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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 fresh water 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 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. Goswami et al. [2], Murphy et al. [3] and Marin et al. [4] reported toxigenic fungi can grow on a wide variety of crops, including wheat, maize, and soy bean. Grenier and Oswald [5] and Pal et al. [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].

Bennett and Klich [8] and Bryden [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]. Gunnarsson and Petersen [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. Matai and Bagchi [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. Tacon [19], Santacroce et al. [20] and Anater et al. [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. Gareis and Wolff [22] and Iqbal et al. [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. Persi et al. [24] and Nomura et al. [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. Abdel-Wahaab et al. [27] observed, residues of sterigmatocystin (a mycotoxins 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 verteberates 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 B_1 (AFB_1) in the aquaculture feedstuffs, and epizootic of hepatomas in rainbow trout by a number of researchers under the direction of scientists J. Halver, R. 0. 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. Fallah [34] and Hussain and Anwar [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].

Rodríguez-Cervantes et al. [39] and Alinezhad et al. [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. Ashley and Halver [41] reported first, aflatoxicosis outbreak in rainbow trout hatcheries in the USA, was related to hepatoma, where trout was fed with AF-contaminated feed. Ashley [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 metabolization by cytochrome P450. Farabi et al. [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. Coppock et al. [44] observed, some fish species are extremely sensitive to AFB1 mainly because of differences in the patterns of enzymes involved in AFB1 metabolism. Bailey et al. [45] reported the carcinogenic effect of AFB1 in channel catfish, *Ictalurus punctatus*; Nile tilapia, *Oreochromis niloticus* and the ornamental guppy, *Poecilia reticulata.* Chàvez-Sànchez et al. [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. Hendricks [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.

Bauer et al. [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]. Sahoo et al. [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. Sahoo et al. [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. Pier et al. [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. Pier et al. [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. El-Sayed et al. [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, *Pelteobagrus fulvidraco*, after a 12-week trial with the presence of AFB1 in the diet at a level of 0.2 mg/kg. Manning et al. [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. Tuan et al. [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. Deng et al. [61] monitored the toxigenic effects of AFB1 in blue tilapia *Oreochromis aureus* over 20 week 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]. Persi et al. [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. Doster [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.

Fuchs and Hult [71] and Hagelberg et al. [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. El-Sayed et al. [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. Diab et al. [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.

Bernhoft et al. [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 proprieties. Due to this great diversity, different detoxification strategies are required to deal with this complex group of compounds, Ismaiel et al. [78] and Crisan [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 Fu*sarium,* 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 diacetoxyscirpenol 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 pondering 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. Manning et al. [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 anomalies 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 occurrentation 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, 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 B_1 (FB$_1$), FB$_2$ and FB$_3$, with FB$_1$ 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 verteberates 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]. Voss et al. [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 B_1 (FB$_1$) have been shown to reduce the productivity of fish. Nile tilapia fingerlings were fed FB$_1$ at 0, 10, 40, 70 and 150 ppm for 8 weeks. The FB$_1$ was extracted from cultures of *Fusarium moniliforme.* Mortalities in all treatment groups were low and were not

dose related. Feeding diets containing 150 ppm FB_1 shows decreased hematocrit. There was evidence that sphingolipid metabolism was disrupted in fish fed FB_1. Observed decreased weight gains among fishes fed with FB_1 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]. Spring and Burel [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 similar age, signs of toxicity were observed at dietary levels as low as 10 ppm FB1. Tuan et al. [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. David et al. [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. Wo'zny et al. [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 Zhang et al. [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. Greco and Pose [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 effect of ZEA toxin on fish has not been evaluated, but it interferes the reproduction in many animals. Manning et al. [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]. Yildirim et al. [121] and Thiel [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. Gonçalves et al. [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. Starostina [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 proprieties. 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 <1 μg/ 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, skeletomyocytes 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 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[1]* and Deecaraman Munusamy[2]

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

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