Review

Fusarium Toxins in Chinese Wheat since the 1980s

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Abstract: Wheat Fusarium head blight (FHB), caused by Fusarium species, is a widespread and destructive fungal disease. In addition to the substantial yield and revenue losses, diseased grains are often contaminated with Fusarium mycotoxins, making them unsuitable for human consumption or use as animal feed. As a vital food and feed ingredient in China, the quality and safety of wheat and its products have gained growing attention from consumers, producers, scientists, and policymakers. This review supplies detailed data about the occurrence of Fusarium toxins and related intoxications from the 1980s to the present. Despite the serious situation of toxin contamination in wheat, the concentration of toxins in flour is usually lower than that in raw materials, and food-poisoning incidents have been considerably reduced. Much work has been conducted on every phase of toxin production and wheat circulation by scientific researchers. Regulations for maximum contamination limits have been established in recent years and play a substantial role in ensuring the stability of the national economy and people’s livelihoods.

Keywords: China; wheat; Fusarium species; mycotoxicoses; Fusarium toxins; toxin management

Key Contribution: This review gives an overview of scientific data about wheat contamination with main Fusarium mycotoxins and Fusarium species in the past 40 years. Furthermore; the efforts for toxin management by the government and scientists are described.

1. Introduction

Wheat (Triticum aestivum L.), which belongs to the grass family, is widely distributed throughout the world and has a large planting area and total yield. Wheat is not only a vital nutrient-rich food source but also an important industrial raw material and animal feed component, and its distribution and use in China is similar to its global characteristics. With the adjustment of the agricultural structure, wheat has been the third largest food crop after maize and rice. According to the relevant data from the 2018 China Statistical Yearbook, wheat acreage has stabilized at 245,080 km² over the past ten years, accounting for 14.73% of cereal production in 2017. China’s total production of wheat has reached 134 million tons and has increased 22% from 2007. However, despite the increase, the deficit in the trade balance increased to a billion dollars, which means that China needs to import approximately 4.4 million tons of wheat every year; this importation makes it imperative to breed wheat for increased yield. China is the largest wheat producer, supplying 17% of the total yield globally. More importantly, China is also the largest wheat consumer and accounts for 16% of the total consumption of wheat every year [1]. Wheat flour-based products, such as steamed buns and noodles, are staple foods for more than
half of China’s population and can be traced back thousands of years. Thus, assuring the quality and safety of wheat and its products is vitally significant to the national economy and people’s livelihoods.

Like other crops, due to the influence of agricultural environments and inputs, there are various safety issues, such as heavy metals and pesticide residues, in wheat-derived products, [2,3]. According to previous studies, mycotoxins are an even greater challenge for wheat quality [4–6]. Fusarium head blight (FHB), or scab, mainly caused by members of the *Fusarium graminearum* species complex (FGSC), is a destructive fungal disease in most of the world’s major wheat-growing areas [7]. From an economic perspective, FHB seriously affects wheat yield, resulting in income reductions for farmers and a substantial financial loss to society. Recently, the impact of FHB on food safety and human health has aroused considerable public concern because the diseased grains are frequently contaminated with toxic secondary metabolites. Among these, type B trichothecenes and zearalenone (ZEN) are the most serious and prevalent toxins in China. Trichothecenes, mainly deoxynivalenol (DON), 3-acetyl-deoxynivalenol (3ADON), 15-acetyl-deoxynivalenol (15ADON), and nivalenol (NIV), can cause acute poisoning symptoms, such as vomiting and dizziness in humans and weight loss and anorexia in animals. The mechanism of action of trichothecenes is based on the inhibition of protein synthesis [8]. Additionally, DON presents immunotoxicity, cytotoxicity, teratogenicity, and carcinogenicity [9–12]. ZEN and its metabolites have strong estrogenic activities and can cause reproductive alterations [13]. ZEN is also reported to be hepatotoxic, hematotoxic, immunotoxic and genotoxic [14]. Therefore, even low levels of these toxins in raw grains can make them hazardous to human or animal health.

Concerning the possible substantial effect of toxins on the country’s economy and society, the Chinese government has made many efforts aimed at ensuring cereal safety, such as setting strict limit and rigorous analytical method standards, revising agricultural product quality security laws, and establishing national special projects for agro-product safety risk evaluations. *Fusarium* toxins are produced by *Fusarium* species in suitable environmental conditions, and once they were present, there is no effective way to completely eliminate them from food. Even so, agricultural scientists have developed physical, chemical and biological methods to interfere with *Fusarium* species infection and toxin accumulation in all phases of wheat production. The present review aims to systematically analyze the occurrence characteristics of the main *Fusarium* toxins in wheat, the varying trend in human poisoning incidents, and the utility of toxin management measures in the past 40 years to provide a reference for scientific monitoring and effective prevention and control of mycotoxin contamination in China.

### 2. Human Mycotoxicoses Caused by *Fusarium* Toxins

Wheat flour and its products have always accounted for a large proportion of the traditional Chinese diet and have a long history, especially in the north of the country. Due to the widespread occurrence and the complicated toxic effects of poisonous FHB metabolites, their presence in food should be regarded as a potential food safety hazard. Mycotoxicosis outbreaks in humans have been associated with the intake of food contaminated with these toxins and are thus a matter of great concern to consumers.

Historically, there were several reports about mycotoxicoses in humans after the consumption of scabby wheat grains, particularly in the 1980s. A total of 21 outbreaks of human intoxication occurred successively from 1984 to 1991 in the main wheat-growing provinces [15]. Some cases of scabby wheat-related food poisoning published in professional journals are listed in Table 1. The typical clinical symptoms are gastrointestinal disorders, including abdominal pain and fullness, nausea, diarrhea, vomiting, fatigue, and fever.
Table 1. Outbreaks of moldy wheat-related food-poisoning incidents in humans since the 1980s.

| Year | Region          | Consumer | Victim | Reference |
|------|-----------------|----------|--------|-----------|
| 1985 | Lingtao, Gansu  | 1549     | 1351   | [16]      |
| 1985 | Puyang, Henan   | 217      | 101    | [17]      |
| 1988 | Yulin, Guangxi  | 160      | 40     | [18,19]   |
| 1988 | Tongghatan, Jiangxi | 9    | 9      | [20]    |
| 1989 | Zigong, Sichuan | 7        | 7      | [21]      |
| 1989 | Baihe, Shanxi   | 5016     | 701    | [21]      |
| 1991 | Xincai, Henan   | 840      | 479    | [22]      |
| 1991 | Linquan, Anhui  | 93       | 67     | [23]      |
| 1991 | Fuyang, Anhui   | 354      | 263    | [24]      |
| 1991 | Xuyi, Jiangsu   | 141      | 117    | [24]      |
| 1996 | Putian, Fujian  | 3        | 2      | [25]      |
| 2000 | Kedong, Helongjiang | 6    | 6      | [26]    |
| 2003 | Dongming, Shandong | 4    | 4      | [27]      |
| 2003 | Baihe, Shanxi   | 5043     | 701    | [28]      |

In 1985, a severe FHB epidemic occurred in wheat in a suburb of Puyang County, Henan Province. A large proportion of local inhabitants showed typical symptoms including gastrointestinal disorders and nervous system disturbances after eating scabby wheat grains, and the incidence of related diseases was 45% [17]. Most of the patients returned to health after two hours of symptoms. After this incident, DON was considered the most important causative toxicant responsible for human intoxications.

After a large flood in 1991, extensive outbreaks of human toxicoses affecting a large number of people who consumed moldy wheat grains occurred in parts of Henan, Anhui, and Jiangsu provinces, as appropriate conditions, such as heavy rainfall and low temperature, for an FHB epidemic and mycotoxin production occurred after the flood [22–24]. High amounts of DON were found in food that was linked to an episode of ‘red-mold intoxication’ involving 130,000 people with acute gastrointestinal disorders in Anhui Province in 1991 [29].

In the 21st century, human poisoning caused by Fusarium toxins decreased and moved from group outbreaks to individual incidents. For example, in 2000, a whole family in Northeast China developed acute poisoning symptoms twice after eating products derived from flour from home-grown wheat [27]. The latest large-scale food safety incident reported in Northwest China was demonstrated to be associated with the consumption of flour products processed from diseased wheat grains. In 2003, of 5043 people in 10 villages who consumed contaminated foods, 701 (13.9%, no lethal cases) presented intoxication. The most common symptoms of the victims were nausea, numbness of the throat, and a burning sensation of the esophagus; symptoms disappeared within approximately 3 hours without medical attention. This human food toxicity incident happened in June and July, when large quantities of wheat grains became moldy but were still harvested despite inferior quality resulting from long-term precipitation. Other reasons for this large-scale incident were a lack of health awareness and poor traditional eating habits of the local residents [28].

In addition to acute toxicity, Fusarium toxins are associated with some human chronic diseases (Table 2). Kashin-Beck disease (KBD) is a chronic, endemic osteochondropathy that occurs mainly in the distant provinces of northeastern and northwestern China [30]. In KBD-endemic areas, wheat has been frequently infected with Fusarium species, and the disease has been suspected to be associated with the consumption of Fusarium-contaminated grains. Earlier findings by Luo et al. [31] on the level of Fusarium toxins in wheat from Shanxi and Inner Mongolia found that the prevalence rate and content of DON 3ADON, NIV, and ZEN were significantly higher in the high-risk area of KBD than in the low-risk area. It seemed that there was a dose-effect relationship between toxins contamination level and degree of KBD occurrence. In Qinghai Province, the DON content in the wheat flour samples from the KBD area was significantly higher than that of the non-KBD area, and the authors indicated that the characteristic distribution of DON contamination in wheat flour was consistent with the KBD prevalence [32]. Similar results regarding DON contamination were reported in wheat flour from Shandong and Gansu provinces [33]. However, the precise etiology of KBD was still not clearly defined, and T-2 toxin and selenium levels were implicated as important causes. Fortunately, a recent epidemiological investigation reported that the KBD prevalence decreased from 1990 to 2007 [34].
Table 2. Occurrence of *Fusarium* toxins in high KBD or cancer incidence regions.

| Year   | Regions                    | Sample Size | Toxin   | Incidence (%) | Average Content (µg/kg) | Content (µg/kg) | Reference |
|--------|----------------------------|-------------|---------|---------------|-------------------------|----------------|-----------|
| 1989   | Shannxi (KBD high incidence) | 5           | DON     | 100.0         | 514.0                   | 343.0–1051.0   | [31]      |
|        |                            |             | 3ADON   | 100.0         | 363.0                   | 15.0–731.0     |           |
|        |                            |             | NIV     | 100.0         | 183.0                   | 17.0–373.0     |           |
|        |                            |             | ZEN     | 40.0          | 15.0                    | 5.0–25.0       |           |
|        | Shannxi (KBD low incidence) | 5           | DON     | 100.0         | 184.0                   | 73.0–410.0     |           |
|        |                            |             | 3ADON   | 0             | 0                       | 0              |           |
|        |                            |             | NIV     | 60.0          | 10.0                    | 8.0–13.0       |           |
|        |                            |             | ZEN     | 0             | 0                       | 0              |           |
|        | Inner Mongolia (KBD high incidence) | 6 | DON     | 100.0         | 101.0                   | 0              |           |
|        |                            |             | 3ADON   | 50.0          | 24.0                    | 0              |           |
|        |                            |             | NIV     | 33.3          | 9.0                     | 0              |           |
|        |                            |             | ZEN     | 0             | 0                       | 0              |           |
|        | Inner Mongolia (KBD low incidence) | 7 | DON     | 100.0         | 75.0                    | 0              |           |
|        |                            |             | 3ADON   | 28.6          | 57.0                    | 0              |           |
|        |                            |             | NIV     | 0             | 0                       | 0              |           |
|        |                            |             | ZEN     | 0             | 0                       | 0              |           |
| 2010   | Qinghai (KBD high incidence) | 23          | DON     | 87.0          | 302.0                   | 0              | [32]      |
|        | Qinghai (non-KBD)          | 27          | DON     | 29.6          | 199.0                   | 0              |           |
| 2010   | Gansu (KBD high incidence)  | 20          | DON     | 75.0          | 142.8                   | 12.8–205.3     | [33]      |
|        |                            | 20          | DON     | 80.0          | 137.4                   | 28.5–180.7     |           |
|        |                            | 20          | DON     | 75.0          | 127.3                   | 20.6–176.1     |           |
| 2010   | Shandong (KBD low incidence)| 20          | DON     | 10.0          | 12.9                    | 10.2–15.6      |           |
|        |                            | 20          | DON     | 20.0          | 18.1                    | 8.9–27.3       |           |
| 1989   | Henan Linxian (esophageal cancer high risk) | 15 | DON     | 46.7          | 59.0                    | 7.0–309.0      | [35]      |
|        |                            | 15          | NIV     | 0             | 0                       | 0              |           |
| 1989   | Henan Shangqiu (esophageal cancer low risk) | 15 | DON     | 46.7          | 18.0                    | 7.0–36.0       |           |
|        |                            | 15          | NIV     | 46.7          | 15.0                    | 13.0–21.0      |           |
Table 2. Cont.

| Year | Regions                              | Sample Size | Toxin       | Incidence (%) | Average Content (µg/kg) | Content (µg/kg) | Reference |
|------|--------------------------------------|-------------|-------------|---------------|-------------------------|----------------|-----------|
| 1995 | Linxian, Henan (esophageal cancer high risk) | 25          | DON         | 92.0          | 83.0                    | 9.0–193.0      | [36,37]   |
|      |                                      |             | 15ADON      |               | 0                       | 0              |           |
|      |                                      |             | NIV         |               | 29.0                    | 13.0–50.0      |           |
|      | Henan Shangqiu (esophageal cancer low risk) | 15          | DON         | 60.0          | 40.0                    | 15.0–125.0     |           |
|      |                                      |             | 15ADON      |               | 0                       | 0              |           |
|      |                                      |             | NIV         |               | 12.0                    | 4.0–22.0       |           |
| 1997 | Linxian, Henan (esophageal cancer high risk) | 15          | DON         | 66.7          | 28.0                    | 0–138.0        |           |
|      |                                      |             | 15ADON      |               | 0                       | 0              |           |
|      |                                      |             | NIV         |               | 95.0                    | 0              |           |
|      | Henan Shangqiu (esophageal cancer low risk) | 15          | DON         | 0             | 0                       | 0              |           |
|      |                                      |             | 15ADON      |               | 0                       | 0              |           |
|      |                                      |             | NIV         |               | 0                       | 0              |           |
| 2000 | Linxian, Henan (esophageal cancer high risk) | 9           | DON         | 77.8          | 732.0                   | 0–1614.0       | [38]      |
|      |                                      |             | NIV         |               | 100.0                   | 190.0–1476.0   |           |
|      | Cixian, Hebei (esophageal cancer low risk) | 18          | DON         | 100.0         | 1031.0                  | 176.0–4280.0   |           |
|      |                                      |             | NIV         |               | 731.0                   | 102.0–2105.0   |           |
| 2010 | Shandong (esophageal cancer high risk)  | 20          | DON         | 100.0         | 195.2                   | 70.1–302.8     | [39]      |
|      |                                      |             |             |               | 100.0                   | 85.4–287.5     |           |
|      | Shandong (esophageal cancer low risk)  | 20          | DON         | 10.0          | 12.9                    | 10.2–15.6      |           |
|      |                                      |             |             |               | 20.0                    | 18.1           |           |
|      |                                      |             |             |               |                         | 18.9–27.3      |           |
During the process of researching the etiology of esophageal cancer, DON was found to be one of the predominating contaminating mycotoxins in the grains and foodstuffs in the high-incidence area in China [39]. Co-contamination of DON, 15ADON, and NIV in wheat samples from Henan Province, where cancer is highly prevalent, was studied in 1989, 1995 and 1997 [36,37]. Linxian samples showed higher levels of DON than those from Shangqiu, which has a low esophageal cancer incidence. These studies suggested that fungal contamination of foods and residents’ exposure to mycotoxins could be considered possible factors involved in the development of cancer. In a survey of Shandong samples harvested in 2010, significantly higher levels of DON were identified in all wheat samples from high-risk areas than in wheat samples from low-risk areas [38]. Hsia et al. [39] reported that NIV naturally existed at high levels in dietary food in high-risk cancer areas and suggested that people who consumed a diet with high levels of NIV had a significantly greater risk of developing esophageal cancer than those who consumed a diet with low levels of NIV. The occurrence of esophageal cancer is a result of multiple factors, including the poor eating habits (tobacco smoking and alcohol drinking), the lack of nutrients and trace elements, genetic determinants, and the intake of food containing high concentration of nitrite compounds and mycotoxins. It is speculated that the chronic consumption of cereals contaminated with mycotoxigenic Fusarium species can increase the odds of the disease, although no correlation between Fusarium toxins and esophageal cancer has been published [40]. Nonetheless, as the most important natural poisons, the threat should not be taken lightly. In general, most outbreaks of human mycotoxicoses from Fusarium toxins followed the occurrence of severe FHB. In the last few years, the damage caused by FHB has become increasingly serious; however, the incidence and the number of victims of human mycotoxicoses have followed the opposite trend. Along with the improvement in living standards, moldy grains are no longer used for food, but they can still serve as major feed components for poultry and livestock. This harm to the development of the animal husbandry industry is not mentioned here, yet it needs to be solved urgently. There are three main causes for this phenomenon. The first is the development and popularization of science and technology. Consumers have a remarkable increase in the understanding and knowledge of scabby wheat and Fusarium toxins, thus contributing to the development of good eating habits. Another reason is the improvement of Chinese living standards. People have more dietary choices and can discard diseased or low-quality cereals. The regulatory authorities for all levels of agricultural product quality and safety also play a crucial role. Moldy wheat grains have been eliminated from the market, and the quality of wheat products is under strict surveillance; thus, safe and superior quality foods are provided to consumers. All these factors reduce the risk of the occurrence of food safety incidents.

3. Toxin-Producing Fusarium Strains

The first FHB outbreak in China can be traced back to 1936; scientists began to research the pathogen of this disease approximately 20 years later [41] and found that most strains from China can produce large amounts of DON and ZEN [42,43]. Based on relevant research in recent years, F. graminearum was identified as the main pathogen of FHB in China, despite the presence of a large variety of Fusarium species isolated from diseased wheat grains. As early as the 1980s, research on FHB pathogens in 21 provincial regions in China identified 18 Fusarium species, among which F. graminearum dominated and accounted for 94.5% of the total [44]. Subsequently, similar results were obtained from studies in Henan, Fujian, Hunan, Ningxia and Qinghai provinces [45–48].
In recent years, genetic and molecular approaches have led to a new understanding that narrowly defines \textit{F. graminearum} sensu stricto (s. str.) as a species complex with significant genetic diversity, clear divergence of biological species, and an obvious geographical distribution. Currently, FGSC consists of at least 16 phylogenetically distinct species [49]. \textit{F. graminearum} s. str. is the most widely distributed species and occurs in most FHB areas around the world [50], while \textit{F. asiaticum} is the main FHB pathogen present in Asia [51,52].

FGSC species can produce several mycotoxins; type B trichothecenes are the most common toxic metabolites found in infected cereals [53]. FGSC strains usually present one of three trichothecene profiles: (i) deoxynivalenol and 3-acetyldeoxynivalenol (3ADON chemotype); (ii) deoxynivalenol and 15-acetyldeoxynivalenol (15ADON chemotype); or (iii) nivalenol and its acetylated derivatives (NIV chemotype) [54]. The chemotype composition appears to be species dependent [55]. In China, most of the \textit{F. graminearum} s. str. isolates are 15ADON producers, while \textit{F. asiaticum} isolates contain 3ADON and NIV chemotypes. Table 3 presents the trichothecene type compositions of \textit{F. graminearum} s. str. and \textit{F. asiaticum} in wheat.

In terms of geographic distribution, the vast majority of \textit{F. asiaticum} isolates have been collected from warm southern areas [56,57], and \textit{F. graminearum} s. str. is mainly distributed in cool northern regions [58,59]. The composition of the populations has been stable over time. The population structure and genetic variation in FHB pathogens have been studied in detail in Jiangsu Province, which has a long history of rice growing and a large rice-growing area that covers 30 million acres. The \textit{F. asiaticum} strain that produced 3ADON has always dominated [60,61], and no similar evidence of temporal trends in the North American wheat population or Chinese barley population has been found [62–66]. Extensive wheat-rice rotation is critical for \textit{F. asiaticum} overwintering, and perithecium production typically favors rice straw under warmer conditions. The better fitness of \textit{F. asiaticum} on rice and DON producers on wheat has led to the prevalence of 3ADON-producing \textit{F. asiaticum} in most wheat-rice rotation areas in Southern China. As a result, a 3ADON-producing \textit{F. asiaticum} population may have been present in this region for a long time, and we suggest that this might have been the main factor underlying the absence of variation in trichothecene genotype frequencies from 1976 to 2014. Recently, based on available data from the literature, we concluded that a cropping system with wheat/maize rotation selects for \textit{F. graminearum}, while a wheat/rice rotation selects for \textit{F. asiaticum} [67].

Due to the promotion and application of straw-returning methods, more perithecia form and more ascospores are released in the subsequent year. Crop debris in the field feeds and increases the amount of primary FHB inoculum. Climatic or agricultural conditions favor wheat infection by \textit{Fusarium}, which eventually leads to higher levels of toxins in wheat. A dominant FHB population means that the main toxins have been substantially retained over a long period of time, and the quantity of FHB pathogens is likely to continually increase. Based on this phenomenon, it can be assumed that the epidemic risk of FHB and harmful levels of \textit{Fusarium} toxins could continue to increase for a long time in the future.
Table 3. The ratio of *F. graminearum* and *F. asiaticum* strains with varied chemotypes in partial studies in China.

| Year         | Region | Sample Sizes | Fg15ADON | Fg3ADON | FgNIV | Fa3ADON | FaNIV | Fa15ADON | Reference |
|--------------|--------|--------------|----------|---------|-------|---------|-------|----------|-----------|
| 1975–1980    | China  | 2450         |          | 94.5%   |        |         |       |          | [44]      |
| 1975–1981    | Hunan  | 185          |          | 97.2%   |        |         |       |          | [45]      |
| 1978–1981    | Fujian | 1081         |          | 99.1%   |        |         |       |          | [46]      |
| 1985         | Henan  | 241          |          | 98.0%   |        |         |       |          | [47]      |
| 1985–1987    | Ningxia| 350          |          | 63.8%   |        |         |       |          | [48]      |
| 1991–1992    | Qinghai| 27           |          | 56.5%   |        |         |       |          | [68]      |
| 1993–1995    | Qinghai| 1005         |          | 54.3%   |        |         |       |          | [69]      |
| 1999         | China  | 299          | 22.7%    |         | 51.8% | 17.7%   | 7.7%  |          | [55]      |
| 2000         | Zhejiang| 208         |          |         | 42.3% | 57.7%   |       |          | [56]      |
| 2007–2014    | Henan  | 327          | 89.0%    |         | 6.7%  | 0.9%    | 0.3%  |          | [70]      |
| 2008         | China  | 444          | 38.1%    |         | 38.5% | 21.9%   | 1.6%  |          | [71]      |
|              | Sichuan| 90           | 6.7%     | 3.3%    | 3.3%  | 25.56%  | 52.2% |          |           |
|              | Chongqing| 6          |          |         |       |         |       |          |           |
|              | Hubei  | 201          | 12.4%    | 8.0%    | 0.5%  | 58.7%   | 4.5%  | 10.5%    |           |
|              | Henan  | 25           | 100.0%   |         |       |         |       |          |           |
|              | Anhui  | 42           | 45.2%    | 7.1%    | 4.8%  | 35.7%   | 7.1%  |          |           |
|              | Jiangsu| 69           | 15.9%    | 10.1%   |       | 63.8%   | 10.1% |          |           |
| 2008–2010    | Jiangsu| 292          | 5.5%     |         |       | 84.6%   | 9.9%  |          |           |
|              | Anhui  | 71           | 21.1%    |         |       | 59.2%   | 19.7% |          |           |
|              | Henan  | 88           | 89.8%    |         |       | 8.0%    | 2.3%  |          |           |
|              | Hebei  | 23           | 100.0%   |         |       |         |       |          |           |
|              | Shandong| 31          | 83.8%    |         |       | 12.9%   | 3.2%  |          |           |
|              | Hubei  | 25           | 92.0%    |         |       |         |       | 8.0%     |           |
Table 3. Cont.

| Year     | Region          | Sample Sizes | Fg15ADON | Fg3ADON | FgNIV | Fa3ADON | FaNIV | Fa15ADON | Reference |
|----------|----------------|--------------|----------|---------|-------|---------|-------|----------|-----------|
| 2008     | Fujian         | 59           |          | 76.0%   | 24.0% |         |       |          | [57]      |
| 2009     |                | 100          | 4.0%     | 81.0%   | 15.0% |         |       |          |           |
| 2009     | Hubei          | 168          | 9.5%     | 69.6%   | 6.6%  | 7.7%    |       |          | [74]      |
| 2011–2012| Shandong       | 95           | 94.7%    | 4.4%    | 1.1%  |         |       |          | [75]      |
| 2011     | Jiangsu/Anhui  | 350          | 4.0%     | 82.9%   | 4.3%  | 4.9%    |       |          | [60]      |
| 2012     | Jiangsu/Anhui  | 541          | 8.7%     | 1.5%    | 75.1% | 9.4%    | 5.4%  |          |           |
| 2013     | Northeast China| 118          | 64.4%    |         |       |         |       |          | [58]      |
| 2014     | Sichuan        | 103          | 18.5%    | 7.8%    | 71.8% | 1.0%    |       |          | [67]      |
|          | Hubei          | 57           |          | 87.7%   | 7.0%  | 5.3%    |       |          |           |
|          | Anhui          | 93           | 1.1%     | 87.1%   | 10.8% | 1.1%    |       |          |           |
|          | Jiangsu        | 67           | 3.0%     | 89.6%   | 7.5%  |         |       |          |           |
|          | Fujian         | 217          | 2.8%     | 10.6%   | 67.7% | 18.9%   |       |          |           |
| 2014–2015| Shandong       | 120          | 84.2%    | 4.2%    | 1.7%  | 10.0%   |       |          | [76]      |
| 2016     | Northeast China| 84           | 44.1%    | 3.6%    | 1.2%  | 4.8%    | 22.6% |          | [59]      |
4. Natural Occurrence of *Fusarium* Toxins in Wheat

China is a traditional agricultural country, and wheat is an important food ingredient. FHB severity has exhibited an increasing trend; therefore, the investigation of and surveillance for *Fusarium* toxins in wheat and its products are of great significance. Tables 4 and 5 show the main *Fusarium* toxins in wheat grains and wheat flour, respectively.

*Fusarium* toxin contamination shows various regional differences. The mean content and standard-exceeded rate of toxin was the highest in wheat and flour samples from Anhui and Jiangsu provinces, where FHB occurred severely and frequently. During the wheat heading and flowering period, a high temperature and humidity environment in the middle and lower reaches of the Yangtze River provided favorable conditions for the propagation of *Fusarium*, the occurrence of the disease and the accumulation of toxins. Although recent trends have indicated that FHB is spreading towards Northeast and Northwest China, the wheat quality in these regions is high. For example, a minimal incidence and concentration of DON and ZEN was detected in wheat from Heilongjiang [59]. A recent study reported the prevalence and concentration of DON in wheat harvested during 2013 from the northwest regions of China, suggesting varied and low levels of DON contamination in the region [77]. Especially in Xinjiang and Tibet, the safety quality of wheat and flour is in good condition [77–79]. These findings suggest that cold or drought environment conditions might be unfavorable for toxin production. Even so, some limitations, such as small sample sizes and deficient research, cannot be ignored.

*Fusarium* toxin contamination shows clear temporal dynamics; the epidemiologic degree of FHB has a clear relationship with the toxin contamination level. The occurrences of *Fusarium* toxins were studied in detail in Jiangsu, Anhui, and Henan provinces over a long period of time, and there was high concentration of *Fusarium* toxins over the standard rate in 1985, 1989, 1991, 2010, 2012, and 2015. This is an interesting discovery, as these unusual years were reported to have massive outbreaks of FHB, except for 1991, in which a large flood occurred. In 1985, Henan Province had the worst outbreak in 40 years; almost all the wheat grains were contaminated with DON, NIV, and ZEN in high amounts. The contamination rate for samples containing toxins higher than the tolerance limit of 1000 µg/kg was close to 50%, and the highest number of DON-positive samples reached 40,000.0 µg/kg [80]. In flour samples derived from wheat collected in 1989, the frequency of DON detection approached 100%, and the average DON content was 1334.0 and 577.7 µg/kg in Anhui and Jiangsu, respectively [81,82]. There was an exceedingly high rate (81.5%) of corresponding contamination in wheat, with a maximum concentration of 13,300.0 µg/kg [83]. In the last decade, the FHB epidemic has become more frequent and severe; moreover, toxin contamination, particularly by DON, is more common and serious. In 2010, 2012, and 2015, the average amounts of DON in Anhui wheat samples were 2701.0, 4501.6, and 17,753.8 µg/kg, respectively [84–86]. The amounts in Jiangsu wheat samples in the corresponding years were >1000.0, >3000.0, and >2000.0 µg/kg, respectively [85,87–89]. FHB outbreaks aggravate toxin contamination despite the inconspicuous effect on ZEN accumulation.

Recently, masked DON, a derivative of DON, has become a focus of attention for in-depth research. D3G (deoxynivalenol-3-glucoside) is a primary type of masked DON and is the most studied. D3G was for the first time detected in naturally contaminated maize and wheat in 2005 [90]. Until now, the toxicological research about D3G is rare. As the protein synthesis inhibitor, the activity of D3G was much lower than that of DON [91]. Although there was no direct evidence that D3G was more toxic than its precursor, the existing research data showed that D3G could release DON by a hydrolysis reaction in the metabolic process [92–94]. Similar studies have raised concerns about the metabolites of D3G in humans or animals and the occurrence of this toxin in wheat grains and their products. A total of 192 wheat samples from 2007–2008 collected in 7 provinces were analyzed for D3G accumulation, and the toxin was found in 52.0% wheat samples with an average content of 43.0 µg/kg [95]. In a recent study, high incidence rates and levels of D3G were detected in wheat samples from Jiangsu and Anhui provinces in 2015–2016. A total of 96.3% of wheat from Jiangsu was positive for D3G, with contamination rates ranging from 12.0 to 18061.0 µg/kg [89], while 99.5% of wheat from...
Anhui was contaminated by D3G, with contamination rates ranging from 28.3 to 2957.2 µg/kg [86]. The detection rate of D3G in wheat flour was to a certain degree, but the contamination level was obviously reduced. D3G was detected in 104/125 flour samples from 12 provinces (0.1–52.8 µg/kg) [96] and 38/158 wheat flour samples from 5 provinces (8.7–33.3 µg/kg) [97]. In 2010, 33.4% of Shandong wheat flour samples, 30.8% of Hubei wheat flour samples, and 5.46% of Hebei wheat flour samples contained D3G with average contamination rates of 1.1, <20.0, and 1.9 µg/kg, respectively [98–100]. During wheat processing, D3G was transferred to prepared products, such as bread and noodles, and caused toxic effects by producing DON after contact with intestinal digestive enzymes [101]. Thus, the fact that masked Fusarium toxins are also a potential risk to human health cannot be ignored.

From several national surveys, it was reported that multitoxin, mainly DON and ZEN, were widespread and severe in Chinese wheat grains, especially in the past decade. Although the overall contamination situation varied significantly in different years, wheat quality safety conditions increased in severity with the prevalence of FHB. The detection rate of Fusarium toxins in wheat flour remains at a certain level; nevertheless, most flour samples have toxin levels below Chinese regulatory limits and those of wheat grains. During wheat cleaning and flour milling, proper processing removes some toxins and is an effective measure in reducing toxin contamination. Considering the frequency and degree of the FHB epidemic, prolonged, successive, and extensive monitoring of Fusarium toxins in wheat and its products is essential for ensuring food safety and promoting human health.
Table 4. Recent mycotoxin survey data in wheat grains in China.

| Year | Regions | Sample Sizes | Toxins | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|------|---------|--------------|--------|---------------|------------------------|--------------|---------------------|-----------|
| 1983 | Anhui   | 40           | DON    | 100.0         | 1161.4                 | 22.5         |                     | [83]      |
| 1986 | Anhui   | 182          | DON    | 44.5          | 312.9                  | 7.1          |                     |           |
| 1989 | Anhui   | 81           | DON    | 100.0         | 2640.0                 | 0–13,300.0   | 81.5                |           |
| 1991 | Anhui   | 26           | DON    | 100.0         | 2105.8                 | 57.7         |                     |           |
| 1986 | Anhui   | 150          | DON    | 53.3          | 340.0                  | 0–4000.0     |                     | [102]     |
| 1991 | Anhui   | 83           | ZEN    | 22.9          | 32.0                   | 0–300.0      |                     | [22]      |
| 2007–2008 | Anhui | 25          | 3ADON  | 44.0          | 6.3                    | 1.8–18.4     |                     | [95]      |
|      |         |              | D3G    | 64.0          | 45.5                   | 2.2–238.4    |                     |           |
|      |         |              | NIV    | 72.0          | 53.3                   | 1.8–229.9    |                     |           |
|      |         |              | 15ADON | 12.0          | 2.6                    | 2.3–3.0      |                     |           |
|      |         |              | DON    | 100.0         | 46.5                   | 3.7–169.3    | 0                   |           |
|      |         |              | ZEN    | 20.0          | 12.9                   | 3.3–36.1     | 0                   |           |
| 2010 | Anhui   | 21           | DON    | 90.5          | 2701.0                 | 521.0–4975.0 | 81.0                | [84]      |
| 2012 | Anhui   | 22           | DON    | 95.4          | 4501.6                 | 465.0–9930.0 |                     | [85]      |
| 2015 | Anhui   | 370          | DON    | 100.0         | 17,753.8               | 109.6–86,255.1 |                  | [86]      |
|      |         |              | D3G    | 99.5          | 414.4                  | 28.3–2957.2  |                     |           |
|      |         |              | NIV    | 87.8          | 250.2                  | 0–2399.7     |                     |           |
|      |         |              | 3ADON  | 80.0          | 39.6                   | 0–284.1      |                     |           |
|      |         |              | 15ADON | 67.3          | 13.2                   | 0–184.7      |                     |           |
|      |         |              | ZEN    | 68.7          | 25.7                   | 0–1091.4     | 5.1                 |           |
Table 4. Cont.

| Year     | Regions | Sample Sizes | Toxins | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|----------|---------|--------------|--------|---------------|-------------------------|--------------|---------------------|-----------|
| 1986     | Jiangsu | 202          | DON    | 26.7          | 40.0                    | 0–400.0      | 0                   | [83]      |
|          |         | 54           | ZEN    | 64.8          | 51.0                    | 0–300.0      |                     |           |
| 1991     | Jiangsu | 7            | DON    | 71.4          | 2900.0                  | 1560.0–5000.0|                     | [23]      |
| 2007–2008| Jiangsu | 24           |        |               |                         | D3G 62.5     | 59.5 1.7–179        | [95]      |
|          |         |              |        |               |                         | NIV 29.2     | 12.4 1.9–29.5       |           |
|          |         |              |        |               |                         | 3ADON 29.2   | 5.5 2.1–11.3        |           |
|          |         |              |        |               |                         | 15ADON 4.2   | 2.4 0–2.4           |           |
|          |         |              |        |               |                         | DON 95.8     | 73.0 2.8–408.3      | 0         |
|          |         |              |        |               |                         | ZEN 16.7     | 3.9 1.7–6.6         | 0         |
| 2010     | Jiangsu | 35           | DON    | 88.6          | 1221.0                  | 259.0–3900.0| 51.4                | [84]      |
| 2010     |         | 41           | DON    | 100.0         | 1075.2                  | 151.6–2550.2| 44.0                |           |
|          |         |              | ZEN    | 46.3          | 216.0                   | 10.1–3048.9 | 9.8                 |           |
| 2011     | Jiangsu | 64           | DON    | 32.8          | 82.1                    | 14.5–1579.8 | 3.1                 | [87]      |
|          |         |              | ZEN    | 0             | 0                       | 0           | 0                   |           |
| 2012     |         | 75           | DON    | 96.0          | 306.7                   | 16.3–41157.1| 48.0                |           |
|          |         |              | ZEN    | 5.3           | 3.2                     | 50.2–72.6   | 2.6                 |           |
| 2012     | Jiangsu | 62           | DON    | 95.1          | 3260.9                  | 260.0–11,200.0| 51.4                | [85]      |
| 2013     |         | 66           | ZEN    | 37.9          | 11.8                    | 6.5–110.0   |                     | [88]      |
| 2014     | Jiangsu | 66           | ZEN    | 46.9          | 22.0                    | 15.0–194.3  |                     |           |
| 2015     |         | 70           | ZEN    | 54.3          | 39.3                    | 25.1–307.3  |                     |           |
| 2015     | Jiangsu | 443          | DON    | 100.0         | 2087.0                  | 166.0–14,960.0|                   | [89]      |
|          |         |              | D3G    | 96.0          | 545.0                   | 83.0–5092.0 |                     |           |
| 2016     |         | 439          | DON    | 100.0         | 2601.0                  | 12.0–18,061.0|                   |           |
|          |         |              | D3G    | 97.0          | 819.0                   | 0–6708.0    |                     |           |
Table 4. Cont.

| Year | Regions | Sample Sizes | Toxins | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|------|---------|--------------|--------|---------------|-------------------------|--------------|---------------------|-----------|
| 1985 | Henan   | 19           | DON    | 100.0         | 17,500.0                | 1.0–40,000.0 | 100.0               | [17]      |
|      |         |              | ZEN    | 10.5          | 375.0                   | 250.0–500.0  | 10.5                |           |
| 1985 | Henan   | 191          | DON    | 99.0          | 923.0                   | 15.9–3337.8  | 47.1                |           |
|      |         |              | NIV    | 81.0          | 128.2                   | 12.5–608.6   |                     | [80]      |
|      |         |              | ZEN    | 100.0         | 15.3                    | 3.3–149.9    |                     |           |
| 1986 | Henan   | 100          | DON    | 74.0          | 14.2                    | 6.7–175.4    | 0                   |           |
|      |         |              | NIV    | 4.0           | 9.5–49.0                |             |                     |           |
| 1986 | Henan   | 97           | DON    | 57.7          | 40.0                    | 0–400.0      | 0                   | [102]     |
|      |         |              | ZEN    | 11.7          | 8.0                     | 0–50.0       |                     |           |
| 1991 | Henan   | 35           | DON    | 100.0         | 1500.0                  | 1000.0–3500.0| 100.0               | [23]      |
| 1991 | Henan   | 24           | DON    | 96.8          | 2850.0                  | 177.0–14,000.0|                     | [103]     |
|      |         |              | 15ADON | 64.5          | 365.0                   | 59.0–1800.0  |                     |           |
|      |         |              | NIV    | 3.2           | 578.0                   | 0–578.0      |                     |           |
|      |         |              | ZEN    | 67.7          | 209.0                   | 9.0–1400.0   |                     |           |
| 1998 | Henan   | 31           | DON    | 89.3          | 223.0                   | 53.0–1240.0  |                     | [29]      |
|      |         |              | 15ADON | 0            | 0                       | 0            |                     |           |
|      |         |              | NIV    | 0            | 0                       | 0            |                     |           |
|      |         |              | ZEN    | 25.0          | 108.0                   | 1.0–217.0    |                     |           |
| 1999 | Henan   | 28           | DON    | 85.3          | 294.0                   | 74.0–941.0   | 0                   |           |
|      |         |              | 15ADON | 0            | 0                       | 0            |                     |           |
|      |         |              | NIV    | 0            | 0                       | 0            |                     |           |
|      |         |              | ZEN    | 58.8          | 23.0                    | 5.0–113.0    |                     |           |
| Year          | Regions | Sample Sizes | Toxins | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|--------------|---------|--------------|--------|---------------|-------------------------|--------------|---------------------|-----------|
| 2007–2008    | Henan   | 28           | D3G    | 75.0          | 24.6                    | 2.8–171.1    | 0                   | [95]      |
|              |         |              | NIV    | 0             | 0                       | 0            | 0                   |           |
|              |         |              | 3ADON  | 14.3          | 3.6                     | 0–4.9        | 0                   |           |
|              |         |              | 15ADON | 46.4          | 4.1                     | 0–17.7       | 0                   |           |
|              |         |              | DON    | 100.0         | 74.6                    | 2.9–363.6    | 0                   |           |
|              |         |              | ZEN    | 17.9          | 3.3                     | 0–8.1        | 0                   |           |
| 1986         | Shanghai| 100          | DON    | 100.0         | 340.0                   | 0–2000.0     | 0                   | [102]     |
|              |         |              | ZEN    | 33.0          | 11.0                    | 0–780.0      | 0                   |           |
| 1995         | Shanghai| 100          | DON    | 53.0          | 280.9                   | 0–1919.7     | 10.0                | [104]     |
|              |         |              | NIV    | 35.0          | 103.4                   | 0–1428.0     | 0                   |           |
| 2009–2012    | Shanghai| 198          | DON    | 80.8          | 64.7                    | 0.5–604.0    | 0                   | [105]     |
| 2011–2012    | Shanghai| 38           | 3ADON  | 100.0         | 10.3                    | 0.7–35.2     | 0                   |           |
|              |         |              | 15-DON | 100.0         | 1.4                     | 0.5–6.2      | 0                   |           |
| 2007–2008    | Hebei   | 25           | D3G    | 60.0          | 88.9                    | 5.6–388.0    | 0                   | [95]      |
|              |         |              | NIV    | 24.0          | 12.3                    | 1.8–57.5     | 0                   |           |
|              |         |              | 3ADON  | 48.0          | 12.5                    | 1.6–70.8     | 0                   |           |
|              |         |              | 15ADON | 88.0          | 236.1                   | 1.5–1256.2   | 0                   |           |
|              |         |              | DON    | 80.0          | 167.3                   | 1.7–636.2    | 0                   |           |
|              |         |              | ZEN    | 56.0          | 126.1                   | 4.7–930.4    | 0                   |           |
| 1986         | Gansu   | 135          | DON    | 57.0          | 2050.0                  | 0–20,000.0   | 0                   | [102]     |
|              |         |              | ZEN    | 40.6          | 15.0                    | 0–300.0      | 0                   |           |
| 2013         | Shannxi | 81           | DON    | 96.1          | 515.3                   | 79.0–3030.0  | 8.64                | [106]     |
|              | Ningxia | 26           | DON    | 100.0         | 804.4                   | 71.0–2330.0  | 26.92               |           |
|              | Gansu   | 52           | DON    | 86.5          | 294.4                   | 0–1798.0     | 1.92                |           |
|              | Xinjiang| 22           | DON    | 0             | 0                       | 0            | 0                   |           |
| Year   | Regions       | Sample Sizes | Toxins | Incidence (%) | Average Content \((\mu g/kg)\) | Range \((\mu g/kg)\) | Exceedance Rate (%) | Reference |
|--------|---------------|--------------|--------|---------------|-------------------------------|-------------------|---------------------|-----------|
| 2000–2016 | Tibet        | 199          | DON    | 0             | 0                             | 0                 | 0                   | [77]      |
|        |               |              | ZEN    | 0.5           |                               | 0.5               |                     |           |
| 2007–2008 | Sichuan     | 30           | D3G    | 0             | 0                             | 0                 |                     | [95]      |
|        |               |              | NIV    | 73.3          | 17.7                          | 3.0–39.1          |                     |           |
|        |               |              | 3ADON  | 0             | 0                             | 0                 |                     |           |
|        |               |              | 15ADON | 0             | 0                             | 0                 |                     |           |
|        |               |              | DON    | 50.0          | 16.4                          | 3.0–47.8          | 0                   |           |
|        |               |              | ZEN    | 20.0          | 5.1                           | 2.0–8.8           | 0                   |           |
| 2007–2008 | Chongqing   | 30           | D3G    | 73.3          | 72.5                          | 9.8–235.3         |                     | [95]      |
|        |               |              | NIV    | 100.0         | 199.5                         | 7.8–1035.8        |                     |           |
|        |               |              | 3ADON  | 60.0          | 9.1                           | 1.9–34.6          |                     |           |
|        |               |              | 15ADON | 46.7          | 9.6                           | 2.1–71.0          |                     |           |
|        |               |              | DON    | 100.0         | 133.3                         | 12.0–590.7        | 0                   |           |
|        |               |              | ZEN    | 80.0          | 199.4                         | 2.3–3425.1        |                     |           |
| 2016   | Heilongjiang  | 55           | DON    | 0             | 0                             | 0                 | 0                   | [59]      |
| 1984   | China         | 29           | DON    | 51.7          | 401.7                         | 0–2450.0          | 6.9                 | [107]     |
|        |               |              | NIV    | 37.9          | 267.3                         | 0–6644.0          |                     |           |
|        |               |              | ZEN    | 44.8          | 6.8                           | 0–32.0            | 0                   |           |
| 2003   | China         | 48           | ZEN    | 100.0         | 98.0                          | 0–470.0           | 72.9                | [108]     |
| 2005   | China         | 190          | DON    | 66.3          | 50.0                          | 0–612.7           | 0                   | [109]     |
| 2007   | China         | 229          | DON    | 38.0          | 73.9                          | 0–600.8           | 0                   | [110]     |
|        |               |              | ZEN    | 16.0          | 1.6                           | 0–72.4            |                     |           |
| 2008   | China         | 41           | DON    | 97.6          | 425.5                         | 9.8               |                     | [111]     |
|        |               |              | ZEN    | 68.3          | 152.4                         | 41.5              |                     |           |
| 2010–2013 | China      | 681          | DON    | 66.5          | 72.8                          | 774.8–14276.0     |                     | [112]     |
|        |               |              | AcDON  | 66.8          | 74.7                          | 797.7–14604.2     |                     |           |
**Table 5.** Recent mycotoxin survey data in wheat flour in China.

| Year       | Regions       | Toxins | Sample Sizes | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|------------|---------------|--------|--------------|----------------|-------------------------|---------------|---------------------|-----------|
| 1983–1991  | Anhui         | DON    | 132          | 92.4           | 1065.6                  | 0–173.0       | 40.9                | [83]      |
| 1988       | Hebei         | DON    | 50           | 54.0           | 75.0                    |               | 0                   | [113]     |
| 1988–1989  | Anhui         | DON    | 100          | 90.0           | 1008.6                  |               | 43.0                | [114]     |
| 1988–1989  | Shanghai      | DON    | 25           | 100.0          | 79.8                    |               | 0                   | [115]     |
| 1989       | Anhui         | DON    | 84           | 100.0          | 1334.0                  |               | 58.3                | [81]      |
| 1989       | Jiangsu       | DON    | 50           | 96.0           | 577.7                   |               | 18.0                | [82]      |
| 1996       | Shanghai      | DON    | 30           | 86.7           | 101.2                   |               | 0                   | [104]     |
| 2009       | China (13 provinces) | DON    | 292          | 100.0          | 178.4                   | 0.5–2995.1    | 1.7                 | [116]     |
|            |               | ZEN    |              | 53.4           | 5.1                     | 0.3–55.0      | 0                   |           |
|            |               | NIV    |              | 88.4           | 8.1                     | 0.3–218.2     |                     |           |
| 2010       | China (12 provinces) | DON    | 125          | 96.8           | 179.0                   | 0.1–1016.8    | 0.8                 | [96]      |
|            |               | 3ADON  |              | 64.0           | 2.2                     | 0.1–19.8      |                     |           |
|            |               | 15ADON |              | 95.2           | 4.2                     | 0.1–25.5      |                     |           |
|            |               | D3G    |              | 83.2           | 10.1                    | 0.1–52.8      |                     |           |
|            |               | NIV    |              | 86.4           | 10.3                    | 0.1–76.5      |                     |           |
|            |               | ZEN    |              | 72.8           | 3.5                     | 0.1–52        | 0                   |           |
| 2010       | China (28 provinces) | DON    | 5678         | 58.7           | 317.0                   | 0–56,100     | 4.7                 | [117]     |
| 2011       |                |        |              |                |                        |               |                     |           |
| 2012       |                |        |              |                |                        |               |                     |           |
| 2013       |                |        |              |                |                        |               |                     |           |
| Year       | Regions | Toxins | Sample Sizes | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|-----------|---------|--------|--------------|---------------|-------------------------|---------------|---------------------|----------|
| 2010–2013 | China   | DON    | 3848         | 71.7          | 126.0                   | 218.0–6922.0  |                     | [112]    |
|           |         | AcDON  | 3860         | 71.8          | 91.5                    | 219.2–6922.0  |                     |          |
| 2010-     | Shandong| DON    | 359          | 97.2          | 84.3                    | 0–825.9       | 0                   | [98]     |
|           |         | 3ADON  |              | 11.1          | 0.1                     | 0–3.6         |                     |          |
|           |         | 15ADON |              | 14.2          | 0.5                     | 0–11.1        |                     |          |
|           |         | NIV    |              | 40.4          | 1.4                     | 0–23.9        |                     |          |
|           |         | D3G    |              | 33.4          | 1.1                     | 0–15.7        |                     |          |
|           |         | ZEN    |              | 0             | 0                      | 0             |                     |          |
| 2010-     | Hubei   | DON    | 26           | 69.2          | 129.4                   | 0–2133.2      | 3.9                 | [99]     |
|           |         | D3G    |              | 30.8          | <20.0                   | 0–252.4       |                     |          |
| 2010-     | Hebei   | DON    | 348          | 91.4          | 240.0                   | 0–1129.0      | 0.6                 | [100]    |
|           |         | 15ADON |              | 34.2          | 1.9                     | 0–6.0         |                     |          |
|           |         | NIV    |              | 16.4          | 3.2                     | 0–19.1        |                     |          |
|           |         | ZEN    |              | 13.2          | 8.4                     | 0–98.8        | 0.3                 |          |
|           |         | D3G    |              | 5.5           | 1.9                     | 0–3.9         |                     |          |
|           |         | 3ADON  |              | 2.1           | 3.2                     | 0–2.6         |                     |          |
| 2011      | Hebei   | DON    | 31           | 16.1          | 137.0                   | 2.4–639.0     | 0                   | [118]    |
|           |         | 3ADON  |              | 6.4           | 0.7                     | 0.6–0.8       |                     |          |
|           |         | 15ADON |              | 0            | 0                      | 0             |                     |          |
| 2012      | Hebei   | DON    | 348          | 91.4          | 240.0                   | 11.5–1130.0   | 0.6                 | [118]    |
|           |         | 3ADON  |              | 34.2          | 1.9                     | 1.1–6.0       |                     |          |
|           |         | 15ADON |              | 3.2           | 2.1                     | 1.5–2.6       |                     |          |
| 2013      |         | DON    | 293          | 99.6          | 156.0                   | 6.2–878.0     | 0                   |          |
|           |         | 3ADON  |              | 0            | 0                      | 0             |                     |          |
|           |         | 15ADON |              | 0            | 0                      | 0             |                     |          |
| Year  | Regions                      | Toxins | Sample Sizes | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|-------|-------------------------------|--------|--------------|---------------|------------------------|--------------|---------------------|-----------|
| 2013  | China (10 provinces)          | DON    | 50           | 30.0          | 58.1                   | 0–862.0      | 0                   | [119]     |
| 2013  | China (5 provinces)           | DON    | 158          | 84.2          | 4084.8                 | 23.5–25,375  | 68.0                | [97]      |
|       |                               | D3G    |              | 24.1          | 13.9                   | 8.7–33.3     |                     |           |
|       |                               | 3ADON  |              | 84.2          | 14.9                   | 10.6–177.5   |                     |           |
|       |                               | 15ADON |              | 60.8          | 14.7                   | 13.4–23.5    |                     |           |
|       |                               | NIV    |              | 22.2          | 26.9                   | 1.8–94.0     |                     |           |
|       |                               | ZEN    |              | 77.2          | 85.8                   | 13–158       | 24.0                |           |
| 2013  | Fujian                       | DON    | 59           | 89.8          | 11.2                   |              |                     | [120]     |
|       |                               | ZEN    |              | 11.9          |                       |              |                     |           |
| 2013  | Guangdong                    | DON    | 30           | 86.7          | 87.9                   | 0–860.8      | 0                   | [121]     |
| 2013–2016 | Shannxi                   | DON    | 504          | 86.9          | 311.0                  | 6.0–3670.0   | 6.7                 | [122]     |
|       |                               | 3ADON  |              | 59.9          | 33.7                   | 21.9–535.0   |                     |           |
|       |                               | 15ADON |              | 8.3           | 5.7                    | 4.5–105.0    |                     |           |
|       |                               | ZEN    |              | 0.2           | 2.6                    | 0–31.0       |                     |           |
| 2013  | Tibet                        | DON    | 85           | 27.1          | 47.0                   | 0–630.0      | 0                   | [78]      |
|       |                               | ZEN    |              | 74.0          | 5.4                    | 0–13.9       | 0                   |           |
| 2014  | Xinjiang                     | DON    | 84           | 51.2          | 20.3                   | 8.7–152.6    | 0                   | [79]      |
|       |                               | 15ADON |              | 28.6          | 15.3                   | 5.6–159.2    |                     |           |
| 2014  | Henan                        | DON    | 65           | 69.2          | 218.3                  | 0           | 0                   | [123]     |
| 2014  | Hebei                        | DON    | 293          | 99.7          | 156.0                  | 0–878.4      | 0                   | [124]     |
| 2014–2015 | Henan                     | DON    | 295          | 8.8           | 14.4                   | 0–750.0      | 0                   | [125]     |
|       |                               | 3ADON  |              | 0            | 0                      | 0           |                     |           |
|       |                               | 15ADON |              | 0            | 0                      | 0           |                     |           |
|       |                               | ZEN    |              | 0            | 0                      | 0           |                     |           |
| Year       | Regions | Toxins | Sample Sizes | Incidence (%) | Average Content (µg/kg) | Range (µg/kg) | Exceedance Rate (%) | Reference |
|------------|---------|--------|--------------|---------------|------------------------|--------------|---------------------|-----------|
| 2016–2017  | Jiangsu | DON    | 35           | 100.0         | 308.9                  | 44.6–924.6   | 0                   | [126]     |
|            |         | 3ADON  |              | 28.6          | 7.1                    | 0–54.9       |                     |           |
|            |         | 15ADON |              | 17.1          | 3.2                    | 0–23.7       |                     |           |
|            |         | ZEN    |              | 17.1          | 1.2                    | 0–16.9       | 0                   |           |
|            |         | DON    | 50           | 62.0          | 91.9                   | 0–401.8      | 0                   |           |
|            |         | 3ADON  |              | 6.0           | 1.1                    | 0–21.0       |                     |           |
|            |         | 15ADON |              | 2.0           | 0.3                    | 0–14.7       |                     |           |
|            |         | ZEN    |              | 0             | 0                      | 0            | 0                   |           |
| 2017       | China   | DON    | 75           | 85.3          | 455.7                  | 12.5–1285.4  | 20.0                | [127]     |
|            |         |        | 15           | 100.0         | 426                    | 51.6–1308.9  | 13.3                |           |
5. *Fusarium* Toxin Management

Since FHB can lead to economic losses and health concerns, some comprehensive strategies for the reduction in the occurrence of FHB and *Fusarium* mycotoxins need to be developed. A combination of planting resistant cultivars, adapting agricultural practices, and applying chemical and biological controls for reducing fungi invasion and toxin production may help to control the occurrence of FHB and its associated mycotoxins.

5.1. Expansion of the Basic Knowledge about Toxin Production

Similar to pigments and antibiotics, *Fusarium* toxins are secondary metabolites produced by *Fusarium* species during its natural growth; these metabolites are closely associated with cell differentiation, growth, and the response to the external environment. Successful whole genome sequencing of several *Fusarium* species has provided useful data for researchers to study the biosynthesis pathways and regulatory mechanisms of mycotoxins [128] and has led to the complete resolution of the trichothecene gene cluster (TRI-cluster) [129,130] and zearalenone biosynthetic gene cluster [131,132]. Environmental factors, including pH [133,134], carbon sources [135], nitrogen sources [136,137], H₂O₂ [138], availability of free water (aₒ), incubation temperatures [139] and regulatory signaling pathways, including the mitogen-activated protein kinase (MAPK) [140], cyclic adenosine phosphate-protein kinase A (cAMP–PKA) [141,142], and target of rapamycin (TOR) pathways [143], can influence toxin accumulation. These molecular mechanisms offer targets for the inhibition of DON synthesis by genetic engineering technology.

Several studies on detailed species and chemotype identification, population genetic diversity, and biological characteristics of FHB pathogens from wheat in China have been performed [60,66,144]. 3ADON-producing populations with high toxin accumulation are more dominant. The identification of advantageous populations, temporal dynamics evolution trends and ecological adaptations could provide a theoretical basis for confirming a regulatory focus, breeding for FHB resistance, and developing targeted disease and mycotoxin control strategies.

5.2. Maturation of Chemical Control Measure of FHB

Spraying carbendazim during the wheat flowering period is a common method for controlling FHB and has played a crucial role in integrated disease control programs since the 1970s. However, the monitoring results of *Fusarium* toxins in wheat samples calls into question the true effects of chemical control on toxin production. In the past, control was measured only by the decrease in the visual disease index and the recovery of economic losses; serious toxin contamination was largely ignored. As such, the efficacy of carbendazim on toxin accumulation is questionable. Poor reductions in toxin accumulation may be due to the increase in *Fusarium* species that are resistant to carbendazim and the improved synthesis ability of DON in resistant strains compared with that of conventional strains [145,146]. High doses of the fungicide and the high proportion of resistant strains in the field may be associated with the serious toxin contamination in wheat samples from Jiangsu and Anhui provinces. In some regions with low carbendazim resistance, this compound can still reduce the disease index, diseased kernel rate and DON content remarkably [147].

Phenamacril, a new type of acrylate fungicide, was developed by China; phenamacril provides successful control of a variety of plant diseases caused by *Fusarium*. Field experiments indicated that phenamacril showed better efficacy against FHB than carbendazim, and the yield increase effect was equivalent to that of carbendazim [146]. Moreover, the application of phenamacril reduced the total DON level in wheat grains by more than 80% compared with the untreated controls, and phenamacril exhibited great potential in toxin management [147,148]. Currently, this fungicide has been popularized and applied in most wheat-growing areas.
Another kind of fungicide that can significantly reduce the ability of pathogens to infect plants and synthesize toxins is theazole antifungals, including metconazole, propiconazole, prothioconazole, and tebuconazole, which belong to the class of demethylation inhibitors. Several studies have proved that tebuconazole alone at varied concentrations or in combination with other fungicides was effective in inhibiting FHB and DON, and the drug showed optimal performance at the early anthesis stage or later anthesis stage [147–150]. The sensitivities of FHB pathogens to metconazole and the efficacy of this fungicide in FHB and DON control in China were reported in a recent study; metconazole exhibited better efficacy than phenamacril and carbendazim [151]. Propiconazole also had a certain role in toxin management [148], but it was reported that this fungicide may have the opposite effect on toxin control at low doses. Sublethal doses of propiconazole triggered H$_2$O$_2$ production in vitro and further induced DON accumulation in the pathogen [152].

According to a new study, validamycin, a type of fungicide for the control of crop diseases caused by *Rhizoctonia* species, had a remarkable effect on reducing DON synthesis by *F. graminearum* [153,154]. Further research on the molecular mechanism revealed that validamycin decreased glucose production by targeting trehalase and blocking the glycolytic pathway, thereby reducing pyruvate and DON production [153]. This finding provides us with important reference values and guidance in the screening of appropriate fungicides against harmful metabolites, as no fungicidal activity of validamycin against *F. graminearum* was discovered in vitro.

There are many agricultural practices to combat pathogens, diseases, and contaminants; however, chemical control is still the most powerful and effective measure. The effect of fungicides on mycotoxins is complicated and can be influenced by various factors, such as toxin-producing fungus, environmental conditions, and treatment dosage. More research on the mechanisms of toxin production and compound mode of action is needed to provide theoretical support for the scientific and reasonable use of fungicides. Chinese government is vigorously implementing the strategy of the dosage reduction and efficiency increase of chemical pesticides, as pesticide residue is a threat to food safety and cannot be ignored. More rational and efficient application of these substances is extremely essential.

### 5.3. Development of Process Control Technology

Wheat can experience a serious loss of tissue composition after infection with scab, resulting in a change in the wheat kernel appearance. Diseased grains usually have shriveled surfaces, declined particle diameters, decreased hardness, and decreased weight; therefore, specific gravity separation is the best method to remove infected wheat kernels before storage and processing. Historically, wind force was used to separate diseased and normal grains based on simple devices, and notable results were obtained. Liang et al. [155] suggested that DON content could be effectively controlled by removing scabby grains with wind and sifting. More recently, a specific gravity separator combined with winnower has played an important role in wheat cleaning and purification. Li et al. [156] conducted particle size and specific gravity separation of raw material and found the redistribution of DON samples. After the elimination of impurities and infected grains, edible wheat was obtained with a 68.94% decrease in total DON compared with the level of DON in the original samples. Bian et al. [157] and Zhu et al. [158] further improved the conventional gravity separation technology; the mass fraction for the DON-contaminated fraction increased while the proportion decreased, indicating that the improved technology effectively and efficiently discarded DON-contaminated wheat grains.
It is well known that scabby wheat kernels present different shades of red due to the infection of *Fusarium*, and electric color sorting technology based on color characteristics can separate the contaminated grains to effectively manage toxins. The soft independent modelling of class analogies (SIMCA) model based on near infrared spectrum and hyperspectral imaging technology has been successfully applied in the identification of scabby grains and DON levels, with a recognition accuracy above 90% [159–161]. Shen et al. [162] established quantitative models for DON with attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) and developed a method for the rapid determination of DON in wheat and its products by associating the absorption values of samples with various DON contents with different bands. With the combined gravity and color sorting technology and equipment in the cleaning process, the DON content decreased from 1.56 mg/kg to 1.18 mg/kg [163].

Cleaning is the first step in wheat processing and plays a vital role in wheat flour safety. At present, color and gravity sorters have been implemented in most flour milling enterprises and are of great importance to mycotoxin reduction and the quality improvement of wheat flour and its products.

5.4. Improvement of the Standard System

To protect public health from the negative impacts of *Fusarium* toxins, many countries and food safety regulators, including China, have introduced maximum or recommended toxin levels for food and feed. Specific regulations at the national level are released by authoritative bodies (Table 6). The former National Health and Family Planning Commission (NHFPC) and China Food and Drug Administration (CFDA) jointly issued national food safety standards (GB 2761-2017), in which the main mycotoxin limits of food were specified. The regulatory limits of mycotoxins in the revised national food safety standards in the infant formula (GB 10765), older infant formula (GB10766), young children (GB 10767), and raw milk (GB 19301-2010) general rules for aged-food (draft for comments) were determined to be in accordance with GB 2761. The former General Administration of Quality Supervision, Inspection and Quarantine of the People’s Republic of China (AQSIQ) and Standardization Administration of China (SAC) promulgated hygienic standards for feed (GB 13078) and fully stipulated limit values for toxicants in feedstuffs and products. These standards help the government protect the health of citizens through food safety guarantees. As technical barriers in international trade, they may also contribute to the protection of domestic markets and industry development.

The national standard system of mycotoxin detection has been improved (Table 7), and some detection standards provide technical support for agricultural product quality and safety supervision, particularly for the most advanced analytical instruments, such high-performance liquid chromatography (HPLC), ultraperformance liquid chromatography (UPLC), and high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). This progression reflects the level of technological innovation in the application and promotion of standards.

However, safety and detection standard systems for agriculture products are in some developing countries and regions are still incomplete. China focuses mostly on primary agricultural products, and agro-products from varied processes for different purposes and consumer bases lack specific standards. For instance, there are no specific rules for direct consumables. Moreover, the process of establishing standards is slightly behind. China does not have established maximum levels for D3G, NIV, and other common toxins. As for minor crops, most lack limitation standards and related testing standards. Combined contamination of multitoxin is a common feature of cereal grains, and a standard for the simultaneous determination of multitoxin is a top research priority.
6. Conclusions and Challenges for the Future

In the present review, we gathered available Chinese data from the last half century on the occurrence of *Fusarium* species and toxins in wheat as well as the resultant food-poisoning incidents. Because of climatic conditions and cropping systems, there are increased amounts of infection sources and greater risks of FHB epidemics and *Fusarium* toxin contamination. Fortunately, with the advancement of society and the development of new materials, the human mycotoxicosis incidence has decreased gradually.

*Fusarium* toxin contamination in cereals remains an inevitable problem worldwide. In recent years, risk assessment and mycotoxin monitoring of cereals has been strengthened, and research in related fields has been promoted. However, achieving the goal of effectively controlling mycotoxin contamination in cereals is still a long way away. Integrated mycotoxin management practices, including preharvest control (e.g., tillage and crop rotation, selection of resistant varieties, proper sowing dates and density, irrigation and fertilization regimes, weed elimination, insect management, and chemical and biological control), harvest control (e.g., proper harvest time, professional mechanical equipment, mechanical damage reduction, effective cleaning, and impurity removal), and postharvest control (e.g., timely and efficient drying, good storage practices, and classified applications) should be employed to manage all possible risk factors to prevent mycotoxin contamination. In the future, with the effective implementation of good agricultural practices (GAPs), good manufacturing practices (GMPs), and hazard analysis critical control points (HACCPs), food safety, and consumer health can be improved and guaranteed as much as possible.

| Table 6. Limits of DON and ZEN relate to cereals for food and feed in China. |
|-------------------------------------------------------------|
| **Food Category** | **Toxin** | **Limit (µg/kg)** | **Standard Code** |
| cereal and its product: corn, corn flour (corn gluten meal, corn flake), barley, wheat, oatmeal, wheat flour | DON | 1000 | GB2761 |
| | | 5000 | |
| | plant feedstuffs | 1000 | GB13078 |
| | | 3000 | |
| | calf, lamb, concentrate supplement in lactation period | 1000 | |
| | other concentrate supplement | 3000 | |
| | pig formula feed | 1000 | |
| | other formula feed | 3000 | |
| cereal and its product: wheat, wheat flour, corn, corn flour (corn gluten meal, corn flake) | ZEN | 60 | GB2761 |
| | corn and its processed products (corn bran, corn gluten feed, corn steep powder excepted) | 500 | |
| | corn bran, corn gluten feed, corn steep powder, corn distiller’s grains products | 1500 | GB13078 |
| | other plant feedstuffs | 1000 | |
| | calf, lamb, concentrate supplement in lactation period | 500 | |
| | piglet formula feed | 150 | |
| | gilt formula feed | 100 | |
| | other pig formula feed | 250 | |
| | other formula feed | 500 | |
Table 7. Current detection standard for DON and ZEN by Chinese regulations.

| Standard Code | Standard Category                      | Standard Name                                                                 | Method                                                                 | Toxin                      |
|---------------|----------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------|
| GB 5009.111-2016 | Mandatory national standard           | Determination of deoxynivalenol and its acetylated derivatives in food        | Isotope-dilution LC-MS/MS; Immunoaffinity chromatography-HPLC; thin layer chromatography | DON                        |
| GB/T 30956-2014 | Recommendatory national standard       | Determination of deoxynivalenol in feeds                                     | Immunoaffinity chromatography-HPLC                                     |                            |
| GB/T 8381.6-2005 | Recommendatory national standard       | Method for determination of deoxynivalenol in formula feed                   | Thin layer chromatography                                              |                            |
| SN/T 3137-2012 | Recommendatory industry standard       | Determination of deoxynivalenol, 3-acety-ldeoxynivalenol, 15-O-4-acetyl-deoxynivalenol, and their metabolite in food for export | HPLC-MS/MS                                                             | DON                        |
| SN/T 3136-2012 | Recommendatory industry standard       | Determination of aflatoxins, ochratoxin, fumonisin B1, deoxynivalenol, T-2 and HT-2 toxins in peanut, grains, and their products for export | HPLC-MS/MS                                                             |                            |
| LS/T 6110-2014 | Recommendatory industry standard       | Detection of deoxynivalenol in cereal                                        | Rapid quantitative method of colloidal gold technique                   |                            |
| LS/T 6113-2015 | Recommendatory industry standard       | Detection of deoxynivalenol in grain                                         | Rapid quantitative method of colloidal gold technique                   |                            |
| LS/T 6127-2017 | Recommendatory industry standard       | Detection of deoxynivalenol in grain                                         | UPLC                                                                   |                            |
| LS/T 6133-2018 | Recommendatory industry standard       | Determination of 16 mycotoxins in cereal                                      | HPLC-MS/MS                                                             |                            |
| KJ 201702      | Rapid detection standard               | Rapid detection of deoxynivalenol in food                                   | Colloidal gold immunochromatographic                                   |                            |
| Standard Code       | Standard Category                  | Standard Name                                                                 | Method                                                                                         | Toxin |
|---------------------|-----------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------|
| GB 5009.209-2016    | Mandatory national standard       | Determination of zearalenone in food                                          | HPLC; HPLC-MS/MS; Immunoaffinity chromatography-fluorescence spectrometer                      |       |
| GB/T 19540-2004     | Recommendatory national standard  | Determination of zearalenone in feeds                                         | Thin layer chromatography; Enzyme-linked immunosorbent assay                                    |       |
| GB/T 28716-2012     | Recommendatory national standard  | Determination of zearalenone in feeds                                         | HPLC method with immunoaffinity column clean-up                                                |       |
| SN/T 3235-2012      | Recommendatory industry standard  | Determination of multi-groups of banned drug residues in foodstuffs of Animal origin for export | LC-MS/MS                                                                                       | ZEN   |
| SN/T 4058-2014      | Recommendatory industry standard  | Determination of residues of zeranols in foodstuffs of animal origin for export | HPLC and HPLC-MS/MS method with Immunoaffinity column clean-up                                 |       |
| NY/T 2071-2011      | Recommendatory agriculture standard | Determination of aflatoxins, zearalenone, and T-2 in feed                      | LC-MS/MS                                                                                       |       |
| LS/T 6109-2014      | Recommendatory agriculture standard | Detection of zearalenone in cereal                                            | Rapid method of colloidal gold technique                                                       |       |
| LS/T 6112-2015      | Recommendatory agriculture standard | Detection of zearalenone in grain                                             | Rapid quantitative method of colloidal gold technique                                           |       |
| LS/T 6129-2017      | Recommendatory agriculture standard | Determination of zearalenone in grains                                         | UPLC-MS/MS                                                                                     |       |
| LS/T 6133-2018      | Recommendatory industry standard  | Determination of 16 mycotoxins in cereal                                       | HPLC-MS/MS                                                                                     |       |
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