Food and Chemical Toxicology 123 (2019) 520–521

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Editorial: Mechanism of mycotoxins

Mycotoxins are toxic secondary metabolites produced by filamentous fungi, and are worldwide natural contaminants of food and feed - causing a variety of health problems not only for humans, but also for animals. In 2017, the Rapid Alert System for Food and Feed (RASFF) notified mycotoxins among the top 10 food and product hazard categories.

Fungi are ubiquitous and are capable of producing more than one mycotoxin. Food in turn can be infected by more than one fungus. Consequently, consumers can be exposed to more than one mycotoxin in their diet. Legislations only take into account the risk of the presence of a few single mycotoxins, and more mycotoxins and their combinations in foods and animal feed should be considered for risk evaluation.

Fusarium is one of the most important fungal genera of plant pathogens, and many *Fusarium* species are able to produce mycotoxins. *Fusarium* species are commonly related to pre-harvest contamination of cereal crops, and these results in yield reduction and consequent economic losses. Mostly, however, mycotoxins are associated to various acute and chronic effects in humans and animals.

This special issue of Food and Chemical Toxicology comprises 10 original contributions and four reviews. The issue reports new findings regarding toxic mechanisms and offers a general account of the techniques used to study the potential toxicity of mycotoxins and their combinations.

The *in vitro* and *in vivo* effects of Fumonisin B1 (FB1) in co-exposure with other *Fusarium* toxins such as zearalenone (ZEA), deoxynivalenol (DON), nivalenol (NIV), T-2 toxin (T-2) and emerging mycotoxins like fusaproliferin (FUS), beauvericin (BEA), moniliformin (MON), and enniatins (ENNs) are reviewed by Correa et al.

The *in vitro* models using porcine intestinal epithelial cells and brain capillary endothelial cells represent predictive tools for absorption, transport and direct impairment of xenobiotics. Many fusariotoxins have been tested in these models, and useful information on their toxicity pathways and risk potentials, in the species-specificity context, has been reviewed by Bertero et al.

Terciolo et al. summarizes the mechanisms of action of trichothecenes in different animal species, their toxicological effects and their physiological impact and gastrointestinal regulation in relation to emesis and food intake.

An overview (Marín et al.) addresses the currently developed major biomarkers and the biological matrices where they may be found, such as urine, plasma and breast milk, together with internal exposure levels, potential co-occurrence with environmental chemicals, and the analytical methods employed.

Multi-mycotoxin occurrence in wheat-based products including flour, bread, biscuits, breakfast cereals and pasta has been evaluated in Romania (Stanciu el al.) to establish the risk associated with exposure to both regulated and unregulated *Fusarium* mycotoxins. The authors conclude that there are no potential risks associated with the detected mycotoxins, namely HT-2 toxin, T-2, NIV and ZEA, because the estimated daily intakes (EDIs) are lower than the tolerable daily intakes (TDIs).

Some authors (Carballo et al.) have considered it important to study ready-to-eat foods for assessing the actual intake of mycotoxins. The presence of 27 mycotoxins was evaluated in 328 samples of ready-to-eat foods that are commonly consumed in Spain, mainly by the adult population. The results showed the contamination levels in all food groups to be lower than those often obtained from raw foods and even in cooked food.

One of the most common uncertainties is related to the biotransformation of DON and its mechanisms of elimination *in vivo*. Stool samples were collected from Wistar rats and were analyzed by ultra-high performance liquid chromatography coupled with tandem mass spectrometry detection. The results obtained demonstrated the excretion of DON and the metabolite DOM-1, which exhibits the least toxic properties (Miró-Abella et al.).

Attention to the risk posed to human and animal health has also been extended to ENNs. Since there is currently little information regarding the detection of ENNs and their biotransformation products in tissues and biological fluids, it is complicated to evaluate the potential risk related to exposure to ENNs. Therefore, Rodriguez et al. have investigated the biotransformation processes of ENN B in human urine samples, with the identification of several metabolites in urine.

The comparative *in vitro* cytotoxicity of the emerging *Fusarium* mycotoxins BEA and ENNs in porcine intestinal epithelial cells has been discussed by Fraeyman et al. These authors demonstrated the following increasing order of cytotoxic potency: BEA > ENN A > ENN A1 > ENN B1 > ENN B, this probably being correlated to higher incorporation to the plasma membrane.

The co-occurrence of mycotoxins in food can lead to underestimation of their toxicity. Cytotoxic effects induced by patulin (PAT), DON and T-2 individually and their combinations have been investigated by Fernández-Blanco et al. using *in vitro* method. The results suggest that the co-occurrence of these three mycotoxins in food may increase their cytotoxic effects compared to the cytotoxic effect produced by each mycotoxin alone.

Evaluation has been made of DON, 3-acetyl-DON (3-AcDON) and 15-acetyl-DON (15-AcDON) *in vitro* and *in silico* (Taroncher et al.). The *in vitro* cytotoxicity of DON and its derivatives individually and combined was determined. The DON + 15-AcDON mixture exhibited additive effects, while the rest showed synergistic effects. *In silico* methods assess individual mycotoxins. The *in silico* Swiss ADME tools showed high gastrointestinal absorption and metabolism.

Cytotoxicity, cell cycle and genotoxicity of the mycotoxins DON, 3-AcDON and 15-AcDON were evaluated in HepG2 cells. 3-AcDON

https://doi.org/10.1016/j.fct.2018.11.044

Available online 20 November 2018

showed the highest cytotoxic effect in these cells. The detected cell cycle alterations were associated to the micronucleus (MN), with maximum induction being reached in mycotoxin combinations (Juan-Garcia et al.).

Transcriptomic analysis based on RNA-seq addressing ENN B cytotoxicity in human Jurkat lymphoblastic T cells showed mitochondria to be the main organelles exhibiting more related differentially expressed genes. Alonso-Garrido et al. demonstrated that differentially expressed genes are involved in biological processes, molecular functions and pathways related to mitochondrial metabolism and respiration.

Vettorazzi et al. in turn studied the response between sexes at gene expression level in kidneys of rats treated with ochratoxin A (OTA). Ochratoxin A induced dose-dependent responses in males and females, though the dose effect appeared to be stronger in males.

The guest editors of this special issue, Guillermina Font and María José Ruiz, are grateful to the authors for their contributions and particularly to the referees for their invaluable work.

We also thank José Luis Domingo, Editor-in-Chief of Food and Chemical Toxicology; Jagna Mirska, journal publisher; and Saritha Bhawarlal, journal manager of Elsevier, for their continuous support in the development of this special issue.

Guillermina Font, Maria-Jose Ruiz
Laboratory of Toxicology, Faculty of Pharmacy, University of Valencia, Av. Vicent Andrés Estellés s/n, 46100 Burjassot, Valencia, Spain
E-mail address: Guillermina.Font@uv.es (G. Font).