## **Information Regarding Toxins**

Mycotoxins are toxic compounds that occur naturally as byproducts of many different types of molds (fungi). Mycotoxin-producing molds can grow on foods such as spices, nuts, and grains, both before and after harvest. They often thrive in foods that are stored improperly in humid conditions. Most mycotoxins are stable compounds that remain harmful to humans even after contaminated food is processed and cooked at recommended temperatures.<sup>1</sup>

Contaminated food usually contains multiple kinds of fungi, and it can be difficult to determine which strains of fungi are responsible for the mycotoxins present and their consequent effects on humans.<sup>2</sup> One strain of fungus may produce several different mycotoxins under certain conditions, and different strains of fungi may produce the same kind of mycotoxins. <sup>3</sup> In general, most studies on mycotoxins' effects on humans are relatively recent, and much is still unknown about their impact.<sup>4</sup> Emerging evidence suggests that climate change may be contributing to the growing prevalence of mycotoxin-contaminated food. <sup>5</sup>

The symptoms of mycotoxins' harmful effects are collectively referred to as mycotoxicosis. Mycotoxicosis can look different in each case, depending on the duration of exposure, dosage, type of toxin, health of the person exposed, and the potential for combined effects with other chemicals. Some people may be more susceptible to mycotoxicosis due to gene mutations that can either increase or decrease the toxic effect of mycotoxins in the body.

## **Trichothecenes**

Trichothecenes (TCNs) are one of the largest groups of mycotoxins that are largely produced by *Fusarium* species of fungi. TCN-producing fungi thrive in foods that are exposed to moisture when improperly stored or packaged. The TCNs accumulate in plant tissues and remain throughout processing, eventually contaminating finished agricultural goods. Water polluted by agricultural run-offs of TCN-infected crops is also a major source of mycotoxin contamination in the environment. Tropical regions are more prone to fungal damage due to

<sup>&</sup>lt;sup>1</sup> https://www.who.int/news-room/fact-sheets/detail/mycotoxins

<sup>&</sup>lt;sup>2</sup> https://www.cpsc.gov/s3fs-public/CPSCStatementmoldmycotoxinhealtheffectsJuly2015.pdf, page 9

<sup>&</sup>lt;sup>3</sup> Fumagalli F, Ottoboni M, Pinotti L, Cheli F. Integrated Mycotoxin Management System in the Feed Supply Chain: Innovative Approaches, § 2.1, Mycotoxin Co-Occurence. Toxins. 2021; 13(8):572. https://doi.org/10.3390/toxins13080572

<sup>&</sup>lt;sup>4</sup> https://www.cpsc.gov/s3fs-public/CPSCStatementmoldmycotoxinhealtheffectsJuly2015.pdf, page 9.

<sup>&</sup>lt;sup>5</sup> Ibid, § 3 Mycotoxins and Climate Change.

<sup>&</sup>lt;sup>6</sup> Liew, W. P., & Mohd-Redzwan, S. Mycotoxin: Its Impact on Gut Health and Microbiota, Occurrence of Mycotoxicosis. Frontiers in Cellular and Infection Microbiology. 2018; 8, 60, page 2. https://doi.org/10.3389/fcimb.2018.00060

<sup>7</sup> Ibid.

<sup>&</sup>lt;sup>8</sup> Liew, W. P., & Mohd-Redzwan, S. Mycotoxin: Its Impact on Gut Health and Microbiota, Occurrence of Mycotoxicosis. Frontiers in Cellular and Infection Microbiology. 2018; 8, 60, page 2.

<sup>&</sup>lt;sup>9</sup> Mahato, D., Pandhi, S., Kamle, M., Gupta, A., Sharma, B., Panda, B... Kumar, P. (2022). Trichothecenes in food and feed: Occurrence, impact on human health and their detection and management strategies, Toxicon, 208, page 63. https://doi.org/10.1016/j.toxicon.2022.01.011.

warm, humid climates that favor fungal growth. Insect infestation and rains during harvest also increase the potential for fungal contamination of foods. <sup>10</sup>

When TCNs are absorbed by the body, they interfere with protein synthesis in cells, eventually leading to irreparable cell damage and cell death. TCNs can cause a wide spectrum of effects, but in general, they target the cells lining the intestine, <sup>11</sup> as well as the skin, kidneys, liver, blood, and immune system. <sup>12</sup> Symptoms include weakness, vomiting, diarrhea, hypotension, loss of appetite, changes to the neuroendocrine system, reduced bone marrow, and suppression of the body's immune response. <sup>13, 14</sup> Chronic exposure to trichothecenes can cause alimentary toxic aleukia. <sup>15</sup>

Studies of the effects of TCNs on humans are scarce, but one study of pigs exposed to *Fusarium* mycotoxins (including TCNs) found significant levels of inflammation and cell death in the pigs' livers. <sup>16</sup> In humans, the liver is an important site of metabolism and detoxification of the blood, and is one of the organs likely to be significantly impacted by absorption of mycotoxins. <sup>17, 18</sup>

Deoxynivalenol (DON), also known as vomitoxin, is one of the most common TCN mycotoxins found in grains around the world. In an outbreak of TCN mycotoxicosis in China due to moldy rice, affected persons developed classic food poisoning symptoms such as chills, vomiting, abdominal pain, and diarrhea. <sup>19</sup> Several outbreaks of mycotoxicosis caused by exposure to DON have been reported in India, China, and the US. <sup>20</sup> There is relatively little known about the specific toxic effects of other kinds of TCNs. <sup>21</sup> Preventing exposure to TCNs is essential as there are no specific treatments or cures for TCN-induced mycotoxicosis. <sup>22</sup>

<sup>&</sup>lt;sup>10</sup> Ibid, page 64.

<sup>&</sup>lt;sup>11</sup> Trichothecenes in food and feed: Occurrence, impact on human health and their detection and management strategies, page 68.

<sup>&</sup>lt;sup>12</sup> Polak-Śliwińska, M., & Paszczyk, B. (2021). Trichothecenes in Food and Feed, Relevance to Human and Animal Health and Methods of Detection: A Systematic Review, § 3,Trichothecenes: Human and Animal Health. Molecules (Basel, Switzerland), 26(2), 454. https://doi.org/10.3390/molecules26020454.

<sup>13</sup> Ibid.

<sup>&</sup>lt;sup>14</sup>https://emergency.cdc.gov/agent/trichothecene/casedef.asp#:~:text=The%20trichothecene%20mycotoxins%20a re%20a,among%20exposed%20humans%20or%20animals.

<sup>&</sup>lt;sup>15</sup> https://realtimelab.com/trichothecenes/

<sup>&</sup>lt;sup>16</sup> Dolenšek, T., Švara, T., Knific, T., Gombač, M., Luzar, B., Jakovac-Strajn, B. (2021). The Influence of *Fusarium* Mycotoxins on the Liver of Gilts and Their Suckling Piglets. Animals (Basel), 11(9), page 12. https://doi.org/10.3390/ani11092534

<sup>&</sup>lt;sup>17</sup> Ibid, page 2.

<sup>&</sup>lt;sup>18</sup> https://www.cpsc.gov/s3fs-public/CPSCStatementmoldmycotoxinhealtheffectsJuly2015.pdf, page 10.

<sup>&</sup>lt;sup>19</sup> Liew, W. P., & Mohd-Redzwan, S. (2018). Mycotoxin: Its Impact on Gut Health and Microbiota, Occurrence of Mycotoxicosis. Frontiers in Cellular and Infection Microbiology. 8, 60, page 3.
<sup>20</sup> Ibid.

<sup>&</sup>lt;sup>21</sup> Streit, E., Schatzmayr, G., Tassis, P., Tzika, E., Marin, D., Taranu, I... Oswald, I. P. (2012). Current situation of mycotoxin contamination and co-occurrence in animal feed--focus on Europe. Toxins, 4(10), page 791. https://doi.org/10.3390/toxins4100788

<sup>&</sup>lt;sup>22</sup> Mahato, D., Pandhi, S., Kamle, M., Gupta, A., Sharma, B., Panda, B... Kumar, P. (2022). Trichothecenes in food and feed: Occurrence, impact on human health and their detection and management strategies, Toxicon, 208, page 69. https://doi.org/10.1016/j.toxicon.2022.01.011.

## **Difficulties in Detection**

When plants become contaminated with mycotoxin-producing fungus, they may attempt to protect themselves from damage by altering the mycotoxin's chemical structure to reduce its toxic effects. This occurs in a process called conjugation, where the plant combines the structures of its own sugars with the mycotoxins. This "masked" or "modified" form of the mycotoxin can be difficult to detect by usual methods but remains harmful to humans, due to the potential for deconjugation during the digestive process. When deconjugated, the mycotoxins are released in their original form. Several kinds of modified mycotoxins have been discovered recently, but many others are still unknown. Current research is limited regarding modified mycotoxins and the way they are released in human digestion.

## **Other Mycotoxins**

In 2004, 125 people in Kenya died of mycotoxicosis after consuming maize contaminated with aflatoxins, another potent kind of mycotoxin. In 2005, more than 75 dogs died in the U.S. after eating pet food also contaminated with aflatoxins. Hundreds of other dogs experienced severe liver problems. <sup>27</sup> Mycotoxins have also been responsible for many epidemics in history, including an outbreak of alimentary toxic aleukia that killed roughly 100,000 people in Russia between 1942 and 1948.<sup>28</sup>

Gliotoxin is another kind of mycotoxin that is an emerging object of focus in mycotoxin studies, so research into its effects on humans is limited.<sup>29</sup> Gliotoxin falls in a class of mycotoxins called ETPs that are produced by a wide variety of molds, including several species of *Aspergillus*.<sup>30</sup> *Aspergillus fumigatus* is a type of mold that is present both indoors and outdoors around the world. It abundantly produces spores that are continuously inhaled by humans but are normally rendered harmless by the body's innate immune response.<sup>31</sup>

Aspergillus fumigatus also produces gliotoxins that suppress the body's immune response by impairing activation of T-cells and inducing cell death in monocytes (a type of

<sup>&</sup>lt;sup>23</sup> Liew, W. P., & Mohd-Redzwan, S. Mycotoxin: Its Impact on Gut Health and Microbiota, Occurrence of Mycotoxicosis. Frontiers in Cellular and Infection Microbiology. 2018; 8, 60, page 2.

<sup>&</sup>lt;sup>24</sup> Polak-Śliwińska, M., & Paszczyk, B. (2021). Trichothecenes in Food and Feed, Relevance to Human and Animal Health and Methods of Detection: A Systematic Review, § 8, Legislation on Trichothecenes in Food and Feed. Molecules (Basel, Switzerland), 26(2), 454. https://doi.org/10.3390/molecules26020454.

<sup>&</sup>lt;sup>25</sup> Ibid.

<sup>&</sup>lt;sup>26</sup> Ibid.

<sup>&</sup>lt;sup>27</sup> https://www.apsnet.org/edcenter/disimpactmngmnt/topc/Mycotoxins/Pages/RecentOutbreaks.aspx

<sup>&</sup>lt;sup>28</sup> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6354945/

<sup>&</sup>lt;sup>29</sup> https://www.frontiersin.org/articles/10.3389/fmicb.2019.02908/full

<sup>30</sup> https://realtimelab.com/gliotoxin/

<sup>&</sup>lt;sup>31</sup> Bugli, F., Sterbini, F., Cacaci, M., Martini, C., Lancellotti, S., Stigliano, E... Posteraro, B. (2014). Increased production of gliotoxin is related to the formation of biofilm by *Aspergillus fumigatus*: an immunological approach, *Pathogens and Disease*, 3(70), page 379. <a href="https://doi.org/10.1111/2049-632X.12152">https://doi.org/10.1111/2049-632X.12152</a>

white blood cell). <sup>32,33</sup> When people with weakened lungs or suppressed immune systems are exposed to *Aspergillus fumigatus*, they can develop Aspergillosis, a fungal disease that can range from mild symptoms to very severe illness. <sup>34</sup> Although most cases of aspergillosis occur sporadically in individuals, outbreaks can occur when vulnerable populations are exposed to high levels of airborne Aspergillus. <sup>35</sup>

Symptoms of exposure to gliotoxins include lung disorders, brain dysfunction, bone marrow dysfunction, and in severe cases, tumors of the brain and lung.<sup>36</sup> Exposure may also aggravate conditions affecting the central nervous system, such as Multiple Sclerosis.<sup>37</sup> Treatments for Aspergillosis include antifungal medications and surgery, but there is no specific treatment to combat the effects of gliotoxin.<sup>38</sup>

<sup>&</sup>lt;sup>32</sup> https://www.sciencedirect.com/topics/neuroscience/gliotoxin

<sup>&</sup>lt;sup>33</sup> https://healthmatters.io/understand-blood-test-results/gliotoxin

<sup>&</sup>lt;sup>34</sup> https://www.cdc.gov/fungal/diseases/aspergillosis/symptoms.html

<sup>35</sup> https://www.cdc.gov/fungal/diseases/aspergillosis/statistics.html

<sup>36</sup> https://realtimelab.com/gliotoxin/

<sup>&</sup>lt;sup>37</sup> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6722733/

<sup>38</sup> https://www.cdc.gov/fungal/diseases/aspergillosis/treatment.html