Mycotoxin Patterns in Fish Feedstuffs

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Definition

he first part of this study evaluates the occurrence of mycotoxin patterns in feedstuffs and fish feeds. Results were extrapolated from a large data pool derived from wheat (n = 857), corn (n = 725), soybean meal (n = 139) and fish feed (n = 44) samples in European countries and based on sample analyses by liquid chromatography/tandem mass spectrometry (LC-MS/MS) in the period between 2012–2019. Deoxynivalenol (DON) was readily present in corn (in 47% of the samples) > wheat (41%) > soybean meal (11%), and in aquafeeds (48%). Co-occurrence of mycotoxins was frequently observed in feedstuffs and aquafeed samples.

1. Introduction

Aquaculture, in contrast to capture fisheries that have remained stable over the last decades, continues to grow and contribute to the increasing food supply for human consumption, reaching worldwide production of 80 million metric tonnes (Mt) in 2016 [1]. To sustain its growth, the aquaculture industry is highly dependent on commercial feed sources [2][3][4]. Indeed, the production of aquafeeds increased from 8 Mt in 1995 to 48 Mt in 2015 [1]. A recent global feed survey revealed that the annual growth of aquafeed production for 2018 was 4% [5], and was projected to reach 65 Mt in 2020 [6]. However, the inclusion rate of traditionally used finite and expensive marine protein and fat sources from wild-caught fish (i.e., fishmeal and fish oil) in the diets of farmed fish species will continue to decline and the industry has already shifted to crop-based ingredients to meet the rising demand for aquafeeds [2][6][7]. For instance, collective data from the Norwegian salmon (Salmo salar) industry reflect the change in modern aquaculture diet composition and confirm the reduced dependency on fishmeal derived from wild-caught fish; while in 1990 salmon diets consisted of 90% marine ingredients, already in 2013 their inclusion rate was less than 30%, which increased the share of plant protein sources to 37% [8]. Plant-based ingredients increasingly replace marine-based ingredients and, therefore, an enhanced level of understanding of the nutritional quality of raw materials derived from plant sources is becoming increasingly important for aquafeeds.

Plant-based feed ingredients currently used in aquafeeds as substitutes for marine ingredients include soybean meal, rapeseed/canola meal, maize/corn, wheat bran and wheat [3]. Even in diets for carnivorous species like Atlantic salmon, the main protein and lipid sources used within the feed in 2012 were derived from crops, such as soybean meal (21.3% average inclusion rate) and rapeseed oil (18.3% average inclusion rate), with the main starch source being wheat (9.9% average inclusion rate) [8]. However, in contrast to marine ingredients that contain well-balanced protein contents to meet the amino acid requirements of aquatic farmed animals, the continuing transition towards higher inclusion of plant-based ingredients poses a real challenge for aquafeed producers due to nutritional limitations [9][10]. The higher inclusion of less-expensive plant sources may introduce a series of anti-nutritional factors (e.g., protease inhibitors, phytates, saponins, glucosinolates, tannins, non-starch polysaccharides) and/or increase the occurrence of animal feed contaminants; factors that might affect the quality and safety of aquafeeds [11][12][13][14][15]. Frequently occurring natural feed contaminants are mycotoxins, which are mainly detected in plant-based feedstuffs [16][17][18][19][20]. Increasingly [21][22][23][24][25], the presence of mycotoxins is reported in aquafeeds.

2. Mycotoxin-Producing Fungi

Mycotoxins are secondary metabolites produced by fungi that invade crops in the field during plant growth and/or fungi that colonize the crops before harvest and predispose the commodity to mycotoxins after harvest during drying, transportation and storage [19][26]. Common toxigenic genera are Aspergillus, Penicillium, Fusarium, Alternaria and Claviceps which proliferate with climatic conditions considered favourable (close to their preferred temperature and moisture) [27][28][29]. The global distribution of mycotoxigenic fungi is temperature-dependent; Penicillium spp. are common in cool climates, Aspergillus spp. in the tropics and Fusarium spp. in temperate areas [30]. Fungal growth requirements for minimal and optimal water activity (a_w) differ among genera. Fusarium and Alternaria are plant pathogens and hygrophilic (1.00 a_w), meaning they proliferate in substrates with high water availability and, therefore, predominate in the fields at pre-harvest. Aspergillus and Penicillium are xerophilic (<0.95 a_w), meaning they can proliferate at low water availability and are the main mycotoxigenic fungi post-harvest, during storage [31]. Post-harvest measures such as proper storage conditions can possibly prohibit the growth of xerophilic fungi [32] but pre-harvest conditions such as a continuously changing climate [33] cannot be controlled, for which reason the presence and growth of hygrophilic fungi from the fields remains unpredictable.

The occurrence of mycotoxigenic fungi, however, does not necessarily lead to the production of mycotoxins. For instance, Aspergillus spp. were detected in aquafeed samples but not the corresponding mycotoxins [34]. Such observations reinforce questions of “How, why and when do fungi produce mycotoxins?” These respective questions largely remain unanswered since most research is focused on the toxicological aspects of mycotoxins and their effects on host organisms [35]. Mycotoxin production may be triggered after environmental abiotic stimuli (light, nutrient, pH) and biotic interactions of different microbes (i.e., fungal–bacterial or fungal–fungal) that lead to up-regulation of biosynthetic gene clusters to secure the ecological niche of fungi in hostile environments by exhibiting antimicrobial functions [36]. Indeed, incubation of commercial fish feeds under different storage conditions can influence fungal growth and mycotoxin production. Specifically, the application of warm (temperature ~ 27 °C) and humid (~70% relative humidity) conditions may trigger the release of ochratoxin A (OTA), with variations due to distinct hotspots with optimal conditions for fungal growth and production of mycotoxins [37]. Therefore, the presence of mycotoxigenic fungi under storage conditions does not necessarily mean the presence of mycotoxins in aquafeeds.

3. Classification of Fusarium Mycotoxins: “Traditional”, “Emerging” and “Masked”

Fusarium species as soil-borne microbes are the most common pathogens in cereal crops flourishing in a wide geographic range, also in Europe [38][39]. The toxicologically most important Fusarium mycotoxins are trichothecenes, zearalenone (ZEN) and fumonisins (FUM) [40]. ZEN occurs more commonly than its metabolites. FUM group is represented by fumonisin B_1 (FB_1), B_2 (FB_2), and B_3 (FB_3), FB_1 being the most abundant member [28]. Trichothecenes can be divided into four types (A, B, C, D); the concerns regarding type A and type B trichothecenes are higher due to their higher toxicity and occurrence in crops [41][42]. Known mycotoxins that belong to type A trichothecenes are T-2/HT-2 toxin, diacetoxyscirpenol (DAS) and neosolaniol (NEO). Among the type A trichothecenes, T-2 toxin is the most toxic mycotoxin regardless of the exposed animal species, is soluble in non-polar solvents (e.g., ethyl acetate and diethyl ether) and is rapidly metabolised to HT-2 toxin [43][44][45]. Known mycotoxins that belong to type B trichothecenes are DON, nivalenol (NIV), fusarenon X (FX) and fusaric acid (FA). Among the type B trichothecenes, worldwide [41][46] DON is the most commonly found mycotoxin in cereal grains.

Besides the “traditional” Fusarium mycotoxins described above, Fusarium species produce other metabolites called “emerging” mycotoxins such as fusaproliferin (FUS), beauvericin (BEA), enniatins (ENNs), and moniliformin (MON) [47]. Furthermore, Fusarium mycotoxins can occur as plant-derived derivatives which are often not detectable during routine mycotoxin analyses and, therefore, called “masked” mycotoxins, after having been biologically modified by plant defense mechanisms after crop infection [20][46]. The most commonly-detected masked mycotoxin conjugates are β-linked glucose-conjugates of trichothecenes: DON-3-glucoside (DON3Glc), nivalenol-3-glucoside (NIV3Glc), HT-2 glucoside (HT2Glc), and ZEN-14-glucoside (ZEN14Glc) [48]. Masked mycotoxins are derived from conjugation reactions following a glucosidation reaction, but can also involve glucuronidation or sulfatation (Phase II of plant metabolism), and are usually less harmful than the parent mycotoxins [46][49].

However, masked forms might be “reactivated” during animal digestion by the action of gut microbiota, which may cleave the polar group and consequently liberate the parent toxin [46]. The concept of toxin reactivation has been confirmed for DON3Glc and NIV3Glc in rats [50][51] and for DON3Glc and ZEN14Glc in pigs [52][53]. To avoid confusion [54], one should not only distinguish free mycotoxins from masked mycotoxins, but also from matrix-associated and other modified mycotoxins. To further emphasize the distinction, acetylated derivatives of DON such as 15-acetyl DON (15AcDON) and 3-acetyl DON (3AcDON) are fungal metabolites (free mycotoxins). These toxins are commonly detected along with DON in feedstuffs and animal feeds [16]. In other words, mycotoxins can be present in many forms.

In Europe, AFB_1 is the only mycotoxin regulated by the Directive 2002/32/EC of the European Parliament and of the Council of 7 May 2002 on undesirable substances; for fish species the maximum allowed concentration in feed materials is 20 µg/kg (ppb), and for complete feed is 10 ppb [55]. For other mycotoxins, including important Fusarium mycotoxins such as DON, ZEN, T-2 and HT-2 toxin, FB_1 and FB_2, the EC has established only recommended limits for their presence in feedstuffs and feed (Table S1) [56][57][58]. Among these recommended limits only those for FB_1 and FB_2 refer directly to fish species. In addition, European Commission (EC) regulations/recommendations are based on the occurrence of a single mycotoxin, although feeds are usually contaminated by numerous mycotoxins simultaneously that might, in some instances, result in synergistic effects [59].

4. Discussion

We aimed to unravel the profile of mycotoxins present in feed ingredients and thus in fish feeds in Europe, despite the lack of consistent, randomly collected field data. Our study included data from samples submitted by industry, and thus we make the assumption that we cannot fully exclude bias associated with suspicious materials also submitted for analysis. Nonetheless, the current study generated a large set of data and showed patterns related to mycotoxin contamination that are highly relevant to the animal and fish feed industry. We found DON occurrence in 44 European fish feed samples with an average contamination of 136 µg/kg and maximum contamination of 469 µg/kg. So far, comparable data on DON contamination have been derived from much smaller data sets analyzing 11 samples of commercial carp feed (average contamination 289 µg/kg, maximum 825 µg/kg) [21], or 10 samples of commercial fish and shrimp feeds (166 µg/kg and 282 µg/kg) [60]. The much larger number of samples in our data set logically produced more reliable outcomes. Is DON occurrence in feed always detrimental for the fish? Not necessarily. Potentially, high temperatures (>150 °C) during the extrusion process might significantly reduce FUM and ZEA and moderately reduce AFLAs, but extrusion may only slightly reduce contamination with DON in finished feeds [61][62]. For instance, extrusion temperatures above 150 °C only led to a slight reduction of ~20% in DON levels in wheat grits [63]. Overall, complete elimination of mycotoxin is not feasible during feed extrusion and, therefore, prevention of mycotoxin contaminated feeds is of utmost importance for feed manufacturers.

The current survey revealed a risk of association of DON with other Fusarium toxins, including emerging and masked mycotoxins. An earlier study based on literature data [59] reported common combinations of different mycotoxins in European cereal samples and addressed their combined risks on different animals, but not fish. Only one study investigated the combined effects of DON with AFB_1 on the fish cell line BF-2, and combined effects of DON with ZEN on zebrafish larvae [64]. The results implied the existence of effects synergetic between DON + AFB_1 but antagonistic between DON + ZEN. Future research is needed to investigate similar effects and more diverse combinations of mycotoxins in in vivo feeding experiments. Furthermore, emerging and masked mycotoxins generally are not detectable in routine controls in feed mills, and no regulatory/recommendation limits exist [46]. Thus, feed producers might consider subjecting their raw materials to periodical state-of-the-art mycotoxin analyses performed by external, certified labs to screen the full spectrum of mycotoxins present. Even then, commercial fish feeds when stored under warm (25 °C) and humid conditions (>60% relative humidity) for a month, can release OTA [37]. Thus, to prevent fungal growth and potential mycotoxin contamination after feed production, aquafeed producers and fish farmers have to ensure proper storage conditions.

To the best of our knowledge, this is the first comprehensive study that has attempted to summarize the effects of DON in different fish species using a systematic review approach. Based on our review, we see no evidence for bioaccumulation of DON in fish tissues [65][66][67] and see no reason to raise concerns with respect to consumer health. However, consumption of DON-contaminated feeds by fish, even at levels below the EC recommendation limit (5000 μg/kg), can result in adverse although non-lethal effects on fish such as impaired feed intake, growth performance, immunity, detoxification capacity, and tissue damage and oxidative stress. By collecting all reported adverse effects of DON, our review extended a previous risk assessment [68] and allowed for a new and updated estimation of critical DON levels for rainbow trout, defined as at risk of affecting 5% of a fish population (CC5). This renewed information could have a direct and practical implication for aquafeed producers when designing their mycotoxin management plans.

Undoubtedly the number of studies investigating single effects of DON on farmed fish species has been increasing, but the data have not been collectively used to assess feed intake and growth performance responses. Our meta-analysis provided new insights into aquaculture nutrition that suggest an exponential relation exists between decreases in feed intake and growth response, and increasing levels of DON (mg/kg) in aquafeeds. These adverse effects of DON appear more severe when natural DON is used for feed formulation instead of pure forms of this toxin, as in experimental studies. Other meta-analyses for pigs and poultry similarly showed negative effects on feed intake and growth performance of mycotoxins, including DON [69][70][71]. In summary, our study predicts that the current average contamination of 136 μg DON per kg fish feed leads to 3.5% reduction in feed intake and 3.7% reduction in growth of trout. In a worst-case scenario (maximum DON contamination level of 469 μg/kg), we predict an even greater reduction of 9.9% in growth of trout. Fusarium fungal growth, DON contamination and risks of reduced feed intake and growth cannot always be predicted, or ignored. To prevent loss of production therefore, particularly when using diets with high inclusion of plant ingredients for more sensitive species such as rainbow trout, feed manufacturers may consider adding anti-mycotoxin products to aquafeeds and altogether eliminate the risk of mycotoxin exposure.

Another important outcome of our meta-analysis is the attribution of reduced growth performance of DON-challenged fish to reduced feed intake. Feed refusal is a common symptom in animals that have consumed DON and might simply be a response to poor organoleptic characteristics of the contaminated feeds [72] or be considered a natural defence mechanism to minimize risks associated with exposure to the toxin. The mechanism through which DON reduces feed intake may be associated with a direct action on the brain or may be indirect through the secretion of gut hormones [73]. The latter phenomenon remains unexplored in fish, however. In the future, direct effects of DON on fish growth should be studied without confounding effects caused by reduced feed intake. Indeed, to better investigate direct effects of DON on fish growth, future experimental designs need to overcome differences in feed intake between experimental groups by pairwise and equal feeding.

Taken together, mycotoxin contamination is an emerging concern for European aquaculture and requires a multidisciplinary approach. Diverse expertise is needed and, therefore, collaboration and communication of stakeholders from the whole value chain and scientific support from fields such as fish nutrition, toxicology, health and welfare, microbiology, feed processing and technology and plant sciences are crucial. Our findings suggest a strong impact of dietary DON on feed intake and fish growth, and regulatory authorities should reconsider their current DON recommendation limit to ensure economic profitability and protect fish welfare.

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Keywords

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