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Mycotoxins in food grains: Threat to food chain

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Abstract
Cereals are a staple food across the world and feed more than half of the world's population. Most countries produce large quantities of cereals, and the rate of contamination is likely to be high. Cereal contamination will primarily be caused by fungal association, which can occur anywhere from pre-harvest to storage level. A different group of fungi infects cereals, among all *Fusarium*, *Aspergillus*, and *Penicillium* species are the most common in most food grains. These are three major fungal species that produce mycotoxins, which induce spoilage and disease, resulting in a loss of quantity and quality of food grains. Mycotoxins have an impact on human and animal health this is due to the consumption of mycotoxins along with food grains. AFB1, Deoxynivalenol (DON), Zearalenone (ZEA), *Fumonisins*, and *Ochratoxin* are all prevalent in the cereal grains which have the most toxic effects on human health when it is consumed at higher levels. The majority of methods for completely eradicating fungal infection in cereal crops are presently unavailable. They have become a major public health concern, owing to their negative health impacts, such as carcinogenicity, and neurotoxicity.

Keywords: mycotoxins, fusarium, carcinogens, health effects, food grains

1. Introduction
Cereal is the word derived from cares, the name of the Roman goddess of harvest and agriculture. Cereals and cereal items are commonplace in most people's diets [1]. India is predominantly an agriculturally based country with nearly three-fourths of the people dependent on agriculture. In India, Agriculture contributes 16% of the total Gross Domestic Product (GDP). As the state, of Karnataka, is blessed with varied agro-climatic conditions, 54.84 lakh hectares' area is being grown cereals with a production rate of 129.36 lakh tonnes. Cereals are the basic staple food and provide much of the energy and protein for many populations. Whole grain cereal consumption is linked to greater diet quality and nutrient-dense foods that provide protein, lipids, B vitamins (including thiamin, niacin, and riboflavin), vitamin E, and minerals (calcium, magnesium, potassium, phosphorus, iron, and sodium) [2]. Due to the inclusion of dietary fiber and bioactive substances, the value of cereals in the diet, particularly wholegrain cereals, is currently being investigated. Dietary fiber components are distributed unevenly throughout a grain, with the highest concentration in the outer tissues [3].

Cereal grains are grown in greater quantities and play a major role in energy supply to humans than any other type of crop with 2534 MT comprising 245.5 MT in India. A total amount of 1104 MT is consumed as food by humans and 876 MT as feed for animals which finally will be consumed as meat by humans. In some developing nations, grain in the form of rice, wheat, or maize constitutes a majority of daily substances Grain, such as rice, wheat, or maize, accounts for the bulk of daily calories in some poor countries. Cereal consumption in developed countries is more moderate and varied, but still significant, in the form of cereal-based food products such as corn flakes, bread, biscuits, flour, oats, poultry, and animal feeds, and also used in industries to make beverages, medicines, brown rice, and other products for both humans and animals [4].

According to FAO, the world cereals output prediction for 2021 was raised by 0.8 percent, up from the outturn in 2020. Global coarse grain output has been lifted marginally in April month, to 1206 million tones, due to a small rise in the maize production forecast in Ukraine (FAO). As per 3rd Advance Estimates, the estimated production of major Food grains **(**305.44 MT) during 2020-21 and among them, Rice (121.46 MT), Wheat (108.75 MT), Coarse Cereals (49.66 MT), Maize (30.24 MT) are produced at different climatic conditions [5].

2. Consumption

The prediction for worldwide cereal usage in 2021-22 has been cut by 12.4 million tonnes. Wheat utilization in 2021/22 has decreased by 2.4 million tonnes due to lower feed demand than it is expected to rise by 1.2 percent from the level of 2020-21. The use of coarse grains in 2021-22 has also been reduced by 10.5 million tonnes from the prior prediction, owing to lower maize and barley consumption.

3. Losses due to contamination

Harvesting is the initial phase in the grain supply chain, and it is a crucial process in determining the overall quality of the crop. Crop harvesting is primarily done by hand in underdeveloped countries, with sickles, knives, scythes, and cutters being used. In developed countries, combine harvesters are used to harvest almost all of the crops [5]. While meeting the growing global food demand remains a serious challenge, more than a third of food is lost or wasted during postharvest processes. Reduced postharvest losses, particularly in developing countries, could be a long-term solution for increasing food availability, reducing reliance on natural resources, eradicating hunger, and improving farmers' livelihoods. Cereal grains are the most common source of staple food in most developing countries, and they have the highest calorific postharvest losses of all agricultural commodities. Due to technical inefficiency, up to 50%–60% of cereal grains can be lost during the storage stage [5]. Food loss across the food supply chain, from crop harvest to consumption, is referred to as postharvest loss [6]. Postharvest loss refers to direct physical and quality losses that lower the crop's economic worth or make it unfit for human consumption. In extreme circumstances, these losses can amount to up to 80% of overall production [7].

4. Contamination of cereals via different modes

Spoilage will be most prevalent during humid and rain, variation in the weather invites spoiling by molds, bacteria, and yeasts. Microorganisms from soil, insects, and other sources infect cereals like wheat, rye, and corn. Bacteria, molds, and yeasts are commonly found in cereal grains and cereal products. On grains, fungi, particularly molds, are the most common natural microflora [8]. Molds are the most common cause of cereal microbiological degradation. During growth, harvest, and storage, cereals can be contaminated by a variety of pathogenic and spoilage microorganisms [9, 10]. They typically include tens to hundreds of thousands of fungal propagules (e.g., spores and mycelia) and thousands to millions of bacteria per gram at the time of harvest (Table 1). Fungi populations can range from 107 to 109 CFU/g1, but bacterial numbers can range from 106 to 108 CFU/g1 [11, 12]. Bacteria can degrade grains as well, but yeasts produce little spoiling issues. Bacillaceae, Micrococcaceae, Lactobacillaceae, and Pseudomonadaceae are the most usually associated bacterial families with grains [13].

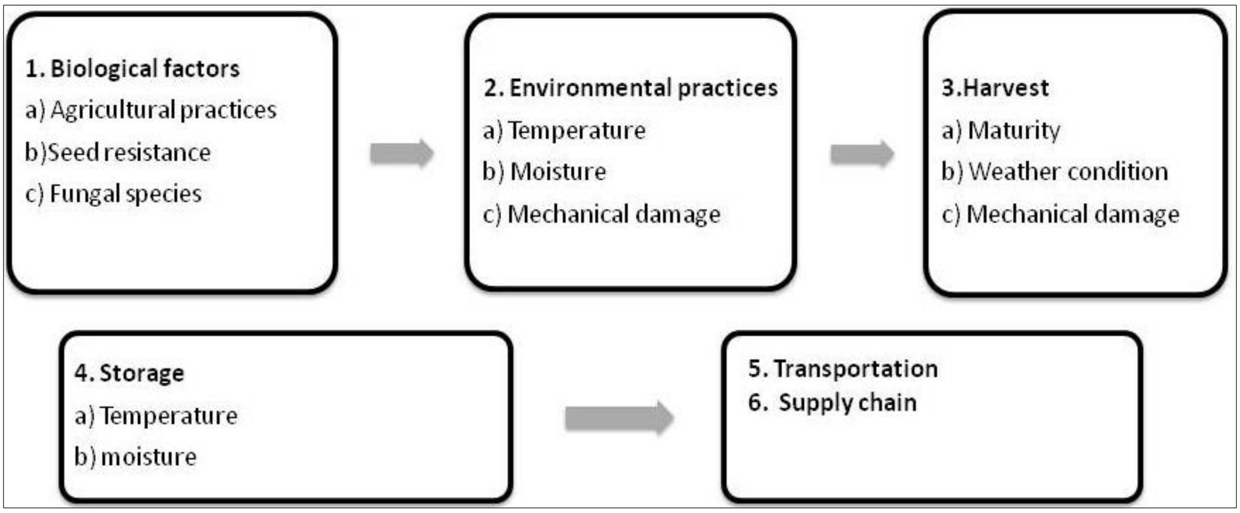

Fig 1: Contamination of cereals via different modes

There are two types of spoilage occurred by molds, field and storage molds. Field molds are usually found before harvest and storage molds are found after harvest (Storing, drying, supplying). Molds cause changes in the cereals such as discoloration, blemish, and blights, such changes are unacceptable for consumption and lead to loss (Table 1 and Fig 1). Different types of molds affect the cereals mainly, *Aspergillus*, *Penicillium*, *Alternaria*, *Mucor*, *Cladosporium*, *Fusarium*, and *Rhizopus* [13]. *Alternaria*, *Fusarium*, *Helminthosporium*, and *Cladosporium* are the most common molds that infest wheat [14].

Aspergillus, *Alternaria*, and *Fusarium* are the most common mold genera that produce mycotoxins before and after harvesting. Under ideal growing conditions, mycotoxins can be created at any point during the processing or storage of cereal crops. *Aspergillus*, *Penicillium*, and *Fusarium* are the mold genera that produce mycotoxins. *Aspergillus*, *Alternaria*, and *Fusarium* are the most common mold genera that produce mycotoxins before harvest (Table 1). Molds produce dangerous secondary compounds called Mycotoxins [12, 14]. Under ideal growing conditions, mycotoxins can be created at any point during the processing or storage of cereal crops. *Aspergillus*, *Penicillium*, and *Fusarium* are the mold genera that produce Mycotoxins [13].

The most common fungus detected in the storage environment is *xerophilic Aspergillus*, *Eurotium*, and *Penicillium* [16]. Storage fungus can grow on kernels with a moisture content of 13–15% (aw 0.70). Storage fungi are commonly found in the dust and air of the storage environment, as well as in various farm environments [16]. Mycotoxin production is a species or strain-specific trait, and a toxigenic fungus may usually create many toxins. Furthermore, numerous distinct poisons are frequently present in contaminated raw materials, and their synergistic effects are poorly known

Table 1: Mycotoxins or diseases caused by major bacterial and fungal species in different food grains

Crops	Diseases or mycotoxins	Bacterial and fungal species
Wheat	Bacterial leaf stalk	*Xanthomonas translucens*
Wheat	basal glume rot	*Pseudomonas syringae*
Rice	Rice seed rot	*Fusarium, Pythium*
Rice	Blast fungus	*Magnaporthe oryzae*
Maize	Bipolaris Leaf Spot	*Bipolaris setariae* (Saw.) Shoem
Maize	Aflatoxins B1 (AFB1), AFB2 AFB1, AFB2 AFG1, AFG2	*Aspergillus flavus, Aspergillus paracitus*
Cereals	Ochratoxin A (OTA)	*Aspergillus carbonarius, Penicillium verrucosum*
Maize	A-type trichothecenes T-2 and HT-2, diacetoxyscirpenol (DAS)	*F. acuminatum, F. langsethiae, Fusarium poae, F. sambucinum, F. sporotrichoides*
Maize	B-type trichothecenes, deoxynivalenol, nivalenol (NIV)	*F. cerealis, F. culmorum, F. graminearum, F. poae*
Maize	Fumonisin B1 (FB1)	*F. verticillioides, F. proliferatum, F.nygamai*

5. Contamination due to bacteria

Bacteria can degrade grains with a high fat and water content, such as peanuts, walnuts, nuts, and nut products. The most common spoilage associated with the bacteria is Bacillaceae, Micrococcaceae, Lactobacillaceae, and Pseudomonadaceae. The bacterial species that often grow on grain are generally non-pathogenic, yet infection with bacterial pathogens like *Salmonella* and *Escherichia coli* can be harmful. It is possible that it was polluted by birds or rodents [17]. *Bacillus* species are the most prone to cause difficulties in the manufacturing process later in the supply chain.

Many of the bacterial human pathogens present are environmental pollutants; however fecal organism numbers are modest unless animal feces were employed as an organic fertilizer during production. Except in the case of very damp grain, where bacteria are highly active during the final stages of moist grain heating, bacteria play a minor role in grain rotting. When grain is stored with too much moisture or becomes wet during storage, there is a chance of heat accumulation in the grains. A series of fungi may then develop, creating metabolic heat and water, allowing thermophilic bacteria to flourish. Due to the minimal water activity in dry grain, bacteria are unable to proliferate (aw) and remain in food flours after milling [12].

6. Health effects

Fungi are extremely common microorganisms that can be found all over the planet. Fungi spread in the air as spores, mycelia, and hyphal fragments. When inhaled, such particulates are thought to contribute to negative health impacts in people who are prone to disease. Individuals who develop specific IgE to fungal antigens, those with respiratory diseases prone to the irritating effects of exposure, and immunocompromised patients susceptible to infections are examples of such people [18]. Concerns regarding human exposure to microorganisms in indoor spaces have been focused on fungi for several years. Because it is now understood that exposure to fungal agents is associated with a wide spectrum of unfavorable health effects with a considerable impact on public health, interest in bioaerosol exposure has expanded significantly [19]. Due to their severe effects on human health and their presence in food, around a dozen mycotoxins have gotten the most attention out of the hundreds that have been discovered so far.

Fig 2: Impact of Mycotoxins on different food grains and their health effects

7. Major fungal species and their effects

Aflatoxin

Aflatoxins are produced by specific molds (*Aspergillus flavus* and *Aspergillus parasiticus*) that thrive in soil, rotting plants, hay, and cereals, and are among the most toxic mycotoxins [12]. Cereals (corn, sorghum, wheat, and rice), oilseeds (soybean, peanut, sunflower, and cotton seeds), spices (chilli peppers, black pepper, coriander, turmeric, and ginger), and tree nuts are all susceptible to *Aspergillus* spp (pistachio, almond, walnut, coconut and Brazil nut). In the form of aflatoxin M1, the poisons can also be identified in the milk of animals fed contaminated grain. Large amounts of aflatoxins can cause acute poisoning (aflatoxicosis) and can be fatal, usually due to liver damage [10, 12].

Aflatoxins have also been found to be genotoxic, which means they can harm DNA *A. flavus* and *A. parasiticus* produce aflatoxin B1 (AFB1) and aflatoxin B2 (AFB2), with AFB1 being the most toxic of all aflatoxins [20]. Aflatoxin M1 (AFM1) is detected in *a. parasiticus* fermentation broth and aflatoxin M2 is also produced when AFB1 and AFB2 are metabolized by an infected liver. AFM1 can be spread through milk [21]. Due to the consumption of these toxic metabolites may lead to Fever, malaise, and anorexia are the first indications of Aflatoxin-induced liver toxicity, followed by abdominal discomfort, vomiting, and hepatitis; nonetheless, cases of acute poisoning are uncommon and rare (Fig 2). Aflatoxins impair the effectiveness of immunization in children, increasing the risk of infection [22, 23].

Fusarium

The term *Fusarium* was coined by Link in 1809 to describe a genus of plant pathogenic fungi that can harm plants, animals, and people [24]. *Fusarium* species are noted for their diversity of connections with both live and dead plants and animals, as well as their abundance in nature [25]. Different *Fusarium* species have been isolated and characterized from different food sources among all *Fusarium oxysporum*, *Fusarium verticillioides, Fusarium sporotrichioides, and Fusarium graminearum* are one of the major foodborne pathogens

Fusarium oxysporum

On typical media like potato dextrose agar, *Fusarium oxysporum* forms a white, pale blue, purple, or light orange mycelial colony. In sporodochia, slightly arched macroconidia with 1 to 4 septa are most common, whereas unicellular, colorless, and round microconidia are generated on short conidiophores branching from the mycelium in a false-headed fashion [26, 27]. Mycelial cells and/or some macroconidial cells thicken their cell walls to create chlamydospores, which are long-lasting and can persist in soil for decades [28]. Major health effects of *Fusarium* toxins include Panama disease, caused by the fungus *F. oxysporum* f. sp. cubense, which is one of the most damaging diseases to banana plants, affecting production all over the world. *F. oxysporum* f. sp. *batatas* is the causal agent of sweet potato wilt disease. *F. oxysporum* f. sp. pisi, the pathogen that causes pea wilt, is a well-known seed-borne disease that is mostly found in North America, Europe, Australia, and New Zealand [29].

Fusarium oxysporum and *Fusarium* moniliforme are two types of *Fusarium*. The respiratory tract, gastrointestinal tract, and dermal areas are all possible entrance points for disseminated infection (Fig 2). Because cutaneous lesions can be seen at an early stage of the disease and in roughly seventy-five instances of disseminated *Fusarium* infection, the skin can be a crucial and early hint to diagnosis. Painful red or violaceous nodules, which commonly become ulcerated and covered by a black eschar, are common skin lesions [10, 17, 30].

Fusarium verticillioides

Fusarium verticillioides is widely distributed throughout the world and is particularly associated with maize where it can cause stalk rot and cob rot that results in significant yield losses and reductions in grain quality [31]. *F. verticillioides* produces the characteristic long chains of microconidia but small aggregates of few spores occur occasionally. It may be 1 or 2 celled, oval to club-shaped with a flattened base. The number of macroconidia produced increases if strains are grown on media with maltose or soluble starch as a carbon source. Macroconidia are several celled, long, slender slightly falcate, or straight and thin-walled. Apically curved and tapered to a point, basally it is notched or foo shaped. It consists of 3 to 5 septate. Chlamydospores are round, 1 or 2-celled, thick-walled spores produced terminally or intercalary on older mycelium, sometimes they may not be produced [32].

The mortality rate for human patients with systemic *Fusarium* infections is >70% [33] and HIV- infected patients are susceptible to such *Fusarium* infections. *Fusarium* species produce an intriguing array of secondary metabolites that are associated with plant disease, as well as with cancer and other growth defects in humans and domesticated animals [24]. Mycotoxins produced by some of these fungi are also used as biological weapons [34, 35].

F. verticilloides is known to be allergic to humans [36] and to be capable of systematically infecting cancer [37]. The most common human health problem associated with *F. verticillioides* is skin lesions [38, 39], wounds [40, 41] keratitis [42], and Polycystic kidney disease (PKD) and is not associated with hospital settings, but nosocomial outbreaks of diseases attributable to this fungus do occur (Fig 2) [43]. *F. verticillioides* is resistant to most clinical antifungals like itraconazole, miconazole, amphotericin B [44], and flucytosine [45] reported as the most effective. *F. verticillioides* also causes direct disease in some animals like edema in pigs and freshwater fish [46].

Fusarium sporotrichioides

Fusarium sporotrichioides is a fungal plant disease that is one of several *Fusarium* species that cause crop damage, most notably *Fusarium* head blight in wheat, and is thus of significant agricultural and economic importance [47]. Ecologically, the species is widespread, occurring in both tropical and temperate climates. Although *F. sporotrichioides* primarily infects crops, mycotoxins produced by the fungus can harm humans if infected cereals are consumed. One such example is the outbreak of alimentary toxic aleukia (ATA) in Russia, which was thought to be caused by an *F. sporotrichioides*-infected crop [48].

In northern temperate areas, *Fusarium sporotrichioides* can be found in cereals. T-2 toxins and additional metabolites are produced by this species, including diacetoxyscirpenol, which is also produced naturally but is not included in this monograph a type-A tricothecenes are T-2 toxins [49]. Early growth of *Fusarium sporotrichioides* is normally white, but later growth might be yellow, brownish, red, pink, or purple [50]. Although other species such as *F. poae* and *F. avenaceum* are normally more numerous in these locations, *F. sporotrichioides* is one of the most common causal agents of head blight throughout Scandinavia, as well as Eastern and Northern Europe. Wheat infection by *Fusarium* species is linked to favorable temperature and humidity conditions, with higher humidity being more permissive to infection, especially during the blooming period, or anthesis, of wheat [47].

The main impacts of *Fusarium* toxins on humans include an illness known as alimentary toxic aleukia, which was initially discovered in Siberia in the old Soviet Union and is thought to be caused by eating T-2 toxin-contaminated grain. Aleukia commonly manifests itself in four stages: Hyperaemia of the oral mucosa develops in the first stage, which is followed by weakness, fever, nausea, and vomiting. The high temperature persists in more severe cases, along with acute oesophagitis, gastritis, and gastroenteritis. Circulatory failure and seizures might occur in rare circumstances. Leukopenia, granulopenia, and increasing lymphocytosis occur in the second stage (Fig 2). Severe hemorrhagic diathesis, severe necrotic pharyngitis, and laryngitis characterize the third stage, which can lead to death in some cases due to total laryngitis closure [51].

Fusarium graminearum

For many years, *F. graminearum* has been the focus of intense research to better understand the genetic basis of its life cycle, pathogenicity, evolution, and population biology as a result of its devastating effects [52]. Environmental factors, particularly temperature and moisture, influence the spread and severity of *Fusarium graminearum*-causes *Fusarium* head blight [53]. *Fusarium* head blight, root rot, and foot rot (crown rot) are diseases that cause significant yield losses in a range of crops around the world, including wheat, maize, oat (*Avena sativa* L.), barley (*Hordeum vulgare* L.), and rice (*Hordeum vulgare* L.) [9, 26, 54].

The ascomycete fungal pathogen *Fusarium graminearum* causes *Fusarium* head blight in wheat and barley (teleomorph stage: Gibberella Zeae). This sickness causes major losses in agricultural productivity and, more crucially, quality due to the contamination of several fungal mycotoxins, which constitute a serious threat to human and animal health [55]. The fungus that generates tricothecenes is *Fusarium graminearum*.

The toxicity of trichothecenes is due to the presence of an epoxide at the C12, and C13 sites (The principal mycotoxins that induce toxicity in people and animals via oral intake are T-2 toxin (Type A) and DON (Type B) [55]. The high frequency of ZEA (Zearalenone) co-occurrence with FBs and DON suggests that these mycotoxins are involved in a variety of synergistic and additive interactions. Scabby grain toxicosis has been related to ZEA in Japan, China, Australia, and the United States, with symptoms including nausea, vomiting, and diarrhea [56]. The effects of ZEA on the reproductive system have been discovered in toxicological investigations, including an enlarged uterus, changed reproductive tract, decreased fertility, and aberrant levels of progesterone and estradiol. Furthermore, consuming ZEA during pregnancy decreased fetal weight and the survival percentage of embryos [57]. ZEA is a non-steroidal estrogenic mycotoxin that has been linked to reproductive problems in agricultural animals (swine, cattle, and sheep), as well as hypoestrogenic syndromes in humans (Fig 2) [58].

8. Conclusion

Grain contamination can come from a variety of sources, including air, dust, soil, water, insects, rodents, birds, animals, bacteria, humans, storage and transportation containers, as well as handling and processing equipment. The majority of contamination is microbial, but heavy metals and industrial pollutants also play a role. Mycotoxins are among the most hazardous pollutants found in a variety of foods, especially in cereals. Toxins, when utilized along with feed, these mycotoxins will be hazardous to people as well as animals. Hygienic practices and processes will avoid most mycotoxins.

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