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Article Review

Mycotoxins: Review on types, toxicity, conventional and updating techniques of detection and counteraction in feeds and foods of animals and human

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ABSTRACT

Mycotoxins, a global challenge, represent one of the most significant hazards that affect foods and feeds. It produced naturally as secondary metabolites by various species of toxigenic fungi. It can cause chronic or acute toxicity due to their immunosuppressive, carcinogenic and mutagenic properties in animals and human. Every year, mycotoxins cause massive economic losses in the animal feed sector and animal husbandry. Human affected by mycotoxins either indirectly through consumption of contaminated animal products (meat, eggs and milk) by mycotoxins' residue or directly through consumption of contaminated foods (nuts, coffee, corn, barley, wheat, peanuts, peas) and their by-products. This review gives an overview of the most important and prevalent mycotoxins in animal feeds, health and economic mycotoxins impacts on animals. In addition, the main conventional and advanced approaches in mycotoxins analytical detection techniques and decontamination strategies to mitigate and counteract mycotoxin contamination of feedstuffs were also reported. There are different analytical techniques to precisely qualities and quantities mycotoxins. They included Fluorometer, chromatography-based devices and immunological based techniques besides other recent advanced techniques. Various mycotoxins detoxification strategies have been developed included physical, chemical and biological strategies to reduce or eliminate mycotoxins in feed ingredients or complete compound feeds, however they cannot totally decontaminate mycotoxins. Hence, they varied in their limitations or abilities to meet the requirements of practical application according to many factors including their binding efficiency, environmental protection, feeds and foods safety, palatability or cost-effectiveness.

INTRODUCTION

Mycotoxins, the toxic products of fungal metabolism, called as unavoidable contaminantsthat contaminated both animal feeds and human food products **(Gowda et al. 2013)**, especially corn, barley, wheat, peanuts, peas,

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nuts, millet, silage, gluten, soybean meal and their by-products. Globally, recent mycotoxin surveys have indicated that they affected much higher than 25% of the world's crops annually **(Lee and Ryu, 2017)**. Subsequently their consumption resulted in health hazards both in livestock and human beings leading to a greater economic and public health implication **(Ma et al. 2018).**

Nearly all animal species especially productive ones as poultry, cattle, sheep and swine are affected by various types of mycotoxins in a various degrees of response. Mycotoxins can cause chronic or acute toxicity. They can display hepatotoxic, nephrotoxic, immunotoxic, mutagenic, carcinogenic and/or teratogenic activities in many animal species **(Zhao et al. 2019)**.

Mycotoxins produced fungi can be divided according to the site and time of contamination into three groups: (a) Field fungi (b) Storage fungi (c) Advanced deterioration fungi. Meanwhile, not all fungal growth results in the production of mycotoxins **(Awuchi et al. 2021)**.

The severity and type of mycotoxin contamination affected by various factors including the productive fungus, where most of them were produced mainly by *Aspergillus, Penicillium* and *Fusarium* species, their chemical structure and environmental factors like excessive field and storage moisture, hotness, humid climate, pH and insect infestation **(Haque et al. 2020)**.Mycotoxins are also classified according to their biological activities as; carcinogenic (e.g. aflatoxin B1, ochratoxin A, fumonisin B1), oestrogenic (zearalenone), neurotoxic (fumonisin B1), nephrotoxic (ochratoxins, citrinin, oosporein), dermonecrotic (trichothecenes) and immunosuppressive (aflatoxin B1, ochratoxin A, and T-2 toxin) **(FAO, 1997)**.

Some of mycotoxin impacts on animals include; poor performance, reduced productivity, decreased immunity leading to impaired resistance to infection, significant liver, kidney and intestinal pathological changes, besides compromised reproduction **(Gashaw, 2015)**. Economic losses due to mycotoxicosis are derived directly from livestock morbidity, mortality and wastage of contaminated feed, increased veterinary service costs and feed disposal **(Ng'ang'a and Niyonshuti, 2022)**.

2- Predominant mycotoxins in feeds and their toxicity

Although over 500 mycotoxins have been identified, There are some primary classes of mycotoxins like: Aflatoxins, Ochratoxins and Fusarial toxins (Fumonisins, Zearalenone, Trichothecenes including Deoxynivalenol and T-2 toxin), which are easily detected in feedstuffs by standard laboratory tests and have a great ability to induce their owen harmful biological action in the body **(Zhao et al. 2021)**.The **Codex Alimentarius, (1995), EC, (2006a, b and 2013) and EFSA et al. (2020)** have established the recommended and maximum tolerable limits of mycotoxins, beyond which the commodity is unsafe and not accepted.

Among the Aflatoxins (B1, B2, G1 and G2), B1 is more prevalent, toxigenic and carcinogenic compouand **(Zhang et al. 2019)**. It is detected as residue in eggs and meat. Meanwhile in dairy cattle it is metabolized to Aflatoxin M1 in liver and is excreted in milk, its residual concentration should not exceed 0.5 µg/kg (ppb) as per FDA regulations or 0.05 ppb in European Union regulations **(Gizachew et al. 2016)**. The maximum allowed concentration in feed materials should not exceed 20 ppb, and for complete feed is 10 ppb **(EC, 2002)**. Ruminants appear to be less vulnerable to aflatoxins rather than other monogastric animals because their rumenal flora has the capacity to transform some mycotoxins into less carcinogenic metabolites or biologically inactive compounds **(Fink-Gremmels et al. 2008)**.

Ochratoxins have dangerous effects on animals. It predominantly affects the kidneys and harms the liver at high concentrations. Because of its strong albumin protein affinity, ochratoxin A (OTA), a primary ochratoxin, accumulates in animal tissues. OTA has been proved to be a potent nephrotoxic, immunotoxic, neurotoxic, hepatotoxic, and teratogenic compound. The most relevant effects of ochratoxins in cells are the inhibition of protein synthesis, lipid peroxidation, DNA damage and oxi-

dative stress **(Heussner and Bingle, 2015)**.

Regarding to Fusarial toxins, all of Fumonisins, Zearalenone, Trichothecenes including Deoxynivalenol and T-2 toxin are primarily produced by Fusarium molds **(Kócsó et al. 2021).** Among fumonisins (FUM: FB1, FB2, FB3) FB1 is the most plentiful, which can cause hepatotoxicity, neurotoxicity, nephrotoxicity, immune and developmental toxicities and cancer in humans, especially esophageal cancer, and animals **(Chen et al. 2021)**.

Fumonisins showed its effects on animal species through interfering with sphingolipid metabolism **(Merrill et al. 2001)**, where leukoencephalomalacia in horses is the most common syndromes associated with it, severe pulmonary edema, left ventricular dysfunction and hepatotoxicity in pigs.

Zeralenone (ZEA) has a biological effectiveness due to its similar structure to estrogen and thus competing with 17 β-estradio for estrogen receptor binding sites, consequently leading to fertility and reproductive disorders in livestock like: disturbed conception, abortion, infertility, vulval edema, and feminization of males **(Gao et al. 2017)**. Its permissible limits not exceed 0.250 ppm **(Zinedine et al. 2007)**. ZEA may be involved in carcinogenesis in human.

The consumption of trichothecenes results in hasty irritation to intestinal mucosa leading to alimentary hemorrhage, vomiting and diarrhea, while direct contact leads to dermatitis. T -2 toxin (T-2), type A trichothecenes, is more toxic but less prevalent. Monogastric animals are very sensitive particularly chicks and young pigs. It inhibits protein and DNA synthesis and weakens cellular immune responses. As well, it linked to oral and intestinal lesions, hematopoietic system destruction, and decreased egg production **(Li et al. 2011)**.

Deoxynivalenol (DON), a type B trichothecene, widely occurring and can induce anorexia, vomiting (hence known as "vomitoxin"), and endanger intestinal and immune functions in different animals by inhibiting the synthesis of nucleic acids and proteins and damage the hematopoietic systems (**Zhang et al. 2020).**

Patulin (PAT) is a fungal metabolite and organic compound produced by at least 60 species of fungi, but mostly produced by *Penicillium expansum*. PAT has neurotic and immunotoxic effect in animals. It was used as antibiotic but it showed toxic effect on human and cause hemorrhage, ulcerations, vomiting and nausea **(Vidal et al. 2019).**

3- Mycotoxins sampling and detection in feeds

3.1 Sampling and preparation procedures

Mycotoxins usually are not evenly distributed in stored commodities and tend to generated in isolated pockets; hence it is very important to obtain a random representative sample for determining mycotoxins **(Whitaker, 2004)**. The European Commission (EC) has defined necessities for collecting samples and performance criteria for analytical techniques to obtain comparable data **(Koesukwiwat et al. 2014)**. Therefore, to validate procedure to meet all performance criteria: proper sampling, extraction and clean up procedures and determining methods must be fully assessed. Sample preparation is very important which involves two important steps of extraction and clean-up. Extraction methods using appropriate solvents are strongly affected the recovery of the specific compounds and therefore the accuracy of the results **(Elkenany and Awad, 2021)**.

3.2 Analytical techniques of mycotoxins detection

3.2.1 Conventional techniques

Different common analytical methods were applied for detection of mycotoxins, where some of them can be applied to samples that contain numerous mycotoxins.

3.2.1.1 Fluorometer

Fluorometer is a qualititative and quantitative apparatus use advanced biotechnology for quick and highly accurate analysis of mycotoxins as aflatoxin, ochratoxin, zeralenone, fuminosin and T2 toxin in poultry and large animals' feeds including cereal grains as corn, soybean, gluten, pelleted rations, concentrates and silage milk as ppb using immunoaffinity

method **(Truckess et al. 1991 and Scott and Kanhere, 1995)**.

3.2.1.2 Chromatography based equipments

It refers to chromatographic separation combined with a suitable detection system: ultraviolet (UV), mass spectrometry (MS), or fluorescence (FLD). The MS method has many advantages such as high sensitivity, selectivity, and accuracy, compared to the two other methods.

Thin layer chromatography (TLC) is a prevalent technique applied for qualitative mycotoxin analysis, due to its capability to investigate great numbers of samples, low operating cost and less equipment required **(Sargeant et al. 1961).**

High performance liquid chromatography (HPLC) with diverse detectors is used as a quantitative reference technique for routine analyses and as confirmatory technique for the modern techniques **(Hernndez-Hierro et al. 2008)**. It is expensive and needs qualified persons. It needs solvents as a mobile phase besides normal and reversed phase columns C18 as a stationary phase, where they are applied for separating and purifying toxins basing on their polarity, physical and chemical structure **(Krska et al. 2005)**.

Ultra-high performance liquid chromatography (UPLC) is lately carried out to detect mycotoxins in herbal medicines. It is more sensitive and less time consuming which is more appropriate for determination of trace complex medicine **(Wen et al. 2014)**.

Mass spectrometer is the detector of choice rather than tandem mass spectrometer **(Berthiller et al. 2007)**. Fluorometric detector for HPLC is common because of its sensitivity, low cost and simplicity, hence it is required for most mycotoxins. Also, other detectors for HPLC are applied, particularly Ultra Violet-spectrometric.

Tandem MS (MS/MS), where two MS equipment are coupled together, is a highly sensitive, specific, and reliable tool for detecting contaminants in foods/feeds and has become the most popular approach for multianalyte analyses **(Soleimany et al. 2012)**.

LC-tandem MS (LC-MS/MS) has been increasingly used for the accurate quantitative analysis of mycotoxins in foods/feeds **(Agriopoulou et al. 2020)**.

Gas chromatography (GC) is frequently used for detection of some volatile mycotoxins, followed by electrophoretic methods, modern thin-layer chromatography and others **(Xu et al. 2006)**.

3.2.1.3 Immunological techniques

Rapid Screening Technologies for Mycotoxin Analysis

Immunological techniques are rapid qualitative analyses carried out for detecting mycotoxins. Immunological methods mostly used for rapid screening. These techniques characterized by simplicity of sample preparation, low costs. Conversely, it sometime gives false -positive results.

Lateral flow immunoassay, ELISA, and immunosensors are immunochemical detection methods based principally on antibody-antigen binding **(Li et al. 2009)**.

Lateral flow test

Symmetric technology lateral flow assay uses specific kits and S-Flow reader operated with the Lateral Logic software to quantify results in (ppb), besides using specific curves to calculate the results **(Drakouli et al. 2019)**

Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA is immune response between antigen and specific antibody in presence of catalytic enzyme **(Lequin, 2005)**. It is commonly used because it is rabid, simple and somewhat inexpensive technique. It needs commercial kits. Meanwhile, the complex co-extracted samples, leads to unspecific reactions of antibodies, results in miscalculation **(Rahmani et al. 2009)**.

Immunosensors

Immunosensors are of the most commonly used analytical methods for mycotoxin detection. Antibodies, antigens, and their fragments, are used for bimolecular recognition in immunosensors. Labeled and label-free immunosensors combined with different transducers have been considerably developed for mycotoxin assessment **(Li et al. 2021)**.

3.2.2 Recent techniques of fungus/ mycotoxins detection

3.2.2.1 DNA-chip with microarray system

Early detection of mycotoxin production in food/feed material could be achieved through the advances in molecular biology techniques. DNA-chip with microarray system containing oligonucleotide primers that are homologues to genes of mycotoxins produced fungal species can be employed to forecast the mycotoxin production. Meanwhile, the success of such PCR based molecular techniques relies highly on the reliability of the reference gene sequence **(Atoui et al. 2012)**.

3.2.2.2 Biosensors

Biosensors are less sensitive and reliable but are simpler to use by non-specialized personnel directly in the field and without the requirement of laboratory infrastructure. It consists of various elements such as a molecularly imprinted polymer (MIP), an aptamer, a DNA/ RNA molecule, an enzyme, a tissue, living cells, and antibodies. A transducer is also necessary to connect these parts, which transforms the observed physical or chemical changes into a quantifiable signal. Depending on the signal transduction mechanism, three categories of biosensors exist: optical, electrochemical, and piezoelectric **(Li et al. 2021)**.

3.2.2.3 Spectroscopic Methods FT-NIR

Infrared (IR) spectroscopy-based methods are the most promising for the detection of mycotoxins since they require small samples, limited technical expertise, cheap, need no sample pre-treatment, relatively simple and eco-friendly **(McMullin et al. 2015)**.

4- Different strategies used for mycotoxins control

4.1 Preventive measures

They are very important practices include 1. Improvement of plant fungal resistant capabilities, 2. Proper pre-harvest, harvest and post -harvest approaches, 3. Management storage prosperities like; low temperature, re-drying the product and removal of contaminated seeds, 4. Utilize fungicides and preservatives against fungal growth and 5. Use suitable insecticides to avoid insects' damage on grains throughout storage period **(Shapira et al. 2004)**.

4.2 Counteracting mycotoxin produced fungal contamination

Prevent growth and invasion of pathogenic fungi in agricultural commodities is very important in preventing mycotoxin contamination. It can be attained by physical, chemical and biological treatments **(Liu et al. 2020).**

4.2.1 Traditional fungal growth inhibitors

4.2.1.1 Physical methods

Physical methods may realize through drying seeds, moisture level (< 9-11%), low temperature and humidity or dilution of the contaminated feed with safe feed.

4.2.1.2 Chemical methods

Chemical methods may applied through use of antifungal agents (acetic acid, propionic acid, benzoic acid, citric acid and their sodium salts, copper sulfate): 0.2–0.4 % in feed, use of fumigants as ammonia: 0.2-0.4% besides addition of herbal extracts (garlic, onion, clove oil, turmeric powder, thyme) : 0.25-0.5% **(Gowda et al. 2013)**.

4.2.2 Recent techniques in controlling of toxigenic fungal growth

4.2.2.1 Biological methods

Biological methods are considered one of the most newly strategies to combat the fungal growth that consequently reduced mycotoxins incidence. They can be applied through using of the Anti-fungal enzymes, chitinase and Beta

-1,3 glucanase found in plant seeds, they could be enzymatically hydrolysed such polysaccharides in fungal cell wall into smaller products resulting in killing of mycelia or spore of fungi. Subsequently future approaches were prepared to increase of that seeds rich in such anti -fungal enzymes likely to resist the infestation of fungi **(Gowda et al. 2013)**.

The use of microorganisms such as fungi and bacteria to degrade mycotoxins in foods has been widely used, (lactic acid bacteria can bind with fumonisins B1 and B2), though bacterial probiotics **(Scott, 2012)**

4.2.2.2 Genetic modification

Genetic modification of mold susceptible plants is capitalizing on the plant's own defense mechanisms. For instances, Enhanced expression of an alpha-amylase inhibitor in Aspergillus could result in reduced aflatoxin synthesis. Hybrid varieties of cereals with Bt (Bacillus thermophilus) genes have shown reduced Aflatoxin production, probably due to higher resistance of plants against pest and insects **(Gowda et al. 2013)**.

4.2.2.3 Using of biosynthetic cluster gene

Another way of control including use of aflatoxin biosynthetic cluster gene disruption techniques, that Furthermore leads to production of non-toxigenic bio-competitive strains of Aspergillus flavus throughout the soil to out -compete the toxigenic isolate **(Price et al. 2006)**.

4.3 Counteracting the produced mycotoxins

4.3.1 Present-day methods for mycotoxin detoxification in feed

Inactivated or detoxified of mycotoxins can be achieved by physical, chemical **(Pankaj et al. 2018 and Hu and Wu. 2019)** and biological means.

4.3.1.1 Physical methods

Physical approaches may applied through thermal processing techniques like cooking under pressure, boiling, baking, frying or roasting **(Kabak, 2009)**, removal of contaminated seeds by hand picking **(Matumba et al. 2015)** or photoelectric detecting machines **(Cui, 2013)**, or using ionizing (x-rays, γ-rays and electron beam) and non-ionizing radiations (ultraviolet rays, infrared and microwave) on feedstuffs **(He and Zhou 2010)**.

However, all these processes are labor intense, reduce the nutritional values of feed ingredients (destroy vitamins and denature proteins) and use an excessive amount of energy which limit their large-scale application.

Adsorbents

Adsorption binders included activated charcoal **(Teleb et al. 2004)** and aluminosilicate minerals **(Adamovic et al. 2011)**, such as, Zeolites **(Sumantri et al. 2018)**, Bentonites **(Bhatti et al. 2017)** and hydrated sodium calcium aluminosilicates (HSCAS) as alkaline cations. They are able to form a complex with mycotoxins in a various degree of binding capacity, thus prevent their absorption to blood, reduce their bioavailability and allowed their passage from the gastrointestinal tract. Other clays, such as kaolin, sepiolite and montmorillonite act also through binding but less effectively than HSCAS and bentonite **(Nadziakiewicza et al. 2019)**.

However, these compounds can bind minerals and antibiotics like monensin, must be applied in vitro on feeds for a period before consumption, effective only against polar mycotoxins (aflatoxins and ochratoxins) and larg quantities were required for good efficiency. Some of the binders are not biodegradable and could pose environmental problem.

4.3.1.2 Chemical methods

There are some chemical agents that act through destruction the structure of the mycotoxins, to generate mildly toxic or nontoxic products **(Jalili and Son, 2011 and Agriopoulou et al. 2016)**. They include acids, bases (caustic soda, ammonia), reducing agents (Bisulphites), oxidants (ozone, sodium hypochlorite, hydrogen peroxide), formaldehyde and chlorinated agents have been used to degrade mycotoxins in contaminated feeds par-

ticularly aflatoxins.

However, chemical detoxification techniques does not meet the FAO requirements, because they are not totally safe for health, change feeds nutritional quality, chemical composition, texture, and flavor, expensive and have some harmful side effects on the environment, hence they not well accepted by consumers **(Kabak et al. 2007)**.

4.3.1.3 Biological /microbiological methods

As a promising strategy, biodegradation of mycotoxin by microorganism or enzymes attracted the attention of scientists **(Chlebicz and Śliżewska, 2020 and Qiu et al. 2021)**. This method of detoxification is widely recognized as specific, efficient and environment-friendly. This technology acts on the toxic group of the mycotoxin molecules, where it broken down and destroyed by the secondary metabolites produced by microorganisms or their secreted intracellular and extracellular enzymes, while producing non-toxic or less toxic degradation products **(Liu et al. 2022)**.

Microorganism

Using yeast *Saccharomyces cerevisiae* and lactic acid bacteria has received much attention through binding different toxins in vivo on its inner cell wall surface specific sugars, where the mannan-oligosaccharides (MOS) or beta-glucan (esterified glucomannans **(Coloviˊc ˇ et al.. 2019)**. Subsequently, reducing the mycotoxin hazard and acting as an immunomodulators. This method gained extensive attention where, the levels of inclusion of yeast-based binders are much lower than clay-based binders. For example, about 500 gm of glucomannans from yeast cell-wall have the same adsorption capacity as 8 kg of clay **(Gowda et al. 2013)**. Probiotic strain of *Lactobacillus acidophilus* CU028, *Lactobacillus casei* and *Lactobacillus rhamnosus* strains alone or in combination with chlorophyllin have shown to bind aflatoxin especially in gut conditions.

Enzymes

The main fungal enzymes known to have degradation activity are carboxylesterase, peroxidase, laccase (copper-containing oxidases), Cytochrome P450 system and oxidase. This technology used the recombinantly expressed detoxifizyme gene by gene cloning **(Cao et al. 2011)**. Where, laccase has the ability to degrad the heat-stable mycotoxin like zearalenone. Hence, it involved in many industrial application **(Viksoe-Nielsen and Birthe, 2009).**

However, biological action on mycotoxins has also some limitations, because some of them might secrete harmful metabolites or cannot survive in the gastrointestinal tract of the animals. These limitations motivated scientists to Look for another advanced techniques to combat mycotoxins.

4.3.2 Recent innovative techniques for mycotoxins control

A simple, highly efficient, and safe degradation technology is urgently required for the mycotoxin detoxification.

4.3.2.1 Biotransformation

Dual cultivation of *Aspergillus niger, Mucor racemosus, Alternaria alternata, Rhizopus oryzae* and *Bacillus stearothermophilus* with toxigenic strain of *Aspergillus flavus* results in 70-80% degradation of aflatoxins. Certain microbes are also able to metabolize mycotoxins (*Corynebacterium rubrum*) in contaminated feed or to biotransform them (*Rhizopius, Trichosporo mycotoxinivorans, Rhodotorula rubra, Geotrichum fermentans*). However, these biological processes are generally slow and have a varied efficiency.

Ruminants are considered to be relatively resistant to aflatoxins, due to biodegrading and biotransforming ability of rumen microbes compared to monogastric animals. This would be a great benefit in biological detoxification of aflatoxins and with the help of genetic engineering techniques, profits of this can be better recognized **(Moral et al. 2020)**.

4.3.2.2 Nanotechnology solutions

Nanobiotechnology is a novel promising solution, effective, eco-friendly and low-cost

strategy for the control of mycotoxigenic fungi and mycotoxins in the agriculture and food industry. Using of carbon-based nanomaterials (e.g., nanodiamonds and magnetic graphene) and chitosan polymeric nanoparticles have shown a high mycotoxin binding capacity due to their physicochemical properties; large surface area, very tiny size, colloidal stability under different pH, enhanced reactivity and strong adsorbing ability **(Horky et al. 2018)**.

Magnetic nanoparticles

Magnetic modifiers made up of pure metals, metal alloys and metal oxides. Iron and zinc oxides, silver, copper, or selenium nanoparticles are gaining massive attention in mycotoxin research because of their effective binding capacity **(Horky et al. 2018 and Loi et al. 2023)**.

4.3.2.3 Nanozymes

Nanozymes are inorganic nanoparticles with enzyme-like properties in redox reactions. They combine the properties of nanomaterials and oxidases in a more stable and efficient system **(Loi et al. 2023)**.

4.3.2.4 photocatalytic degradation

In recent years, photocatalytic degradation as a progressive oxidation technology have exhibited an enormous potential in the detoxification of mycotoxins due to their merits of low cost, environmental-friendly, easy operation at only mild pressure and temperature conditions, and without any secondary pollution **(Murugesan et al. 2021)**. The up-to-date nanomaterials have played a key role on the photocatalytic degradation of mycotoxins and have gradually been an attractive study hotspot in mycotoxin detoxification fields.

4.3.2.5 Plasma treatment

Plasma is an ionized gas (formed from application of electric current through neutral gas) that generates several reactive charged and neutral species, including photons, positive and negative ions, and oxygen and nitrogen reactive species with unique physical and chemical properties **(Mandal et al. 2018)**. It can be divided into thermal and non-thermal (cold) plasma, depending on the type of gas generation methods, and working temperature.

Cold Plasma

Cold plasma works at around room temperature (30–60°C), it has strong antimicrobial effects and for this reason, it finds multiple applications in sterilization, decontamination, and disinfection in the food industry. The reactive species generated by the cold plasma are highly active oxidants that may increase the permeability of the cell membranes by damaging the cell walls, leading to DNA fragmentation and leakage, destruction of cellular proteins, cell apoptosis and the deformation of mycelial spore. It is promising, low-cost, and environmentally friendly method for the decontamination of mycotoxins. The capability of cold plasma to inactivate fungal growth and mycotoxin production has been well recognized **(Loi et al. 2023)**.

However, this process still needs standardization and improvement to overcome the low penetration capacity. As well, suitable plasma equipment is still at the laboratory stage.

4.3.2.6 Polyphenols,flavonoids, plant extracts and essential oils

Phytonutrients mainly polyphenols and flavonoids have recently been applied in various food systems due to their biological activities, particularly antibacterial, antioxidant and anti-inflammatory properties. Their molecular mechanisms against mycotoxins varies and may be attributed to: (I) their bioactivity through their antioxidant properties and lipophilicity, (II) inhibition of mycotoxin production through structural modifications of the fungal membrane, (III) downregulation of the gene's expression involved in the mycotoxin production and (IV) inhibition of the enzymatic activity **(Ahmed et al. 2022)**. Hence, they have antifungal and antimycotoxigenic properties, besides their immunomodulating, safe and well tolerated effects on animals. As well, natural essential oils has advantages as a high efficiency, eco-friendly and low-drug-resistance tool.

4.4 Nutritional supplementation strategies to alleviate the adverse effects of mycotoxins

Concerning to the fact that none of the mycotoxin decontamination strategies has the ability to complete removed or detoxified various types of mycotoxins, besides taken in consideration that even a low consumption level of a mycotoxin can cause chronic toxicity including a reduction of the performance and immunosuppression in animal. Therefore, nutritional strategies have also a great role in animal general health support through modulation of mycotoxin detoxification system, overcome oxidative stress and shortage of nutrient absorption resulted from mycotoxins.

For instances, addition of hepatotropic nutrients like methionine amino acids,in amount more than its requirements, has protected the chicks from growth depressing effects of AFB1, possibly through an increased rate of detoxification by glutathione, a sulfur amino acid metabolite. Supplementation of phenylalanine has shown to alleviate toxicity of ochratoxin. Addition of vegetable oil (safflower oil, olive oil) to aflatoxin contaminated feed improves the performance of chicks **(Gowda et al. 2013)**.

Applying of antioxidants like Butylated hydroxy toluene (BHT) is effective in ameliorating the adverse effects of mycotoxins, neutralizing the free radicals and lipid peroxidation **(Klein et al. 2002)**. Similarly, Vitamin C, B and E, and Selenium supplementation. Of late, there is a growing interest in the use of phytochemicals (silymarin, flavonoids, curcumin, Allixin and polyphenolics, resveratrol) as antioxidants in increasing the activity of antioxidant enzymes (glutathione peroxidase, catalase, and super oxide dismutase) **(Gowda et al. 2013)**.

Conclusions and perspectives

Contamination of processed foods and feeds endangered human and animals health. This review provided an insight on the most predominant types of mycotoxins, besides a number of different important traditional and new analytical approaches for the accurate determination of mycotoxins' levelsincluded fluorometer, chromatography based devices, immunological based techniques and biosensors. As well, this article summarizes a number of strategies to reduce mycotoxin contamination using physical, chemical, biological and biotechnological approaches. However, traditional physical and chemical procedures have several drawbacks, including limited efficacy, safety concerns, palatability losses, reduce feeds nutritive value, high cost and have some side effects on animal and human health. Adsorbents and microorganisms/enzymes use may be more desirable and currently used as feed additives. Biotechnological intervention in terms of developing transgenic fungal resistant crops and biological control using non-toxigenic, competitive fungal species holds a better promise in managing toxigenic fungi. Advancement in molecular techniques using fungal oligonucleotide probes with PCR based microarray analysis would help in early forecasting detection of potential mycotoxin production, suggesting for critical control strategies.

For further researches, more studies needed to give a better understanding of fungal control approaches regarding climatic changes and their effect on severity and stability of toxigenic fungi and mycotoxins, besides weigh out the potential abilities of the already used and the advanced detoxification techniques. Until now, no single technique is equally efficient against a broad variety of mycotoxins that can cooccur in various commodities. Hence,further researches on the safety of strategies combination to an integrated decontamination approach should developed to maximize mycotoxin removal from food/feeds to the most possible extent.

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