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# Botanicals in Ameliorating Mycotoxicosis in Poultry

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**ABSTRACT**

Mycotoxicosis is a serious threat to poultry, caused by ingesting contaminated feed with toxigenic fungi or mycotoxins. It is characterized by loss of performance, poor immune response, and/or even death within a short period. The traditional approaches for the control of mycotoxicosis are based on the use of synthetic feed additives or toxin binders, which have certain limitations, such as the appearance of residues in poultry products, the emergence of drug resistance, and consumer's demand to use natural material for sustaining the health of animals. Therefore, this review was planned to explore the promising role of botanicals in ameliorating mycotoxicosis in poultry. The pathogenesis of mycotoxicosis involves the initiation of oxidative stress. Phytogenic or botanicals such as turmeric, garlic, ellagic acid, and curcumin exhibit anti-inflammatory, antioxidant, antifungal, and immunomodulatory properties. These properties help to detoxify mycotoxins, improve immune responses, protect against oxidative stress due to reactive oxygen species, and mitigate inflammation. Despite the use of synthetic compounds, farmers can employ a sustainable and natural approach i.e. the use of botanicals to control mycotoxicosis.

**Key words:** Phytogenic; Mycotoxins; Medicinal plants; Plant extracts; Essential oils

## INTRODUCTION

The term mycotoxin is a combination of two words myco and toxin which are derived from the Greek word “mykes” meaning fungus and the Latin word “toxicum” meaning poison. Mycotoxins are also known as unavoidable pollutants or natural poisons which are the secondary metabolites of fungi, pose significant health hazardous risks for humans, poultry, and livestock and the disease caused by them is known as mycotoxicosis (Alam et al. 2024). Most of the mycotoxins are produced by three genera of fungi- *Penicillium*, *Aspergillus* and *Fusarium*- and hundreds of different mycotoxins produced by fungi (>500) have been identified and chemically characterized. However, attention has been given to only those which have agricultural or medical importance, such as ochratoxin (OTA), deoxynivalenol (DON), aflatoxin B1 (AFB1), zearalenone (ZEA), fumonisin B1 (FB1), nivalenol (NIV) and T-2 toxin (T-2) (Wu et al. 2014).

Most of the mycotoxins occur in poultry feed and are characterized by the problem caused by them in poultry. The mycotoxins that pose a threat to the poultry industry include ergot alkaloids, trichothecenes, aflatoxins, or others produced by fumonisins, citrinin, ochratoxins, oosporein, or *Fusarium* (Naseem et al. 2018a; Hoerr 2020). According to the World Mycotoxin Survey 2024, 5383 samples from 64 countries, detected prevalence which includes DON (81%), ZEA (68%), FB1 (63%), fumonisin B2 (56%), AFB1 (17%), T-2 (17%), OTA (12%), and NIV (8%) (DSM-Firmenich 2024). Another survey addressing the prevalence of mycotoxins in 100 poultry feed samples estimated the prevalence in the reverse order fumonisin (86%), cyclopiazonic acid (76%), griseofulvin (42%), penitrem A (30%), sterigmatocystin (10%), OTA (5%), and aflatoxin (3%) (Labuda and Tancinova 2006). Twaruzek and colleagues conducted a survey from 2015 to 2020 to estimate the prevalence of mycotoxins in feedstuff, analyzed 3980 samples, and indicated the prevalence in the following order DON (97.8%), NIV (93.8%), T-2 (88.4%), ZEA (95.6%), OTA (33.3%), and AF (3%) (Twarużek et al. 2021). These surveys indicate that DON is most prevalent in feedstuff throughout the world.

Mycotoxicosis in poultry is caused by nutritional deficiencies, different mycotoxins, or a combination of mycotoxins with pathogens and leads to multiple organ toxicity such as immunotoxicity, reproductive toxicity,

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nephrotoxicity, neurotoxicity, hepatotoxicity, and gastrointestinal tract toxicity (Wu et al. 2014; Imran et al. 2020). The low dose of mycotoxins in poultry results in the occurrence of chronic mycotoxicosis which is characterized by loss of performance, pathological changes such as intramuscular or subcutaneous hemorrhages, and poor immunity. On the other hand, acute mycotoxicosis is caused by high levels of mycotoxins which is characterized by significant loss of production and death within a short time and can be diagnosed by typical clinical symptoms and post-mortem lesions (Table 1). In addition to this, subnormal poultry production without infections, stress, clinical signs, or nutritional deficiency, also indicates mycotoxicosis in poultry (Twarużek et al. 2021).

Poultry industry is an important, successful, and lucrative sector of agriculture in various parts of the world. Poultry meat contains less fat and is economical to purchase. Therefore, to meet the daily requirements of poultry meat and eggs, the health of birds is an important parameter (Shakoor et al. 2021; Urgesa 2023; Okonkwo et al. 2022). As mycotoxicosis is directly involved in performance loss in the poultry industry, its control and treatment are crucial. The contaminated feed must be replaced with unadulterated feed. When the birds get uncontaminated feed, they usually recover from the mycotoxicosis, but this does not compensate for the production loss of birds. The formulation of feed and water-based treatments can fulfill the requirements of trace minerals, vitamins, lipids, and proteins (Hoerr, 2020). Prevention of the occurrence of mycotoxins in the feed of poultry is an effective control method to maintain the health and production of poultry. Certain toxin binders such as activated charcoal, zeolites, or mineral clays (sodium bentonite and aluminosilicate) are given with feed that absorbs toxins and removes them from the body (Murugesan et al. 2015). However, where the synthetic preparations have proven therapeutic beneficial, these also have certain drawbacks such as the development of resistance, the appearance of drug residues in the poultry products, and consumer demand to use organic preparations for the consumption of poultry.

In recent years, people are more concerned about the quality and type of food they eat. They prefer poultry products from those farms that rear birds by providing them with their natural habitat and providing them with organic feed and additives. The interest of people in organic products is expected to continue in the future. Therefore, a recent trend in advancement in the utilization of plant-derived products for the well-being of animals has increased (Valenzuela-Grijalva et al. 2017; Elihasridas et al. 2023). Plant-derived products have been in use for centuries for the treatment of various ailments of animals. Mostly in developing countries, the Indigenous people use ethnoveterinary practices for the health, well-being, and treatment of diseases in animals. Besides this, the smallholders could not afford the cost associated with expensive chemotherapies and in rural areas, the unavailability of veterinary facilities is another constraint. Medicinal plants used for the treatment of diseases may offer substitutes for synthetic drugs and studies have indicated the therapeutic potential of plant products (Joseph et al. 2023; Bangulzai et al. 2022; Batool et al. 2023).

Based on the therapeutic potential of plant products, this exclusive review aimed to address the potential of plant products or phytogenic products in ameliorating mycotoxicosis in poultry and their activity against mycotoxins.

## Characterization of mycotoxins and their pathogenesis

There are many fungi producing mycotoxins which reduce the performance of birds when consumed with feed (Fig. 1). *Claviceps purpurae* produce toxic alkaloids which cause ergotism in poultry. Ergot occurs worldwide in rye, weed seed, and other cereals in cooler grain-rearing settings. Lysergic acid is the active chemical of ergot alkaloid which produces neurological symptoms in affected birds. Ergotism is characterized by neurological, vascular, or endocrine disorders. Poultry that are affected by ergot show reduced performance such as decreased feed intake, egg production, growth, and diarrhea. The pathological lesions include the development of ulcers and vesicles on wattles, comb, toes, and beak. The wattles and comb also become discoloured and atrophied (Dänicke 2017).

**Table 1:** Clinical symptoms and post-mortem lesions caused by mycotoxins in poultry

| Mycotoxins | Recommended risk threshold in ppb | Signs and symptoms | Pathological lesions | References |
|---|---|---|---|---|
| Aflatoxin B1 | 2 | Poor egg production and hatchability, decreased concentration of serum protein, decreased immunity | Swollen liver and kidney, enlarged spleen and fatty liver, testicular atrophy and reduced volume of semen, increased apoptosis of spermatogenic cell | Twarużek et al. (2021) |
| Ochratoxin | 10 | Reduced consumption of feed, efficiency, weight gain, egg production, egg quality, and immunity | Swelling of glomeruli and disruption | Alam et al. (2024) |
| Zearalenone | 50 | Decreased egg production and quality | Cloacal swelling, enlargement of the oviduct, reproductive tract cysts, and reduced testicular weight | dsm-firmenich, (2024) |
| Fumonisin B1 | 500 | Weakness, poor immunity, and deformity of legs | Hyperplasia of the liver, enlarged kidney, stomach, and weight gain | Kolawole et al. (2024) |
| T-2 toxin | 50 | Reduced consumption of feed, efficiency, weight gain, egg production, and immunity, abnormal behavior | Pathological lesions in the oral cavity, impaired plumage | Okasha et al. (2024) |
| Deoxynivalenol | 150 | Reduced consumption of feed, efficiency, weight gain, egg production, and immunity, abnormal behavior | Pathological lesions in the oral cavity, impaired plumage | Dänicke, (2017) |

Ppb = Parts per million

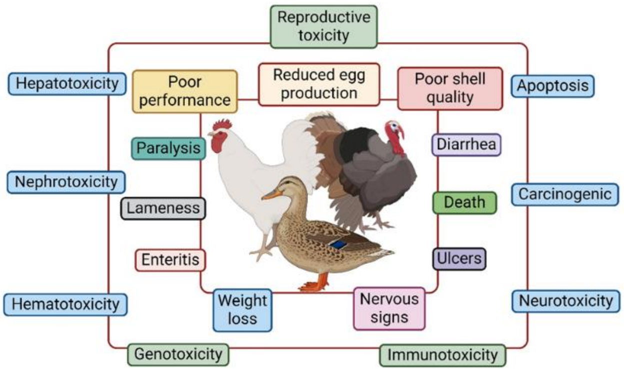


**Fig. 1:** Effects of mycotoxins in poultry. The figure is created by using BioRender.

Multiple mycotoxins are produced by the genus *Fusarium*, which is injurious to the health of poultry and characterized by cardiac, reproductive, digestive, and skeletal disorders. These toxins include zearalenone, fumonisins, trichothecenes, moniliformin, fusaproliferin, beauvericin, and enniatins. Trichothecenes mycotoxins are produced by plant and soil fungi including *Calonectria*, *Gibberella*, and *Fusarium*. There are two types of trichothecenes type A and B. The toxins in type A include neosolanial, T-2 toxin, diacetoxyscirpenol, and others while the toxins of type B include DON, nivalenol, fusarenone-X, vomitoxin, and others. These toxins occur in cereal grains, corn, and feed. DON is the most prevalent mycotoxin in the world. In poultry, trichothecenes toxicity is characterized by refusal of feed by the birds, necrosis of skin or oral mucosa coming in contact with the toxins, poor egg production, shell quality, and immunity, gout, rickets, feathers malformation, and acute digestive disease (Polak-Śliwińska and Paszczyk 2021).

*Fusarium* (*F.*) *verticillioides*, *F. subglutinans* and other *Fusarium* species produce moniliformin toxins which are nephrotoxic and cardiotoxic in poultry. These occur in soybeans, shelled corn, and other cereal grains. *F. verticillioides* also produce other toxins such as zearalenone, fusariocin A, and fumonisins. In poultry, moniliformin toxicity is characterized by decreased laying rate, delayed production peaks, diarrhea along with uneven feed consumption, blood smear, and fecal stains on eggshells (Kolawole et al. 2024). The mycotoxin fumonisin includes B1, B2, and B3 out of which the occurrence of B1 mycotoxin is common. Clinically in poultry, it is characterized by reduced feed intake, black adhesive diarrhea, weight loss, poor egg production, lameness, and even increased death rate. The pathological changes include enlarged proventriculus, gizzard, kidney, and liver, rickets, and atrophy of lymphoid organs (Kolawole et al. 2024). Furthermore, the toxigenic culture fusarochromanone of *F. verticilliodes, F. roseum, F. equiseti*, *Aspergillus* (*A.*) *niger*, and *A. Flavus* results in bone deformities, tibial dyschondroplasia, in poultry.

An estrogenic mycotoxin zearalenone produced by *Gibberella zeae* is the second most prevalent fungus in the world and occurs in corn or other grains (Boumaaza et al. 2022). The tolerance of chicken is more than turkey or swine against ZEA, therefore providing an outlet for the consumption of grains not suitable for turkey or swine. Although it is less toxic in chicken, however, its presence indicates the occurrence of another fungus – *Fusarium*. In the feed of broiler breeders, it results in poor reproductive performance leading to reduced egg production, cystic inflammation of the oviduct, ascites, and low concentration of progesterone in serum. The other *Fusarium* toxins include enniatins, beauvericin, and fusaproliferin resulting in poor egg production, immunodepression, and cytotoxic effects (Liu and Applegate 2020; Ashraf et al. 2022).

Another important mycotoxin that poses a threat to humans and disrupts the food chain is aflatoxin which is produced by *A. flavus*, *A. parasiticus*, and *P. puberulum* (Naseem et al. 2018b; Saleemi et al. 2020; Basiouni et al. 2023). It is highly toxic, carcinogenic, and has regulatory concerns. AFB1 affects the liver and is the most toxic type of aflatoxin. Chickens are somewhat resistant to aflatoxins, whereas quails show intermediate toxicity. The poults of turkey and duckling are highly sensitive to this mycotoxin. Aflatoxicosis is characterized by mortality, hemorrhages, anemia, loss of egg production, nervous signs, impaired growth and ambulation, lameness, paralysis, and liver toxicity (Wang et al. 2023).

Ochratoxin is one of the most common mycotoxins in poultry and causes nephrotoxicity. It is mainly produced by *A. ochraceous* and *Penicillium viridicatum* and is classified into 4 groups A-D, out of which OTA-A is the most toxic. In Balkan nephropathy of poultry and swine, OTA in combination with FB1 and penicillic acid was the risk factor. It occurs in corn, corn gluten meal, pelleted feed, and bakery products. Clinically, ochratoxicosis is characterized by enteritis, diarrhea, pigmentation, and poor weight gain. The pathological lesions include enteritis, visceral gout, and discoloration of the liver and kidneys (Tahir et al. 2022; Bhatti et al. 2022). Citrinin is also a mycotoxin produced by various fungi including *Penicillium*, *Aspergillus*, and *Monascus*, and occurs in rice, corn, and other cereal grains. The mycotoxicosis of citrinin is characterized by degenerative changes in kidney tubules, swollen kidneys, and poor weight gain leading to uneven growth of chicks. The other mycotoxins include oosporein, cyclopiazonic acid, sterigmatocystin, rubratoxins A and B, penicillic acid, tenuazonic acid, and patulin which also cause toxicities in poultry (Okasha et al. 2024).

The pathogenesis of mycotoxicosis is studied in poultry and laboratory animals. There are three main routes via mycotoxins that are exposed to animals such as dermis, oral, and parenteral routes leading to toxicity in the gastrointestinal tract (GIT), liver, cardiovascular system, nervous system, reproductive system, and kidneys (Ramaiyulis et al. 2023). GIT is the main site of accumulation of mycotoxins in the body of the animals than any other organ. When animals ingest feed contaminated with mycotoxins, it leads to damage to intestinal villi causing enteritis and ulcers in the gut which ultimately disrupts the homeostasis of the normal intestinal flora of the animals (Jin et al. 2021). The pathogenesis results in the production of reactive oxygen species and free radicals which ultimately disrupt biological processes of the cells. However, the antioxidants (either endogenous or exogenous) cope the oxidative stress by preventing or scavenging the production of reactive oxygen species and protecting the cells of the animals from the toxicity induced by the mycotoxins. The cellular pathways involved in uplifting the health of poultry or laboratory animals by preventing oxidative stress include nuclear factor erythroid 2 related factor (Nrf2), nuclear factor kappa-β (Nf-kβ), and mitogen-activated protein kinase (Lingappan 2018). Still, further studies are required to know more about the mechanism of cellular pathways involving mycotoxins in poultry, the initiation of oxidative stress, and the defensive mechanism of animals to cope with reactive oxygen species (Fig. 2).

**Phytogenic products for the treatment of mycotoxicosis**

The plant materials consist of a diverse range of chemical compounds that possess therapeutic potential for the treatment of various infections (Saleh et al. 2023). The active compounds found in plants vary greatly depending on the part of the plant used, harvesting season, and geographic area as plants directly obtain minerals and other nutrients from the soil (Dağ et al. 2023; Saleem et al. 2023). Due to the therapeutic properties of plants such as anti-inflammatory, antioxidant, antigenotoxic effects, and antimicrobials, these are often explored to evaluate their efficacy in poultry (Salako et al. 2022 Mustafa et al. 2023). In this context, plant products are used in research against mycotoxicosis in poultry in two ways. First is their ability to inhibit the growth of fungi in the feed of poultry and second is their ability to mitigate toxicity in birds (Table 2). Under practical circumstances, the complete prevention of fungal infections of feed may not be possible. However, many plant products have been reported to possess anti-mycotic properties such as *Thymus vulgaris*, *Piper nigrum*, *Rosmarinus officinalis*, *Curcuma longa*, and *Syzygium aromaticum* (Mirnawati et al. 2023). Since the pathogenesis of mycotoxicosis involves oxidative stress, immunosuppression, liver damage, and inflammation (Fig. 3), the plant products that possess antioxidant, immune booster, anti-inflammatory, and hepatoprotective properties might serve as an organic therapeutic approach for the control of mycotoxicosis in poultry (Umaya et al. 2021; Devi et al. 2023; Mohamed et al. 2023).

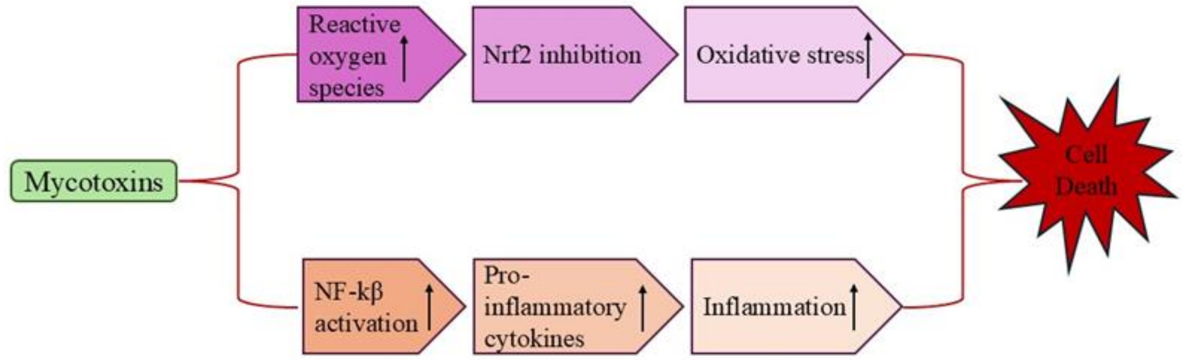


**Fig. 2:** Flow diagram showing the pathogenesis or mechanism of action of mycotoxins in poultry. The figure is created by using BioRender.

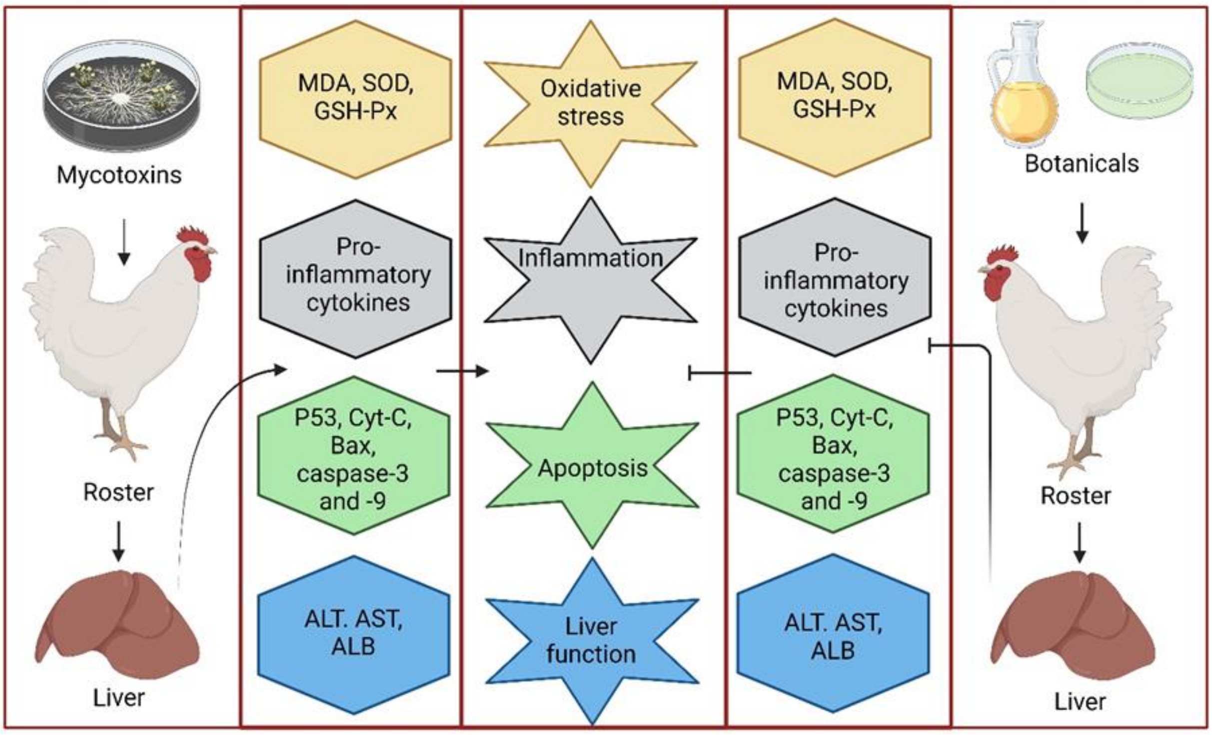


**Fig. 3:** Mode of action of mycotoxins and botanicals against mycotoxins in poultry. The figure is created by using BioRender.
ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; ALB = Albumin; MDA = Malondialdehyde; SOD = Superoxide dismutase; GSH-Px = Glutathione peroxidase

**Table 2:** Studies on the effect of botanicals and their compounds on mycotoxicosis

| Plant source | Protective agent | Fungi/ mycotoxin | Mechanism of action | References |
|---|---|---|---|---|
| Essential oils | | | | |
| *Aflamomum danielli* | Monoterpenes | Ochratoxin | Ameliorate oxidative stress and inflammation | Aroyeun et al. (2009) |
| *Satureja khozistanica* | B-carotene | Fumonisin B1 (FB1) | Ameliorate oxidative stress and inflammation | Gorran et al. (2013) |
| *Thymus daenensis* | Thyme oil | FB1, *Aspergillus* (*A.*) *flavus* | Ameliorate oxidative stress and genotoxicity | Gorran et al. (2013); Tian et al. (2019) |
| *Satureja macrosiphonia* | Linalool | Fumonisin B1 | Ameliorate oxidative stress | Gorran et al. (2013) |
| *Curcuma amada* | Ginger, 6-gingerol | *A. flavus*, Aflatoxin B1 and B2 (AFB1) | Inhibit AFB1 | Nerilo et al. (2020) |
| *Carum carvi* | Anti-fungal peptide | *A. flavus* and *A. parasiticus* | Alteration in fungal cell membrane permeability | Nerilo et al. (2020) |
| *Juniperus communis* | Organic acids, α-pinene | *A. flavus* and *A. parasiticus* | Ameliorate oxidative stress | Nerilo et al. (2020) |
| *Citrus limon* | Polyphenols, terpenes, and tannins | deoxynivalenol (DON) | Ameliorate oxidative stress, damage cell membrane of fungi | Perczak et al. (2019) |
| *Cymbopogon martini* | Geraniol | DON | Inhibit AFB1 | Perczak et al. (2019) |
| *Cinnamon* | Terpenes and cuminaldehyde | FB1 | Ameliorate oxidative stress | Xing et al. (2013) |
| Crude extracts | | | | |
| Wild stevia | NA | *Fusarium verticillioides*, *A. flavus*, *A. niger*, and *A. ochraceous* | Ameliorate oxidative stress and inflammation | Abdel-Fattah et al. (2018) |
| *Origanum vulgare* | NA | AFB1 | Ameliorate oxidative stress and inflammation | Ponzilacqua et al. (2019) |
| *Rosmarinus officinalis* | NA | AFB1 | Ameliorate oxidative stress and inflammation | Ponzilacqua et al. (2019) |
| *Psidium cattleianum* | NA | AFB1 | Ameliorate oxidative stress and inflammation | Ponzilacqua et al. (2019) |
| *Passiflora alata* | NA | AFB1 | Ameliorate oxidative stress and inflammation | Ponzilacqua et al. (2019) |
| *Schisandra chinensis* | NA | AFB1 | Ameliorate oxidative stress and apoptosis | Gyamfi and Aniya, (1998) |
| *Premna integrifolia* | NA | AFB1 | Ameliorate oxidative stress and apoptosis | Singh et al. (2019) |
| *Thonninga sanguinea* | NA | AFB1 | Ameliorate oxidative stress and apoptosis | Gyamfi and Aniya, (1998) |
| Phytochemicals | | | | |
| *Punica granatum* | Ellagic acid | AFB1 | Protect from mutagenicity induced by AFB1 | Khan et al. (2019) |
| *Curcuma longa* | Curcumin | AFB1 | Hepatoprotective | Khan et al. (2019) |
| *Vitis vinifera* | Resveratrol | Mycotoxicosis | Activate detoxification pathways and inhibit the metabolism of xenobiotics | Tabeshpour et al. (2018) |
| *Solanum lycopersicum* | Lycopene | ZEA, OTA, AFB1, T-2 toxin | Protect against oxidative stress, inflammation, and reproductive, and hormonal damage caused by mycotoxins | Hedayati et al. (2019) |
| Fruits (blackberry, raspberry, cranberry, grapes, and cherry), vegetables (red onion and cabbage), and medicinal herbs | Cyanidine | OTA, AFB1 | Ameliorate oxidative stress | Sorrenti et al. (2012) |
| *Ruta graveolens* | Rutin | T-2 toxin | Reversed T-2 toxin-induced lipid peroxidation | El-Sawi and Al-Seeni (2009) |

NA = Not applicable

## Essential oils

The composition of essential oils varies depending on the extraction method and solvent used for the extraction of essential oils (Hussain et al. 2023). They contain a complex mixture of compounds and are mainly composed of aromatic compounds, terpenes, and their derivatives, aliphatic compounds, and nitrogen-containing sulfur compounds. Terpenoids such as monoterpenes are the most abundant class of compounds found in essential oils and account for more than 70% of the composition of essential oils (Ahmad et al. 2023). The biological activity of essential oils extracted from plants is mainly determined by diterpenoids and sesquiterpenes (Cui et al. 2015; Al-Saeed et al. 2023). The common methods of extraction of essential oils from plant material include distillation, pressing, organic solvent extraction, lipolysis, adsorption extraction, enzyme fermentation, etc. (Moumni et al. 2020; Kanwal et al. 2024).

Research to check the anti-fungal properties of essential oils is based on their ability to inhibit the growth of fungi-producing mycotoxins. There are few studies that have been conducted demonstrating the mycotoxin detoxifying potential of essential oils. Some studies have demonstrated the effect of essential oils at certain concentrations. For example, the essential oil of *Aflamomum danielli* detoxifies OTA at a concentration of 2000 mg/kg with 100% efficacy. While it showed 90-95% efficacy at a concentration of 1000mg/kg (Aroyeun et al. 2009). Gorran et al. (2013) investigated the detoxifying potential of three plants (*Satureja khozistanica*, *Thymus daenensis*, and *Satureja macrosiphonia*) essential oils against fumonisin B1. The essential oils were extracted with three solvents namely water, ethanol, and 70% ethanol. In another similar research, only the aqueous extract significantly reduced fumonisin B1 and the most effective plant extract was *Thymus daenensis.* It significantly inhibited *A. flavus* growth (Gorran et al. 2013; Tian et al. 2019). Their results led to the conclusion that different extraction methods produce essential oils that possess varying mechanisms of degradation of mycotoxins. In addition to this, the essential oils of lemon and palmarosa were effective in degrading DON and the essential oil of cinnamon could degrade fumonisin B1 (Xing et al. 2013; Perczak et al. 2019). Nerilo and colleagues evaluated the antifungal activity of the essential oil of ginger against *A. flavus* and inhibited the production of AFB1 and AFB2. Furthermore, it was found that the ginger essential oil is mainly composed of geranial and α-zingiberene. The essential oils of *Carum carvi* and *Juniperus communis* also possess antifungal properties against *A. flavus* and *A. parasiticus* (Nerilo et al. 2020).

Plant essential oils possess the degradation ability against mycotoxins and may be utilized for the control of mycotoxicosis in poultry. However, the efficacy of essential oils varies according to different extraction processes, and further comparative studies are still required to optimize the extraction process. Furthermore, the detoxifying mechanism and *in vivo* toxicity of these oils have not been studied and require the attention of researchers to fill this gap.

**Plant extracts**

The natural flora is enriched with many medicinal plants that possess therapeutic properties. According to the World Health Organization, about 80% population of the world is still dependent on botanicals as a traditional remedy to cure different ailments (WHO 2001). The activity of plants as anti-fungal and anti-mycotoxigenic was investigated against phytopathogenic strains of fungi such as *F. verticillioides*, *A. flavus*, and *A. ochraceous*. Abdel-Fattah and colleagues reported the detoxifying potential of plant extracts of wild stevia against *F. verticillioides*, *A. flavus*, *A. niger*, and *A. ochraceous* (Abdel-Fattah et al. 2018). Similarly, the aqueous extracts of *Origanum vulgare, Rosmarinus officinalis, Psidium cattleianum*, and *Passiflora alata* exhibited detoxifying potential against AFB1 mycotoxins (Stoev et al. 2019). In rats, that suffered from hepatotoxicity due to mycotoxins, the extracts of *Schisandra chinensis*, *Thonninga sanguinea*, and *Premna integrifolia* provided protection by enhancing antioxidant and detoxification and inhibiting oxidative stress and apoptosis (Gyamfi and Aniya, 1998; Singh et al. 2019).

In broiler chickens exposed to OTA mycotoxins, having nephrotoxicity, hepatotoxicity, and immunosuppression, the extracts of *Silybum marianum* and *Withania somnifera* showed partial protection (Stoev et al. 2019). Similar to essential oils extracted with different methods, the plant extracts prepared with different solvents and duration of exposure of mycotoxins to plant extracts, possess variable efficacy against the fungi and mycotoxin inhibition (Mehnaz et al. 2023). In addition to this, the daily household spices namely ginger, garlic, clove, black cumin, lemon grass, and fenugreek also possess detoxifying potential against AFB1 (Negera and Washe 2019).

**Phytochemicals**

Plants possess a natural defense mechanism against pathogenic microorganisms, harsh environmental conditions, and insects by producing various secondary metabolites (Abbas and Alkheraije 2023). The non-nutritive secondary metabolites are known as phytochemicals. The phytochemicals possess a protective ability against microorganisms and the toxins produced by toxigenic pathogens. At present, many different groups of phytochemicals have been discovered which are promising for the discovery of future drugs. They are different from others due to their chemical structures and their examples include flavonoids, phenolic compounds, alkaloids, saponins, terpenoids, aromatic acids, organic acids, glucosinolates, carotenoids, carotenoids, tannins, etc. They provide protection directly or indirectly as they possess antimicrobial, antiparasitic, antimutagenic, anticarcinogenic, antigenotoxic, antioxidant, anti-inflammatory, and antiproliferative properties (Das et al. 2020; Kiran et al. 2022; Sindi et al. 2023).

Ellagic acid and curcumin are being used as feed and food additives isolated from plants. These compounds can protect from mutagenicity induced by AFB1. The mechanism behind this is their capability to prevent AFB1 metabolism and enhance glutathione-S-transferase activity involved in the xenobiotic's detoxification (Abd El-Ghany, 2020). Curcumin also exhibits other therapeutic activities *in vivo* and *in vitro* such as antiproliferative, anticarcinogenic, and antimutagenic (Khan et al. 2019). Another phytochemical is resveratrol which can be isolated from the skin of grapes and possesses many therapeutic potentials (protect against the proliferation of cancers such as prostate, pancreatic, and breast cancers by activating detoxification pathways and inhibiting metabolism of xenobiotics) including the protection from mycotoxicosis both *in vitro* and *in vivo* (Tabeshpour et al. 2018). Lycopene possesses broad-spectrum activity against multiple fungi. It could be isolated from red vegetables and vegetables, tomatoes, and papaya. It protects against oxidative, reproductive, and hormonal damage due to ZEA in mice. Furthermore, it also protects from T-2 toxin, OTA, and AFB1-induced oxidative stress (Hedayati et al. 2019). Sorrenti and colleagues reported the hepatocytes and enterocytes' protective effect of cyanidine that could be isolated from fruits (blackberry, raspberry, cranberry, grapes, and cherry), vegetables (red onion and cabbage), and medicinal herbs. The phytochemical cyanidine has protective efficacy against OTA and AFB1 toxicity (Sorrenti et al. 2012). Likewise, rutin is another phytochemical that has a protective role against toxicity induced by T-2 toxins (El-Sawi and Al-Seeni 2009).

**Mechanism of action of phytogenic against mycotoxicosis and their effect on poultry health**

Plants possess many therapeutic properties (anticarcinogenic, antioxidant, anti-microbial, and antimutagens) capable of protecting animals from toxic and genotoxic effects induced by mycotoxins. The antioxidants provided by the plant materials protect cell membranes and macromolecules by irradicating free radicals from the cells. The phytochemicals found in different plant materials prevent the toxic effect of fungi by disrupting the permeability and functions of cell membranes, inhibiting mitochondrial and cytoplasmic enzymes involved in the synthesis of various components of the cell wall of fungi, and altering homeostasis (redox balance, osmotic pressure, and cellular compartment) thereby inducing cytotoxicity in fungi (Bülbül et al. 2023). Furthermore, they also act by inducing xenobiotic detoxification and inhibiting biochemical pathways. The compounds present in the plant material could be used as a feed additive to induce the enzymes that activate enzymes for Phase II detoxification or inhibit enzymes that activate Phase I carcinogens (Wu et al. 2017).

In this aspect, firstly, phytogenic exert their protective effects against mycotoxicosis in poultry via their oxidative properties (Khan et al., 2023). Oxidative stress can be induced by mycotoxins – ochratoxins, aflatoxins, and T-2 toxins – by generating reactive oxygen species leading to DNA damage, oxidation of protein, and lipid peroxidation (Mnisi et al. 2023). In the pathogenesis of mycotoxicosis, oxidative stress is one of the main factors. Botanicals which are rich in flavonoids, phenolic compounds, and other antioxidants, can scavenge the free radicals and inhibit oxidative reactions in poultry caused by contaminated feed with fungi or their metabolites. For example, the extracts of turmeric contain curcumin which has been shown to increase the antioxidant enzymes activity such as superoxide dismutase, catalase, and glutathione peroxidase. These enzymes have a role in neutralizing reactive oxygen species and protecting cellular components from oxidative damage (Khan et al. 2019). Likewise, phytochemical resveratrol, a polyphenol found in grapes, possesses antioxidative properties and exerts its therapeutic effects by upregulating the expression of antioxidant genes and reducing lipid peroxidation in poultry exposed to mycotoxins (Khan et al. 2017a; Tabeshpour et al. 2018).

Secondly, the impairment of the immune system in case of mycotoxicosis in poultry is observed which results in making birds vulnerable to secondary infections or diseases (Tarhane er al., 2023). The immunosuppressive effects during mycotoxicosis in poultry include reduced production of antibodies, decreased phagocytic activities of macrophages, and impaired lymphocyte functions (Khan et al. 2019). Phylogenetics has the ability to modulate the immune responses in poultry, thereby ameliorating the immunosuppressive effects induced by mycotoxins (Khan et al. 2017b; Imran et al. 2023). For example, allicin (a phytochemical present in garlic) has been shown to possess immunomodulatory properties such as enhancing the activity of macrophages and activating the antibodies production and various other immune cells, thereby protecting poultry affected by mycotoxin by mitigating immunosuppressive effects (Negera and Washe 2019).

Thirdly, inflammation is also one of the factors of pathogenesis in the case of mycotoxicosis in poultry. Botanicals having anti-inflammatory properties can treat inflammation, thereby reducing tissue damage and improving the overall health of the birds. For example, curcumin is well known for its anti-inflammatory properties and can prevent the activation of nuclear factor-kappa B (a regulator of inflammatory responses). By inhibiting the production of nuclear factor-kappa B, curcumin decreases the proinflammatory cytokine (tumor necrosis factor-alpha and interleukin-6) production (Tabeshpour et al. 2018).

Fourthly, the biotransformation of mycotoxins into less toxic metabolites detoxifies the mycotoxins leading to their excretion from the body (Das et al. 2020). Various detoxifying enzymes (glutathione S-transferase, UDP-glucuronosyltransferase, and those enzymes in the cytochrome P450 family) can facilitate the excretion of mycotoxins from the body. The phytogenics that possess the ability to enhance the activities of the above-mentioned enzymes accelerate the process of detoxification (Khan et al. 2019). For example, flavonoids have the ability to enhance the expression of cytochrome P450 enzymes and glutathione S-transferase leading to the biotransformation of aflatoxins into their less toxic metabolites, thereby reducing their bioavailability and toxicity (Das et al. 2020).

Lastly, phytogenics exert their protective effects by directly binding and absorbing mycotoxins - reducing their bioavailability and toxicity, maintaining the integrity and function of the gut – preventing mycotoxin's effects on the gastrointestinal tract, enhancing absorption of nutrients and their utilization – preventing the interference caused by mycotoxins in the absorption of nutrients leading to poor growth performance and productivity, and have synergistic effects against mycotoxicosis in poultry (Aljohani 2023).

**Challenges and perspective of using ethnomedicine in poultry for mycotoxicosis**

Botanicals derived from plants contain many bioactive compounds that possess antifungal, antioxidant, and immunomodulatory properties (Ponzilacqua et al. 2019). Natural products including phytochemicals, plant extracts, and essential oils are promising in the control and prevention of mycotoxicosis in poultry. Despite their therapeutic properties, there are also certain challenges that must be addressed to ensure their maximum therapeutic activity. For example, there is a huge variation in the composition and potency of the phytogenic. The geographic region from where the plant material is collected, cultivation conditions and extraction methods are significantly responsible for such variations in their composition thus affecting the efficacy of natural products (Valenzuela-Grijalva et al. 2017). Therefore, standardization of botanicals and understanding the mechanism of action of various compounds need to be the focus of researchers to optimize their use in poultry feed. Another challenge is the correct estimation of dosage and the administration of phytogenic to mitigate the toxicity that might be caused by overdose or inappropriate route of administration. Furthermore, to prevent their subtherapeutic effects, the estimation of therapeutic dose is also crucial. Lastly, the economic feasibility that incurs due to the extraction process and their standardization, and regulatory issues that vary from region to region must also be addressed to ensure their proper use in the feed of poultry for the prevention of mycotoxicosis (Das et al. 2020).

Advancements in the development of analytical techniques such as proteomics and metabolomics can provide deeper insight into the interaction of botanicals with mycotoxins and biology of the poultry. The understanding of such interactions may facilitate the development of targeted botanical formulations with increased efficacy and specificity. Furthermore, the advancement in the delivery system such as nano-encapsulation can be beneficial in the improvement of the stability and bioavailability of phytogenics, ensuring their controlled release and optimal absorption from the gut of poultry. Additionally, the evaluation of the synergistic combination of phytogenics with other synthetic or natural additives might enhance the overall effect of phytogenics against mycotoxicosis in poultry. Finally, the utilization of an integrated approach in the control of mycotoxicosis in poultry such as combining botanicals with management techniques (biosecurity measures, good hygiene, and proper feed storage) might be promising in ameliorating mycotoxicosis in poultry (Thipe et al. 2020).

## Conclusion

Mycotoxicosis caused by the ingestion of mycotoxins or mycotoxin-producing fungi poses a threat to poultry leading to various adverse health effects, poor performance, and economic losses. The traditional approach for the control of mycotoxicosis in poultry is the use of synthetic additives. Botanicals contain various bioactive compounds that possess antifungal, antioxidant, anti-inflammatory, and immunomodulatory properties and may serve as the best natural alternative to synthetic additives for detoxifying mycotoxins. Therefore, these therapeutic properties can be beneficial in ameliorating mycotoxicosis in poultry.

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