Review Article

Fusarium spp. Mycotoxin Production, Diseases and their Management: An Overview

Saba Shabeer[1], Riffat Tahira[2] and Atif Jamal[3*]

[1]Department of Bioscience, COMSATS University, Islamabad, 44000, Pakistan; [2]Social Sciences Research Institute (PARC), AARI, Jhang Road, Faisalabad, Pakistan; [3]Crop Diseases Research Institute, National Agricultural Research Centre, Park Road, Islamabad, 45500, Pakistan.

Abstract | In total, more than 1.5 million fungal species exist in the world, amongst them pathogenic species can attack plants at different stages causing considerable damage amounting to millions of rupees. One of the plant pathogenic fungi is *Fusarium* spp. *Fusarium* species are very well-known soil-inhabiting fungi that cause many economically important diseases of crops.Many species are included in the *Fusarium* genus, which are not only pathogenic to plants but also cause different diseases in humans and livestock.Apart from diseases, one of the most dangerous characteristics of this fungus is the ability to produce dangerous secondary toxic metabolites, which are commonly known as mycotoxins. Some of the important toxins produced by different species of *Fusarium* are fumonisins and trichothecenes.*Fusarium* species are present around the world and have a very wide host range including many economically important species of crops and plants. Most of the plant diseases are caused by *F. solani, F. oxysporum* and *F. graminearum. Fusarium* species can infect grains in storage, but they are more prevalent in the field where they cause infection in crops and then may invade grains and cause infection in storage. Different methods including chemical, cultural, and biological control strategies are employed to control this fungus. In this review, mycotoxin production, characterization, identification, and different economically important diseases associated with *Fusarium* species as well as their control are discussed in detail.

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***Correspondence** | Atif Jamal, Crop Diseases Research Institute, National Agricultural Research Centre, Park Road, Islamabad, 45500, Pakistan;
Email: atif75j@gmail.com
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Introduction

Fusarium is an important and well-known genus known as imperfect fungi. This genus consists of important plant pathogenic filamentous fungi (Suga and Hyakumachi, 2004). Over 20 species are included in the genus *Fusarium*, out of which 14 are plant pathogenic (Early, 2009). In these 14 species, *Fusarium solani, Fusarium oxysporum and Fusarium chlamydosporum* are the most common ones (De Hoog *et al.*, 2000). *Fusarium* species are present around the world from tropical to temperate regions and even in harsh climates (Early, 2009).The species of the genus *Fusarium* also produce different mycotoxins and secondary metabolites. Zearalenone and gibberellin are two important groups of metabolites that are used to enhance the growth of cattle and also as plant growth regulators respectively (Yu *et al.*, 2004). Whereas, different mycotoxins like fumonisins and trichothecenes produced by *Fusarium* spp. can be fatal for animals and humans (Rheeder *et al.*, 2002). If *Fusarium* contaminated food is consumed by animals

and humans then it may cause mycotoxicosis in them (Kosmidis and Denning, 2017). *Fusarium* spp. may also act as important biodegrading agents and it can sustain in the soil for up to 16 years without any host as well as in dead and decaying plant material (Early, 2009). *Fusarium* species have a very broad host range. They cause economic losses in all cereal crops in North America and western Europe,cotton, wheat and barley in China, rice plants in Taiwan, Thailand and Japan, in all important crops in the tropics and worldwide in timber trees in the forest (Voigt, 2002).

All species of *Fusarium* can produce different secondary metabolites whose functions are still unknown or not properly understood. These secondary metabolites are different toxins that cause virulence during the development of diseases in plants. When mycotoxin contaminated grains are consumed by humans and livestock it may cause great health impact (Bakker *et al*., 2018). Symptoms produced by mycotoxins may vary depending upon the type as well as the concentration of mycotoxin (Bennett and Klich, 2003). The mycotoxins produced by different *Fusarium* species are trichothecenes, fumonisins and zearalenone (Table 1). Trichothecenes are the mycotoxins produced by 24 different species of *Fusarium*. These 24 species that produce trichothecenes are *Fusarium acuminatum, F. oxysporum, Fusarium avenaceum, F. poae, Fusarium camptoceras, F. proliferatum, F. chlamydosporium, F. sambucinum, F. compactum, F. scirpi, F. crookwellense, F. semitectum, F. culmorum, F. solani, F. equesiti, F. sporotrichioides, F. graminearum, F. subglutinans, F. moniliforme, F. tricinctum, F. nivale, F. tumidum, F. nygamai, F. venenatu* (Bullerman, 2007; Mulè *et al*., 1997; Pitt and Hocking, 1997; Sweeney and Dobson, 1998). Zearalenone is the mycotoxins of *Fusarium graminearum* and some *Fusarium sambucinum* related species but they are not associated with the disease on wheat (Munkvold, 2017). Zearalenone is a beneficial mycotoxin as it is being used to increase the growth of cattle (Yu *et al*., 2004). Fumonisins mycotoxins are produced by the *F. verticilloides* (Desjardins and Plattner, 2000) and some other species of *Fusarium* like *Fusarium moniliforme, F. proliferatum* (Keller and Sullivan, 1996), *Fusarium napiforme* (Nelson *et al*., 1992) and *Fusarium nygamai* (Thiel *et al*., 1991). They are related to ear rot in corn, but they are not needed for disease-causing in corn (Desjardins and Plattner, 2000). Their adverse effects on the health of livestock as well as humans have been reported. They are very toxigenic for kidney and liver as well as they are also carcinogenic in nature (Stockmann-Juvala and Savolainen, 2008). All the mycotoxins that are produced by different species of *Fusarium* and their effects are summarized in Table 1.

Control of mycotoxins produced by different Fusarium species

Mycotoxins produced by different fungal species can be detoxified by using chemicals, but it is not a commonly used method as crops subjected to these chemical treatments may become unsuitable for human consumption. However, different chemical treatments involved for the detoxification of mycotoxins are ammoniation, treatments with different acids, bases, oxidizing (e.g. ozone) or reducing (e.g. sodium bisulfite) agents and enzymatic degradation (Munkvold *et al*., 2019).

Awell-studied method of mycotoxin management through chemicals is the treatment of contaminated products with ammonia or ammonium hydroxide. In a study, the treatment of contaminated products with 2% ammonia caused reduction in fumonisinsup to 79% (Charmley and Prelusky, 1994). Treatments with calcium or sodium hydroxide have shown remarkable detoxification in feeds contaminated by aflatoxins, T-2, zearalenone and diacetoxyscirpenol from 45% to 99% depending upon the nature of the toxin as well as feed moisture level (Charmley and Prelusky, 1994; Karlovsky *et al*., 2016). Sodium bisulfite treatments were proved to be effective against deoxynivalenol in only animal feed corn as well as treatments with ozone and chlorine gas were only effective in detoxification of different mycotoxins in corn but not wheat (Young, 1986; Young *et al*., 1986). Formaldehyde and ammonium hydroxide were proved to be effective in decontaminating zearalenone affecting corn and corn grits,but the products treated with formaldehyde are unstable for human consumption (Charmley and Prelusky, 1994).

For the inactivation of mycotoxins through enzymatic treatments different products are commercially available which includes Mycofix, FUMzyme, Biomin BBSH 797, and Biomin MTV. Only a few enzymes have been discovered for the detoxification of fumonisins which includes esterases obtained from a yeast called *Spinifera exophiala* and amino transferase obtained from a bacterium *Sphingomonas* sp. Whereas, for the detoxification of different trichothecenes, UDP-glycosyltransferase was proved to be effective

Table 1: *List of mycotoxins produced by Fusarium spp. along with compounds of mycotoxins, mycotoxins producing species and their effect on humans and animals.*

S. no	Name of mycotoxin	Compound of mycotoxin	Mycotoxin producing spp.	Effect of mycotoxin	Reference
01.	Trichothecenes	Diacetoxyscirpenol T-2 toxin Nivalenol Deoxynivalenol HT-2 toxin	*F. acuminatum, F. oxysporum, F. avenaceum, F. poae, F. camptoceras, F. proliferatum, F. chlamydosporium, F. sambucinum, F. compactum, F. scirpi, F. crookwellense, F. semitectum, F. culmorum, F. solani, F. equesiti, F. sporotrichioides, F. graminearum, F. subglutinans, F. moniliforme, F. tricinctum, F. nivale, F. tumidum, F. nygamai,F. venenatu*	Chronic and fatal toxicosis in human and animals such as Alimentary toxic Aleukia, Akakabi-byo (red mold disease) and Swine feed refusal	(Bullerman, 2007; Desjardins and Plattner, 2000; Mulè *et al.*, 1997; Pitt and Hocking, 1997)
02.	Fumonisins	Fumonisins B1 Fumonisins B2 Fumonisins B3	*F. verticillioides, F. proliferatum, F. napiforme, F. dlamini* and *F. nygamai*	Leukoencephalomalacia in horses, esophageal cancer and birth defects in humans	(Desjardins, 2006; Marin *et al.*, 2013)
03.	Zearalenone	-	*F. gramineraum, F. culmorum, F. cerealis, F. equiseti, F. verticillioides* and *F. incarnatum*	Estrogenic syndromes in swine and used to increase the growth of cattle	(Desjardins, 2006; Marin *et al.*, 2013; Pusateri and Kenison, 1993)
04.	Beauvercin and Enniatins	-	*F. avenaceum, F. trincinctum, F. sporotrichioides, F. langsethiae, F. sambucinum, F. verticilliode, F. sporotrichioides, F. proliferatum* and *F. subglutinans*	No effects	(Desjardins, 2006; Logrieco *et al.*, 1998; Thrane, 2001)
05.	Butenolide	-	*F. graminearum*	Fescue foot in cattle and toxicity in mice	(Desjardins, 2006)
06.	Equisetin	-	*F. semitectum* and *F. equiseti*	Toxic to mice, effect Human immunodeficiency virus and gram-positive bacteria	(Desjardins, 2006)
07.	Fusarins	-	*F. verticilliodes* and *F. graminearum*	Cause mutation	(Desjardins, 2006)
08.	Fusaproliferin	-	*F. proliferatum* and *F. subglutinans*	Cause toxicity in Artemia Salina, L,6,10 IARC/LCL 171 human B lymphocytes and SF-9 insect cells as well as it has pathogenic effects on embryos of chicken	(Marin *et al.*, 2013)
09.	Moniliformin	-	*F. avenaceum, F. tricinctum, F. proliferatum, F. subglutinans,* and *F. verticillioides*	Cause interruption of gluconeogenesis and inhibit glutathione peroxidase and reductase	(Chen *et al.*, 1990; Pirrung *et al.*, 1996)

while for the degradation of zearalenone different enzymes including laccases were reported to be effective (Karlovsky *et al.*, 2016; Loi *et al.*, 2017).

Biological detoxification of mycotoxins includes the use of different microorganisms or the use of different enzymes obtained from microorganisms. In some cases, there are reports of degraded products that are still toxic but, in some cases, there is the complete degradation of mycotoxins using mycotoxin-detoxifying microorganisms. Reduction in the level of deoxynivalenol up to 54%-56% has been seen in the feed when it is incubated with intestinal microflora of chickens (Charmley and Prelusky, 1994). For the detoxification of each of the common mycotoxins, at least one specific microorganism has been discovered (Zhu *et al.*, 2016). Many microorganisms identified as mycotoxin degrading agents are bacteria especially *Bacillus* species.

The life cycle of Fusarium spp.

Fusarium spp. follow both asexual and sexual life cycles. During both sexual and asexual stages, mycelial structures that are haploid are being established. Few species of *Fusarium* produce sexual (meiotic) spores viz ascospores and three types of asexual (mitotic) spores viz. microconidia, macrocondia and chlamydospores that are produced from conidiophores, from sporodochium and within or on hyphae, respectively. Both stages produce spores that are airborne in nature and hence may cause infection and mycotoxin contamination in plants (Dweba *et al.*, 2017). The generalized life cycle of *Fusarium* spp. is depicted in Figure 1. Not all species of *Fusarium* produce all kinds of spores and the sexual cycle of only less than 20% of *Fusarium* spp. is known (Ma *et al.*, 2013).

Sexual state of Fusarium spp.

Teleomorph, which is the sexual state, is known of few *Fusarium* species. All sexual states of known *Fusarium* species are part of Ascomycota but included in different genera viz. Genus Gibberella and Genus Nectria etc. The teleomorphic species of *Fusarium* can be both heterothallic and homothallic. During meiosis, the chromosomes of few of these species was seen under light microscope but due to the small chromosome size of *Fusarium* species, the accurate number of chromosomes or karyotyping is not determined therefore, for this purpose pulsed field gel electrophoresis (PFGE) has been used (Suga and Hyakumachi, 2004). All the known perfect states of *Fusarium* species are given in Table 2.

Morphological and microscopic characteristic of Fusarium spp.

Fusarium spp. can grow on many media. When different *Fusarium* spp. are grown on potato dextrose agar, they may show white, lavender, pink, salmon, or gray-colored velvety to fuzzy cottony growth. Hyphae of *Fusarium* species is hyaline and septate, and it varies from 3 to 8µm in diameter. The species of *Fusarium* produce both macro as well as microconidia. Macroconidia produced by different *Fusarium* species are hyaline, multicellular, septate, and sickle-shaped which may appear in form of clusters while the microconidia are hyaline, unicellular, and ovoid to straight or slightly curved in shape. Sometimes chlamydoconidium are also produced by *Fusarium* species which may present as a single spore or in the shape of clusters or chains (Bullerman, 2003; Nucci and Anaissie, 2009).

Molecular identification of Fusarium spp.

Different molecular techniques which include Random Amplified Polymorphic DNA (RAPD) analysis, specific diagnostic PCR primers and DNA sequencing are being used to identify *Fusarium* species. The polymerase chain reaction (PCR) is considered

Table 2: *Asexual state of Fusarium species with their known sexual state.*

S. No	Asexual state of *Fusarium* species (Anamorph)	Sexual/Perfect state of *Fusarium* species (Teleomorph)	Reference
01.	*Fusarium graminearum*	*Gibberellazeae*	Khan *et al.*, 2020
02.	*Fusarium moniliforme*	*Gibberellafujikuroi*	Chang and Sun, 1975
03.	*Fusarium solani*	*Nectriahaematococca*	Windels, 1991
04.	*Fusarium roseum var. avenaceum*	*Gibberellaavenacea*	Cook, 1967
05.	*Fusarium tumidum*	*Gibberellatumida*	Broadhurst and Johnston, 1994
06.	*Fusarium sacchari*	*Gibberellasacchari*	Leslie *et al.*, 2005
07.	*Fusarium sambucinum*	*Gibberellapulicaris*	O'Donnell, 1992
08.	*Fusarium verticillioides*	*Gibberella moniliformis*	Jurgenson *et al.*, 2002
09.	*Fusarium acuminatum*	*Gibberella acuminata*	Elmer, 1996
10.	*Fusarium Lateritium*	*GibberellaBaccata*	Afanide *et al.*, 1976
11.	*Fusarium circinatum,*	*Gibberellacircinata*	Gordon *et al.*, 2006
12.	*Fusarium pseudograminearum*	*Gibberellacoronicola*	Aoki and O'Donnell, 1999
13.	*Fusarium heterosporum*	*Gibberellagordonii*	Sheraliev and Bukharov, 2001
14.	*Fusarium udum*	*Gibberella indica*	Rai and Upadhyay, 1982
15.	*Fusarium gibbosum*	*Gibberellaintricans*	Dutkiewicz *et al.*, 2016
16.	*Fusarium proliferatum*	*Gibberella intermedia*	Salvalaggio and Ridao, 2013
17.	*Fusarium xylarioides*	*Gibberellaxylarioides*	Geiser *et al.*, 2005

Table 3: *Molecular identification of Fusarium spp. using specific primer sets.*

S. no	Primers	*Fusarium* spp.	Amplification (size bp)	Sequence	Reference
01.	ITS 1 and ITS4	Universal fungal primers	550-570 bp	ITS1(5′TCC GTA GGT GAA CCT GCG G 3′) ITS4 (5′TCC TCC GCT TAT TGA TAT GC 3′)	(Abd-Elsalam *et al.*, 2003; Ferrer *et al.*, 2001)
02.	ITS-Fu-f & ITS-Fu-r	*F. oxysporum* f. sp. *Vasinfectum, F. oxysporum, F. moniliforme, F. solani*	398 bp	ITS-Fu-f(5`-CAACTCCCAAACCCCTGTGA-3`) ITS-Fu-r(5`-GCGACGATTACCAGTAACGA-3`)	(Abd-Elsalam *et al.*, 2003)
03.	ITS5 & as7	*F. proliferatum, F. verticellioides, F. subglutinans, F. nygamai, F. oxysporum, F. compactum, F. sporotrichioides, F. tricinctum, F. graminearum, F. poae, F. camptoceras, F. culmorum, F. pseudonygamai, F. avenaceum, F. thapsinum, F. acuminatum, F. babinda, F. chlamydosporum, F. dlamini, F. heterosporum, F.cf. langsethiae, F. pseudograminearum and F. xylarioides*	930 bp	ITS5(5'GGAAGTAAAAGTCGTAACAAGG3') as 7 (5'CTTCCCTTTCAACAATTTC AC3')	(Kachuei *et al.*, 2015)
04.	Fg16F & Fg16R	*Fusarium gramineraum*	420-520 bp	Fg16F(CTCCGGATATGTTGCGTCAA) Fg16R(GGTAGGTATCCGACATGGCAA)	(Nicholson *et al.*, 1998)
05.	OPT18F & OPT18R	*F. culmorum*	470 bp	OPT18F (F-GAT GCC AGA CCA AGA CGA R-AG) OPT18R (GAT GCC AGA CGC ACT AAG AT)	(Schilling *et al.*, 1996)
06.	FAC-F & FAC-R	*F. acuminatum*	600 bp	FAC-F (GGG ATA TCG GGC CTC A) FAC-R (GGG ATA TCG GCA AGA TCG)	(Williams *et al.*, 2002)
07.	FEF & FER	*F. equiseti*	400 bp	FEF (CAT ACC TAT ACG TTG CCT CG) FER (TTA CCA GTA ACG AGG TGT ATG)	(Mishra *et al.*, 2003)
08	Fp82F & Fp82R	*F. poae*	220 bp	Fp 82F(CAAGCAAACAGGCTCTTCACC) Fp 82R(TGTTCCACCTCAGTGACAGGT)	(Parry and Nicholson, 1996)
09.	SUBF & SUBR	*F. subglutinans*	630 bp	SUBF(CTGTCGCTAACCTCTTTATCCA) SUBR(CAGTATGGACGTTGGTATTATATCT)	(Mulè *et al.*, 2004)
10.	VERF & VERR	*F. proliferatum*	420 bp	VERF(TGTCAGTAACTCGACGTTGTTG) VERR (CTTCCTGCGATGTTTCTCC)	(Mulè *et al.*, 2004)

as the most reliable and rapid technique for the identification of different *Fusarium* species (Kachuei *et al.*, 2015). Different primer sets have been designed for the identification of *Fusarium* species (Table 3).

Pathogenicity factors of Fusarium spp.

Fusarium spp. uses different cellular signaling pathways and different toxins or enzymes which may include MAPKs, Ras proteins, G-proteins, Velvet complex, cAMP pathways and cell wall degrading enzymes to enter their hosts and cause infection. These pathogenicity factors maybe generally produced by different species of *Fusarium* or they may be host-specific (Poppenberger *et al.*, 2003).

Diseases caused by Fusarium spp.

Species of *Fusarium* cause many diseases like root rots, seedling blight (Bakker *et al.*, 2016), vascular wilts (Michielse and Rep, 2009), infection in reproductive tissues as well as in developing seeds (Kazan *et al.*, 2012) and diseases in storage (Gachango *et al.*, 2012). The *Fusarium* species have a wide host range. They can cause diseases in different cereal crops like maize, rice, wheat, barley, rye, oat and malt, etc. as well as in other vegetables and fruit crops like melons, pepper, potato, tomatoes and banana, etc. (Early, 2009). Most of the plant diseases are caused by *Fusarium solani* (50%) and by *Fusarium oxysporum* (20%) (Kosmidis and Denning, 2017). A comprehensive table has been

made which shows all the diseases caused by *Fusarium* spp. in different plants (Table 4).

Disease symptoms

Fusarium spp. produces different types of symptoms on hosts. Some of the common symptoms produced by this fungus are described below.

Vascular wilt diseases

Wilt diseases are mostly caused by different species of *Fusarium*. Mostly all wilts show common symptoms like the infected parts of the plant lose their turgidity, their color changes to light green or yellowish green then to brown and they wilt and finally die. Wilting is due to the blockage in xylem tissue of plants by the spores, mycelium, or polysaccharides of fungus which results in the less flow of water in tissues of plants. The fungus also produces different mycotoxins like fusaric acid and lycomarasmin in vessels that flow from vessels to the leaves. In leaves, they affect the process of photosynthesis by reducing the production of chlorophyll (Voigt, 2002).

Rot diseases

Rots may affect the roots, foot, or stem of plants. Rots maybe caused by one or more than one pathogen (Waller and Brayford, 1990). The plant parts which are rotted may seem like water soaked and the color of the infected area turn brownish and finally black. Plant stops growing and roots, as well as stems, die due to rotting (Voigt, 2002). In the case of cereals, the rotting of the stalk happens which results in the

Table 4: *List of diseases caused by Fusarium spp. on different hosts.*

S. no	*Pathogen* spp.	Disease caused	Host	Reference
01.	*Fusarium sacchari*	Sugarcane wilt	Sugarcane	(Viswanathan *et al.*, 2011)
02.	*Fusarium moniliforme*	Pokkah Boeng	Sugarcane	(Vishwakarma *et al.*, 2013)
03.	*Fusarium fujikuroi*	Bakane	Rice	(Wulff *et al.*, 2010)
04.	*Fusarium decemcellulare*	Green point gall	Cacao	(Hansen, 1966)
05.	*Fusarium manginifera*	Flowering malformation	Mango	(Marasas *et al.*, 2006)
06.	*Fusarium oxysporum*f.sp. *elaeidis*	*Fusarium* wilt	Oil palm	(Flood, 2006)
07.	*Fusarium oxysporum* f. sp. *Lycopersici*	*Fusarium* wilt	Tomato	(Walker, 1971)
08.	*Fusarium oxysporum* f. sp. *Cubense*	Panama disease	Banana	(Ploetz, 2006)
		Fusarium wilt	Abaca	(Waite, 1954)
09.	*Fusarium pallidoroseum*	Crown rot	Banana	(Krauss and Johanson, 2000)
10.	*Fusarium graminearum*	*Fusarium* head blight	Wheat, Corn, Barley	(McMullen *et al.*, 1997)
11.	*Fusarium solani*	Papaya internal fruit rot	Papaya	(Alvarez and Nishijima, 1987)
		Root rot	Cassava	(Bandyopadhyay *et al.*, 2006)
		Canker	Passion fruit	(Ploetz, 2003)
		Slow decline	Pepper	(Oliveira and Pereira, 1983)
12.	*Fusarium oxysporum* f. sp. *Ciceris*	*Fusarium* Wilt	Chickpea	(Knights, 2004)
13.	*Fusarium moniliforme*	*Fusarium* ear rot of corn	Corn	(Davis *et al.*, 1989)
14.	*Fusarium decemcellulare*	Dieback of mango	Mango	(Qi *et al.*, 2013)
15.	*Fusarium oxysporum* f. sp. *Angsanae*	Wilt	Angsana	(Crowhurst *et al.*, 1995)
16.	*Fusarium xylarioides*	Wilt	Coffee	(Rutherford, 2006)
17.	*Fusarium oxysporum* f. sp. *Vasinfectum*	*Fusarium* wilt	Cotton	(Holliday, 1980)
18.	*Fusarium oxysporum* f. sp. *Passiflorae*	*Fusarium* wilt	Passion fruit	(Ploetz, 2003)
19.	*Fusarium circinatum*	Pitch canker	Pine	(Gordon, 2006)
20.	*Fusarium guttiforme*	Fusariosis	Pineapple	(Ventura, 1994)
21.	*Fusarium oxysporum* f. sp. *Rosellae*	*Fusarium* wilt	Rosella	(Ooi and Salleh, 1999)
22.	*Fusarium oxysporum* f. sp. *Vanilla*	Stem and root rot	Vanilla	(Ben-Yephet *et al.*, 2003; Liew *et al.*, 2004)
23.	*Fusarium solani* f. sp. *Eumartii*	Foot rot	Tomato, Potato, eggplant & pepper	(Romberg and Davis, 2007)
24.	*Fusarium oxysporum* f. sp. *phaseoli*	*Fusarium* wilt or yellows	Beans	(de Vega-Bartol *et al.*, 2011)

softening of internodes and change of outer color into brown while the inner color changes into pink or reddish. Roots are also affected which results in the discoloration of leaves, breaking of the stalk and premature death while in case of maize ear rot, pink or red mould may appear on ears. In early infection by ear rot, complete rotting of ears happens which leads to the development of pinkish mould between ears and husk (Voigt, 2002).

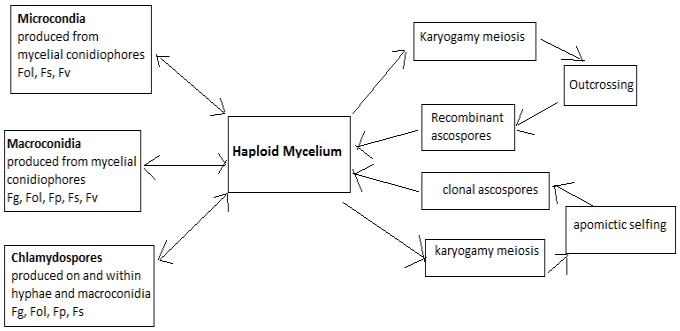

Figure 1: *The General life cycle of Fusarium spp. plasmogamy and karyogamy results in the production of recombinant and clonal meiotic (sexual) spores in the outcrossed and selfed perithecium which in turn forms haploid mycelium. This haploid mycelium can produce three different types of spores that are mitotic in nature viz: micro and macro conidia which can colonize the host and chlamydospores which overwinters and whenever the conditions are favorable, they develop into perithecium and again starts the cycle. Abbreviations: Fg, Fol, Fusarium oxysporum f. sp. lycopersici; Fp, Fusarium pseudograminearum; Fs, Fusarium solani f. sp. pisi; Fv, Fusarium verticillioides(redrawn from Dweba et al., 2017; Ma et al., 2013).*

Seedling blight diseases

The blight of seedlings mostly caused on corn and small grains as dark brown lesions that resemble brown rot and blight in both at pre- and post-emergence stage. The seedings may not develop properly, chlorosis will occur which finally results in the death of seedling (Voigt, 2002).

Head blight or Scab diseases

Scab appears on spikelet as water-soaked lesions which later decolorize. During warm and humid conditions, the head fully gets infected through mycelia and conidia and the kernels get dry and shriveled. Mycelium of fungus overgrows and appears as white, pink, or brown growth on infected kernels (Voigt, 2002).

Dry rot diseases

Dry rot may infect bulbs, corms, and tubers on both pre- and post-harvest stages. The most common hosts of dry rot diseases are onion, lily, gladiolus, and potatoes. The injuries caused during harvesting are the main way of pathogen invasion. Brown colored small lesions will form on tubers which increase in size and later wrinkles will form. Tubers become hard and mummified (Voigt, 2002).

Management of diseases caused by Fusarium species

cultural control

Cultural control practices help to reduce the primary inoculum which is responsible for the development of secondary infection. Diseases in plants caused by *Fusarium* spp. can be controlled by achieving low plant density, using proper phosphate, potassium, and nitrogen fertilizers, and using resistant varieties of plants. Rotation of crops, tillage and proper seedbed preparation can also reduce the primary inoculum present in crop residues. The first-ever method used to control the plant diseases was crop rotation (Sumner, 1994). But it is not useful in the case of *Fusarium* spp. which are not specialized because they have a wide host range (Waller and Brayford, 1990). Losses caused by *Fusarium* spp. can be decreased by crop rotation with resistant or non-host crops, attaining suitable soil drainage and by using healthy and treated stock (Agrios, 1997). Disease development can also be controlled by changing the date of sowing because it is affiliated with the epidemic development. Crops like chickpea have been sown in southern Spain in early winters instead of early springs which helped in slowing the epidemics of *Fusarium* wilt which resulted in less disease development (Navas-Cortés *et al.*, 1998). Sowing the crops in early winter instead of early spring resulted in more soil moisture and less temperature which are not favorable for *Fusarium* wilt thus it affects the disease development (Voigt, 2002). Primary inoculum of *Fusarium* can also be decreased by flooding fields for a large period or dry fallowing because it results in a low oxygen level which is not favorable for pathogen development (Manners, 1993). Infection of *Fusarium* in seeds can be controlled by decreasing the temperature and moisture in storage for several months because it decreases the activity of *Fusarium graminearum* in grains (Gilbert *et al.*, 1997). By achieving the temperature below 10°C, growth and mycotoxin production can be lowered in *F.graminearum, F. moniliforme and F. proliferatum* (Ryu and Bullerman, 1999; Ryu *et al.*, 1999). Food preservatives like sorbic acid, acetic acid, formic acid and propionic acid, etc. can be used to decrease the mycelial growth and production of spores and mycotoxins by different *Fusarium* spp. like *F. proliferatum* (Marin *et al.*, 1999) and *F. oxysporum*

(Tzatzarakis *et al*., 2000) in food.

Chemical control

The use of chemical control strategies such as fungicide seed treatment and the application of fungicides on crops along with cultural control strategies can be effective to control diseases. Studies have been done to check the effect of treatments on seeds which helped in better understanding of different chemical treatment effects on viability, germination, emergence and vigor of seeds as well as the weight of roots (Gilbert and Tekauz, 1995; Gilbert *et al*., 1997). Rots caused by *Fusarium* spp. can be controlled by applying benomyl sprays on plants or by treating propagative plant materials with benomyl. Benzimidazoles and Benomyl works very well against the infections caused by *Fusarium* species. Benzimidazoles are very effective against the *F. avenaceum, F. culmorum, F. equiseti and F. solani*, but it is not effective against the *F. sambucinum* which causes tubers in potatoes because it is highly resistant to benzimidazole and its derivatives (Kawchuk *et al*., 1994). While prochloraz and tebuconazole are effective against *F. culmorum* and *F. poae* which are the causal agents of ear blight on wheat (Doohan *et al*., 1999). In storage conditions, diseases on crops can be managed by applying fungicides at the post-harvest stage. For example, a pathogen causing dry rot of potato tubers only enters its host through physical injuries. After it enters its host, it develops inside the host and causes infection but its development inside the host can be controlled by treating the potatoes with thiabendazole at the post-harvest stage (Secor and Gudmestad, 1999). When plants are treated with benzimidazole then on the surface of plants they convert into methyl benzimidazole carbamate (MBC, carbendazim) which acts as a systemic fungicide and are fungistatic in nature (Manners, 1993). Organomercury fungicides act both as eradicants and protectants and they are used to control *Fusarium* diseases in cereal grains (Häni, 1981; Manners, 1993). In China, bakanae disease of rice has been successfully managed by treating seeds with formalin and organic mercury (Cook, 1967). But formalin and organic mercury-based fungicides have toxic effects on plants. Another safe method to control *Fusarium* diseases is by treating the soil with fumigants like methyl bromide before the sowing of crops. This fumigant enters in the pores of soil, spread thoroughly and has no toxic effect (Ben-Yephet *et al*., 1994). Soil is treated with both volatile fumigant methyl bromide and insecticide chloropicrin together. Metalaxyl, diazoben, pentachloronitrobenzene (PCNB), ethazol, captan and chloroneb are the most common organic fungicides which are used to treat the soil. They are more effective, safe but are expensive than sulfur-based and copper-based fungicides. Captan which act as a protectant, reacts with sulfhydryl groups and stops the activity of enzyme which contains thiol (Manners, 1993). Many *Fusarium* spp. develop resistance against fungicides and fungicide may not remain effective against those isolates which will ultimately increase the diseases caused by *Fusarium* (Secor and Gudmestad, 1999). Therefore, along with chemical control we must use other control measures like use of proper cultivation techniques, proper treatment of seeds and usage of clean and healthy seed and propagating stock etc. (Voigt, 2002).

Biological control

***Fusarium* against *Fusarium*:** Some species of pathogens contain virulent, avirulent or hypovirulent strains. These two avirulent or hypovirulent strains can be used against the virulent strain. These virulent or hypovirulent strains can protect the crop against its virulent strain (Sneh, 1998). The avirulent strains increase the resistance of host plants against its pathogen by competing with the virulent strains. Some strains of *Fusarium* also produce anti-fungal compounds like alpha-pyrones produced by *F. semitectum* which play an important role in the protection of plants (Evidente *et al*., 1999). For example, Wilts caused by *Fusarium oxysporum* in different crops was managed by using avirulent strains of the same fungus (Fravel and Engelkes, 1994).

Fungi against *Fusarium*: Mycorrhizal association with the roots have successfully managed the disease caused by *F. oxysporum* in Douhla fire seedlings and *F. solani* in soybean same as in the case of ectomycorrhizal and endomycorrhizal associations which increases the plant health resulted in less development of pathogens like *F. oxysporum, F. solani, F. culmorum and F. graminearum* in their respective hosts (Schönbeck *et al*., 1994). The *Trichoderma* is also one of the successful bio-control agents of *Fusarium*. It affects the growth of *Fusarium* by causing parasitism (Ogawa *et al*., 2000). *Trichoderma* spp. effects and degrade the chitin which is the main constituent of the cell wall of fungus (Manocha and Govindsamy, 1998). *Trichoderma viridae* successfully controlled the diseases caused by *F. moniliforme* as well as reduced

its mycotoxin production by 85% (Yates *et al*., 1999). *F. oxysporum* f. sp. *lycopersici* which causes wilt was controlled in tomatoes by 30% using *Penicillium purpurogenum* as a bio-control agent (Larena and Melgarejo, 1996).

Bacteria against *Fusarium*: Rots and damping-off diseases caused by *Fusarium* have been successfully managed by using *Bacillus cereus* which is a soil-borne bacteria whereas, *Pseudomonads* are being successfully used against *F. oxysporum* because they produced antibiotics such as N-butylbenzene sulfonamide which inhibits the activity of *F. oxysporum* (Kim *et al*., 2000). *Pseudomonads* especially *P. fluorescens* and *P. putida* are abundantly present in soil rhizosphere. They make soil suppressive against the wilts causing *Fusarium* by producing siderophores (Alabouvette *et al*., 1998). *P. putida* promotes the production of phenolic compounds in cucumber which are antifungal in nature. This helps in the increase of resistance against the pathogen (Ongena *et al*., 2000). The health of potato plants has been increased by the induction of *Pseudomonas* which promotes siderophores that are hydroxamate type which resulted in the production of hydrocyanic acid and indole acetic acid (Gupta *et al*., 1999). Salicylic acid is an important signaling molecule in plant defense systems which plays an important role in the induction of resistant mechanisms in plants (Mauch-Mani and Métraux, 1998). If the activation of salicylic acid is affected, then it increases the susceptibility level of the host against its pathogens (Delaney *et al*., 1994). Rhizobacteria increase the plant health by inducing ISR in plants through the production of compounds like indole-3-acetic acid and cytokinin along with the reduction of ethylene (Buchenauer, 1998).

Mycoviruses against *Fusarium:* Studies have shown that mycoviruses cause a reduction in the virulence of fungi known as hypovirulence therefore they can be used as bio-control agents (Nuss, 2005). Different mycoviruses have been discovered from different *Fusarium* species. *Fusarium graminearum* virus 1 (FgV1)/ *Fusarium graminearum* virus DK21 (FgV-DK21), *Fusarium graminearum* virus 2 (FgV2), *Fusarium graminearum* virus China 9 (FgV-ch9), *Fusarium graminearum* hypovirus 1 (FgHV1), *Fusarium graminearum* hypovirus 2 (FgHV2)and *Fusarium graminearum* mycotymovirus 1 (FgMTV1) have been discovered from different isolates of *Fusarium graminearum* and they affect them by causing hypovirulence, less mycotoxin production, altered growth and irregular morphology (Chu *et al*., 2002, 2004; Darissa *et al*., 2012; Li *et al*., 2016, 2015; Wang *et al*., 2013; Yu *et al*., 2011) same as in case of *Fusarium boothi* large flexivirus 1 (FbLFV1), *Fusarium virguliforme* virus 1, *Fusarium virguliforme* virus 2 (FvV1 and FvV2), *Fusarium circinatum mitovirus* 1, *Fusarium circinatum mitovirus* 2-1 and *Fusarium circinatum mitovirus* 2-2 (FcMV1, FcMV2-1 and FcMV2-2) having same effects on *Fusarium boothi, Fusarium virguliforme* and *Fusarium circinatum* respectively (Marvelli *et al*., 2014; Mizutani *et al*., 2018; Muñoz-Adalia *et al*., 2016).

Conclusions and Recommendations

Fusarium is an important genus among fungi including different plant as well as human pathogenic species. They not only cause infection but are also responsible for different mycotoxins that are toxic for both animals and humans. There is a dire need to control this menace so that losses can be minimized and to this end different control strategies can be employed to manage and control this fungus.

Novelty Statement

An up to date comprehensive review about *Fusarium* spp. For the first time in this review, mycotoxins and diseases caused by *Fusarium* spp. are discussed. All the possible control strategies for controlling this pathogen are discussed with special reference to biological control, an environmentally safe method. All the information is tabulated for the ease of students and researchers.

Author's Contribution

Saba Shabeer: Data collection, draft-ing the article, revision of the article.
Riffat Tahira: Revision of the article.
Atif Jamal: Conception of the work, revision of the article and final approval.

Conflict of interest
The authors have declared no conflict of interest.

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