Occurrence of Mycotoxins in Certain Freshwater Fish Species and the Impact on Human Health: A General Review

Muralidharan Velappan and Deecaraman Munusamy

Abstract

Mycotoxins are toxic secondary metabolites produced by organisms of the fungus kingdom, which are capable of causing disease and death in humans and animals when present in food. Recent studies evinces fish consumption might become another way for mycotoxins to enter the human food chain. Although the increasing research publications related to the occurrence and prevention of mycotoxin contamination in fish feeds, there was limited studies on bioaccumulation of mycotoxins research in common freshwater fish species. Further this was assumed fish species of salmonid and cyprinids are very sensitive to feed-borne mycotoxins so far. Studies have demonstrated, fish may also carry mycotoxins residue along the food chain, thus compromising human health. This review describes mainly mycotoxin contaminations in certain freshwater fish species and the impact on human health due to their potential proven toxicity. This review also provided comprehensive information on mycotoxins contamination levels in muscle and liver tissue of some freshwater fish species such as Nile tilapia, Labeo rohita, and Catla catla during capturing in freshwater lakes and also fish sold at wet market and hypermarket in Chennai, Tamilnadu.

Keywords: Mycotoxins, bioaccumulation, freshwater fish, wet market, hypermarket, Chennai

1. Introduction

In many developing countries, fish grew in economic importance during the second half of the twentieth century and by the end of the 1990s, the fisheries sector had become an important source of food, employment and foreign exchange. Worldwide since 1960 consumption of fish has been increasing, on an average fish consumption has varied among continents and countries within each continent, and it always been higher in richer than in poorer countries. Several studies evinces that per capita fish intake will continue to increases worldwide to the next three decades, and the increasing consumption will result as a typical indicator used to measure the country’s economic health. In contrast the existing studies of positive income in fish trade, which generally ranges between normal and inferior, however the manner in which consumption responds to increase in wealth seems not only to the level of accomplishment of wealth, but also the quantities of fish that are
Aflatoxins

 eaten by the consumers. During the end of the twentieth century, in the developing countries, fishing pressure on inshore underwent increases steadily. This is mainly due to growing populations, changes in the technology, modernization of fishing methods, and access to an increasing number of buyers. According to the Food and Agriculture Organization of the United Nations, overfishing was bringing more inshore fish stocks into a state of overexploitation and the situation was becoming more serious threat for many communities.

Mycotoxins are toxic secondary metabolites produced by organisms of the fungus kingdom and is capable of causing disease and death in humans and animals including aquatic species. Several study reports evinces symptoms like vomiting, abdominal pain, jaundice, pulmonary edema, coma, convulsions, and death are considered as acute aflatoxicosis in humans, chronic symptoms of Long-standing exposure to aflatoxins has been associated with liver diseases, including cancer, cirrhosis, hepatitis [1]. Since 1956, the scientific expert committee jointly convened by FAO/WHO Expert Committee on Food Additives (JECFA) is the international body responsible for evaluating the health risk from naturally occurring toxicants and residues of veterinary drugs in food. [2–4] reported toxigenic fungi can grow on a wide variety of crops, including wheat, maize, and soy bean. [5, 6] have reported presently more than around 300–400 mycotoxins which are produced by 350 filamentous fungi were identified till date. The most common mycotoxins which are produced by moulds are Aspergillus, Penicillium, fusarium, and Alternaria, the occurrence of mycotoxicosis only after the consumption of mycotoxin-contaminated by humans and animals [7].

[8, 9] noted that the fungal genera of Aspergillus, Fusarium, and Penicillium are most frequent sources of harmful mycotoxins. A number of studies from different regions of Europe evinces Aspergillus prefers warmer tropical areas, whereas Fusarium and Penicillium grow in European temperate areas [10] However, Aspergillus flavus causes a broad spectrum of disease in human beings, ranging from hypersensitivity reactions to invasive infection, Aspergillus flavus and Aspergillus parasiticus are the major producers of mycotoxins that contaminates foodstuffs such as groundnut, maize, etc., [11]. The toxic symptoms of mycotoxins intake are collectively known as mycotoxicosis are the consequence of ingestion of grains or forage containing toxic metabolites produced by filamentous fungi. Fungi that produce toxins often do so only under specific conditions of warmth, moisture and humidity. Mycotoxins produce their toxic effects in several ways, including impairment of metabolic, nutritional or endocrine functions. According to [12, 13] study reports some mycotoxins are produce teratogenic or carcinogenic. Apart from plant feed stuffs such as soybean meal and cereal grains as a great source of mycotoxins in fishes [14, 15], an aquatic weed, Eichhornia crassipes, commonly known as water hyacinth, is one of the most troublesome aquatic weed and also an alternative to fish diets as partial or total fish meal replacement, a fungal phytopathogen Alternaria alternata (AL-14) a new strain on water hyacinth has been recorded as lower dissolved oxygen level leading to reduction of aquatic fish production [16]. [17] reported that water hyacinths collection from various sources and some important components namely hemicellulose 22–43.4 percent; cellulose 17.8–31 percent; lignin 7–26.36 percent; and magnesium 0.17 percent. [18] also reported the component levels of fresh water hyacinths ash which contains 28.7 percent K2O, 1.8 percent Na2O and 21 percent Cl. [19–21] reported that increased risk of contamination on plant-based diets to the fishes, more specifically increased mycotoxins-contamination tropical regions and developing countries where fish feeds are often made by the farmers themselves under inappropriate conditions with improper milling and storage condition. [22, 23] were observed some mycotoxins contaminating edible tissues in fishes mainly Aflatoxins (AFs), zearalenone (ZEN), and ochre toxin A (OTA), which represents food safety risk. [24, 25] found the residues of aflatoxin
B1 (AFB1) in fish muscle under experimental conditions, while [26] hypothesized the presence of mycotoxins in fish tissues could be the result from previous contamination of water ponds or from an accumulation of mycotoxins in mud ponds. [27] observed, residues of sterigmatocystin (a mycotoxin closely related to AFs) in edible tissue of Nile tilapia, *Oreochromis niloticus*, after the intragastric dosing. Earlier study reports of [28] shows ZEN (a resorcylic acid lactone) and its derivatives are the only known mycotoxins with estrogenic potential and are classified as endocrine-disrupting substance. While analyzing the occurrence of emerging Fusarium mycotoxins in aquacultural fish, [29] reported *Fusarium verticillioides* and *Fusarium proliferatum* are the common ingredient in fish feeds, further he concluded that the risk of contamination with *Fusarium* toxins is higher in maize and wheat than for soybean, however they were isolated in a very small percentage they may cause adverse effects to fish.

Since most studies have concentrated the effects of aflatoxins at high levels in fish feeds, and the establishment of aflatoxins on higher vertebrates not on the effects on lower vertebrates. This study mainly discusses the various mycotoxins contamination levels in edible portion of muscle and liver tissues of freshwater fishes of *Nile tilapia*, *Labeo rohita*, and *Catla catla*.

2. Mycotoxins

The occurrence of mycotoxins in aquatic feeds and their effects on target species are topics that continue to gain attention due to the general trend of replacing expensive animal protein sources such as fishmeal with cheaper plant-derived proteins. Mycotoxins intoxication occurs when fish and shrimp consume mycotoxins-contaminated feedstuffs [30]. Moreover, the impact of mycotoxins changes depending on the kind of fish that consumes them, especially Aflatoxin B1, was widely investigated mycotoxins as a source of contamination of foods and aquaculture feed worldwide. However great scientific discoveries were made in aflatoxin B1 (AFB1) in the aquaculture feedstuffs, and epizootic of hepatomas in rainbow trout by a number of researchers under the direction of scientists J. Halver, R. O. Sinnhuber, G. S. Bailey, J. D. Hendricks and colleagues, and very restricted study to a limited number of fish species till date [31].

Mycotoxins primarily found in areas with hot and humid climate, favourable for the growth of molds, they can also be found in temperate zones. In addition, mycotoxins exposure is mostly by ingestion [32]. Several studies performed by [33] shows *A. flavus* and *A. parasiticus* are the major dominant species isolated from fish feed from tropical countries. [34, 35] were found fish feed from Egypt and Iran were contaminated with *A. flavus*. Similarly [36, 37] reported fish feeds were contaminated with *A. flavus* at 35% and 55%, whereas *Aspergillus tamarii* were isolated at a frequency of 9.1% and 8% in fish feeds from Brazil, East Africa East Africa and Iran. *Aspergillus niger* (6%, 13.9%, 36%, and 39.1%) and *A. ochraceus* (10.2%) are the potential ochratoxigenic fungi were isolated from fish feed from East Africa, Iran, Portugal, and Brazil [38].

[39, 40] reported that AFB1, the most dangerous aflatoxin, displays hepatotoxic, carcinogenic, mutagenic, eratogenic, and immunosuppressive effects on a range of animal species, including aquatic vertebrates. [41] reported first, aflatoxicosis outbreak in rainbow trout hatcheries in the USA, was related to hepatoma, where trout was fed with AF-contaminated feed. [42] reported the lethal poisoning by AFs in many other fishes. Most importantly AFB1 mechanism of action is the formation of AFB1–8, 9-epoxide during metabolism by cytochrome P450. [43] reported that AFB1–8, 9-epoxide forms an adduct with macromolecules in cells,
with an affinity in decreasing order of macromolecules of DNA > RNA > protein. [44] observed, some fish species are extremely sensitive to AFB1 mainly because of differences in the patterns of enzymes involved in AFB1 metabolism. [45] reported the carcinogenic effect of AFB1 in channel catfish, *Ictalurus punctatus*; Nile tilapia, *Oreochromis niloticus* and the ornamental guppy, *Poecilia reticulata*. [46] has been observed marked differences in the susceptibility of different fish species and fish classes with fish fry, for instance, aflatoxicosis being more sensitive and succumbing quicker than adult fish. Dissimilarities in Aflatoxin sensitivity in salmonids with rainbow trout displaying extremely sensitive, while coho salmon, *Oncorhynchus kisutch*, were more resistant. [47] reported the occurrence of three forms of Aflatoxicosis: acute, subacute, and chronic. Acute aflatoxicosis in fish appears after ingestion of moderate to high doses of AFs.

[48] observed, in a experimental study on rainbow trout evinces sublethal doses of AFB1 produces anemia, pale gills, reduced packed cell volume values, edema, haemorrhaging, liver damage, and alterations to nutrient metabolism in rainbow trout. Similarly [49] also reported, acute toxicity was noticed in rohu, *Labeo rohita* following intraperitoneal (i.p.) application of AFB1, with doses of 7.5, 11.25, and 13.75 mg/kg AFB1 caused anorexia, sluggish movement, rapid opercular movement, and also found dose-dependent mortality by the end of the 10-day of the experiment. Histopathological alterations in liver with subcapsular focal congestion, necrotic and vascular changes and gill lamellae, meningitis, brain congestion, degeneration and inflammatory injury of the heart, degenerative and necrotic changes to the kidney tubules, and sloughing of the intestinal mucosa [50, 51]. [52] observed AFB1 at concentrations of 1.25 and 2.5 mg/kg (i.p.) in rohu caused cachexia, and preneoplastic liver lesions, along with changes to the spleen, intestine, gill, and pancreas over the 90-d trial. [53] were analyzed in rohu, doses of 1.25 and 5.0 mg/kg (i.p.) AFB1 caused disruption of the immune system over 90 days, evinces as a reduction in total protein, globulin levels. [54] also noticed chronic aflatoxicosis after long-term intake of low to moderate doses of AFs. Furthermore, this chronic form of the disease is reported as carcinogenic and genotoxic effects, followed by teratogenic, hormonal, neurotoxic, and hematological changes. [55] demonstrated in sea bass *Dicentrarchus labrax*, AFB1 at concentration of 0.018 mg/kg in feed evinces induced liver damage, increased in serum transaminases and alkaline phosphatase activity with significant decrease in plasma proteins after 42-day of exposure. [56] observed circulation disturbances and reaction induced infiltration around the bile duct, degeneration of liver tissues, nerve cells and renal damages, with the changes of polymorphonuclear in the renal tubules after 120- day of exposure AFB1 at concentrations of 0.2 mg/kg in common carp, *Cyprinus carpio*. Similarly [57] reported that negatively affected growth performance, bactericidal activity, lysozyme activity, and concentration of total serum proteins in yellow catfish, *Peleobagrus fulvidraco*, after a 12-week trial with the presence of AFB1 in the diet at a level of 0.2 mg/kg. [58] reported AFs in naturally contaminated feed in a concentration of 0.16 mg/kg had no adverse effects on the Production variables of weight gain, feed intake, and feed efficiency ratio (FER) in channel catfish, *I. punctatus*. Similar results were shown by [59] a 12-week study on juvenile channel catfish fed diets containing up to 0.22 mg AFs/kg. No significant reduction in body weight gain, FER, survival, or haematocrit values was noticed. [60] reported, the species of the genus *Oreochromis* tends to evinces low susceptibility to AFB1 exposure. The effect of diets with 0.25, 2.5, 10, and 100 mg/kg AFB1 on Nile tilapia for 8 weeks. Diets containing 100 mg/kg AFB1 caused weight loss, severe hepatic necrosis, and mortality, while 10.0 mg/kg evoked hepatic injury characterized by an excess of lipofuscin and irregular sized hepatocellular nuclei. Diets containing more than 2.5 mg/kg AFB1 evinces negative values of haematocrit and growth patterns.
No significant effects were observed diet containing 0.25 mg/kg AFB1. [61] monitored the toxigenic effects of AFB1 in blue tilapia Oreochromis aureus over 20 weeks by using food containing 0.019, 0.085, 0.245, 0.638, 0.793, and 1.641 mg/kg AFB1. Subsequently reduced cases of mortality rate was noticed in Nile tilapia throughout the experiment and toxic impacts were the only observed in the diet with 0.245 mg/kg or higher between 10 and 20 weeks. At levels of 0.245 mg/kg AFB1, and reduction in the growth rate was noticed along with hepatic damage, and accumulations of inflammatory cells and eosinophilic materials were found in the liver at 0.638 mg/kg of AFB1. [62, 63]. Therefore, based on the several study results, weight gain does not appear to be a sensitive parameter to detect mycotoxins contamination. According to [64] serum Alanine Aminotransferase (ALT) and Lactic Acid Dehydrogenase (LDH) along with lactate concentrations seems to be the delicate to fish with the responses to Deoxynivalenol (DON). Little is known about the impact of ecotoxicology and the consequence of exposure to aquatic organisms [65]. Careful monitoring of the AFs content in fish is essential, particularly in south and Southeast Asia. Thus it can be observed the various effects of mycotoxins reported in fish, as well as the related doses and time that fishes were exposed.

2.1 Ochratoxins

Ochratoxins are a group of mycotoxins produced by some Aspergillus species (mainly A. ochraceus and A. carbonarius, but also by 33% of A. niger industrial strains) and some Penicillium species, especially P. verrucosum [66]. [67] reported that Ochratoxins A (OTA) is the most prevalent and relevant fungal toxin of this group. According to reports of the International Agency for Research on Cancer (IARC) categorized OTA as possibly carcinogenic to humans under Group 2B carcinogen. As per the reports of [68] Ochratoxins A (OTA) evinces an immunosuppressive, teratogenic, and nephrotoxic compound. However, prevalence of OTA is the highest in South Asian and Eastern European food samples, the average contamination is much higher in South Asia [69]. Human studies are showed that OTA is associated with kidney diseases, such as Balkan endemic nephropathy (BEN). BEN is a chronic tubulointerstitial disease which slowly progressed into terminal renal failure. [70] described the main target organs of OTA toxic impact are the liver and kidney in fishes, and also he recorded an acute toxicity and metabolization of OTA in rainbow trout were developed with 10-days mortalities after single i.p. doses of OTA at 4.0, 6.0, and 8.0 mg/kg body weight. Histopathological study evinces normal architecture of liver specimen in trout dosed with OTA 4.0 mg/kg with many necrotic parenchymal cells. But the apparent effect of OTA on the affected liver was an increased the number of cytoplasmic and nuclear vacuoles at the highest doses of OTA with 8.0 mg/kg evinces necrosis in all parts of the kidney tissues.

[71, 72] observed an experimental study on rainbow trout with one single intravenous injection of 14C-labeled OTA, further they also noticed this mycotoxins was excreted through the urine and bile in 35.8 and 57.1%, over 24 h, which indicates that the hepatobiliary mode of excretion is more important than urinary excretion in fish. Similarly [73, 74] noticed highest concentrations of OTA in tissue 24 h after exposure were in the pyloric ceca, intestine, and liver and the elimination half-life of OTA in fish is 0.68 h. which evinces much shorter than mammals and birds. [75] observed the acute toxicity of OTA and behavioural changes in marine-reared adult sea bass. They also recorded an acute oral 96-h lethal concentration 50 value of 0.277 mg/kg body weight. Histopathological investigation revealed marked changes in fin and general congestion of the kidneys, gills, and on the periphery of the liver. [76] investigated in an experimental approach on ochratoxicosis in Nile tilapia and its amelioration by some feed additives. He also observed OTA intoxicated positive
control group were sluggish swimming, poor growth and off feed before death with reduction in survival was 53% and growth performance. Gross pathological lesions were also observed in liver, kidneys and spleen. Biochemistry results evinces ALT, AST, creatinine and urea were significantly raised with reduced total protein TP, albumin and globulin also compared in ochratoxicated fish group with negative control group.

[77] demonstrated dietary exposure of channel catfish (Ictalurus punctatus) and sea bass (Dicentrarchus labrax) to OTA led to reduced weight gains, poorer feed conversion rates, lower survival and changes of haematocrit values. Moreover, histopathological changes were observed in liver and posterior kidney tissues and changes of immune parameters were observed in channel catfish, similarly Nile tilapia (Oreochromis niloticus) showed increasing dietary OTA levels resulted in decreased growth, and poor feed utilization. In contrast, there have been no studies examining the effect of OTA on contamination levels in muscle and liver tissue of freshwater fish species viz., Nile tilapia, Labeo rohita, and Catla catla during capturing in fresh water lakes and also fish sold at wet market and hypermarket in Chennai, Tamilnadu.

2.2 Fusarium mycotoxins

Fusarium mycotoxins are a broad class of compounds with different chemical structures, physical and toxicological properties. Due to this great diversity, different detoxification strategies are required to deal with this complex group of compounds, [78, 79] has proved several studies, adsorption is not a feasible strategy to tackle fusarium mycotoxins, as it is only effective towards aflatoxins and, to a lesser extent, ochratoxins. Fusarium mycotoxins cause acute and chronic toxic effects and have been shown to cause a broad variety of toxic effects in animals [80].

2.3 Trichothecenes

Trichothecenes are a very large family of chemically related mycotoxins produced by various species of Fusarium, Myrothecium, Trichoderma, Trichothecium, Cephalosporium, Verticimonosporium, and Stachybotrys [81]. Hazardous concentrations of trichothecenes have been detected in maize, wheat, oats, and other commodities used as ingredients in aquaculture feeds [82] The toxicity of trichothecenes is primarily in protein biosynthesis inhibitors, neurotoxins, Immunosuppressive factors, or nephrotoxins and evoke acute and chronic symptoms after uptake [83]. In general, trichothecenes have the ability to affect general cell metabolism due to the tendency of active site thiol groups to attack the 12, 13 carbon epoxide ring, these inhibitory effects mostly seen in actively proliferating cells in the gastrointestinal tract or bone marrow [84]. Trichothecenes represents large group of over 150 chemically related mycotoxins known to date. Structurally each trichothecene consisting of a single six-membered ring containing a single oxygen atom, bounded by two carbon rings, the core ring structure contains an epoxide or tricyclic ether, at the 12, 13 carbon positions, as well as a double bond at the 9, 10 carbon positions, these two functional groups are primarily responsible for trichothecene ability to inhibit protein synthesis and incur cytotoxic effects. Removal of these groups results in a complete loss of toxicity. [85]. Further the classification system breaks up the trichothecene family into four groups namely type A, B, C, and D, based on chemical structure, with type A including T-2 toxin, HT-2 toxin, a deacetylated metabolite of T-2 toxin, neosolaniol, and diacetoxy-sicpenol and type B, represented by deoxynivalenol (DON), nivalenol, and its 3-acetyl and 15-acetyl derivates. [86]. Despite the distinct functional groups of
trichothecene classification types give each and unique chemical properties, their classification type does not specifically indicate their relative toxicity, while type D trichothecenes are pondered to be the most toxic, comparatively, A and B types have mixed toxicity [87]. Trichothecenes toxic effects in animals include decreased plasma glucose, reduced blood cell and leukocyte count, weight loss, alimentary toxic aleukia, as well as pathological changes in the liver and stomach. The mechanism involved in T-2 and DON toxicity is generally via oxidative stress-mediated deoxyribonucleic acid (DNA) damage and apoptosis [88, 89]. Furthermore, T-2 and DON are well-known inhibitors of protein synthesis resulting from the binding of peptidyl-transferase, which is located in the 60s ribosomal subunit. The most important trichothecene mycotoxicosis in animals, including fish are the T-2 toxin and DON [90].

2.3.1 T-2 toxin

T2 toxin, are trichothecene mycotoxins produced by fungal metabolites of the genus Fusarium. They are commonly present in foods and feed of cereal origin, and it was reported T-2 toxin was first isolated from the mould F. tricinctum (F. sporotrichoides). The main toxic effects of T-2 toxin induces DNA damage and cell death on prolonged administration, while these effects can be partially blocked by antioxidants, such as glutathione, coenzyme Q10, or α-tocopherol. In contrast toxic effects have been shown both in experimental animals and in livestock (unpublished data from Sigma Aldrich). Till date, very few investigation have been done on biological effects of T-2 toxin in fish diets. Earlier study reports of [91] reported that feeding of T-2 toxin around 16 week >2.5 mg/kg resulted in stunted growth in rainbow trout with reduced feed intake and hematocrit and hemoglobin concentrations evinces dose-dependent depression, while in Adult trout fed 15.0 mg/kg T-2 toxin had focal intestinal hemorrhaging and enlarged spleens and gall bladders. [92] also reported the T-2 toxin, is responsible for significant reduction in growth, significantly poor feed conversion, adversely affected hematocrit value, low survivability and histopathological abnormalities of stomach and kidneys in juvenile channel catfish. In addition, LD of T-2 in trout evinces, severe oedema and fluid accumulation in the body cavity and behind the eyes are produced in addition to the loss of the intestinal mucosa. Consumption of T-2 toxin contaminated feed at concentrations of 1.0 and 1.8 mg/kg in the rainbow trout immune system by studying non-specific cellular and humoral immune responses and its effect on red and white blood cells. Both the concentrations evinces significantly increased erythrocyte counts and a decrease in mean corpuscular volume, while haemogram analysis evinces decreased mean corpuscular haemoglobin to both experimental concentrations. In contrast, decreases in plasma haemoglobin was the only significant at the higher T-2 toxin concentration level. However, higher concentration of T-2 toxin resulted in a significant increase of leukocyte and lymphocyte count, while absolute phagocyte count and less mature neutrophil granulocyte forms remained unchanged at both the concentrations. Immunological assay evinces, non-specific humoral immunity was decreased significantly in both experimental groups when compared with the control study. Paradoxically, T-2 toxin in feed at a concentration range of 1.0–1.8 mg/kg influences the immunological defence mechanisms of rainbow trout [93].

2.3.2 Deoxynivalenol

Deoxynivalenol (DON), also known as vomitoxin, is a type B trichothecene, an epoxy-sesquiterpenoid. This mycotoxin occurs predominantly in grains such as wheat, barley, oats, rye, and corn, and less often in rice, sorghum, and triticale,
Aflatoxins

Further it is the most economically important mycotoxin [94, 95]. The effects of deoxynivalenol (DON) on fish are still not clear. In vitro study evinces fishes are sensitive animals to (DON) toxin. However this toxin does not seem to be a threat to the health of the fish, and not the case for deoxynivalenol (also called vomitoxin) which is the least toxic trichothecene, and some study reports evinces this can even cause harm to fish and humans [96]. The impact of experimental animals rats after oral exposure of (DON) exhibits both developmental and reproductive toxicity including reduced fertility, embryo toxicity, and skeletal abnormalities, effects on body weight and relative epididymal weight and postnatal mortality [97]. In general, exposure of (DON) among fishes does not cause higher mortality. However, doses of up to 2.6 mg/kg of this (DON) toxin were fed to rainbow trout, symptoms develops poor feeding and reduced feed conversion efficiency, which further leads to poor weight gain and growth rate. Although, feeding a rainbow trout diet with 6.4 mg/kg of deoxynivalenol causes reduced in mortality after Flavobacterium psychrophilum infection. Similarly, exposure in channel catfish to deoxynivalenol (2.5 to 10.0 mg/kg) increased their survival rate after Edwardsiella ictalurid infection, but no significant negative effects on weight gain and feed conversion efficiency. Therefore, (DON) seems to have some protective effect against Gram positive or Gram negative bacterial infections in some species of fishes [98]. Histopathological examination recorded by [99] morphological changes in the liver, including subcapsular edema, hemorrhages, and fatty infiltration of hepatocytes, while hemorrhages were found in the intestinal tract. According to [100] study reports evinces there was no significant changes in biometric parameters were recorded so far, significant changes were observed in hematological parameters, such as low mean corpuscular hemoglobin values and biochemical parameters, such as a decrease in glucose level, serum cholesterol, and ammonia [101].

2.4 Fumonisins

Fumonisins (FUMs) are mycotoxins produced by F. verticilloides. Worldwide, the occurrence these mycotoxins a common contaminants of maize and maize by-products. Further several reports evinces these (FUMs) mycotoxins mainly consist of fumonisin B₁ (FB₁), FB₂ and FB₃, with FB₁ being the most toxic. Clinical signs associated with fumonisin toxicity varies significantly between the species and the primary target organ, further, safe levels of fumonisin in the feed are quite variable between species [102, 103]. Experimental study evinces FB1 is also a cancer promoter and initiator in rat liver cells, hepatotoxicity in higher vertebrates such as horses, pigs and vervet monkeys. In vitro cell culture evinces cytotoxicity in mammalian cells and phytotoxicity among various plants. Earlier study reports evinces (FUMs) in home-grown corn have been associated with an elevated risk for human oesophageal cancer in Transkei and China [104]. [105] observed, consumption of feed containing FBs leads to disruption of sphingolipid metabolism and accumulation of sphinganine (SA) in the liver, kidney, and serum in animals. Comparative study was carried out by [106] where the toxic dose for FB1 in fish has a broad range, with pigs and horses [107]. Fumonisin B₁ (FB₁) have been shown to reduce the productivity of fish. Nile tilapia fingerlings were fed FB₁ at 0, 10, 40, 70 and 150 ppm for 8 weeks. The FB₁ was extracted from cultures of Fusarium moniliforme. Mortalities in all treatment groups were low and were not dose related. Feeding diets containing 150 ppm FB₁ shows decreased hematocrit. There was evidence that sphingolipid metabolism was disrupted in fish fed FB₁. Observed decreased weight gains among fishes fed with FB₁ at 40, 70 and 150 ppm levels. However, fishes are fed 10 ppm of FB₁ evinces decreased weight gains for the first 2 weeks, but body weights at 4 weeks not significantly different from controls. Some study
evinces Channel catfish are more sensitive and toxic to FB1 [108]. [109] reported that Channel catfish are more tolerant with FB1 than carp. Exposure of 1-year-old common carp to be feed contaminated with FB1 0.5 and 5.0 mg/kg body weight resulted loss of body weight and alterations of physiological parameters in target organs, including increased activities of liver enzymes. In another study with carp of a similar age, signs of toxicity were observed at dietary levels as low as 10 ppm FB1. [110] reported in farm animals feed contaminated with FB1, histological sections revealed scattered lesions in the exocrine, endocrine pancreas and interrenal tissues, and this mostly due to ischemia or increased endothelial permeability. FB1 contamination was also found to impair the immune response of fishes were inoculated with killed Edwardsiella ictaluri cells. Microscopic hepatic lesions was observed in fish fed diets contaminated with more than 20 ppm. In contrast to these findings, a similar study was reported, there is no histological evidence of toxicity in adult channel catfish fed a diet containing more than 300 ppm FB1 for periods of up to five weeks. [111] described on Nile tilapia fingerlings, feeding FB1 at 10, 40, 70 or 150 mg/kg feed for eight weeks, affected the growth performance was evident. Similarly, experimental study in fish fed diets containing FB1 at levels of 40,000 μg/kg evinces decreased average weight gains, further, haemogram analysis revealed hematocrit was only decreased in tilapia fed diets containing 150,000 μg FB1/kg. On the other hand, few data’s were available that shrimp are sensitive to FB1. So far FB1 has not been extensively studied in shrimp feed contaminants. [112] reported FB1 was not a complete carcinogen in trout, when compared with fumonisin B1 (FB1) in rodents and epidemiological evidence association between FB1 and cancer in humans, for that he designed an experimental approach in rainbow trout with very low spontaneous tumor incidence, firstly, if FB1 was a complete carcinogen, in the absence of an initiator, secondly, promoter of liver tumors in fish initiated as fry with aflatoxin B1 (AFB1) and finally a promoter of liver, kidney, stomach, or swim bladder tumors in fish initiated as the fry with N-methyl-N′-nitro-nitrosoguanidine (MNNG). Despite FBs being the most prevalent mycotoxin in grains (the most common ingredient in commercial aqua feed), and epidemiological evidence suggests the overall concentration is low and does not represent a threat to fish. A slight tendency toward prolonged clotting time and lowered iron concentrations in the liver and ovary after exposing juvenile rainbow trout to 10 mg/kg ZEN i.p. for 24, 72, and 168 h was observed by [113]. ZEN concentrations in commercial fish feed for cyprinids in Central Europe was assessed by [114], while [115] examined some samples of rainbow trout feed in Argentina, he observed concentrations did not exceed an average level of 0.068 mg/kg (Central Europe) and 0.088 mg/kg (Argentina), suggesting that ZEN poses no threat to fish under aquaculture.

2.5 Zearalenone

Zearalenone (ZEA), one of the common estrogenic mycotoxins and is mainly produced by Fusarium fungi. Primarily this (ZEA) mycotoxin attacks young crops, also can develop when cereals were stored even dried fully. In vitro and in vivo study evinces that (ZEA) possess estrogenic activity in mice, swine, donkeys and cattle. According to Southern Regional Aquaculture Centre (SARC) reports, (ZEA) toxin has potent estrogenic effects among farm animals. According to [116] reports, numerous studies have described the (ZEA) toxin worldwide, no data existed in India till date. [117] reported, the exact mechanism of the reproductive physiology in farm animals with (ZEA) toxin has not been clearly documented. Feed concentrations of zearalenone as low as 1 to 4 ppm can cause transient to permanent reproductive damage in breeding swine, depending on the age of the animals. Susceptibility to (ZEA) toxin older animals are sensitive than younger animals. The
Aflatoxins

effect of ZEA toxin on fish has not been evaluated, but it interferes the reproduction in many animals. [118] examined few samples of rainbow trout feed in Argentina, concluded that the concentrations did not exceed an average level of 0.068 mg/kg (Central Europe) and 0.088 mg/kg (Argentina), and also suggested ZEN poses no threat to fish under aquaculture.

2.6 Moniliformin

MON is an uncommon fungal toxin a feed contaminant that is lethal to mainly ducklings [119]. Experimental study were carried out at Auburn University evinces that juvenile channel catfish diets containing moniliformin toxin at 20, 40, 60 and 120 ppm of diet significantly lowered weight gains compared to the control catfish. Moniliformin disrupts the intermediary metabolism of the tricarboxylic acid (TCA) cycle at the conversion of pyruvate to acetyl-CoA, the starting intermediate for the TCA cycle [120]. [121, 122] described, the MON toxicity, based on the disruption of pyruvate metabolism, since the inhibition of pyruvate dehydrogenase and subsequent pyruvate accumulation in the tissues of the affected animal. [123] performed a comparative study on FB1 and MON toxicity in channel catfish, which evinces fish diets containing 20 mg/kg MON or FB1 led to differences in weight gain and FCR. Catfish fed with an FB1 diet had significantly lowered weight gain and poorer FCR than catfish fed a MON diet, which indicates that FB1 is more toxic than MON to channel catfish. Levels of 60 and 120 mg/kg MON (and the combination of MON and FB1) reduced hematocrit and caused smaller hepatocellular nuclei, whereas 60 mg/kg MON significantly increased serum pyruvate levels. [124] reported the toxicity of MON over the mineralization, development of bone structures and its influence on survival, growth and gene expression by using zebrafish (Danio rerio) as a model species for in vivo experiments, while gilthead seabream (Sparus aurata) mineralogenic cell line VSa13 as in vitro model. In vivo and in vitro analysis evinces MON did not decrease bone mineralization. This study also reported minimal in vitro cytotoxicity concentration at 1000 μg L⁻¹ MON, further the occurrence of deformities was also not altered by MON toxicity at the concentration tested (450 μg L⁻¹) inspite of larval growth was affected as shown by the decrease in standard length of exposed specimens after 20 dpf. Moniliformin concentrations higher than 900 μg L⁻¹ significantly decreased larvae survival when compared to control.

2.7 Emerging mycotoxins

According to Fish Site 2016, reports, emerging mycotoxins are a class of compounds that are attracting increasing interest among the scientific community, primarily their high occurrence in feed and food commodities, sometimes at relatively high concentrations, and potential toxicity towards animals and humans. Studies focusing on this class of mycotoxins are still quite low in number, an extensive review published in 2015 showed that among all mycotoxin-related studies, only 7% were directed towards emerging mycotoxins. Over all, existing literature study evinces the naturally occurring fumonisin toxins produced by various fungal species of fusarium fungi reported to have toxic effects on vital organs, immunological disturbances loss of weight, including metabolic alterations, eventually results in cancer and increased mortality. Further, fusarium have been addressed as the most prevalent fungi that infect agricultural commodities, so far there were no study reports of bioaccumulation of fumonisin toxin in the musculature of fishes. They can also produce a broad array of mycotoxins and secondary metabolites, however, consumption of fish does not seem to be
any serious impact reported by food security risk regarding this toxin, more studies are imperative to understand the impacts of these toxins on fish population [125].

2.7.1 Enniatins

Enniatins (ENNs) are known for their antimicrobial, insecticide and antifungal properties. These toxins might have herbicide effects as well. ENNs are commonly found on small cereal grains and derived products in Europe, Africa, Asia, America and Australia, with concentrations ranging from \( \leq 1 \mu g/ \) to 100 mg. Other products can also be contaminated, such as dried fruits, nuts, eggs and fish. The mechanism of action of enniatins is directed towards cellular membrane transport proteins that are inhibited by the toxin. Toxicity of enniatins is particularly severe towards mitochondria [126].

2.7.2 Beauvericin

Beauvericin (BEA) shows strong antimicrobial activity towards various bacterial species, based on sources of the existing literature review, (BEA) has no distinction between Gram-positive and Gram-negative. This toxin also evinces cytotoxic, apoptotic and immunosuppressive activity. Beauvericin acts on the cellular membranes by increasing the permeability and disrupting the cellular homeostasis. In addition, (BEA) has been reported the toxicity to lymphocytes, skeletomycocytes and cardiomyocytes, with birds and minks being the most sensitive species. However, the mechanism of action has not been fully understood yet, but toxicity study evinces towards mitochondria, there is an assumption with the same mechanism of (ENNs) toxins.

2.7.3 Fusaproliferin

Studies focused on Fusaproliferin (FUS) evinces is a fungal toxicity towards human B - lymphocytes and some insect cell lines. (FUS) considered as the most emerging mycotoxin, earlier study also reports evinces teratogenic and pathogenic effects on chicken embryos. More recently, some studies were conducted using brine shrimp \((Artemia salina)\) as a model organism. The toxin often co-occurs with deacetyl-fusaproliferin, although the toxicity of the latter is much lower compared to fusaproliferin. Studies on the synergistic effects between the two fungal toxins have not been elucidated yet.

2.8 Conclusions and future recommendations

The incidence is rapidly increasing mycotoxins, namely toxic fungi are currently of constant interest and concern, and aquatic species have different levels of sensitivity to mycotoxins depending on type and quantity of mycotoxins, duration of exposure, age, species and sex including diet. Outcomes of mycotoxin contamination in fish has been increasing during the last few years including rainbow trout, Atlantic salmon, common carp, gibel carp, zebrafish, beluga, sturgeon hybrids, channel catfish and Nile tilapia. However, the effects of the same mycotoxin on two different fish species under the same experimental conditions have not yet been investigated, which makes it difficult to judge species differences in sensitivity to mycotoxins. Most commonly, it was often assumed that salmonids are very sensitive to mycotoxins, but recent investigation evinces that depending on the biological response, similarly, cyprinids are also reported very sensitive to feed-borne mycotoxins. There were no mycotoxin contamination research conducted on \(Labeo\)
Aflatoxins

rohita, and Catla catla during capturing in fresh water lakes and also fish sold at wet market and hypermarket so far, further research is needed to clarify the issue of species-specific sensitivity to certain mycotoxins. Further, the use of appropriate drying methods and improved storage conditions can certainly minimise the formation of mycotoxins in grains independent of the location where they take place, i.e. on a farm, in a warehouse or during transport. Increasing the knowledge on mycotoxins in fish will influence our future strategies for fish nutrition. We suggest that further research should be conducted on the effects of co-occurring mycotoxins and also recommend not only stricter regulations on fish feed, also fish handling (landing centre to retail market) further to reduce the impacts of mycotoxins on fish health and productivity.

Declaration

No original data is utilized in this review, all information is accessed from published work.

Author details

Muralidharan Velappan* and Deecaraman Munusamy

1 Department of Marine Biotechnology, AMET University, Chennai, India

2 Department of Biotechnology, Dr. M.G.R Educational and Research Institute, Chennai, India

*Address all correspondence to: muralidharanmicro@gmail.com

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
References

[1] World Health Organization, Mycotoxin, 9 May, 2018.

[2] Goswami, R. S. and H. C. Kistler. Heading for disaster: *Fusarium graminearum* on cereal crops. Molecular Plant Pathology. 2004. 5:515-525.

[3] Murphy, P. A., S. Hendrich, C. Landgren, and C. M. Bryant. Food mycotoxins: an update. Journal of Food Science. 2006. 71:51-65.

[4] Marin, S., A. J. Ramos, G. Cano-Sancho, and V. Sanchis. Mycotoxins: occurrence, toxicology, and exposure assessment. Food and Chemical Toxicology. 2013. 60:218-237.

[5] Grenier, B., Oswald, I.P. (2011). Mycotoxin co-contamination of food and feed: Meta-analysis of publications describing toxicological interactions. World Mycotoxin Journal, 4(3), 285-313.

[6] Mahendra Pal, Fikru Gizaw, Firehiwot Abera, Pankaj Kumar Shukla, Hazarika, R.A. (2015). Mycotoxins: A Growing Concern to Human and Animal Health, Beverage & Food World, 42(5)

[7] Grenier, B. and Oswald, I. Mycotoxin co-contamination of food and feed: meta-analysis of publications describing toxicological interactions. World Mycotoxin Journal. 2011. 4 (3): 285-313. DOI: 10.3920/WMJ2011.1281.

[8] Bennett, J. W. and Klich. M. Mycotoxins. Clinical Microbiology Reviews. 2003. 16:497-516.

[9] Bryden, W. L. Mycotoxin contamination of the feed supply chain: implications for animal productivity and feed security. Animal Feed Science and Technology. 2012. 173:134-158.

[10] Iveta Matejova, Zdenka Svobodova, Jan Mares, Helena Modra. Impact of Mycotoxins on Aquaculture Fish Species: A Review. World Aquaculture Society. 2016. DOI: 10.1111/jwas.12371.

[11] Shankar, J. Madan, T. Basir, S. F and Sarma P. U. Identification and characterization of polyubiquitin gene from cDNA library of Aspergillus fumigatus. Indian Journal of Clinical Biochemistry. 2005. vol. 20, pp. 208-212.

[12] Marika Jestoi. Emerging fusarium-mycotoxins fusaproliferin, beauvericin, enniatins, and moniliformin: a review. Critical Review of Food Science Nutrition. 2008. 48(1):21-49. DOI: 1080/10408390601062021.

[13] Iveta Matejova, Zdenka Svobodova, Jan Mares, Helena Modra. Impact of Mycotoxins on Aquaculture Fish Species: A Review. World Aquaculture Society. 2016. DOI: 10.1111/jwas.12371.

[14] Yiannikouris, A. and Jouany, J. P. Mycotoxins in feeds and their fate in animals: a review. Animal Research. 2002. 51:81-99.

[15] Binder, E. M. Managing the risk of mycotoxins in modern feed production. Animal Feed Science and Technology. 2006. 133:149-166.

[16] Kamal Rai Aneja, Romika Dhiman, Neeraj Kumar Aggarwal, and Ashish Aneja, International Journal of Microbiology. 2014. Article ID 758942, 14 pages DOI:10.1155/2014/758942

[17] Carina C Gunnarsson, Cecilia Mattsson Petersen. Water hyacinths as a resource in agriculture and energy production: a literature review. 2005. Waste Management. 27(1):117-29. DOI: 0.1016/j.wasman.

[18] Matai, S. Bagchi, D.K. 1980. Water hyacinth: a plant with prolific bio-productivity and photosynthesis. p. 144-148. In: Gnanam, A,
Aflatoxins

Krishnaswamy, S., and Kahn, J.S. (eds.), Proc. International. Symposium on Biology. 1980. Applications of Solar Energy. MacMillan Co. of India, Madras.

[19] Tacon, A. G. J. Nutritional fish pathology: morphological signs of nutrient deficiency and toxicity in farmed fish. FAO Fish Technical Paper. 1992. No. 330. Food and Agriculture Organization of the United Nations, Rome, pp. 75.

[20] Santacroce, M. P. M. C. Conversano, E. Casalino, O. Lai, C. Zizzadoro, G. Centoducati, and G. Crescenzo. Aflatoxins in aquatic species: metabolism, toxicity and perspectives. Reviews in Fish Biology and Fisheries. 2008. 18:99-130.

[21] Anater, A. L. Manyes, G. Meca, E. Ferrer, F. B. Luciano, C. T. Pimpão, and G. Font. Mycotoxins and their consequences in aquaculture: a review. 2016. Aquaculture 451:1-10.

[22] Gareis, M. and J. Wolff. Relevance of mycotoxin contaminated feed for farming animals and carryover of mycotoxins in food of animal origin. 2000. Mycoses 43:79-83.

[23] Iqbal, S. Z. S. Nisar, M. R. Asi, and Jinaq, S. Natural incidence of aflatoxins, ochratoxin A and zearalenone in chicken meat and eggs. Food Control. 2014. 43:98-103.

[24] Persi, N. J. Pleadin, D. Kovacevi´ Scortichini, G and S. Milone. Ochratoxin A in raw materials and cooked meat products made from OTA-treated pigs. Meat Science. 2014. 96:203-210.

[25] Nomura, H. M. Ogiso, M. Yamashita, H. Takaku, A. Kimura, M. Chikasou, Y. Nakamura, S. Fujii, M. Watai, and H. Yamada. Uptake by dietary exposure and elimination of aflatoxins in muscle and liver of rainbow trout (Oncorhynchus mykiss). Journal of Agricultural and Food Chemistry. 2011. 59:5150-5158.

[26] Julie J Tsafack Takadong, Hippolyte T Mouafo, Linda Manet, Annick M B Baomog, Jorelle, J.B. Adjele, Evrard K Medjo, Gabriel N Medoua. Assessment of the Presence of Total Aflatoxins and Aflatoxin B₁ in Fish Farmed in Two Cameroonian Localities. Int J Food Sci. DOI: 10.1155/2020/2506812.

[27] Abdel-Wahaab, M. A. A. M. Hasan, S. E. Aly, and K. F. Mahrous. Adsorption of sterigmatocystin by montmorillonite and inhibition of its genotoxicty in the Nile tilapia fish (Oreochromis niloticus). Mutation Research, Genetic Toxicology and Environmental Mutagenesis. 2005. 582:20-27.

[28] Zinedine, A. J. M. Soriano, J. C. Moltó, and J. Mañes. Review on the toxicity, occurrence, metabolism, detoxification, regulations and intake of zearalenone: an oestrogenic mycotoxin. Food and Chemical Toxicology. 2007. 45:1-18.

[29] Bullerman, LB. Ryu, D. Jackson, LS. Stability of fumonisins in food processing. Advances in Experimental and Medical Biology. 2002. 504:195-204.

[30] Global results of 22318 analyses on the occurrence of mycotoxins – including aflatoxin, zearalenone, deoxynivalenol (vomitoxin), T-2 toxin, fumonisins and Ochratoxin A— in crops such as corn (maize), wheat, soybean, related by-products and finished livestock feeds. Biomin Mycotoxin Survey Q1 2019 Results.

[31] Maria Pia Santacroce, M. C. Conversano, E. Casalino, O. Lai, C. Zizzadoro, G. Centoducati & G. Crescenzo, Springer Link. 2007. 18: pp 99-130.

[32] Bankole, S. M. Schollenberger, S and Drochner, W. “Mycotoxins in food systems in sub-Saharan Africa: a
review,” *Mycotoxin Research*, 2006. vol. 22, no. 3, pp. 163-169.

[33] Berthiller, F. Sulyok, M. Kraska, R and Schuhmacher, R “Chromatographic methods for the simultaneous determination of mycotoxins and their conjugates in cereals,” *International Journal of Food Microbiology*, 2007. vol. 119, no. 1-2, pp. 33-37.

[34] Fallah, A. A. Aflatoxin M1 contamination in dairy products marketed in Iran during winter and summer. Food Control. 2010. 21:1478-1481.

[35] Hussain, I. Anwar, J. A study on contamination of aflatoxin M1 in raw milk in the Punjab province of Pakistan. Food Control. 2008. 19:393-395.

[36] El-baradei G, Delacroix-buchet A, Ogier JC Bacterial biodiversity of traditional Zabady fermented milk. Int J Food Microbiol. 2008. 121:295-301.

[37] D’Mello, J. P. F. and A. M. C. Macdonald. *Mycotoxins*. Animal Feed Science and Technology. 1997. 69:155-166.

[38] Asghar Sepahvand, Masoomeh Shams-Gahfarokhi, Abdolamir Allameh, Zahra Jahanshiri, Mojdeh Jamali & Mehdi Razzaghi-Abyaneh A survey on distribution and toxigenicity of *Aspergillus flavus* from indoor and outdoor hospital environments. Folia Microbiologica. 2011. 56, 527-534.

[39] Rodríguez-Cervantes, C.H. A.J. Ramos, A.J. Robledo-Marenco, M.L Sanchis,V. Marín, S & M.I. Girón-Pérez. Determination of aflatoxin and fumonisin levels through ELISA and HPLC, on tilapia feed in Nayarit, Mexico. Food and Agricultural Immunology. 2013. 24:3. DOI:10.1080/09540105.2012.684202.

[40] Alinezhad, S., M. Tolouee, A. Kamalzadeh, A. A. Motalebi, M. Nazeri, M. Yasemi, M. Shams-Gahfarokhi, R. Tolouei, and M. Razzaghi-Abyaneh. Mycobiotia and aflatoxin B1 contamination of rainbow trout (*Oncorhynchus mykiss*) feed with emphasis to *Aspergillus section Flavi*. Iranian Journal of Fisheries. 2011. 10:363-374.

[41] Ashley, L.M. and Halver, J.E. Multiple metastasis of rainbow trout hepatoma. Transactions of the American Fisheries Society. 1963. 92:365-371.

[42] Ashley, L. M. Pathology of fish fed aflatoxins and other antimetabolites. A Symposium on Diseases of Fishes and Shellfishes.1970. American Fisheries Society Special Publication No. 5, 366-379.

[43] Farabi, S. M. V. M. Yousefian, M. and Hajimoradloo. A. Aflatoxicosis in juvenile *Huso huso* fed a contaminated diet. Journal of Applied Ichthyology. 2006. 22:234-237.

[44] Coppock, R. W., R. R. G. Christian, and B. J. Jacobsen. Aflatoxins. Pages 1181-1199 in R. Gupta, editor. Veterinary Toxicology: Basic & Clinical Principles, 2nd edition. Elsevier, Inc.2012. San Diego, California, USA.

[45] Bailey, G. S. D. Williams, E. Wilcox, E. Loveland, Coulombe, P.M and Hendricks, J.D. Aflatoxin B1 carcinogenesis and its relation to DNA adduct formation and adduct persistence in sensitive and resistant salmonid fish. Carcinogenesis. 1988. 9:1919-1926.

[46] Chávez-Sánchez, M. C. C. A. Martinez-Palacios, C. A. and Osorio-Moreno, I. Pathological effects of feeding young *Oreochromis niloticus* diets supplemented with different levels of aflatoxin B1. Aquaculture. 1994. 127:49-60.

[47] Hendricks, J. D. Carcinogenicity of aflatoxins in non-mammalian organisms. Pages 103-136 in D. L. Eaton
and J. D. Groopman, editors. The toxicology of aflatoxins: human health, veterinary, and agricultural significance. 1994. Academic Press, New York, New York, USA.

[48] Bauer, D. H. Lee, DJ and Sinnhuber, R. O. Acute toxicity of aflatoxins B1 and G1 in the rainbow trout (*Salmo gairdneri*). Toxicology and Applied Pharmacology. 1969. 15:415-419.

[49] Sahoo, P. K. Mukherjee, S. C. Nayak, S. K. and Dey, S. Acute and sub chronic toxicity of aflatoxin B1 to rohu, *Labeo rohita* (Hamilton). Indian Journal of Experimental Biology. 2001. 39:453-458.

[50] Hamilton, P. Problems with mycotoxins persist, but can be lived with. Feedstuffs. 1990. 62:22-23.

[51] Santacroce, M. P. M. C. Conversano, E. Casalino, O. Lai, C. Zizzadoro, G. Centoducati, and G. Crescenzo. Aflatoxins in aquatic species: metabolism, toxicity and perspectives. Reviews in Fish Biology and Fisheries. 2008. 18:99-130.

[52] Sahoo, P. K. Mukherjee, S. C. Nayak, S. K. and Dey, S. Acute and sub chronic toxicity of aflatoxin B1 to rohu, *Labeo rohita* (Hamilton). Indian Journal of Experimental Biology. 2001. 39:453-458.

[53] Sahoo, P. K. S. C. Mukherjee, S. C. Nayak, S. K. and S. Dey. Acute and sub chronic toxicity of aflatoxin B1 to rohu, *Labeo rohita* (Hamilton). Indian Journal of Experimental Biology. 2001. 39:453-458.

[54] Pier, A. C. Richard, J. L. and Cysewski, S. J. Implications of mycotoxins in animal disease. Journal of the American Veterinary Medical Association. 1980. 176:719-724.

[55] Pier, A. C. Richard, J. L. and Cysewski, S. J. Implications of mycotoxins in animal disease. Journal of the American Veterinary Medical Association. 1980. 176:719-724.

[56] El-Sayed, Y. S. and Khalil, R. H. Toxicity, biochemical effects and residue of aflatoxin B1 in marine water reared sea bass (*Dicentrarchus labrax* L.). Food and Chemical Toxicology. 2009. 47:1606-1609.

[57] Wang, X. Y. Xue, H. Zhang, P. Encarnação, G. A. Santos, and R. A. Gonçalves. Response of yellow catfish (*Pelteobagrus fulvidraco*) to different dietary concentrations of aflatoxin B1 and evaluation of an aflatoxin binder in offsetting its negative effects. Ciencias Marinas. 2016. 42: 15-29.

[58] Manning, B. B. Wise, D. J. Abbas, H. K. and Peterson, B. C. Channel catfish, *Ictalurus punctatus*, fed diet containing aflatoxin from moldy corn do not experience increased mortality after challenge with *Edwardsiella ictaluri*. Journal of the World Aquaculture Society. 2011. 42:598-602.

[59] Manning, B. B. Wise, D. J. Abbas, H. K. and Peterson, B. C. Channel catfish, *Ictalurus punctatus*, fed diet containing aflatoxin from moldy corn do not experience increased mortality after challenge with *Edwardsiella ictaluri*. Journal of the World Aquaculture Society. 2011. 42:598-602.

[60] Tuan, N. A. Grizzle, J. M. Lovell, R. T. Manning, B. B and Rottinghaus, G. E. Growth and hepatic lesions of Nile tilapia (*Oreochromis niloticus*) fed diets containing aflatoxin B1. Aquaculture. 2002. 212:311-319.

[61] Deng, S. X. Tian, L. X. F. J. Liu, S. J. Jin, G. Y. Liang, H. J. Yang, Z. Y. Du, and Liu, Y. J. Toxic effects and residue of aflatoxin B1 in tilapia (*Oreochromis niloticus × O. aureus*) during long-term dietary exposure. Aquaculture. 2010. 307:233-240.
[62] Ashley, L.M. and Halver, J.E. Multiple metastasis of rainbow trout hepatoma. Transactions of the American Fisheries Society. 1963. 92:365-371.

[63] Bailey, G. S. Williams, D. E. Wilcox, J. Loveland, P.M. Coulombe, R.A and Hendricks, J.D. Aflatoxin B1 carcinogenesis and its relation to DNA adduct formation and adduct persistence in sensitive and resistant salmonid fish. Carcinogenesis. 1988. 9:1919-1926.

[64] Pietsch, C. Kersten, S. Burkhardt-Holm, P. Valenta, H and Dänicke, S. Occurrence of deoxynivalenol and zearalenone in commercial fish feed: an initial study. Toxins. 2013. 5:184-192.

[65] Shams, M. Mitterbauer, R. Corradini, R. Wiesenberger, G. Dall’Asta, C. Schuhmacher, R. Berthiller, F. Isolation and characterization of a new less-toxic derivative of the fusarium mycotoxin diacetoxyscirpenol after thermal treatment. Journal of Agricultural and Food Chemistry. 2011. 59(17), 9709-9714.

[66] Forgacs, J. Mycotoxicoses—the neglected diseases. Feedstuffs. 1962. 34: 124-134.

[67] Persi, N. J. Pleadin, D. Kovacevi’ Scortichini, G and S. Milone. Ochratoxin A in raw materials and cooked meat products made from OTA-treated pigs. Meat Science. 2014. 96:203-210.

[68] Ladeira, C. Frazzoli, C. and Orisakwe, O. E. Engaging one health for non-communicable diseases in Africa: perspective for mycotoxins. Front. Public Health. 2017. 5:266. DOI: 10.3389/fpubh.2017.00266.

[69] Schatzmayr, G. and Streit, E. Global occurrence of mycotoxins in the food and feed chain: facts and figures. World Mycotoxin Journal. 2013. 6:213-222.

[70] Doster, R. C. Toxicity and metabolism of ochratoxins in rainbow trout (Salmo gairdneri). PhD dissertation. Oregon State University, Corvallis, Oregon. 1973. USA.

[71] Fuchs, R. and Hult, K. Ochratoxin A in blood and its pharmacokinetic properties. Food and Chemical Toxicology. 1992. 30:201-204.

[72] Hagelberg, S. K. Hult, K and Fuchs, R. Toxicokinetics of ochratoxin A in several species and its Plasma-binding properties. Journal of Applied Toxicology. 1989. 9:91-96.

[73] Doster, R. C. Toxicity and metabolism of ochratoxins in rainbow trout (Salmo gairdneri). PhD dissertation. Oregon State University, Corvallis, Oregon. 1973. USA.

[74] Fuchs, R. and Hult, K. Ochratoxin A in blood and its pharmacokinetic properties. Food and Chemical Toxicology. 1992. 30:201-204.

[75] El-Sayed, Y. S. Khalil, R.H and Saad, TT Acute toxicity of ochratoxin-A in marine water-reared sea bass (Dicentrarchus labrax L.). Chemosphere. 2009. 75:878-882.

[76] Amany M. Diaba, Salem, R.M. El-Keredy M.S. Abeerc Gehan I.E. Alic Nagwan El-Habashi. Experimental ochratoxicosis A in Nile tilapia and its amelioration by some feed additives. International Journal of Veterinary Science and Medicine. 2018. 149-158. DOI:org/10.1016/j.ijvsm.2018.09.004.

[77] Bernhoft, A. Høgåsen, H.R. Rosenlund, M. Moldal, T. Grove, S. Berntsсен, M.H.G. Thoresen, S.I. Alexander, J. Effects of dietary deoxynivalenol or ochratoxin A on performance and selected health indices in Atlantic salmon (Salmo salar). Food Chem. Toxicol. 2018, 121, 374-386.

[78] Ismaiel, A. A. Ghaly, M.F. El-Naggar, A.K. Milk kefir: Ultrastructure,
Aflatoxins

antimicrobial activity, and efficacy on aflatoxin B1 production by Aspergillus flavus. Curr. Microbiol. 2011. 62, 1602-1609.

[79] Crisan, E.V. Effects of aflatoxin on seedling growth and ultrastructure in plants. Appl. Microbiol. 1973, 12, 991-1000.

[80] Placinta, C.M. Mello, J. P. F. D and Macdonald, A. M. C. A review of worldwide contamination of cereal grains and animal feed with Fusarium mycotoxins. Animal Feed Science and Technology.1999 78:21-37.

[81] Arukwe, A. T. Grotmol, T. Haugen, T.B. Knudsen, F.R and Goksøyr. A. Fish model for assessing the in vivo estrogenic potency of the mycotoxin zearalenone and its metabolites. Science of the Total Environment. 1999. 236:153-161.

[82] Meronuck, R. and Xie. W. 1999. Mycotoxins in feed. Feedstuffs 71:123-130.

[83] Pestka, J. J. Zhou, H.R. Moon, Y and Chung, Y.J. Cellular and molecular mechanisms for immune modulation by deoxynivalenol and other trichothecenes: unraveling a paradox. Toxicology Letters. 2004. 153:61-73.

[84] Ueno, Y. Trichothecene mycotoxins: mycology, chemistry, and toxicology. Advances in Nutritional Research.1989. 3:301-353.

[85] Escrivá, L., G. Font, and L. Manyes. In vivo toxicity studies of fusarium mycotoxins in the last decade: a review. Food and Chemical Toxicology. 2015. 78:185-206.

[86] Escrivá, L., G. Font, and L. Manyes. In vivo toxicity studies of fusarium mycotoxins in the last decade: a review. Food and Chemical Toxicology. 2015. 78:185-206.

[87] Meronuck, R. and W. Xie. Mycotoxins in feed. Feedstuffs. 1999 71:123-130.

[88] Wu, F. and G. P. Munkvold. Mycotoxin in ethanol co-products: modelling economic impacts on the livestock industry and management strategies. Journal of Agricultural and Food Chemistry. 2008. 56:3900-3911.

[89] Winnie-Pui-Pui Liew and Sabran Mohd-Redzwan. Mycotoxin: It’s Impact on Gut Health and Microbiota. Frontiers in Cellular and Infection Biology. 2018. DOI:.org/10.3389/ fciimb.2018.00060.

[90] Yuan, G. Y. Wang, X. Yuan, T. Zhang, Zhao, J. Huang, L and S. Peng. T-2 toxin induces developmental toxicity and apoptosis in zebrafish embryos. Journal of Environmental Sciences. 2014. 26:917-925.

[91] Poston, H. A. Coffin, J.L and Combs,G.F. Biological effects of dietary T-2 toxin on rainbow trout, Salmo gairdneri. Aquatic Toxicology. 1982. 2:79-88.

[92] Manning, B. B., M. H. Li, and E. H. Robinson. Aflatoxin from moldy corn cause no reductions in channel catfish Ictalurus punctatus performance. Journal of the World Aquaculture Society. 2005. 36:59-67.

[93] Helena Modra, Miroslava Palikova, Pavel Hyrsl, Jana Bartonkova, Ivana papezikova, Zdenka Svobodova, Jana Blahova & Jan Mares. Effects of trichothecene mycotoxin T-2 toxin on haematological and immunological parameters of rainbow trout (Oncorhynchus mykiss). Mycotoxin Research. 2020. 36, 319-326.

[94] Marin, S. Ramos, A.J. Cano-Sancho, G and Sanchis, V. Mycotoxins: occurrence, toxicology, and exposure assessment. Food and Chemical Toxicology. 2013. 60:218-237.
[95] Mariana Oliveira and Vitor Vasconcelos. Occurrence of Mycotoxins in Fish Feed and Its Effects: A Review. Toxins. 2020. 12, 160: DOI: 10.3390/toxins12030160.

[96] Mariana Oliveira and Vitor Vasconcelos. Occurrence of Mycotoxins in Fish Feed and Its Effects: A Review. Toxins. 2020. 12, 160: DOI: 10.3390/toxins12030160.

[97] Hussein, H. S. and Brasel, J. M. Toxicity, metabolism, and impact of mycotoxins on humans and animals. Toxicology. 2001 167:101-134.

[98] Mariana Oliveira and Vitor Vasconcelos. Occurrence of Mycotoxins in Fish Feed and Its Effects: A Review. Toxins. 2020. 12, 160: DOI: 10.3390/toxins12030160.

[99] Hooft, J. Elmor, A. E. H. I. Encarnação, P and Bureau, D. P. Rainbow trout (Oncorhynchus mykiss) is extremely sensitive to the feed-borne Fusarium mycotoxin deoxynivalenol (DON). Aquaculture. 2011. 311:224-232.

[100] Matejova, I. H. Modra, H. Blahova, J. Franc, A. Fictum, P. Sevcikova, M and Svobodova, Z. The effect of mycotoxin deoxynivalenol on haematological and biochemical indicators and histopathological changes in rainbow trout (Oncorhynchus mykiss). BioMed Research International 2014:5. DOI: 10.1155/2014/310680.

[101] Matejova, I. H. Modra, H. Blahova, J. Franc, A. Fictum, P. Sevcikova, M and Svobodova, Z. The effect of mycotoxin deoxynivalenol on haematological and biochemical indicators and histopathological changes in rainbow trout (Oncorhynchus mykiss). BioMed Research International 2014:5. DOI: 10.1155/2014/310680.

[102] Scott, P. M. Recent research on fumonisins: a review. Food Additives and Contaminants: Part A, Chemistry, Analysis, Control, Exposure and Risk Assessment. 2012. 29:242-248.

[103] Ahangarkani, F. S. Rouhi, and Azizi, I. G. A review on incidence and toxicity of fumonisins. Toxin Reviews. 2014. 33:95-100.

[104] Riley, R. T. and K. A. Voss. Differential sensitivity of rat kidney and liver to fumonisin toxicity: organ-specific differences in toxin accumulation and sphingoid base metabolism. Toxicological Sciences. 2006. 92:335-345.

[105] Voss, K. A. Smith, G. W and Haschek, W. M. Fumonisins: toxicokinetics, mechanism of action and toxicity. Animal Feed Science and Technology. 2007. 137:299-325.

[106] Voss, K. A. Smith, G. W and Haschek, W. M. Fumonisins: toxicokinetics, mechanism of action and toxicity. Animal Feed Science and Technology. 2007. 137:299-325.

[107] Robert W Coppock, Barry J Jacobsen. Mycotoxins in animal and human patients. Toxicology and Industrial Health. 2009. DOI: 10.1177/0748233709348263.

[108] Peter Spring and Christine Burel. Effect of mycotoxins in aqua culture. Mycotoxins in farm animals. Transworld Research Network, Kerala, India. 2008. pp.71-90.

[109] Peter Spring and Christine Burel. Effect of mycotoxins in aqua culture. Mycotoxins in farm animals. Transworld Research Network, Kerala, India. 2008. pp.71-90.

[110] Tuan, N. A. Grizzle, J. M. Lovell, R. T. Manning, B. B and Rottinghaus, G. E. Growth and hepatic lesions of Nile tilapia (Oreochromis niloticus) fed diets containing aflatoxin B1. Aquaculture. 2002. 212:311-319.
Aflatoxins

[111] David, B. Carlson David, E. Williams Jan, M. Spitsbergen, P. Frank Ross Charles, W. Bacon Filmore, I. Meredith Ronald, T. Riley. Fumonisin B1 Promotes Aflatoxin B1 and N-Methyl-N′-nitro-nitrosoguanidine-Initiated Liver Tumors in Rainbow Trout. ScienceDirect. 2001. Volume 172, Issue 1, pp 29-36. DOI:10.1006/taap.2001.9129.

[112] Woźny, M. P. Brzuzan, M. Gusiatin, E. Jakimiuk, S. Dobosz, and Kuźmiński, H. Influence of zearalenone on selected biochemical parameters in juvenile rainbow trout. Polish Journal of Veterinary Sciences. 2012. 15:221-225.

[113] Pietsch, C. S. Kersten, P. Burkhardt-Holm, H. Valenta, and Dänicke, S. Occurrence of deoxynivalenol and zearalenone in commercial fish feed: an initial study. Toxins. 2015. 7:4595-4609.

[114] Greco, M. A. Pardo, and Pose, G. Mycotoxigenic fungi and natural co-occurrence of mycotoxins in rainbow trout (Oncorhynchus mykiss) feeds. Toxins. 2015. 7:4595-4609.

[115] Guo-Liang Zhang, Yu-Long Feng, Jun-Lin Song and Xiang-Shan Zhou, Zearalenone: A Mycotoxin with Different Toxic Effect in Domestic and Laboratory Animals’ Granulosa Cells. Frontiers in Genetics. 2018. Front. Genet. 18: DOI:org/10.3389/fgene.2018.00667.

[116] Constanze Pietsch. Risk assessment for mycotoxin contamination in fish feeds in Europe. Springer. 2019. DOI:10.1007/s12550-019-00368-6.

[117] Greco, M. A. Pardo, and Pose, G. Mycotoxigenic fungi and natural co-occurrence of mycotoxins in rainbow trout (Oncorhynchus mykiss) feeds. Toxins. 2015. 7:4595-4609.

[118] Manning, B. B. Wise, D.J. Abbas, H.K and Peterson, B.C. Channel catfish, Ictalurus punctatus, fed diet containing aflatoxin from moldy corn do not experience increased mortality after challenge with Edwardsiella ictaluri. Journal of the World Aquaculture Society. 2011. 42:598-602.

[119] The factsheet by the Southern Regional Aquaculture Center (SRAC) gives information on managing high pH in freshwater ponds. 2013.

[120] Thiel, P. G. A molecular mechanism for the toxic action of moniliformin, a mycotoxin produced by Fusarium moniliforme. Biochemical Pharmacology. 1978. 27:483-486.

[121] Yildirim, M. B. B. Manning, B.B. Lovell, R.T. Grizzle, J.M and Rottinghaus, G.E Toxicity of moniliformin and fumonisin B1 fed singly and in combination in diets for young channel catfish Ictalurus punctatus. Journal of the World Aquaculture Society. 2000. 31:599-608.

[122] Thiel, P. G. A molecular mechanism for the toxic action of moniliformin, a mycotoxin produced by Fusarium moniliforme. Biochemical Pharmacology. 1978. 27:483-486.

[123] Rui A. Gonçalves, Marco Tarasco, Dian Schatzmayr and Paulo Gavaia. Preliminary Evaluation of Moniliformin as a Potential Threat for Teleosts. Fishes. 2018. DOI:10.3390/fishes3010004.

[124] Emerging Mycotoxins: Overview and Occurrence. Biomin, 2016.

[125] Constanze Pietsch. Risk assessment for mycotoxin contamination in fish feeds in Europe. Springer Link. 2019. 36, pages41-62.

[126] Nazia Hoque, Choudhury Mahmood Hasan, Md. Sohel Rana, Amrit Varsha, Mohamed Hossain Sohrab, and Khondaker Miraz Rahman. Fusaproliferin, a Fungal Mycotoxin, Shows Cytotoxicity against Pancreatic Cancer Cell Lines. 2018. 23(12): pp. 3288.