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Dedicated to our Parents

Preface

Filamentous fungi such as *Aspergillus*, *Fusarium*, *Penicillium*, and *Alternaria* are common contaminants of food, feed, and indoor environment. During unfavourable conditions, they produce toxic secondary metabolites termed mycotoxins. These mycotoxigenic moulds are producers of both "traditional mycotoxins" such as aflatoxins, ochratoxins, fumonisins, trichothecenes, zearalenone, alternariol monomethyl ether, alternariol, and patulin and "emerging mycotoxins" such as penicillic acid, cyclopiazonic acid, gliotoxin, sterigmatocystin, tenuazonic acid, beauvericin, enniatin, fusaproliferin, moniliformin, culmorin, fusaric acid, sterigmatocystin, butenolide, and emodin.

Mushrooms mostly belong to the subdivision Basidiomycotina; however, few of them are included in Ascomycotina. They are healthy food options, but all of them are not edible. Consumption of toxic species of mushrooms may lead to poisoning syndrome, affecting mainly the gastrointestinal tract and the nervous system. Gyromitrin, amanitin, muscarine, isoxazole derivatives and indole derivatives are well-documented mushroom toxins while others like allenic norleucine are not.

Aflatoxins are major contaminants of corn and corn by-products, peanuts, cotton, pistachios, hazelnuts, Brazil nuts, almonds, and dried figs whilst fumonisins are mostly found in maize but are also prevalent in sorghum, wheat, millet and their products, complete and complementary feeding materials for fishes, hens, calves, pigs, rabbits, horses, lambs, ruminants, and pet animals. *Alternaria* toxins AOH and AME have been found to contaminate wheat, sorghum, barley, sunflower seeds, oats, tomatoes, olives, melons, pecans, and peppers. Ochratoxins produced by *Aspergillus* spp., *Penicillium verrucosum*, and *Fusarium* spp. are general contaminants of wheat, barley, oats, rye, coffee beans, and other plant products including beer wines, spices, and chocolate and feed of pigs, poultry birds, and dairy animals. Zearalenone is a naturally occurring mycotoxin of crops, especially maize infected by *Fusarium* spp. ZEA and trichothecenes persist in the products of wheat, rice, maize, barley, oats, soybeans, and sorghum. A high level of patulin occurs in cereals such as barley, corn, wheat and their processed products, fruits like apple and its

products, bananas, grapes, pears, strawberries, apricots, cherries, blueberries, peaches, and plums.

Many fungal metabolites with suspected or known toxicity are designated "emerging mycotoxins". They are known to affect vegetables, cereals and cereal products (bread, beer, and baby food), fruits, processed fruit products, oilseeds, dried fish, naturally fermented sausages, foodstuffs (cheese, miso, sake, and soy sauce), and animal feed. The emerging mycotoxins having less toxic precursors are called T "masked toxins". This category of toxins usually remains undetected during analysis. Despite high incidences of toxicity, they are not legislatively regulated in the food and feed.

Direct or indirect exposure to mycotoxins leads to mycotoxicoses in humans and animals. Aflatoxins are potent carcinogens. Aflatoxicosis together with hepatitis B virus is accountable for thousands of human deaths per year, especially in tropical regions. In chickens, pigs, and cattle, effects of aflatoxins include liver and kidney damage. Ochratoxin A, however, is responsible for urinary tract cancer and kidney damage. Fumonisins cause oesophageal cancer and DNA damage in humans and birth defects in mice. Trichothecenes are highly immunosuppressive while zearalenone has oestrogenic effects in animals and men. Patulin, however, is geno-, hepato-, and nephrotoxic. The inhalation of aflatoxins, ochratoxins, stachybotryotoxins, and *Fusarium* mycotoxins has ill health effects in the occupants of damp indoor environments and mouldy buildings. A cocktail of mycotoxins and indoor contaminants (like smoke) induce respiratory disorders and general intoxication as well. The additive effect of mycotoxins is more hazardous than that of a single one and often leads to more severe co-occurrence poisoning.

Although overlapping symptoms make the diagnosis of mycotoxicoses difficult, some specific clinical signs like weight loss and feed refusal in animals, tremors, hepatic and renal necroses, and lung scarring can be helpful in the differential diagnosis of mycotoxicological effects in humans and animals.

A single method for the control of mycotoxins would not be suitable for all agricultural commodities owing to their different chemical structures. Since very low concentrations of mycotoxins are responsible for toxicity, sensitive and reliable techniques are required for detection. TLC, GC, HPLC, LC-MS, and LC-MS/MS have been established as confirmatory techniques in mycotoxin analysis. Apart from this, ELISA dipstick assay, lateral flow tests NIR, MIR using infrared spectroscopy, molecularly imprinted polymers (MIPs), capillary electrophoresis, fluorescence polarization, labelled optical-read dipstick assays, biosensors based on surface plasmon resonance (SPRs) or fibre-optic probes, and immunological array and nanomaterial-based biosensors are rapid screening methods for detecting the presence of a single or multiple mycotoxins.

The easiest strategy to prevent the formation of mycotoxins is to reduce the growth of moulds. Fertilizers, opportune crop rotation tillage, date of the plantation, selection of genetically modified crops, control of infestation by biological or chemical treatments, removal of the crop, and control of insect and weed are widely discussed aspects to prevent fungal infestation and, thus, mycotoxin production in the fields. Since the discovery of aflatoxins in the 1960s, regulations regarding the

intake of mycotoxins have been implemented by several countries. Generally, the establishment of mycotoxin limits is based on factors such as mycotoxin level in the articles, food consumption and toxicological data, food security issues, and methods of analysis. Due to multi-mycotoxin contamination, the complete destruction of mycotoxins is not possible. Therefore, hazard analysis and critical control point (HACCP) based approach is a control programme for processed foods and feeds including strategies for prevention control, good manufacturing practices, and quality control at all stages of production from field to the final consumer. Uses of additives such as propionic acid, ammonia, and silage additives of microbial and enzymatic origin can turn out to be helpful in controlling mould growth and, consequently, mycotoxin production.

Toxicodynamics and toxicokinetics are two important aspects of mycotoxicological studies explaining the relationship between a toxicant and its biological targets. The kinetics of a mycotoxin can be determined by its route/s of entry and ADMET (Absorption, Distribution, Metabolism, Elimination, and Toxicity) properties. Nonetheless, toxicodynamic methods evaluate the mechanism of action and toxicological effects of the toxicant. In silico methods for mycotoxin risk assessment have also been used to obtain supporting data.

This book has ten chapters. The first chapter covers the historical perspective of mycotoxins along with the timeline while the second one provides an overview including the classification of mycotoxins and mycotoxicoses. Comprehensive information on traditional, emerging, and mushroom mycotoxins is given in Chaps. 3, 4, and 5, respectively. Chapter 6 deals with mycotoxins co-occurrence poisoning whereas new and masked mycotoxins are described in Chap. 7. Mycotoxin detection methods are explained in Chap. 8. The ninth chapter includes mycotoxin management strategies. The last (tenth) chapter of the book covers recent developments in mycotoxicokinetics and mycotoxicodynamics.

The book addresses a wide range of readers including mycologists, clinicians, agricultural scientists, chemists, veterinarians, environmentalists, and food scientists, providing all-around knowledge about mycotoxins to date in a simple manner.

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Contents

Abbreviations

^{1}H NMR	Proton nuclear magnetic resonance
^{3}H-FX	Radioactive Fusarenon-X
3-NPA	3-Nitropropionic acid
AAL toxins	*Alternaria alternata* toxins
AAL-TA	*Alternaria alternata* toxins TA
AAL-TB	*Alternaria alternata* toxins TA
ACROs	Acromelic acids
Af	Aflatoxin
aflJ	Aflatoxin biosynthetic gene
aflR	Regulatory gene *aflR*
AHDA	Amino hexadienoic acid
ALARA	As low as reasonably achievable
ALTCH	Alteichin
ALTs	Altertoxins
AME	Alternariol monomethyl ether
AMV RT	Avian myeloblastosis virus (AMV) reverse transcriptase
AOH	Alternariol
AQA	Analytical quality assurance
ATA	Alimentary toxic aleukia
ATX-I	Altertoxins I
ATX-II	Altertoxins II
ATX-III	Altertoxins III
ATXs	Altertoxins
AUC_{0-t}	Area under the concentration-time curve from time zero to the last measurable concentration
a_w	Water activity
BBB	Blood-brain barrier
BEA	Beauvericin
BUT	Butenolide
bw	Body weight

C-4	Acetyl residues
CaCo-2	Colorectal adenocarcinoma cells-2
CCPs	Critical control points
CEC	Commission of the European Communities
CFCF	Cell-free culture filtrate
CIT	Citrinin
Cl	Clearance
Cmax	Maximum (or peak) serum concentration
CNS	Central nervous system
CPA	Cyclopiazonic acid
CT	Computed tomography
CTN	Citrinin
CUL	Culmorin
CYP 450	Cytochromes P450
CYP1A2	Cytochrome P450 family 1 subfamily A member 2
CYP3A4	Cytochrome P450 family 3 subfamily A member 4
CYP3A5	Cytochrome P450 family 3 subfamily A member 5
D3G	Deoxynivalenol-3-glucoside
DAS	Diacetoxyscirpenol
DDGS	Dried distillers' grains with soluble
DESI	Desorption electrospray ionization
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DOM	Deepoxy-DON
DOM-1	Deepoxy metabolite of DON
DON	Deoxynivalenol
EA	Ergot alkaloids
EC	Oesophageal cancer
EFSA	European Food Safety Authority
ELEM	Equine leukoencephalomalacia
ELISA	Enzyme-linked immunosorbent assay
EMO	Emodin
ENN	Enniatins
ENNs	Enniatins
EU	European Union
F	Bioavailability
F. verticillioides	MRC 826
FA	Fusaric acid
FAO	Food and Agriculture Organization of the United Nations
FAPAS	Food Analysis Performance Assessment Scheme
FB	Fumonisins B
FB1	Fumonisin B_1
FLD	Fluorescence detection
FMEA	Failure mode and effect analysis

FPIA	Fluorescence polarization immunoassay
FTIR	Fourier transform infrared spectroscopy
Fum5 gene	Fumonisin synthase gene
FUS	Fusaproliferin
FX	Fusarenon-X
GABA	Gamma-aminobutyric acid
GAP	Good Agricultural Practices
GC	Gas chromatography
GC-MS	Gas chromatography-mass spectrometry
GDP	Guanosine diphosphate
GHP	Good Hygienic Practices
GI	Gastrointestinal tract
GMP	Good Manufacturing Practices
GSP	Good Storage Practices
GT	Gliotoxin
HACCP	Hazard analysis and critical control point
HPLC	High performance liquid chromatography
IARC	International Agency for Research on Cancer
IBO	Ibotenic acid
IDH	Isoepoxydon dehydrogenase
IEC	Intestinal epithelial cell
IG	Intra-gastric
IP	Intra-peritoneally
iv	Intra-venous
JECFA	Joint FAO/WHO Expert Committee on Food Additives
KDa	Kilodalton
LADME	Liberation, absorption, distribution, metabolism and excretion
LC	Liquid chromatography
LC-MS	Liquid chromatography-mass spectrometry
LC-MS/MS	Liquid chromatography-mass spectrometry/mass spectrometry
LFD	Lateral flow devices
LLC-PK1 renal cells	Epithelial cell line originally derived from porcine kidneys
LOD	Limit of detection
LOQ	Limit of quantification
LSD	Lysergic acid diethylamide
MFH	*N*-methyl-*N*-formylhydrazine
MH	Monomethylhydrazine
MON	Moniliformin
MPA	Mycophenolic acid
MRT	Marginal rate of transformation
MS	Mass spectrometry
MUS	Muscimol
MW	Molecular weight

Na-K ATPase	Sodium potassium pump adenosine triphosphatase enzyme
NASBA	Nucleic acid sequence-based amplification
NIH/3T3	3-day transfer, inoculum 3×10^5 cells from NIH mouse embryonic fibroblast cells
NIR	Near-infrared
NIV	Nivalenol
nor-1 gene	Neuron-derived orphan receptor-1
NRPSs	Non-ribosomal peptide synthetases
OTA	Ochratoxin A
OTB	Ochratoxin B
OT-GSH	OTA-glutathione conjugate
OTHQ	OTA-hydroquinone
OTQ	OTA-quinone
PA	Penicillic acid
PAT	Patulin
PCR	Polymerase chain reaction
PIDI	Provisional tolerable daily intake
PIWI	Provisional tolerable weekly intake
pks-A	Polyketide synthases
po	*Per os*
PPE	Porcine pulmonary oedema
ppm	Parts per million
RNA	Ribonucleic acid
Rnase H	Ribonuclease H
RP-HPLC	Reversed phase high performance liquid chromatography
RT PCR	Real-time polymerase chain reaction
RT	Room temperature
SH	Sulfhydryl groups
SLUDGE	Salivation, lacrimation, urination, defecation, gastrointestinal distress, and emesis
SPE Cartridges	Solid phase extraction cartridge
SPSR	Surface plasmon resonance sensors
SSR	Self-sustained sequence replication
STC	Sterigmatocystin
STE III	Stemphyltoxins III
STE	Stemphyltoxins
$t_{1/2}$	Half-life
T-2	T-2 toxin
T7 RNA	T7 bacteriophage that catalyses the formation of RNA from DNA
T7 RNA polymerase	RNA polymerase from the T7 bacteriophage
TCs	Trichothecenes
TDI	(Maximum) tolerable daily intake
TeA	Tenuazonic acid