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Fusarium head blight and mycotoxins in wheat: prevention and control strategies across the food chain

A.M. Torres[1], S.A. Palacios[1], N. Yerkovich[1], J.M. Palazzini[1], P. Battilani[2], J.F. Leslie[3], A.F. Logrieco[4] and S.N. Chulze[1*]

[1]Research Institute on Mycology and Mycotoxicology (IMICO), UNRC-CONICET, Ruta 36, Km 601, Río Cuarto 5800, Córdoba, Argentina; [2]Institute of Entomology and Plant Pathology, Faculty of Agriculture, Università Cattolica del Sacro Cuore, via Emilia Parmense 84, 29122 Piacenza, Italy; [3]Department of Plant Pathology, 4024 Throckmorton Plant Sciences Center, Kansas State University, Manhattan, KS 66506-5502, USA; [4]National Council of Research (CNR), Institute of the Science of Food Production (ISPA), via Amendola 122/O, 70126 Bari, Italy; schulze@exa.unrc.edu.ar

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REVIEW ARTICLE

Abstract

With 744 million metric tons produced in 2017/2018, bread wheat (*Triticum aestivum*) and durum wheat (*Triticum durum*) are the second most widely produced cereal on a global basis. Prevention or control of wheat diseases may have an enormous impact on global food security and safety. *Fusarium* head blight is an economically debilitating disease of wheat that reduces the quantity and quality of grain harvested, and may lead to contamination with the mycotoxin deoxynivalenol, which affects the health of humans and domesticated animals. Current climate change scenarios predict an increase in the number of epidemics caused by this disease. Multiple strategies are available for managing the disease including cultural practices, planting less-susceptible cultivars, crop rotation, and chemical and biological controls. None of these strategies, however, is completely effective by itself, and an integrated approach incorporating multiple controls simultaneously is the only effective strategy to limit the disease and reduce deoxynivalenol contamination in human food and animal feed chains. This review identifies the available tools and strategies for mitigating the damage that can result from *Fusarium* head blight.

Keywords: deoxynivalenol, *Fusarium graminearum*, disease management strategy, integrated pest management, pre-harvest, post-harvest, zearalenone

1. Introduction

Worldwide production of hexaploid bread wheat (*Triticum aestivum*) and tetraploid durum wheat (*Triticum durum*) was estimated at 744 million tons in 2017 (FAO, 2018), making it the second most widely grown cereal after maize and similar in production level to rice. Wheat can be consumed with a minimum of processing and the wide range of wheat cultivars enables the production of different foods to satisfy a myriad of demands. Bread wheat and durum wheat are both important due to their differential adaptation to climatic conditions and environments, and the different food products they are used to produce. Wheat is considered the main food for 35% of the world's population, providing 20% of global calories and protein (FAO, 2018). Major wheat exporters include Russia (36 million tons), the European Union (26 million tons), the United States of America (25 million tons), Canada (22.5 million tons), Australia (17.5 million tons), and Argentina (13.7 million tons) (USDA-FAS, 2018).

Increases in global population combined with the impacts of climate change and plant diseases, suggest that wheat production will not meet global demand if the current genetic gain in yield of ~1% per year remains unchanged. Demand is expected to increase by 70% by 2050, and average yields need to increase by at least 1.7% per year to reach this goal (FAO, 2009). Successful scenarios all give increased disease control a central role in the production of more high-quality grain (Ray *et al.*, 2013). A major disease problem in wheat production is *Fusarium* head blight (FHB), which causes billions of dollars of losses

worldwide (McMullen *et al.*, 2012; Windels 2000). The major fungal pathogens associated with FHB include strains from the *Fusarium graminearum* species complex (FGSC) and related species such as *Fusarium avenaceum, Fusarium culmorum* and *Fusarium poae* (Leslie and Summerell, 2006). Other species, e.g. *Fusarium acuminatum*, *Fusarium chlamydosporum*, *Fusarium equiseti*, *Fusarium langsethiae*, *Fusarium sporotrichiodes*, *Fusarium cerealis* and *Fusarium tricinctum*, are of lesser importance in the global incidence of this disease (Bottalico and Perrone, 2002; Van der Lee *et al.*, 2015). FHB can cause direct losses through decreased grain yield, lower by-product quality, and reduced seed germination, kernel weight, number of kernels per head, and grain marketability (Dahl and Wilson, 2018; Wilson *et al.*, 2018). Harvested grain also may be contaminated with zearalenone (ZEA) and trichothecenes, such as nivalenol (NIV), deoxynivalenol (DON), and DON's acetyl derivatives 3-acetyl-deoxynivalenol (3-ADON) and 15-acetyl-deoxynivalenol (15-ADON) (Desjardins, 2006; McCormick *et al.*, 2013; McMullen *et al.*, 2012). ZEA is a non-steroidal pseudo-oestrogenic mycotoxin (Hidy *et al.*, 1977; JECFA, 2000) and has been associated experimentally with oestrogenic syndromes in pigs and experimental animals (Zinedine *et al.*, 2007). NIV is more commonly found on rice than it is in wheat (Yang *et al.*, 2018). Commercial antibody kits are generally available for the most common trichothecenes produced by *F. graminearum* (Nguyen *et al.*, 2019).

Trichothecenes cause oxidative stress damage through the generation of free radicals, inhibition of protein synthesis, and interference with intercellular signalling (Rocha *et al.*, 2005). Acute DON poisoning causes emesis and diarrhoea in experimental animals while low dose ingestion is associated to anorexia, growth retardation, immunotoxicity and diminish reproduction and development as consequence of maternal toxicity (Pestka, 2010).

Due to the toxic effects of mycotoxins, maximum regulatory limits for DON and ZEA have been established for wheat and wheat by-products (Table 1). These limits are not harmonised across jurisdictions, and are probably exceeded in the diets of some populations even in the first world (Papageorgiou *et al.*, 2018). The need for global harmonisation of mycotoxin regulation is reflected in the recent MycoTox Charter (Logrieco *et al.*, 2018) call to minimise human and animal exposure to mycotoxins worldwide.

Plants can metabolise mycotoxins and the resulting metabolites are commonly termed modified, or 'masked', mycotoxins (Berthiller *et al.*, 2013; Rychlik *et al.*, 2014).

Table 1. Maximum regulatory limits for deoxynivalenol (DON) and zearalenone (ZEA) established for wheat and wheat by-products in different countries/regions.

Country / region	Product	DON (µg/kg)	ZEA (µg/kg)
Europe[1]	unprocessed durum wheat	1,750	100
	unprocessed cereals other than durum wheat	1,250	100
	cereal for direct human consumption	750	75
	dried pasta	750	–
	bread, pastries, biscuits, cereal snacks and breakfast cereals	500	50
	processed cereal-based foods and baby foods	200	20
Brazil[2]	unprocessed cereals	3,000	40
	bread, pastries, biscuits, cereal snacks and breakfast cereals	750	100
	wheat bran	1000	200
Uruguay[3]	wheat flour, crackers, etc.	1000	100
	processed products	1000	–
USA[4]	finished wheat products for human consumption	1000	–
	grains and grain by-products	10,000	–
Canada[5]	un-processed cereals	2,000	–
	baby foods	1000	–
China[6]	grains and processed products	1000	60

[1] EC, 2006, 2007.
[2] ANVISA, 2017.
[3] MSP, 2001.
[4] FDA, 2010.
[5] Health Canada, 2018.
[6] FAO, 2004.

Plants can add glucose residues to DON and ZEA via glucosyltransferases to produce deoxynivalenol-3-glucoside (DON-3G) and zearalenone-14-glucoside (ZEA-14G), respectively. These glucosides, at present, are not regulated and usually are not detected in standard tests for DON and ZEA. Chemical reactions during food or feed processing or digestion can cleave the glycosidic bond and release the original mycotoxin. Potential risks attributable to these glucosides *per se* are unknown, but the mycotoxin molecules released during processing and digestion should be as capable of interfering with animal and human metabolism as they were prior to being bound in the glucoside (Berthiller *et al.*, 2016; EFSA CONTAM Panel, 2014).

FHB was first reported in 1884 in England (Parry *et al.*, 1995) and since then episodic outbreaks have occurred in different countries around the world (Alconada Magliano and Chulze, 2013; Bilska *et al.*, 2018; Ji *et al.*, 2014; McMullen *et al.*, 2012; Obanor *et al.*, 2013). Over the last 25 years the epidemics have become more frequent and more severe, and escalated to a significant threat to world food safety and security. Major losses have been reported in the USA, Canada, Europe, China and South America, e.g. Alconada Magliano and Chulze (2013), Cai *et al.* (2011), Gilbert and Haber (2013), McMullen *et al.* (2012), Palazzini *et al.* (2015), Windels (2000) and Zhang *et al.* (2013).

The objective of this review is to identify and summarise recent advances in strategies for reducing the impact of FHB, and associated mycotoxin accumulation, across the wheat food chain with a focus on pre- and post-harvest control strategies.

2. *Fusarium* head blight

Ascospores and conidia from *Fusarium* strains associated with *Fusarium* head blight persist on crop residues for long periods of time, when temperatures are conducive and sufficient moisture is available for the fungus to grow and sporulate. Wheat ears are susceptible to fungal colonisation during anthesis, a time when fungal perithecia often are ejecting ascospores. Infected wheat heads whiten prematurely and appear discoloured and wrinkled, which may reduce both yield and grain quality by up to 80% (McMullen *et al.*, 2012).

Pathogens

The *Fusarium graminearum* species complex (FGSC) is comprised of 15 formally described phylogenetic species and one additional species that is informally recognised based on genealogical exclusivity and conidial morphology (Aoki *et al.*, 2012, 2014; O'Donnell *et al.*, 2004; Sarver *et al.*, 2011; Starkey *et al.*, 2007). *F. graminearum sensu stricto* (Leslie and Summerell, 2006) is the main pathogen isolated from wheat in North and South America, Europe and Africa, and can be found in most wheat fields worldwide (Minaar-Ontong *et al.*, 2017; Van der Lee *et al.*, 2015). Although primarily associated with the diseases it causes on wheat and maize, *F. graminearum* can colonise at least 25 other native grass species, and interactions with these native species may play a role in determining a strain's metabolic and pathogenic capabilities (Lofgren *et al.*, 2018). Genetically, populations of this pathogen are highly variable (Kelly and Ward, 2018), with as much variation within a small portion of a single field as across much of North America (Zeller *et al.*, 2003, 2004). *Fusarium asiaticum* is the most important phylogenetic species in China, Japan and Korea and also has been isolated in Uruguay and in United States of America (Gale *et al.*, 2011; Qu *et al.*, 2008; Shin *et al.*, 2018; Umpierrez-Failache *et al.*, 2013; Zhang *et al.*, 2012). Strains of other *Fusarium* species, including *F. acuminatum*, *F. avenaceum*, *F. cerealis, F. chlamydosporum*, *F. culmorum*, *F. equiseti*, *F. langsethiae*, *F. poae*, *F. sporotrichiodes* and *F. tricinctum* also may cause the disease (Bottalico and Perrone, 2002).

Strains within the FGSC usually exhibit one of three primary trichothecene profiles: (1) deoxynivalenol and 3-acetyldeoxynivalenol (3-ADON type); (2) deoxynivalenol and 15-acetyldeoxynivalenol (15-ADON type); or (3) nivalenol and its acetylated derivatives (NIV type). The different toxin types are not uniformly distributed across various wheat-growing regions. In North America, Central Europe, Southern Russia, and South America, the 15-ADON type dominates, and in Northern Europe, China, Australia, New Zealand and Korea the 3-ADON type dominates (Van der Lee *et al.*, 2015; Yli-Mattila *et al.*, 2009). The NIV type has been isolated in China, Japan and other Asian countries and less frequently in Europe, South Africa and the Americas (Gale *et al.*, 2011; Suga *et al.*, 2008; Van der Lee *et al.*, 2015; Zhang *et al.*, 2012). In Canada and the United States, a significant increase in the DON/3-ADON type has been observed in recent years (Gale *et al.*, 2011; Guo *et al.*, 2008, Puri and Zhong, 2010; Ward *et al.*, 2008). A fourth trichothecene toxin type was detected in the United States in 2015 (Varga *et al.*, 2015) and produces NX-2, a trichothecene with a chemical structure similar to 3-ADON. To date, strains producing NX-2 have not been found outside North America (Kelly *et al.*, 2016; Liang *et al.*, 2014). PCR analysis of predicted trichothecene genotype often is used as a proxy for chemical analysis of mycotoxin production. Unfortunately, variation in organisation within the *Tri* gene cluster and the wide variety of mutants that can influence the trichothecene produced have made developing broadly applicable PCR assays difficult (Villafana *et al.*, 2019).

ZEA production by multiple species occurs worldwide, including Canada, the United States, Europe, China, and South America (Chełkowski *et al.*, 2012; Ji *et al.*, 2014;

Schwake-Anduschus *et al.*, 2015; Stanciu *et al.*, 2015; Tittlemier *et al.*, 2013; Tralamazza *et al.*, 2016; Yerkovich *et al.*, 2017). Since toxin types present in populations can change, it is important to continue monitoring strains associated with FHB to understand current mycotoxin contamination potential within the wheat grain chain.

Infection cycle

Understanding the pathogen's life cycle, the infection process, and the role of environmental conditions in the epidemiology of the disease, is important for effective FHB management and control. Ascospores (sexual spores) and macroconidia (asexual spores) are the most important source of inoculum, although hyphal fragments also can serve as inocula. Ascospores are produced in specialised sexual structures, termed perithecia (Guenther and Trail, 2005; Trail and Common, 2000), that can be found on plant debris and require exposure to light for proper development (Kim *et al.*, 2015; Krause, 1930). *F. graminearum* can survive for years as a saprotroph growing in the soil and on dead organic matter, e.g. crop residues. Factors, such as temperature, water, light and O_2 availability, can alter survival time (Leplat *et al.*, 2012). Weed plants can serve as reservoir of the pathogen, with genetically diverse *F. graminearum* strains isolated from the inflorescences of healthy weed plants belonging to gramineous and non-gramineous species growing in or near commercial fields (Mourelos *et al.*, 2014; Postic *et al.*, 2012; Sneideris *et al.*, 2019). High humidity and warm temperatures in the spring favour the development and maturation of perithecia. Ascospores and macroconidia can travel long distances when carried by the wind and also may be dispersed by rain (Keller *et al.*, 2013; Schmale *et al.*, 2006). Once spores land on a suitable host, high humidity is required for spore germination and plant infection (Bushnell *et al.*, 2003). Airborne inoculum levels at and before anthesis are strongly correlated with disease incidence and DON accumulation (Hellin *et al.*, 2018).

Macroconidia of *F. graminearum* germinate within 6 to 12 h post-inoculation on the face of the glume, and by 12 to 24 h post-inoculation hyphae are easily seen and often have reached stomata (Pritsch *et al.*, 2000). The development of FHB after fungal infection depends on the growth stage of the plant, the amount of inoculum, and the weather. Long-term exposure to high humidity and temperatures ≥25 °C promote the disease (Parry *et al.*, 1995). Infection initiates during anthesis, when the wheat flower is directly exposed to the environment. Tissue colonisation depends on cultivar resistance, temperature, humidity, fungal aggressiveness and mycotoxin production (Champeil *et al.*, 2004). Under optimal conditions, the first symptoms of FHB appear 2-4 days after inoculation as slightly brown, water-soaked spots in the spikelets. The infection may be limited to the infected spikelet, or spread across the entire spike. The pathogen disperses from spikelet to spikelet through the rachis. As the infection progresses, the spikelets die, dry up and become bleached resulting in shrivelled kernels (Bushnell *et al.*, 2003).

F. graminearum sensu stricto should be considered a hemibiotroph. After it penetrates the wheat ear there are two distinct phases of infection (Brown *et al.*, 2010; Kazan *et al.*, 2012). Initially the fungus develops a biotrophic relationship with the host in which the invaded tissues remain alive and completely functional. As the infection progresses, the pathogen changes to a necrotrophic state in which it invades the host cells leading to necrosis. Spread of the fungus within the plant occurs more readily in the presence of DON, which blocks a jasmonate-related defence reaction (Bonnighausen *et al.*, 2019), and this mycotoxin functions as a virulence factor in wheat (Bai *et al.*, 2002; Jansen *et al.*, 2005). DON biosynthesis is specifically induced in infection structures, but the toxin is not a prerequisite for the development of these structures or for the initial penetration of wheat tissues (Boenisch and Schäfer, 2011). Thus, the current working hypothesis is that DON is important for suppressing plant defences and enabling the pathogen to break through the rachis node.

Crop phenology

Understanding plant growth and development is an essential component of a wheat management system. The phenological system of Zadoks *et al.* (1974) is widely used for wheat and other small grains, with each stage of plant growth assigned a number. Stages are illustrative and the small differences between stages are important since plant growth is continuous and does not stop at the admittedly arbitrary borders of the different stages in the system. Stage 0 is associated with germination, including all steps from a dry seed up to the appearance of the coleoptile. Stage 1 begins with seedling growth, includes the unfolding of the leaves, and continues until tillering. Stage 2 is specific for tillering. Stage 3 begins with stem elongation and continues until the flag leaf appears. Stage 4 is specific for the boot process. Stages 5 and 6 are associated with inflorescence emergence and anthesis, respectively. Caryopsis development occurs in three stages: Stage 7 is the milk stage, Stage 8 is dough development, and Stage 9 is grain ripening. Secondary growth stages are identified by a second digit to better define closely related differences. The second digits follow the Feckes' scale for intermediate stages, which enables the identification of specific details as needed (Zadoks *et al.*, 1974). For example, codes for the number of leaves are important for determining when fungicide(s) and herbicide(s) should be applied.

Some canopy and ear traits are associated with higher levels of FHB (Jones *et al.*, 2018). Flag leaf length and the number of tillers were the most significant canopy traits,

while spikelet density was the most significant ear trait. Unfortunately reducing flag leaf length, the number of tillers per plant or the density of the spikelets will almost certainly reduce yield in addition to reducing FHB severity.

3. Pre-harvest strategies to reduce *Fusarium* head blight and toxin accumulation

Different strategies for reducing the impact of FHB have been proposed including planting more disease-tolerant cultivars, crop rotation, tillage practices, chemical and biological control and forecasting systems (Chulze *et al.*, 2015; Mesterházy *et al.*, 2003; Wegulo *et al.*, 2015). Different stages of the wheat chain and which strategies can be used in each one to reduce DON accumulation (Figure 1). During the FHB disease cycle, debris, fungal spore release, and weather at anthesis are critical variables for controlling the pathogen. The fungi overwinter on stubble and other plant debris, and under favourable conditions plant infection occurs during flowering. In some regions a wheat-maize rotation is practiced which increases the risk of FHB disease and DON accumulation (Vogelgsang *et al.*, 2011). For integrated management of the disease the best chance for success comes from combining two or more strategies (Acs *et al.*, 2018; McMullen *et al.*, 2012; Mesterhazy *et al.*, 2018a,b; Wegulo *et al.*, 2013).

Biological control of *Fusarium* head blight

FHB management by antagonist microorganisms is a very promising strategy. Biocontrol agents can be applied to stubble to reduce pathogen survival and to limit growth on residue of the previous crop (Palazzini *et al.*, 2013; Wegulo *et al.*, 2015). Biocontrol agents can interact with the pathogen either directly, e.g. parasitism or antibiosis, or indirectly, e.g. induction of resistance, competition, or plant growth promotion (Legrand *et al.*, 2017). Multiple antagonist microorganisms are available and can control FHB pathogens both *in vivo* and *in vitro* (Table 2). Successful antagonism *in vitro*, however, is not always a good predictor of successful *in vivo* activity (Whitaker and Bakker, 2019). Combination applications of chemical controls with biological controls may be possible, but the data to date are relatively limited (Palazzini *et al.*, 2018a).

Reduction of disease severity and the level of DON contamination are both important. Greenhouse applications often are more effective than field applications. Experimental conditions vary considerably and direct comparisons of results from different studies usually cannot be made. Effects may be measured in terms of reduction of fungal growth/sporulation, toxin production or disease severity. The potential use of *Cryptococcus* (Schisler *et al.*, 2011) may encounter regulatory concerns over the ability of some strains of species in this genus to cause human and animal disease. Work on biocontrol of *F. graminearum* with RNAi (Machado *et al.*, 2018; Yu *et al.*, 2018) is still in preliminary stages. Since 2002, a number very different

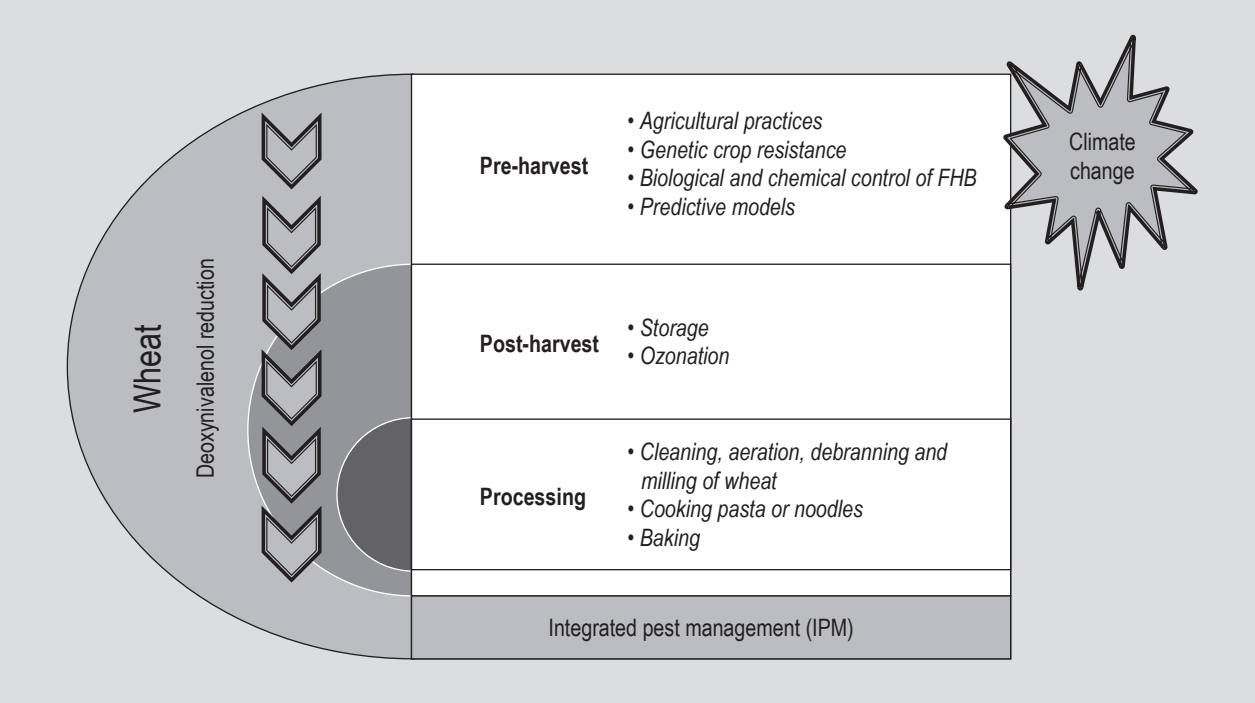

Figure 1. Management to reduce the deoxynivalenol accumulation in wheat.

Table 2. Biocontrol agents for reducing *Fusarium* head blight disease and deoxynivalenol (DON) production by *Fusarium graminearum*.

Biocontrol agent	Experiment location	% Reduction				Reference
		Growth	Sporulation	Disease severity	DON	
Aureobasidium pullulans	greenhouse	–	–	22	–	Wachowska and Głowacka, 2014
Bacillus spp.	*in vitro*	88	96	–[1]	100	Zhao *et al.*, 2014
Bacillus velezensis	field	–	–	25	51	Palazzini *et al.*, 2018b
Clonostachys rosea	greenhouse	–	–	46	33	Xue *et al.*, 2014a,b
Cryptococcus aureus + *Cryptococcus flavescens*	greenhouse	–	–	32	–	Schisler *et al.*, 2011
Paecilomyces spp.	*in vitro*	62	–	–	–	El-Hasan *et al.*, 2018
Pseudomonas spp.	greenhouse	–	–	25 or 50	–	Schisler *et al.*, 2006
	field	–	–	46 or 63	–	
Lysobacter	greenhouse	–	–	80	–	Jochum *et al.*, 2006
Streptomyces albidoflavus	greenhouse	–	–	40	60-100	Palazzini *et al.*, 2007
	field	–	–	30	25	Palazzini *et al.*, 2018b
Trichoderma gamsii	*in vitro*	–	–	–	90	Matarese *et al.*, 2012
Trichoderma spp.	*in vitro*	72-84	–	–	–	El-Hasan *et al.*, 2018

[1] No data.

viruses – dsRNA (Chu *et al.*, 2002; Li *et al.*, 2019; Wang *et al.*, 2013; Yu *et al.*, 2009), negative strand RNA (Wang *et al.*, 2018), and positive single-stranded RNA (Chen *et al.*, 2016) viruses – have been described in *F. graminearum*. In general work with these viruses has not gone very far beyond their description, and infected fungal strains often have few or no morphological differences from the wild type strains (Li *et al.*, 2016). Some viruses, however, are reported to cause major changes in internal fungal metabolism (Bormann *et al.*, 2018; Cho *et al.*, 2012; Yu *et al.*, 2016) and/or to reduce pathogenicity (Chu *et al.*, 2002; Darissa *et al.*, 2012; Tóth *et al.*, 2005). These mycoviruses appear to have potential for biocontrol of *F. graminearum*, but more work appears is needed to develop these viruses as biological control agents.

Chemical control of *Fusarium* head blight

Chemical control, i.e. fungicides, is an available strategy to reduce the risk of FHB and can effectively reduce disease severity and mycotoxin contamination in both naturally and artificially infected plants. Fungicide effectiveness depends on other agronomic practices, e.g. crop rotation, tillage, nitrogen fertilisation, seed treatment and resistant cultivars (Acs *et al.*, 2018; Beyer *et al.*, 2006; Edwards, 2004). Many fungicides have been used to reduce FHB, including triazoles, carbendazim, mancozeb, benomyl, prochloraz, propiconazole and triadiamenol. None of these chemicals, however, suffice by themselves to completely control FHB in wheat (Dweba *et al.*, 2017; Spolti *et al.*, 2013; Yuan and Zhou, 2005).

Fungicides, such as tebuconazole, metconazole and prothioconazole (Paul *et al.*, 2008; Pirgozliev *et al.*, 2002) currently provide the most effective control of FHB in wheat, but this control is not complete. Triazole fungicide application, usually tebuconazole or prothioconazole, can reduce FHB incidence, disease severity and DON accumulation. Application is most effective during anthesis, but application after or prior to anthesis also can reduce disease severity and DON accumulation (Paul *et al.*, 2018). Tebuconazole, one of the most widely tested products, reduced FHB severity 25-77% and DON content 32-89% in field trials (Haidukowski *et al.*, 2005; Paul *et al.*, 2007). Prothioconazole is the most recently registered broad-spectrum fungicide and can reduce FHB disease severity 39-93% and DON accumulation 40-90% relative to untreated controls in field trials (Haidukowski *et al.*, 2012; Mesterházy *et al.*, 2003; Müllenborn *et al.*, 2008; Paul *et al.*, 2007, 2008). Triazole-based fungicides inhibit cytochrome P450 sterol 14α-demethylase (also termed CYP51 and ERG11), an essential enzyme in fungi that is required for ergosterol biosynthesis. Ergosterol is an indispensable component of fungal cell membranes. Reduction of this enzyme's activity reduces fungal membrane integrity and lowers strain viability (Becher *et al.*, 2011). Different alleles of CYP51 differ in their sensitivity to seven different triazoles (Liu *et al.*, 2011).

Repeated applications of the same fungicide to a field can lead to fungicide resistance in the pathogen population. Thus, the use of mixtures of multiple triazoles and/or

triazoles with strobilurins are recommended for more sustainable control (Gilbert and Haber, 2013; McMullen *et al.*, 2008; Ramirez *et al.*, 2004). Strobilurins inhibit growth of the fungus by blocking electron transport in the mitochondrial respiratory chain and thereby reduce aerobic respiration and energy production. Low doses of strobilurins or tebuconazole generally are ineffective in controlling FHB, and DON content may even increase relative to an untreated control (Pirgozliev *et al.*, 2002; Ramirez *et al.*, 2004; Simpson *et al.*, 2001).

In China, FHB frequently occurs in the middle and lower reaches of the Yangtze River, the Huaihe River Valley, and the Eastern coastal region. More recently, disease incidence also has increased in the northern and western wheat growing areas. Benzimidazole fungicides, particularly carbendazim (MBC), have been applied regularly to control FHB for over 30 years during wheat heading and flowering in areas with warm and moist weather. The effectiveness of MBC has been threatened by the emergence of resistant pathogen populations in the field. The frequency of MBC-resistant isolates in some regions of China increased gradually, with the efficacy of MBC against *F. graminearum* decreasing dramatically after 1998. The decrease in carbendazim efficacy paralleled the increased frequency of resistant strains in the population. A new fungicide, cyanoacrylate, also known as JS399, was developed by the Jiangsu Branch of National Pesticide Research & Development South Center (NPRDSC) of China. Both MBC-resistant and MBC-sensitive *F. graminearum* isolates can readily develop resistance to cyanoacrylate. Strains resistant to both fungicides are expected to emerge and potentially create major problems since both fungicides are used extensively in China (Chen and Zhou, 2009).

The selection and timing of fungicide application, the rate of application and the coverage of the spike (Mesterházy *et al.*, 2003, 2011, 2018b) are all variables that can affect the amount of disease controlled. Although excessive fungicide use is regarded as toxic by the general public, mycotoxin contamination usually is more problematic for humans and domesticated animals than is fungicide overapplication. The maximum tolerable Daily Intake (MTDI) for the sum of DON, 3-ADON, 15-ADON and DON-3G in humans is 1 µg/kg body weight/day (EFSA CONTAM Panel, 2017), while the MTDIs for the fungicides range from 18 to 40 µg/kg body weight/day. Fungicides also degrade under field conditions within two weeks of application, while mycotoxins may persist for years and are stable to heat (Mesterházy *et al.*, 2018a). DON contamination of grain can be reduced with the use of fungicides, but fungicides alone do not suffice to prevent FHB. Other factors that are important for the reduction of disease severity, incidence and DON accumulation include the aggressiveness of the infection in the field, weather, and the implementation of agronomic practices known to mitigate FHB.

Genetic crop resistance

Resistant cultivars are an important FHB management strategy. At least five types of resistance to FHB are known (Mesterházy, 1995): type I – resistant to pathogen penetration and the onset of disease; type II – resistant to spread of the pathogen in the plant once the disease is established; type III – resistant to infection of the grain; type IV – tolerance of the disease, i.e. infection occurs but grain yield is not reduced; and, type V – toxin degradation or inhibition of toxin activity. Bread wheat is generally less susceptible to FHB than durum wheat.

Wheat cultivars with different levels and mechanisms of resistance to FHB have been identified (Bai and Shaner, 2004; Bainotti *et al.*, 2017; Wegulo *et al.*, 2013, 2015). Resistance to FHB is quantitative, and is controlled by multiple genes (loci) with individual alleles responsible for small levels of increased resistance. As the different resistance alleles usually must be incorporated individually from exotic backgrounds into commercial breeding lines, developing resistant varieties is a relatively slow process since rare recombination events must be selected to reduce linkage drag (Brar *et al.*, 2019), and high levels of resistance have been difficult to obtain (Bai and Shaner, 2004). Researchers have identified and mapped more than 100 quantitative trait loci (QTLs) that are associated with resistance to FHB (Bai *et al.*, 2018; Buerstmayr *et al.*, 2009; Cainong *et al.*, 2015; Cuthbert *et al.*, 2007; Xue *et al.*, 2010). The pathogen population also contains considerable genetic variation to overcome host resistance (Voss *et al.*, 2010), and managing the disease solely through resistant germplasm seems unlikely in the near future.

Amongst the 100 reported QTLs for FHB resistance, 22 QTL regions on 16 wheat chromosomes have been characterised in more detail. QTLs associated with both reduced FHB severity and lower DON content include: *Fhb1* (chromosome 3BS), *Qfhs.nau-2DL* (2DL), *Qfhs.ifa-5A* (5A), and *Fhb7AC* (7A) (Buerstmayr and Lemmens, 2015). *Fhb1* is derived from the Sumai-3 Chinese wheat cultivar and is, so far, the most important source of FHB resistance. Map-based cloning to identify candidate genes in the *Fhb1* region associated a pore-forming toxin-like gene with FHB resistance (Rawat *et al.*, 2016), and suggested a resistance mechanism involving fungal cell wall interactions. This QTL has been incorporated as a resistance source into multiple cultivars and can explain up to 60% of the phenotypic variation for type II FHB resistance (Buerstmayr *et al.*, 2002). FHB resistant cultivars and breeding lines, including Sumai-3, accumulate very low levels of DON (<2 mg/kg) and have fewer than 10% infected spikelets (Bai *et al.*, 2001). Incorporation of QTLs into commercial lines can be even more difficult as gene pyramiding usually is required for an effective level of resistance to be obtained and both doubled haploids and molecular mapping with

linked markers may be required to select genetic material with commercial potential (Da Silva *et al.*, 2019).

FHB disease severity was reduced 64-74% in transgenic wheat expressing a barley UDP-glucosyltransferase (*HvUGT13248*) (Li *et al.*, 2015b). The transformation of DON to the less toxic DON-3G was 24% more efficient in the transgenic plants than in the non-transformed controls. Plant height of both transformed and non-transformed plants was similar and taken as evidence that expression of the heterologous enzyme did not alter phenotypic characters. Thus, converting DON to DON-3G detoxifies DON *in planta* and reduces FHB disease severity (Li *et al.*, 2015b). DON-3G is less toxic *in planta*, but can be hydrolysed to release DON during digestion or food processing. The released DON molecules can be distributed, metabolised and excreted in the same manner as DON molecules that were never incorporated into a DON-3G intermediate. Although toxicity data for DON-3G is limited and *in vivo* data on chronic toxicity are not available, the EFSA CONTAM Panel determined that DON-3G could be associated with acute and chronic adverse health effects similar to those associated with DON (EFSA CONTAM Panel, 2017).

Agricultural practices

The implementation of good agricultural practices is critical for effective control of FHB. Crop rotation and management of infected residue in the field may reduce FHB severity and DON contamination by up to 30%. *F. graminearum* can persist as a saprophyte in the field between crops on maize and soybean plant residues. Thus, both crop rotation and tillage can be important in reducing the amount of inoculum (McMullen *et al.*, 2012).

Tillage buries infested plant residues below the soil surface, and prevents the formation of perithecia and ascospores, which require light (Leplat *et al.*, 2012). Reducing the number of ascospores present reduces the inoculum available to infect wheat plants when they are susceptible to infection. Perithecia and ascospores can develop more easily on the above ground residue found in fields managed following no-till practices. While no-till cultivation of wheat has many advantages, FHB can increase in no-till fields (Blandino *et al.*, 2010; Duveiller *et al.*, 2014; Klem *et al.*, 2007; Leplat *et al.*, 2012). Ploughing, when combined with a resistant wheat cultivar and fungicide application reduced DON contamination by 94% in comparison to direct sowing of a susceptible wheat cultivar and no fungicide application (Blandino *et al.*, 2012).

Good agricultural practices for reducing FHB should include the use of fertilisers and herbicides. FHB severity and/or DON accumulation increase in grain as nitrogen input increases (Heier *et al.*, 2005; Lemmens *et al.*, 2004). The impact of glyphosate applications on FHB has not been consistent. In minimum-till wheat fields in Canada, the FHB index was higher in fields previously treated with glyphosate (Fernandez *et al.*, 2009a). In another study (Bérubé *et al.*, 2012), glyphosate applied to a soybean crop during the year preceding the wheat crop did not have any effect on the FHB index or DON content. Ryegrass is a widespread weed in wheat-growing regions of Brazil, and glyphosate-resistant ryegrass is common in areas where glyphosate has been applied to agriculturally important crops (Machado *et al.*, 2015). The glyphosate-resistant ryegrass could increase FHB in wheat by serving as a reservoir for increased fungal inoculum during the growing season.

Both chemical and biological seed treatments are available to control seedling blight and to protect wheat seeds and seedlings against seed- or soil-borne pathogens (Dal Bello *et al.*, 2002; Khan *et al.*, 2006; Schaafsma and Tamburic-Ilincic, 2005). The role of these treatments in reducing FHB or DON contamination, which are problems in adult plants, is not clear. *F. graminearum* inoculum can be found in seeds and soil and the fungus can grow systemically within the plant (Moretti *et al.*, 2014). Treating seeds with commercial fungicides is not sufficient to prevent plant infection, since infection also can occur at other stages of growth (Fernandez *et al.*, 2009b). Although seed treatments may not prevent infection, treatment with chitosan (Bhaskara Reddy *et al.*, 1999) may induce the seedlings to accumulate additional phenolic compounds and lignin that increase their resistance to disease. Planting fungicide-treated seeds improves emergence and tillering, which increases plant canopy density as the crop grows and matures. This increase in canopy density favoured increased FHB, but did not alter the amount of DON accumulated (Schaafsma and Tamburic-Ilinic, 2005). It is possible for *F. graminearum* to colonise parts of the plant other than the heads and the grain, e.g. leaves and stems (Moretti *et al.*, 2014). These plant parts may be used for animal feed and provide an alternate route for the introduction of DON, ZEA and related toxins into the diets of these animals. Thus, further work to understand where and how *F. graminearum* colonises these portions of the plants is warranted, with the role of seed treatments in reducing or delaying such colonisation of particular interest.

Predictive models

Forecasting systems (DeWolf and Paul, 2014; Prandini *et al.*, 2009) play a key role in the practical management of FHB since they allow near-real time estimation of FHB disease risks during the growing season. Models have been developed for Argentina (Moschini and Fortugno, 1996; Moschini *et al.*, 2013), Belgium (Detrixhe *et al.*, 2003), Brazil (Del Ponte *et al.*, 2005), Canada (Hooker *et al.*, 2002), Italy (Rossi *et al.*, 2003, 2012), the Netherlands (Franz *et al.*, 2009) and the United States (DeWolf *et al.*, 2003), with

some more focused on FHB and FHB severity and others on toxin accumulation. In the United States, farmers can obtain real-time estimates of predicted disease severity on line (http://www.wheatscab.psu.edu/) based on a combination of flowering status, predicted weather and the resistance of the planted variety. Such estimates can be used to help determine whether fungicide applications are warranted, but cannot be used as a sole guide since chemical control is most effective if applied prior to flowering and most models rely on weather at the time of flowering for estimates of disease severity (De Wolf and Paul, 2014; Moschini *et al.*, 2013; Rossi *et al.*, 2012). The models also assume a typical harvest date for a region, although extended delays in harvesting can increase contamination by DON or ZEA 10-25 fold (Edwards and Jennings, 2018).

FHB is well suited for risk assessment modelling because of the severity of the epidemics, the losses that result from mycotoxin contamination, and the relatively short time for pathogen sporulation, inoculum dispersal, and host infection (DeWolf *et al.*, 2003; Shah *et al.*, 2019). Models often focus on weather forecasts and the susceptibility of the planted cultivar. Modelling mycotoxin production is more difficult than is modelling disease incidence and severity since toxin production is affected by additional factors, e.g. variation in the capacity of different strains to produce toxins, competition with other microbes in the plant, and effects of fungicides on toxin biosynthesis (Landschoot *et al.*, 2013; Ramirez *et al.*, 2004; Xu *et al.*, 2007). Most of existing models are empirical in nature, as the fundamental factors connecting disease progression and toxin production to the environment are not well understood. Thus, the models quantify the impact of readily-obtained practical variables on DON accumulation at harvest, most commonly through the use of multiple regression.

Existing forecasting systems are based primarily on weather data, e.g. temperature, rainfall and moisture, and have been developed for application in particular geographic regions, usually where they were developed. In Argentina, the Predictive Index (PI%) of Moschini and Fortugno (1996) estimates mean head blight incidence from temperature (maximum and minimum daily temperature) and moisture variables beginning eight days before heading and ending when 530 degree days have been accumulated, a period viewed as the susceptible period for infection. Since 2005-2006 wheat growing season, a system for assessing FHB risk has been functioning in the Pampas region of Argentina (Moschini *et al.*, 2013). The system incorporates daily meteorological data from 45 weather stations and short range weather forecasts into predictive FHB models to generate comments and maps showing the potential risk of an FHB epidemic (climayagua.inta.gob.ar).

In the United States, the *Fusarium* Risk Assessment Tool (www.wheatscab.psu.edu/) estimates the risk of an FHB epidemic with more than 10% field severity with weather variables observed 15 days prior to flowering. The goal of this tool is to help growers in all US states where wheat and barley are grown assess the risk of FHB in their area and then apply the best management practices to suppress the disease. FHB risk maps are posted daily, from the beginning of winter wheat flowering until the end of the flowering period for spring wheat. The models from this web site are correct 70-80% of the time.

In Canada, models that predict both FHB severity and DON accumulation risks have been developed. FHB risk maps for the provinces of Saskatchewan and Manitoba are available and based on weather data prior to flowering (https://www.gov.mb.ca/agriculture/crops/plant-diseases/fhb-risk-forecast-wheat.html). Unfortunately, the models and disease descriptors are different in each province. Farmers are encouraged to use these risk maps (www.gov.mb.ca/agriculture/crops/plant-diseases/fhb-risk-forecast-wheat.html; http://www.saskwheat.ca/producer-info/fusarium-risk-assessment-map) as part of an integrated approach to make management decisions about FHB. DONcast® is a commercially available forecasting system that enables farmers to predict DON accumulation in wheat at harvest. This tool was developed in Canada by Weather Innovations Consulting LP (2018) and utilises actual, forecasted and historical weather data together with field-specific agronomic data, such as cultivar, crop rotation and tillage to predict with 80-85% accuracy whether the DON accumulation at harvest will be above or below 1 mg/kg (Giroux *et al.*, 2016). This model also has been tested in Uruguay and France, where its accuracy, 60-80%, is somewhat lower than what it was in Canada (Schaafsma and Hooker, 2005).

In Italy, a mechanistic model that relies on weather data and wheat growth stages is used to predict both FHB risk and DON contamination. The model produces two indices: one for the risk of FHB on wheat and the other for mycotoxin accumulation. Model validations were based on data collected at several locations in northern Italy and gave satisfactory results since the indices calculated with the model coincided with those obtained from the fields (disease symptoms, kernel infection and mycotoxin concentration in the kernel samples) (Rossi *et al.*, 2003). Mechanistic models should work irrespective of the geographic area in which they were developed, while empiric models rely more on local conditions (Camardo Leggieri *et al.*, 2013). Thus, mechanistic models can be core components of a generalised Decision Support System (Rossi *et al.*, 2012).

Climate change and *Fusarium* head blight

FHB is a weather-dependent disease, so climate change may alter both when and where the disease occurs. Continued anticipated growth in CO_2 emissions are projected to

increase the mean global surface temperature in 2100 by 3.7-4.8 °C compared to pre-industrial levels (IPCC, 2013). Consequently, seasonal and regional climates are expected to become more variable and extreme in terms of temperature and precipitation (IPCC, 2007, 2012).

Battilani *et al.* (2016) and Van der Fels-Klerx *et al.* (2016) examined predicted changes resulting from increased temperatures of 2 and 5 °C. Earlier flowering of wheat, changes in pest pressure, and susceptibility of wheat grown in broader geographic regions to FHB and DON contamination all could occur. If elevated CO_2 levels and drought/flooding weather events also were included, then the impacts could be even more severe.

Increases in CO_2 levels alone could change fungal growth and host-pathogen interactions. In general, fungi are tolerant to elevated CO_2 stresses, but when this stress is combined with other environmental stresses their tolerance to increased CO_2 levels decreases (Magan and Aldred, 2007). Three-way interactions between elevated CO_2 (350-400 vs 650-1,200 ppm), temperature increases (2-5 °C) and drought stress, all altered the growth of *F. graminearum*. Changing a_w × temperature altered the ratio of DON, 3-ADON and 15-ADON, produced both *in vitro* and in grain (Medina *et al.*, 2017).

Better understanding and modelling of the impact of climate change requires additional experimental data. Increasing temperature results in both increased disease incidence and increased DON accumulation, and rank correlations between 'normal' and 'warm' treatments were weak suggesting that selection for lines that respond well to a warmer environment need to be conducted in the warmer environment (Tessmann and Van Sanford (2018). When both the fungus and the wheat plants were exposed to 390 and 780 ppm CO_2 (Vary *et al.*, 2015), there was more disease development at the higher CO_2 level. The highest FHB disease levels and associated yield losses occurred when elevated CO_2-acclimated *F. graminearum* was inoculated onto elevated CO_2-acclimated wheat. Thus, climate change could potentially expand the geographic range over which FHB occurs and increase losses due to greater disease severity and toxin contamination.

4. Post-harvest storage and decontamination

Storage

FHB as a disease is a pre-harvest risk, but fungal spoilage and contamination of grains with mycotoxins, such as DON and ZEA may continue during storage if moisture, temperature and aeration are suitable for fungal growth and toxin production (Magan *et al.,* 2010). Both temperature and water activity (a_w) affect the accumulation of DON and ZEA (Garcia-Celá *et al.*, 2018a). Typically, the maximum amount of ZEA, 1,600 µg/kg, is detected at 25 °C and 0.93 a_w with production at the same a_w at 15 °C (550 µg/kg) only about a third of that at the higher temperature. The maximum amount of DON, 806 µg/kg, was detected at 20 °C and 0.95 a_w with almost the same production (720 µg/kg) at the same a_w at 15 °C (Garcia-Celá *et al.*, 2018a).

Adequate storage requires drying the grain to 12-15.5% moisture content, depending on the storage temperature, and then maintaining the grain under these conditions until used (Bala, 2016). The most important control measures to adopt during storage include: (1) removal of *Fusarium*-damaged grains during harvest by using combine settings with an appropriate fan speed to exhaust the 'tombstone' kernels; (2) prompt drying of grain to a storable moisture content; and (3) adequate storage that includes moisture control and control of insects and other pests (Magan *et al.,* 2014).

Dry matter loss by grain is used as a proxy for grain quality. Fungal growth can occur at 20-25 °C and 0.90 a_w, i.e. 19-21% moisture content, in both wheat and barley with dry matter loss of 0.22-0.44% (Magan *et al.*, 2010). The respiration rate of stored wheat can be used to estimate dry matter loss and ZEA contamination. Dry matter losses of <1.0% have a low risk of either ZEA or DON contamination exceeding EU legislative limits (Garcia-Celá *et al.*, 2018b; Mylona *et al.*, 2012).

Managing storage conditions is very important, but fungal growth and mycotoxin production in storage usually originate from infections that initially occur in the field. Thus, the best strategy for reducing *Fusarium* and mycotoxin contamination in storage is to follow good agricultural practices during pre-harvest crop growth and harvest, and minimise the fungal infection that occurs before the grain is placed in storage.

Ozonation

Ozone, O_3, has been widely used in the food industry as an antimicrobial agent. Ozone gas is a strong oxidising reagent that can oxidise double bonds in organic compounds and inactivate microorganisms by reacting with intracellular enzymes, nuclear material, cell walls and membranes, spore coats, and viral capsids (Khadre *et al.*, 2001). Ozone can be used to decontaminate mycotoxins in cereals (Chen *et al.*, 2014; Qi *et al.*, 2016; Savi *et al.*, 2014), and has several advantages over traditional chemical agents, including: (1) rapid decomposition (half-life of 20-50 min) to molecular oxygen; (2) no residue remains after treatment; (3) on-site generation; and (4) no hazardous chemical storage or disposal (Sandhu *et al.*, 2011). Ozone also can be used to decontaminate produce, equipment, food contact surfaces, and processing environment (Khadre *et al.*, 2001). Wheat contaminated with DON can be treated with O_3 to reduce

DON levels (Li *et al.*, 2015a; Sun *et al.*, 2016; Wang *et al.*, 2016).

Ozone may attack DON at the C9-10 double bond leading to its breakdown to simpler acids, aldehydes, ketones and CO_2 (Young *et al.*, 2006). Complete degradation of DON can occur with saturated aqueous ozone (~25 ppm), but with dry ozone no reduction in DON was seen in wheat kernels. Thus, moisture is essential for the reaction between DON and ozone to occur. pH also is an important factor. At pH 4-6 DON was degraded readily, while at pH 7-9 there was little or no degradation. Fungal growth, germination and sporulation all can be limited or completely inhibited by ozone, thus preventing additional toxin biosynthesis after treatment (Kottapalli *et al.*, 2005; Savi *et al.*, 2014; Wu *et al.*, 2006). The efficacy of decontamination or growth limitation depends on a myriad of factors including, but not limited to: O_3 concentration, exposure time, substrate, moisture content, pH, mode of application (gaseous or aqueous), and the fungal species present and their growth stage(s) (Trombete *et al.*, 2017; Young *et al.*, 2006). In general DON degradation increases with O_3 concentration and processing time (Li *et al.*, 2015a). Grain with higher moisture content is easier to decontaminate with ozone than is grain with a low moisture content (Young *et al.*, 2006).

Ozone is GRAS (Generally Recognized as Safe) for the treatment, storage and processing of food and water (FDA, 2001). Moreover, ozone is considered a 'green technology', since its production is environmental friendly and it leaves no residues in the food. Thus, ozonation could have a role as a sanitising agent for organic food production (Trombete *et al.*, 2017). Treatment of wheat grain and flour with O_3 may even improve bread or noodle quality (Li *et al.*, 2012, 2015a; Sandhu *et al.*, 2011; Savi *et al.*, 2014). In particular, flour obtained from wheat treated with ozone had higher tenacity and whiteness, which improved the quality of the flour (Wang *et al.*, 2016).

Ozonation also can degrade ZEA in maize and water. Again, toxin degradation increased with O_3 concentration and treatment time (Dudziak, 2012; Qi *et al.*, 2016). In wheat bran, over half of the ZEA (52%) was degraded after a 15-min exposure to ozone, a rate nearly twice that of the degradation of DON (Santos Alexandre *et al.*, 2018). The quality of the wheat bran was not affected by the treatment. In wheat used for malting, up to 49% of the ZEA present could be degraded following exposure to 20 mg/l O_3 for 40 to 130 min (Reinholds *et al.*, 2016). More work on ZEA degradation by ozone is needed, but clearly ozonation has the potential to significantly reduce both ZEA and DON in contaminated wheat.

5. Post-harvest grain processing

Post-harvest, wheat is subjected to multiple processes including: cleaning, aeration, debranning and milling that can redistribute the mycotoxins present in the grain, with a comprehensive review of the distribution of mycotoxins through the process recently published (Schaarschmidt and Fauhl-Hassek, 2018). Cleaning, sorting and milling of wheat can reduce the mycotoxin content by 57% in finished flour (Tibola *et al.*, 2016). In the cleaning process, kernels with extensive fungal growth, broken kernels, dust and fine materials are removed. During the debranning process, outer layers of the wheat grains are removed prior to the milling process. Debranning can increase the milling performance of wheat and the degree of refinement of flour and semolina (Cheli *et al.*, 2013). Fermentation of grains as part of the malting process with lactic acid bacteria can reduce contamination with DON by 34% and ZEA by 23% as well as increasing germination by 8-9% (Juodeikiene *et al.*, 2018).

In the milling process, mycotoxins may be redistributed and concentrated in particular milling fractions. Mycotoxin levels generally are lower in the inner fractions, e.g. flour and semolina, commonly used for human food, and higher in the outer fractions, e.g. bran, flour shorts, screenings and middlings, used for animal feed (Cheli *et al.*, 2013). Outer fractions may, however, be used for some human foods due to nutritional (essential amino acids, vitamins, antioxidants and mineral content) and physiological benefits such as improved large bowel function, slowed digestion, better absorption of carbohydrate and fat, and reduced risks for some diseases, e.g. obesity, cardiovascular diseases, type 2 diabetes, colon diverticulosis and gastro-intestinal cancers (Hemdane *et al.*, 2016).

DON contamination in finished flour is significantly lower than in milled wheat; however, there are no significant differences in DON levels between milled wheat and bran. DON-3G distribution in the different milling fractions is similar to that of DON, but DON-3G levels in bran were higher than those in flour (Kostelanska *et al.*, 2011; Schwake-Anduschus *et al.*, 2015; Zhang and Wang, 2015). The distribution of ZEA and ZEA-glucosides follows that of DON and DON-3G (Edwards *et al.*, 2011; Schwake-Anduschus *et al.*, 2015; Zheng *et al.*, 2014).

Durum wheat has some different processing considerations since most of this wheat goes to pasta and noodles rather than to flour for bread. Relative to the initial intact grain, DON contamination levels in processed clean wheat, peeled wheat and semolina were 30, 66 and 63%, respectively. DON levels in the by-products increase about 10-fold for foliage waste and ranged from 2-5 higher than the unprocessed grain for the three successive dehulling steps (Brera *et al.*, 2013). Although the inner structures of a wheat kernel are

contaminated at lower levels than the outer portions, even the inner structures can be contaminated by trichothecene-producing *Fusarium* strains. Thus, none of the structures within the kernel effectively block fungal colonisation. Semolina is an excellent substrate for trichothecene biosynthesis, but the bran contains biochemical inhibitors that can limit mycotoxin synthesis (Pinson-Gadais *et al.*, 2007).

Durum wheat also can be processed by pearling. This process removes the outer layers of wheat kernels by abrasion and increases the yield of semolina. Spaghetti made with semolina from pearled wheat is less brown and brighter in colour, and the texture of the cooked spaghetti is not changed (De Brier *et al.*, 2015; Dexter *et al.*, 1994). Pearling also was more efficient than milling in reducing *Fusarium* and DON content in the outer layers of the grain, which were the most contaminated. A 10% reduction in grain tissue through pearling could lead to a 45% reduction in DON in the final product (Rios *et al.*, 2009).

Food processing procedures, such as bread-making and pasta production, also can affect levels of DON and ZEA. At both pilot and industrial scales, modifying the baking step (time/temperature ranges), even within the acceptable technological range, was crucial for minimising DON in the final product (Bergamini *et al.*, 2010). Bread-making includes both fermentation and baking steps. DON levels can be altered, either reduced or increased, during dough fermentation (Vidal *et al.*, 2014). Fermentations at high temperatures that avoided enzyme use reduced DON levels at the end of the fermentation, while fermentations that include enzymes, especially xylanase and α-amylase, could increase DON levels, probably due to enzymatic release of DON bound to polysaccharides (starch and arabinoxylans) and from DON-3G (Vidal *et al.*, 2016a).

Studies of the effects of bread-making on DON-3G content have not been consistent. In one report (Kostelanska *et al.*, 2011), there were no substantial changes in DON-3G levels during the dough preparation process, i.e. kneading, fermentation, and proofing. If bakery improver enzyme mixtures were included, however, an increase of up to 145% of conjugated DON-3G occurred in the fermented dough (Kostelanska *et al.*, 2011), although there was an overall decrease in DON-3G by the time the baking process was complete. In a second report (Vidal *et al.*, 2014), the DON-3G level increased during both kneading and fermentation, but the DON level decreased. This result could occur if the DON is glycosylated during the process. In a third report (Vidal *et al.*, 2017), the presence of α-amylase and xylanase did not affect the DON-3G concentration during fermentation. In a fourth report (Vidal *et al.*, 2016b), the DON-3G level decreased by the end of the fermentation stage regardless of either the fermentation temperature or the addition of exogenous enzymes. Clearly, additional work is needed in this area.

Reports of the effects of baking on DON levels also have been inconsistent. DON-3G levels can be reduced during baking (Simsek *et al.*, 2012). If the initial level of DON is high, then the amount of reduction in DON level also is high (Bergamini *et al.*, 2010). Changes in DON content during baking can be affected by: (1) the scale at which studies are conducted; (2) the size of the baked items; (3) the time of baking; and (4) the addition of exogenous enzymes, e.g. xylanase and α-amylase (Vidal *et al.*, 2016c). Thermal degradation products derived from DON-3G have been found in bread (Kostelanska *et al.*, 2011).

Fermentation and baking reduced ZEA levels by 12% and 80%, respectively. Baking was the most important step in ZEA reduction since this toxin is thermosensitive under the second set of conditions. In pasta production, 10% of the ZEA present was detected in the water used for boiling. Less mycotoxin reduction occurred in pasta production than in baking, probably due to the lower temperature used in pasta cooking (85-98 °C) relative to the baked products (220 °C) (Keller Bol *et al.*, 2016). Bullerman and Bianchini (2007) reported that temperatures greater than 150 °C are needed for good reduction of ZEA during extrusion processing of food and Ryu *et al.* (2003) found that the greatest losses occurred above 175 °C.

Relative to semolina, DON was reduced in dry and cooked pasta by 8 and 41%, respectively (Brera *et al.*, 2013). The larger reduction for cooked pasta was attributed to DON's solubility in water. These results are consistent with previous results (Visconti *et al.*, 2004) in which the highest levels of DON were found in the bran fraction, and DON levels dropped by 23% in cleaned wheat, 63% in semolina, 67% in spaghetti, and 80% in cooked spaghetti. Decline of DON levels in the spaghetti after cooking was attributed to DON leaching into the cooking water.

DON was stable during the kneading and drying steps in spaghetti production (Vidal *et al.*, 2016c), but was consistently reduced by >40% during cooking. The DON that leached into the boiling water was not degraded and the amount of DON that leached into the water depended on the cooking time, with the amount leached increasing as cooking time increased. These results suggest that the exposure to DON in pasta is minimised if the water in which the pasta is cooked is discarded and not retained for use in a soup. DON-3G also is stable throughout the pasta making process and can be leached into the cooking water (Vidal *et al.*, 2016b; Zhang and Wang, 2015; Figure 2).

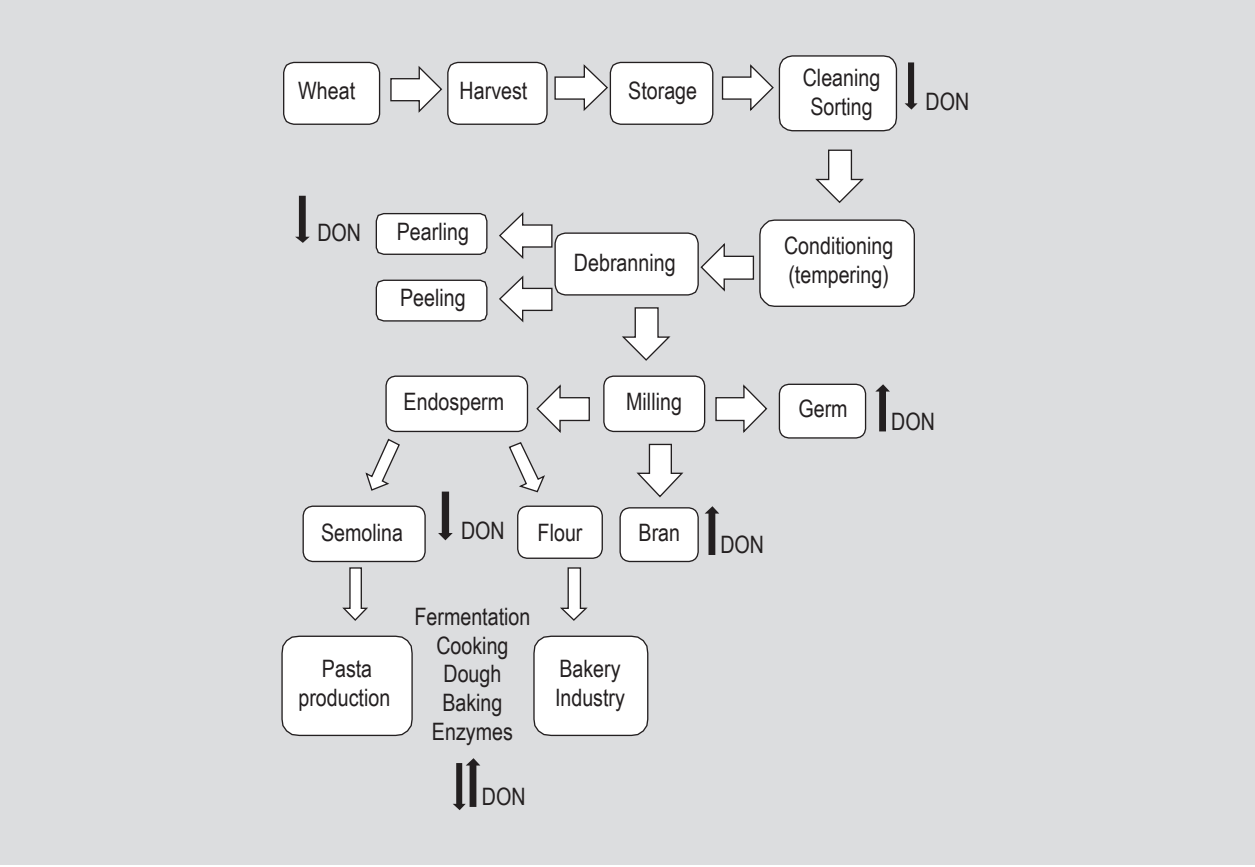

Figure 2. Deoxynivalenol (DON) reduction across the wheat chain.

6. Conclusions

Numerous strategies are available to reduce *Fusarium* head blight and mycotoxin accumulation in the wheat food chain. Among the points to consider are:

- Pre-harvest
  - Continued routine monitoring of biodiversity in the pathogen populations is needed to estimate the risks of mycotoxin contamination and of resistance to fungicides.
  - Changes in the phenology (e.g. early anthesis) of wheat cultivars under some climate change scenarios could significantly increase FHB and DON accumulation.
  - Relative merits of chemical and biological controls should be determined to minimise consumer exposure to fungicides and to ensure an environmentally friendly approach.
  - A combination of moderately resistant cultivars with fungicide use as needed is currently the best defence against this disease.
  - Forecasting models are important tools to support monitoring and predictions of disease damage and mycotoxin contamination during crop growth and at harvest.
  - Survival of pathogen on crop residue should be considered a critical control stage.
- Post-harvest
  - Drying, cleaning, segregation and storage of grain under controlled conditions is critical to ensure safety and quality of final products.
  - Ozonation is a promising strategy for remediating contaminated materials, but the presence and toxicity of residues from incomplete mycotoxin degradation need further study.
- Processing
  - Studies of the effects of glycosylated toxins on human and animal health are needed to determine what role monitoring for the presence of these compounds in grain should play and whether they warrant regulation.
  - Further studies of processing are needed to determine the stability, biodegradation and modification of mycotoxins at pilot and industrial scales.

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