INTERNATIONAL AND NATIONAL LEGISLATION TO CONTROL MICTOXINS IN FOOD: REVIEW

Today, the problem of monitoring mycotoxins has become global in connection with climate change, a violation of the ecological balance for the use of intensive technologies for processing crops, through air pollution and the accumulation of products of photochemical reactions (photooxidants), which leads to a decrease in plant resistance to phytopathogens.

Every year, the problem of mycotoxicosis is exacerbated, as toxic fungi adapt quickly to new technologies and modern plant protection products. The increase in mycotoxins in foods also relates to the widespread use of nitrogen fertilizers and pesticides.

Natural toxins create risks for the health of humans and animals, affect food security and nutrition, reducing people's access to healthy food. The World Health Organization is constantly appealing to national authorities to monitor and ensure that the levels of the most relevant natural toxins in foods are as low as possible and consistent with both national and international requirements.

Ukraine's membership in the WTO, an association with the European Union, and the expansion of international trade require solutions to the issues of free movement of goods, safe and healthy food, and, accordingly, an adequate level of protection of life and health of people. One of the most important ways to solve them is to improve and harmonize national food legislation in line with international standards, including on the control of mycotoxins.

The purpose of our work was to conduct an analysis of literary sources, international and national legislative acts on the control of mycotoxins in food products throughout the food chain.

To prepare the publication, we have used literary sources on the subject of publication, as well as we have conducted a comparative analysis of national and international legislative acts regulating procedures and methods for controlling the residues of mycotoxins in food.

An analysis of numerous sources has shown that the issue of monitoring mycotoxins in foods, improving laboratory control and risk-based approach to preventing foodborne mycotoxicosis worries scientists from different countries, including Ukrainian. The analysis of national legislation shows that national standards on maximum levels of pollutants have been revised in Ukraine and a number of standards have been harmonized for methods of monitoring the residues of mycotoxins in feed for productive animals, food products of animal and vegetable origin.

Key words: mycotoxins, food chain, food, international law, national legislation, control, safety, risks.


Problem statement and analysis of recent research. Mycotoxins are secondary metabolites from toxicogenous fungi and are known as common hazardous contaminants in food and feed [1–3]. Over the past half century, they have been recognized as one of the most dangerous factors for human and animal health.

The contamination of food and feed by mycotoxins depends on the environmental conditions that are susceptible to the growth of mycelium and the formation of mycotoxins. Agricultural products can be infected at any time, from the cultivation of plants in the field, as well as during harvesting, storage or transportation of finished products [4, 5].

Mycotoxins are a source of serious concern about foodborne diseases (mycotoxicosis) in humans. Diseases caused by mycotoxins, as a rule, do not have a characteristic clinical picture or they pass asymptomatic, often complicated by secondary microflora, therefore they are not diagnosed on time. A significant amount of mycotoxins has long-term effects: teratogenic, mutagenic, embryotoxic, carcinogenic, immunosuppressive [6, 7]. Toxicity of mycotoxins is detected at low concentrations in feed. They differ in this from other toxic metabolites produced by microorganisms [8].

There are about 350 types of micromycetes, which form more than 400 mycotoxins. The main producers of dangerous mycotoxins are mold Fusarium, Aspergillus, Myrothecium, Stachybotrys, Trichoderma, Trichotheceum, Penicillum. About 25% of cereals in the world are affected every year by mycotoxins [9, 10]. Mushrooms can produce mycotoxins in any feed during vegetation, harvest or storage [2].
Fungi Penicillium and Aspergillus species produce ochratoxins A, B, S. Ochratoxin A is considered carcinogenic and causes urinary tract cancer and kidney damage in humans. The risks are most often due to the consumption of cereals and their processing products.

Fusarium most often affect food and feed. The spread of fusarium fungi, their variability, as well as the risks to human health and animals that make up their mycotoxins, predetermine the interest of scientists in fusariosis. Grain affected by fusariosis contains mycotoxins, dangerous to humans and animals [11, 12].

Fusarium graminearum produce mycotoxin deoxynivalenol. Zearalenone is a product of various species of Fusarium, in particular Fusarium graminearum, Fusarium culmorum, Fusarium equiseti and Fusarium verticillioides [13, 14].

Patulin is a product of the exchange of various species of molds of the genus Penicillium, Aspergillus and Paecilomyces. P. expansum affects fruits and vegetables, including apples [15, 16]. This mold is destroyed during the fermentation processes and is therefore not found in apple drinks such as cider. No data is available on the carcinogenic effects of patulin, but there are reports of its negative effects on the immune system of animals.

Different mycotoxins are found in Ukraine: aflatoxins, ochratoxins, fumonisins, zearalenone, patulin, deoxynivalenol (DON) and T-2 toxin [6].

Scientists around the world are paying much attention to studying the chemical and toxicological properties of mycotoxins. The results they receive contribute to the expansion of checklists and to the improvement of detection methods.

In the European Union, the relevant directives set maximum levels for a number of mycotoxins permitted in food and animal feed. The Food and Drug Administration (FDA), based on scientifically sound data, regulates and introduces restrictions on the concentration of mycotoxins in food and feed industries since 1985 [17].

For many years, the International Agency for Research on Cancer (IARC) has been working on a program to assess the carcinogenicity of mycotoxins for animals and humans, developing criteria for identification and risk management of mycotoxins [18]. According to the IARC classification of aflatoxin risk groups, ochratoxin A, sterigmatocysteine and fumonisins are classified as carcinogenic mycotoxins.

Today, in many countries, provisions have been adopted on the maximum levels of different mycotoxins. Information, impact assessment and risk management in the presence of mycotoxins in food products are important measures and tools for protecting the health and life of consumers. [19, 20].

In many countries, the list of mycotoxins, the content of which is regulated and controlled in foods, is different. There are differences in periodicity and control methods [21].

The purpose of our work was to conduct an analysis of literary sources, international and national legislative acts on the control of mycotoxins in food products throughout the food chain.

Material and methods of research. To prepare the publication, we have used literary sources on the subject of publication, as well as we have conducted a comparative analysis of national and international legislative acts regulating procedures and methods for controlling the residues of mycotoxins in food.

Results of the research. According to the World Health Organization (WHO), mycotoxins present risks to the health of humans and animals [22], causing significant damage — cancer, immunosuppression, and growth disturbances, which in turn threatens the economies of the countries [23–25].

The international organizations of FAO and WHO are actively involved in providing important information on various aspects of mycotoxin control for all countries of the world. Their recommendations for international trade include sampling and analysis procedures, food monitoring and control systems, the use of contaminated products during feeding animals; detoxification protocols and food safety control. Their initiative has repeatedly reviewed the international legislation on the control of mycotoxins in food and animal feeds, published data on levels of tolerance, legal framework and responsible bodies [26–30].

The Codex Committee on Contaminants in Foods (CCCF) Codex Committee sets or approves maximum permitted levels (MLs), revises existing levels of directives on contaminants and natural toxicants in food and feed; prepares priority lists of pollutants and natural toxicants for risk assessment. CCCF does not overlook the issue of controlling mycotoxins in food and feed [31, 32].
The European Union has recommended maximum levels (limits) for some mycotoxins and has established legislative restrictions for aflatoxins in animal feed [33, 34].

The European Food Safety Authority (EFSA) collects and evaluates mycotoxin monitoring data in food and feed. It also prepares instructions for customers on how to assess the safety and effectiveness of feed additives that help reduce the contamination of feed by mycotoxins. The EFSA Expert Group on contaminants in the food chain (CONTAM) provides risk managers with scientific advice on how to decide on maximum levels of mycotoxins (such as ochratoxin A, deoxynivalenol or zearalenone) in food and feed; analyzes the risks to human and animal health.

In the EU, the maximum permissible levels of pollutant content are set for the following mycotoxins: aflatoxins, ochratoxin A, trichothecene mycotoxins, patulin, citrine.

Aflatoxins are most often found in cereal crops (corn, wheat, barley, oats, rye) and products based on them. They can also be accumulated in oilseeds (especially soya), nuts and berries, and products from them (peanut, peanut butter, pistachios), vegetables (potatoes, lentils, peppers), dried fruits (figs) and beer. Aflatoxins are commonly found in products grown in regions (countries) with hot and humid conditions that are beneficial for their synthesis.

Aflatoxicogenic mushrooms were found in samples of smoked and dried fish, rice, grains, poultry feed [35–37]. There were also cases of aflatoxins in other food products such as frozen fish, dried meat, chips, spices, and the like [38–40].

Aflatoxin contamination of peanuts is one of the most important determinants of its quality and causes significant financial losses to producer and exporting countries. Monitoring of aflatoxins in peanut and its products is very important for the prevention of food-related risks [41, 42].

The EU focuses on aflatoxin M1 (AFM1), which has been classified as a potential human carcinogen (group 2B) [43]. Due to concerns about human health risks, AFM1 regulatory restrictions exist in more than 60 countries of the world, and 34 of these countries, including EU countries, have set the maximum permissible AFM1 in milk (0.05 μg/kg) [44], while levels of other mycotoxins in milk are not regulated. According to research data, almost 9.8% of milk samples exceeded the permissible level for AFM1 established in the European Union [45].

Brazilian researchers [46] found AFM1 in 83% of milk samples. The amount of this mycotoxin did not exceed 3 ng/kg. Their research suggests that the processing and storage of milk have little effect on the residual AFM1 content in dairy products. Thus, the total amount of AFM1 in cheese was lower by 3.2%, yogurt – by 6% compared to raw milk. The average concentration of AFM1 in cheese grain was 1.9 times higher, in serum – 0.6 times lower than in unprocessed milk.

Ochratoxin A is considered one of the most dangerous contaminants for food and feed. It is found in grain crops (wheat, corn, rye, barley, oats), rice, potatoes, lentils, soy beans, coffee, cocoa beans, peas, peanuts and dried fruits (figs, raisins), produced in warm regions with moderate climates, in grain processing products (flour, bread, pasta) can be found in beer, wine and grape juice. Remains of ochratoxin A foreign scientists isolated 5% of samples of slaughter products of farm animals, in particular pigs and poultry [47, 48]. Ukrainian scientists are paying attention to food risks and the need to control ochratoxin [49].

Fumonisins are most commonly found in corn products intended for human and animal consumption [50].

Zearalenone has estrogenic and teratogenic properties, as well as antibacterial action against gram-positive bacteria. Contamination of cereals with this mycotoxin is possible under all climatic conditions. The study of the content of fumonisins and zearalenone in milk showed their low levels, which are not risks to consumers [51, 52]. It was established that even after experimental feeding of zearalenone peak concentrations (up to 13 ng/ml) to lacquering cows its level in milk did not exceed the normative index.

In 2003, the European Commission published a report highlighting data from numerous studies on agricultural products, according to which 57% of about 12,000 tested samples contained deoxynivalenol (DON). Often mycotoxin fumonizone B1 has been observed (46% of the 4,000 tested samples were positive) and zearalenone (32% of approximately 5,000 samples).

Patulin exhibits carcinogenic and mutagenic properties [53]. Occurs in fruits, affected by mold: more often – apples, rarely – pears, apricots, peaches, cherries, grapes, strawberries, blueberries, cranberries, buckthorns. The research of fruit and vegetable production grown in the South of Kazakhstan found that 17.5% of samples of fruit and berries were contaminated with patulin [54]. In 2004, the Eu-
European Community set maximum levels of patulin in food products, in particular – fruit juices, baby food products from apples, including apple juice.

Huang et al. [55] revealed the simultaneous presence of various mycotoxins in milk samples: 15% of the samples were contaminated by two mycotoxins, 45% by three mycotoxins, and 22% by four mycotoxins. According to researchers [56], the presence of several mycotoxins may increase their toxic effects on human and animal health through addictive, synergistic or antagonistic events. Toxic effects in such cases may occur even in the presence of mycotoxins in quantities that are considered non-toxic for some of them [57].

Ukraine is an agrarian state and can supply grain and food products both to its own market and markets of European countries. The Association of the EU and the expansion of international trade lead to the need for harmonization of national legislation regulating the maximum levels of mycotoxins in raw materials and products of plant and animal origin. In accordance with this, national standards for the permissible content of certain pollutants, including mycotoxins [58], for compliance with European requirements were revised [59]. At present, national regulated levels of mycotoxin content in foods are maximally harmonized to European indicators (Table 1).

<table>
<thead>
<tr>
<th>Food</th>
<th>Mycotoxin</th>
<th>State Hygiene Regulations and Norms (No 774/23306), µg/kg</th>
<th>Commission Regulation (EC) No 1881/2006, µg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk and dairy products</td>
<td>Aflatoxin M1</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Meat and meat products</td>
<td>Aflatoxin B1</td>
<td>5.0</td>
<td>Not regulated</td>
</tr>
<tr>
<td>Vegetable oil</td>
<td>Aflatoxin B1</td>
<td>5.0</td>
<td>Not regulated</td>
</tr>
<tr>
<td>Groats, flour, bread</td>
<td>Aflatoxin B1</td>
<td>5.0</td>
<td>Not regulated</td>
</tr>
<tr>
<td>Unprocessed cereals of cereals</td>
<td>Ochratoxin A</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Food products based on cereal grains</td>
<td>Ochratoxin A</td>
<td>0.5</td>
<td>3.0</td>
</tr>
<tr>
<td>Vegetables, fruits, berries, fruit juices</td>
<td>Patulin</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Unprocessed cereals</td>
<td>Deoxynivalenol</td>
<td>1250</td>
<td>1250</td>
</tr>
<tr>
<td>Pasta</td>
<td>Deoxynivalenol</td>
<td>750</td>
<td>750</td>
</tr>
<tr>
<td>Bread</td>
<td>Deoxynivalenol</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Cereals intended for direct human consumption</td>
<td>Zeaalenone</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Bread</td>
<td>Zeaalenone</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Processed foods based on corn</td>
<td>Fumonisins, the sum of B and B2</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Corn for direct consumption</td>
<td>Fumonisins, the sum of B and B2</td>
<td>1000</td>
<td>400</td>
</tr>
</tbody>
</table>

An analysis of national and European requirements for the control of mycotoxins has shown that national rules set the maximum acceptable level for aflatoxin B1 in meat products, cereals, flour and bakery products, this is not provided for in the European regulation.

For cereals and their processing products, national legislation regulates the definition of six mycotoxins (aflatoxin B1, aflatoxin B1, B2, G1, G2 (sum), zearalenone, deoxynivalenol, ochratoxin A, fumonisins B1 and B2), while in the European Union seven are defined (included also T-2, in total with NT-2 toxin). The maximum level of fumonisins according to the domestic requirements is much higher than the European index. And the permissible level of ochratoxin A is 6 times lower than the European one.

In vegetable oils, the content of aflatoxin B1, fumonisins and zearalenone is regulated in Ukraine, whereas in the EU Regulation the aflatoxin B1 is not specified.

For baby food and dietary products, national requirements include monitoring of the content of seven mycotoxins (aflatoxin B1, aflatoxin M1, ochratoxin A, patulin, zearalenone, deoxynivalenol, fumonisins (sum of B1 and B2), which is fully harmonized with the European regulations.

To control mycotoxins, various methods are used, including for screening analysis (thin-layer chromatography – TCHX, ELISA) and for confirmation (high performance fluorescence detection liquid chromatography – HPLC), liquid mass spectrometry – LS-MS). These methods have their disadvantages, advantages and limits of detection that need to be taken into account when choosing a method for analyzing mycotoxins [60]. According to [61], the HPLC-FLD method is preferred for the anal-
ysis of individual mycotoxins, whereas HPLC-MS/MS can be used to simultaneously detect multiple mycotoxins. Various immunological methods, such as ELISA, are commercially available for the screening of mycotoxins in various foods. In addition, for the analysis of mycotoxins in foods, many other promising methods have been proposed, but they require further testing.

Commission Regulation (EC) No 466/2001 and Codex Alimentarius Commission sets common criteria for sampling, performance criteria for sample preparation and control methods for mycotoxins [62, 63]. At present, there are many European standardized methods for determining mycotoxins in different matrices, including feed for productive animals and food [64–67].

In connection with the expansion of international trade, a number of national standards have been harmonized regarding methods for the determination of mycotoxins in various objects, in particular in food products [68–71].

**Conclusions.** 1. An analysis of numerous literary sources has shown that the issue of monitoring mycotoxins in foods, improving laboratory control and risk-based approach to preventing foodborne mycotoxicosis worries scientists from different countries, including Ukrainian.

2. The analysis of national legislation shows that national standards on maximum levels of pollutants have been revised in Ukraine and a number of standards have been harmonized for methods of monitoring the residues of mycotoxins in feed for productive animals, food products of animal and vegetable origin.

**Information on compliance with bioethical norms.** Experimental and clinical studies were not conducted during the preparation of the review publication.

**Information about conflict of interest.** The authors declare no conflict of interest.

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Природні токсини створюють ризики для здоров’я людей і тварин, виходячи з продовольчої безпеки та харчування, зменшуючи доступ людей до здорової їжі. Всесвітня організація охорони здоров’я постійно звільняє національні органи держав контролювати та забезпечувати, щоб рівень найбільш релевантних природних токсинів у продуктах харчування були якомога нижчими і відповідали як національним, так і міжнародним вимогам.

Членство України в СОТ, асоціація з Європейським Союзом, розширення міжнародної торгівлі потребує звільнення питань щодо забезпечення вільного руху товарів, безпечного та здорового харчування і, відповідно, належного рівня захисту життя та здоров’я людей. Одним із важливих питань їх вирішення є упосередження та гармонізація вітчизняного харчового законодавства з міжнародним, у тому числі й таких нормативних актів, що стосуються питань контролю мікотоксинів.

Тому метою роботи було провести аналіз літературних джерел, міжнародних та національних законодавчих актів щодо контролю мікотоксинів у харчових продуктах упродовж харчового ланцюга.

Для підготовки публікації було використано літературні джерела за темою публікації, а також проведено порівняльний аналіз національних та міжнародних законодавчих актів, що регламентують процедури і методи контролю залишків мікотоксинів у харчових продуктах.

Як показав аналіз численних літературних джерел, питання мікотоксинів упродовж харчового ланцюга, усунення небезпеки угрози впливом на харчовий сектор з метою профілактики харчових мікотоксинів, наголошує високу значущість витрення питань легальних нормативних актів та гармонізації національного законодавства. В Україні були переглянуті витрені нормативні акти мікотоксинів, в якій рівень забезпечення національних, міжнародних та обов’язків в рамках та його концепцій, з метою контролю залишків мікотоксинів у харчових продуктах упродовж харчового ланцюга.

Ключові слова: мікотоксини, харчові продукти, міжнародне законодавство, національне законодавство, контроль, безпека, ризики.

Международное и национальное законодательство по контролю микотоксинов в пищевых продуктах: обзор

Хищак О.А., Герард Р.

Сегодня проблема мониторинга микотоксинов приобрела глобальное значение в связи с изменением климата, нарушением экологического баланса при использовании интенсивных технологий возделывания сельскохозяйственных культур, а также из-за загрязнения воздуха и накопления в нём продуктов фитоценозов (фитоценозов), что приводит к снижению устойчивости растений к фитопатогенам.

С каждым годом проблема микотоксинов становится всё более актуальной, поскольку токсичные продукты широко присутствуют в пищевых продуктах, что может привести к серьезным заболеваниям у людей и животных.

Природные токсинов создают риски для здоровьё людей и животных, влияют на продовольственную безопасность и питание, уменьшая доступ людей к здоровой пище. Всемирная организация здравоохранения постоянно призывает национальные органы государств контролировать и обеспечивать, чтобы уровни наиболее релевантных природных токсинов в продуктах питания были как можно ниже и отвечали как национальным, так и международным требованиям.

Членство Украины в ВТО, ассоциация с Европейским Союзом, расширение международной торговли требует решения вопроса о обеспечении спокойствия в торговле товаров, безопасного и здорового питания и, соответственно, надлежащего уровня надёжности пищевого и здоровой пищи. Одним из важнейших путей решения является совершенствование и гармонизация отечественного пищевого законодательства с международным, в том числе и нормативных актов, касающихся вопросов контроля микотоксинов.

Поэтому целью работы было провести анализ литературных источников, международных и национальных законодательных актов по контролю микотоксинов в пищевых продуктах на протяжении всего периода.

Для подготовки публикации были использованы литературные источники, а также проведены сравнительный анализ национальных и международных законодательных актов, регулирующих процедуры и методы контроля остатков микотоксинов в пищевых продуктах.

Как показал анализ многочисленных литературных источников, вопросы мониторинга микотоксинов по пищевой цепи, совершенствование законодательства, включая введение новых исследований, а также усилена тенденция к гармонизации национальных законодательств. В Украине были пересмотрены отечественные нормативные документы, в том числе и законодательства. Об этом свидетельствует анализ национального законодательства. В Украине были пересмотрены отечественные нормативные документы, в том числе новые документы, а также усилена тенденция к гармонизации национальных законодательств.