters measured. The results support the conclusion that 0.2% BENT can alleviate mycotoxicoses induced by AF in ducks.

• Rattanasinthuphong et al (2017) added multi-mycosorbents (MM; Thai BENT, CLI and YCW) (2%), HSCAS (0.2%) to AF-CT (32 – 38 ppb) feed for 42 d in ducks. The result indicated that supplementation with 0.2% HSCAS or 0.2% MM alleviated the toxic effects of AF; however, 0.2% MM demonstrated better preventive results than 0.2% HSCAS.

• Tanpong et al (2017) incorporated YCW (Fixar® VivaDry) (0.05%, and 0.10%) to AF-CT (60 – 120 ppb) diet for 28 days in ducks. The results showed that Fixar® Viva Dry 0.05% was effective in preventing the toxic effects of AF that may be present in poultry diets.

Turkey

• Oguz (1997) produced AF on rice for feeding trials by using Aspergillus parasiticus culture in October 1994 with minor modification of Shotwell's method (1966). After production of AF, fermented rice was then steamed to kill the fungus, dried and ground to a fine powder. The rice powder was then analyzed for AF content. Then it became useful rice powder which was possible to be incorporated into the basal diet to provide desired amounts of AF levels in animal experiments.

• Kaya and Yarsan (1995) reviewed prevention of moldy in feeds and feedstuffs utilization of MYC contaminated feedstuffs with 25 related references.

• Kececi et al (1998) incorporated synthetic ZEO (0.5%) into AF-CT (2.5 ppm) broiler diet and synthetic ZEO provided significant improvements in the adverse effects of AF on performance, hematology and biochemistry.

• Oguz and Kurtoglu (2000) added CLI (1.5 and 2.5%) to AF-CT (2.5 ppm) broiler diet and CLI provided significant improvements in performance. Addition of 1.5% CLI also ameliorated the toxic effects of AF (2.5 ppm) on hematology-biochemistry (Oguz et al 2000a) and reduced the number of affected broilers and the severity of gross and histopathological lesions caused by AF (Ortatatli and Oğuz 2001).

• Oguz et al (2000b) also added CLI (1.5%) into lower levels AF-CT (50 and 100 ppb) broiler diet and CLI significantly recovered the negative effect of AF on performance of broilers. Addition of 1.5% CLI also improved the changes in gross and histopathology of target organs (Ortatatli et al 2005) and humoral immunity (Oguz et al 2003) associated with aflatoxicosis (Kececi et al 1998, Oguz et al 2003, Ortatatli et al 2005).

• Celik et al (2001) incorporated SCE (0.1%) to AF-CT (100 ppb) quail diet and SCE partially neutralized some toxic effects of AF.

• Parlat et al (2001) added SCE (0.1%) to AF-CT (2 ppm) quail diet and SCE provided significant improvements the effect of AF on performance. SCE (0.2%) was also added to AF-CT (5 ppb) quail diet and the negative changes in the performance, egg production and egg quality were significantly ameliorated by adding of SCE (Acay 2006).

• Denli et al (2003) supplemented vitamin A (15. 000 IU) to AF-CT (100 ppb) quail diet and vitamin A partially decreased the negative effects of AF on performance, biochemistry and pathology.

• Denli et al (2004, 2005) incorporated conjugated linoleic acid (CLA; 0.2 and 0.4%) to AF-CT (200 and 300ppb) broiler diet and CLA provided a partial improvement in performance and biochemistry parameters. CLA also decreased the negative effects of AF on liver pathology.

• Eraslan et al (2004a) supplemented SB (0.25 and 0.5%) into AF-CT (1 ppm) broiler diet and SB provided a partial improvement in lipid peroxidation in the liver and kidneys of broilers.

• Eraslan et al (2004b) also added HSCAS (0.5 and 1%) to AF-CT (2.5 ppm) quail diet and HSCAS provided a moderate amelioration the negative effects of AF on performance and biochemistry.

• Oguz and Parlat (2004) added MOS (0.1%) to AF-CT (2 ppm) quail diet and MOS significantly improved the adverse effects of AF on performance of quail.

• Yildiz et al (2004) added SCE (0.2%) to AF-CT (2 ppm) quail diet and the addition of SCE significantly recovered the deleterious effects of AF on performance, egg production and egg weight. The addition of 0.2% SCE also provided significant improvements in hatchability and fertility of quails (Yildirim and Parlat 2003).

• Basmacioglu et al (2005) added EGM (0.1%) to AF-CT (2 ppm) broiler diet and EGM significantly ameliorated the toxic effects of AF on hematology and biochemistry. Addition of 0.1% EGM also reduced the rate of affected broilers and the severity of lesions in the target organs caused by AF (Karaman et al 2005).

• Celik et al (2005) supplemented tribasic copper chloride (200 ppm) to AF-CT (1 ppm) broiler diet and tribasic copper chloride significantly improved the effects of AF on performance and biochemistry.

• Sehu et al (2005) supplemented Mycotox (0.5%) into AF-CT (2.5 ppm) quail diet; the adsorbent did not reduce the toxic effects of AF.

• Denli and Okan (2006) incorporated HSCAS, diatomite and ACH (0.25%) to the AF-CT (40and 80 ppb) broiler diet. HSCAS was the most effective adsorbents among them to ameliorate the toxic effects of AF in performance and biochemistry.

• Essiz et al (2006) added HSCAS (0.5%) and yeast wall (0.5%) and to AF-CT (2.5 ppm) quail diet and they restored plasma malondialdehyde levels altered by AF. The addition of 0.5% HSCAS also moderately decreased the toxic effects of AF (2.5 ppm) in quail in terms of performance, histopathology and immunology parameters (Sehu et al 2007).

• Kabak et al (2006) reviewed strategies to prevent contamination of animal feed and listed all detoxification methods which have been studied in vivo and in vitro and used for MYC decontamination; results with 276 related references.

• Cinar et al (2008) incorporated yeast glucomannan (GM; 0.075%) to AF-CT (2 ppm) broiler diet; yeast GM at this level was not sufficient to alleviate the oxidative damage caused by AF in broilers.

• Keser and Kutay (2009) reviewed chemical methods including adsorbents and biological methods for preventing of MYCs, with 40 related references.

• Ozen et al (2009) supplemented melatonin (10 ppm/bwt) to AF-CT (150 and 300 ppb) broiler diet; melatonin supplementation greatly reduced the nitrosative tissue degeneration caused by AF.

• Demirel et al (2010) reviewed the usage of natural ZEOs in animal production including poultry, with 49 related references.

• Karaman et al (2010) added lipoic acid (60 ppm/bw) to AF-CT (150-300 ppb) broiler diet they; lipoicacid provided moderate improvements in lipid peroxidation and histopathology of target organs.

• Matur et al (2010) added SCE extract (0.1%) to AF-CT (100 ppb) hen diet; addition ofSCE extract reduced the toxic effects of AF on pancreatic lipase and chymotrypsin activity.

• Yildirim et al (2011) supplemented yeast GM (0.075%) to AF-CT (2 ppm) broiler diet; the deleterious effects were partially restored, but the treatment did not prevent tissue damage.

• Oguz (2011, 2016) reviewed meta-analytically the in vivo experimental trials on inactivation of AF by using adsorbents and biological products as a feed additive in poultry feed, with 206 related references.

• Mizrak et al (2014) incorporated sepiolite (1.5 and 3%) and MOS (0.1%) into AF-CT (120 ppb) laying hens' feed for 12 weeks. The addition of MOS and sepiolite to the feed reduced the degree of digestion of AF by 6-12%. Addition of sepiolite to AF-CT diet had the beneficial effects on hen performance, egg quality, and blood and digestion characteristics.

• Yenice et al (2015) supplemented SB (0.5 and 1%) and MOS (0.1%) into AF-CT (120 ppb) laying hens' feed for 12 weeks. SB appears to be more effective than MOS as a toxin-binding agent in counteracting the adverse effects of AF on performance, egg quality, blood and digestion characteristic in laying hens.

• Uyar et al (2016) added Urtica dioica seeds (UDS) extract (30 ml/kg diet) to AF-CT (1 ppm) broiler diet for 21d. Supplementation of UDS extract helped restoration of AF-induced increase in MDA and reduced the antioxidant system towards normality, particularly in the liver, brain, kidney and heart. UDS extract has a protective hepato-renal effect in broilers affected by aflatoxicosis, probably acting by promoting the antioxidative defense systems.

• Yavuz et al (2017) added EGM (0.1% and 0.2%) to AF-CT (2 ppm) feed for 21 d in quails. The addition of 0.2% EGM on AF-CT diet may protect quails from aflatoxicosis, as demonstrated by the alleviation of gross and pathological changes in the liver and lymphoid organs.

United Kingdom

• Wielogarska et al (2016) reviewed the efficacy of detoxifying agent in feed in light of changing global environment and legislations.

United States

• AF was produced on rice by using Aspergillus flavus culture (Shotwell et al 1966) for using in feeding trials with poultry and other animals. This method has become a preferential method in the experiments for investigating AF toxicity and/or evaluation of preventive efficacy of feed additives against AF.

• Kubena et al (1990) added HSCAS (0.2%) and ACH (0.5%) to AF-CT (5and 7. 5 ppm) Leghorn chicks' diet and HSCAS significantly diminished the adverse effects of AF on performance, organ weights and biochemistry, whereas adding ACH had no effect.

• Araba and Wyatt (1991) added SB, HSCAS and ethacal (0.5 and 1%) to AF-CT (5 ppm) broiler diet. Addition of 0.5% SB and HSCAS significantly reduced the negative effects of AF on performance, liver weights and liver lipids.

• Kubena et al (1991) supplemented HSCAS (0.5%) to AF-CT (0.5 and 1 ppm) turkey diet and HSCAS neutralized the effects of AF performance, relative organ weights, hematological and biochemical values associated with 0.5 ppm AF.

• Huff et al (1992) added HSCAS (0.5%) into AF-CT (3. 5 ppm) broiler diet and HSCAS effectively recovered the detrimental effects of AF on serum biochemistry.

• Harvey et al (1993) incorporated ZEOs (CLI, zeomite and mordenite) (0.5%) to AF-CT (3. 5 ppm) broiler diet; zeomite and mordenite decreased the toxicity of AF to growing chicks as indicated by weight gains, liver weight, and serum biochemical values.

• Kubena et al (1993) added HSCAS (0.5%) to AF-CT (2.5 and 5 ppm) broiler diet. The addition of0.5% of the HSCAS compounds significantly recovered the growth inhibitory effects caused by AF. The increases in relative organ weights and the decreases in serum biochemical values caused by AF were significantly improved to differing degrees by HSCAS compounds and HSCAS was found to be protective against the effects of AF in young growing broilers.

• Scheideler (1993) incorporated Ethacal, Novasil, zeobrite and perlite (1%) into AF-CT (2.5 ppm) broiler diet. Initial three adsorbents provided significant improvements in performance and liver lipid, and partial ameliorations in mineral status.

• Stanley et al (1993) supplemented SCE (0.05 and 0.1%) to AF-CT (5 ppm) broiler diet and the addition of 0.1% SCE significantly improved the changes in performance, relative organ weights and serum biochemistry associated with aflatoxicosis.

• Abo-Norag et al (1995) added HSCAS (0.5%) to AF-CT (3. 5 ppm) broiler diet; HSCAS effectively ameliorated the negative effects of AF on performance and serum biochemistry.

• Edrington et al (1997) incorporated super ACH (0.5%) to AF-CT (4 ppm) broiler diet; active charcoal moderately improved the toxic effects of AF on performance, hematology and biochemistry.

• Bailey et al (1998) added three different adsorbents (0.5%) to AF-CT (5 ppm) broiler diet; the adsorbents offered some protection against AF toxicity in chickens (Baileyet al 1998).

• Kubena et al (1998) added HSCAS (0.25%) to AF-CT (5 ppm) broiler diet and significantly reduced negative effects of AF on performance and serum biochemistry.

• Ledoux et al (1999) supplemented HSCAS (Milbond-TX; 1%) to AF-CT (4 ppm) broiler diet and HSCAS completely improved in AF-dependent changes in organ weights, serum chemistry changes, and gross pathology observed in chicks fed AF. HSCAS also effectively reduced the incidence and severity of the hepatic and renal histopathology changes associated with aflatoxicosis.

• Phillips (1999) reviewed dietary clay used in the prevention of aflatoxicosis. In this review AF prevention strategies, chemoprevention, HSCAS and possible nutrient interaction with adsorbents were expressed, with 70 related references.

• Stanley et al (2004) also added yeast culture residue (2 lb/ton) to AF-CT (3 ppm) breeder hen diet; the inclusion of yeast culture in the AF-treated diet improved hatchability and egg production, and lowered embryonic mortality significantly. Serum globulin and albumin were partially recovered with the addition of yeast.

• Bailey et al (2006) incorporated MNT clay (0.5%) into AF-CT (4 ppm) broiler; they reported that MNT clay in broiler diets provided significant protection on growth performance, serum biochemistry, and relative organ weight associated with aflatoxicosis.

• Fairchild et al (2008) added BENT based Astra-Ben (1 and 2%) to AF-CT (4 ppm) broiler diet; the adsorbent provided significant improvements in performance and liver lipid content.

• Rawal et al (2010) reviewed toxicology, metabolism and prevention of AF; clay-based inorganic adsorbents and their effects were also discussed, with 121 related references.

• Zhao et al (2010) added HSCAS and YCW component with two doses (0.1 and 0.2%) to AF-CT (1 and 2 ppm) broiler diet and they provided significant improvements by adding of HSCAS

Table 1. Studies carried out on detoxification of aflatoxins in poultry feed according to the countries and poultry species

Country	Experimental					Review	Total
	Broiler	Quail	Duck	Hen	Turkey		
Argentina	6						6
Australia						1	1
Austria	1			1		1	3
Belgium						2	2
Brazil	12	1		1		1	15
Bulgaria					1		1
Cameroon	1						1
China	16		2			3	21
Colombia					1		1
Croatia						1	1
Cuba						1	1
Czechia						1	1
Denmark						1	1
Egypt	5	1		1			7
France						3	3
Germany						1	1
Greece	2						2
Hungary						1	1
India	15					2	16
Indonesia	2		1				3
Iran	26	2					28
Iraq	7						7
Italy	1			3		1	5
Korea				1			1
Mexico	1		1				2
Nepal			1				1
Nigeria	1				1		2
Pakistan	8	1		2		2	13
Poland						1	1
Saudi Arabia	1						1
Serbia						1	1
Slovak Republic	2						2
South Africa	3					1	4
Spain	2					2	4
Switzerland						1	1
Thailand	2		5				7
Turkey	14	9		3		5	31
United Kingdom						1	1
United States	18		1	1	1	4	25
Uruguay	1						1
Venezuela	3						3
Vietnam	1						1
Total	151	14	11	13	4	38	231

Table 2. Studies carried out on detoxification of aflatoxins in poultry feed according to the first author's countries and binding materials*

Country	BNT	HSC	Y/YCW	EGM	ZEO	ACH	CLI	MNT	OTH	Total
Argentina	3		2		1				1	7
Australia										0
Austria	1				1				1	3
Belgium										0
Brazil	2	1	5	2				3	1	14
Bulgaria									1	1
Cameroon									1	1
China		4	1	2				1	16	24
Colombia									1	1
Croatia										0
Cuba							1			1
Czechia	1				1				1	3
Denmark			1						1	2
Egypt	1	3	2	2					4	12
France										0
Germany										0
Greece	2									2
Hungary										0
India		2	1	4		2			8	17
Indonesia						1			2	3
Iran	8		3	7	4	1	1		15	39
Iraq	1		1						6	8
Italy		1		2			1		1	5
Korea									1	1
Mexico			1						1	2
Nepal									1	1
Nigeria	1	1						1	1	4
Pakistan	3	1	3			1			5	13
Poland		1								1
Saudi Arabia						1			1	2
Serbia										0
Slovak Rep.							1		2	3
South Africa	1		1						3	5
Spain		1							1	2
Switzerland										0
Thailand	2	1	3	2			1		1	10
Turkey	2	3	7	5	2	1	2		10	32
Unit. Kingdom					1					1
United States	4	10	3			2		1	4	24
Uruguay		1		1						2
Venezuela			3						3	6
Vietnam									1	1
Total	32	30	37	27	10	9	7	6	95	253

* Combined uses were considered separately; BNT: Bentonite, HSC: Hydrated sodium calcium aluminoslilicate, Y: Yeast, YCW: Yeast cell wall, EGM: Esterified glucomannan, ZEO: Zeolite, ACH: Activated charcoal, CLI: Clinoptilolite, MNT: Montmorillonite, OTH: Others.

and less improvements by YCW components in performance, biochemistry and histopathology changes associated with aflatoxicosis.
• Jaynes and Zartman (2011) reviewed the AF toxicity reduction in feed by enhanced binding to surface-modified clay additives, with 45 related references.
• Wan et al (2013) incorporated clay adsorbent (0.1%) to AFB1-CT (25, 50 and 100 ppb) duckling feed for 21 d. The addition of 0.1% clay adsorbent can protect against the detrimental effects caused by AF on performance and organ weights in ducks.
• Chen et al (2014b) added HSCAS (0.5%) to AF-CT (0.5, 1, and 2 ppm) to broiler diet for 21 d. Results from this study indicate that dietary supplementation with HSCAS can effectively improve body weight gain and partially ameliorate aflatoxicosis for broiler chicks fed AF-CT feeds.
• Womack et al (2014) reviewed non-biological remediation of AF-CT crops, with 72 related references.
• Fowler et al (2015) supplemented Ca BENT (0.2%) into AF-CT (600, 1200 and 1800 ppb) into broiler feed for 21 d. Results also showed that 0.2% Ca BENT was found to be effective at reducing the accumulation of AFB1 residues in the liver and improving livability in birds fed AF.
• Shannon et al (2017) incorporated raw BENT (0.5%) and concentrated BENT (0.5%) to AF-CT (2 ppm) broiler feed for 21d. Both raw BENT and concentrated BENT were effective in reducing the toxic effects of AF, however the cost of processing of concentrated BENT would make the raw BENT a more economical product for reducing the effects of AF in young broiler chicks.

Uruguay
• Mosca and Marichal (2011) added HSCAS, EGM and multi modular additive (MM) to AF-CT (4. 5 ppm) broiler diet and MM appeared to be the most effective to counteract the adverse effect produced by these MYC combinations (AF plus fumonisin).

Venezuela
• Marin et al (2003) incorporated SCE (0.1%) and selenium (2.5 ppm) to AF-CT (70 ppb) broiler diet; no improvements in biochemistry and hematology by adding the supplements were determined.
• Arrieta et al (2006) supplemented SCE (0.1%) and selenium (2 ppm) into AF-CT (70 ppb) broiler diet; no improvements were seen in biochemical parameters. Also no significant changes were determined by adding low levels of AF in parameters.
• Gomez et al (2009) added SCE (0.1%) and Se (2 ppm) to AF-CT (70 ppb) broiler diet and the results suggested that the ingestion during 42 days period with 70 ppb AFB1 on diet of broiler may have some effects on production parameters.

Vietnam
• Kinh et al (2010) incorporated Mtox (0.25%) to AF-CT (31-44 ppb) broiler diet; Mtox improved growth rate and feed efficiency of broiler chickens significantly.

Conclusions

The evaluation of the preventive efficacy of protective agents is possible by determining significant statistical differences between parameters of AF and AF plus additive groups in the target organs and key parameters in favor of AF plus feed additive groups. In our opinion, the best way to assess the performance of feed supplements against AF toxication for producers and scientists is to evaluate the results "as total" in terms of performance, biochemical-hematological, immunological and gross pathologic and histo-pathological parameters by comparing the AF groups with AF plus feed additive groups.

Evaluation of experiments "as total" is not always easy, because authors from different departments sharing responsibility for designing the experiment and interpreting the results tend to publish special aspects of experimental results in different scientific journals, with focus on their own special field of interest. To assess the "total" preventive efficacy and practical benefit of toxin binders used in experiments, nutritionists in the feed industry may invest some of their time following the titles of articles and/or associate authors and/or materials and methods of articles - unless they rely on recent reviews.

The studies have been carried out mostly in broilers (85%) among poultry species and in humid countries and/or the countries which import feedstuffs from them (Table 1). Experiments to reduce negative effects of AF in poultry feed have been mainly performed with BENTs and HSCAS single or in combination with biological matters such as yeast (SCE) and yeast cell derivates (EGM) (Table 2). Nutritionists in the feed industry and scientists can examine the results and decide which protective agent to use, taking into account the AF dose in feed, levels of protective agent, the experimental period and the species/variety of poultry species. Feed supplements must be inert and non-toxic and have no pharmacological and toxicological effects themselves in the organisms of animals. Possible nutrient interaction and dioxin contamination should also be regarded for using of natural clays.

For application in practice, focus on limiting AF contamination by optimizing harvesting and storage conditions should be stressed instead of expecting miracles from feed additives which have shown positive effects under experimental conditions.

Acknowledgement

This review is an updated version of invited papers published at the beginning of 2011 and 2016 (Oguz, 2011, 2012 and 2016). Since 2016, 25 new articles have been investigated in 42 different countries related to detoxification of AF in poultry feed were published and are included here (Totally 231 articles in 42 different countries until July 2018). Additionally new 2 tables which are given poultry species and binding materials used according to the countries were added.

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