

Martin Weidenbörner

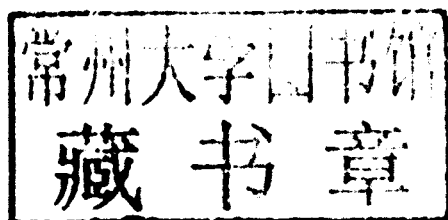
Mycotoxins and Their Metabolites in Humans and Animals



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Helene

Preface

Mycotoxins are secondary toxic mold products which are widespread in foods and feeds. The already published books *Mycotoxins in Feedstuffs* and *Mycotoxins in Foodstuffs* provide a good overview of mycotoxins. It is estimated that 4.5 billion of the world's population are exposed to mycotoxins, which can be found in temperate as well as in continental climates. However, especially in low-income countries (e.g., parts of Africa, Southeast Asia, Central and South America) people are chronically exposed to high levels of mycotoxins. In these countries, staple foods like groundnuts and other nuts, maize, as well as other cereals, are especially affected. For example, in West Africa aflatoxin contamination of humans starts in utero and continues throughout life. Besides the hepatitis B virus (HBV), exposure to high levels of dietary aflatoxins poses a major risk for developing human hepatocellular carcinoma (HCC) in these countries. However, even low levels of aflatoxin ingestion causes a suppression of the immune system and increases susceptibility to diseases in several animal species.

Besides their acute toxicity, mycotoxins have other harmful effects. They are, for example, cytotoxic, genotoxic, hepatotoxic, nephrotoxic, mutagenic, neurotoxic, and teratogenic. Human toxicoses due to mycotoxins have been reported, for example, in China, India, Japan, Kenya, Korea, and Russia. If optimal conditions of temperature, humidity, and a suitable substrate prevail, mycotoxins are produced on agricultural commodities in the field, in storage and/or during processing. Because mycotoxins are known to have these detrimental effects, many countries have set legal limits for these toxic fungal metabolites in order to limit their intake.

Contamination especially by aflatoxins, fumonisins, ochratoxin, deoxynivalenol, and zearalenone of a wide range of food products from around the world is of major concern. These food products are mainly of plant origin. Foodstuffs of animal origin, except milk and derived products, show a lower contamination rate. Furthermore, their mycotoxin concentration is usually low. Therefore, food items of animal origin generally pose a minor danger to consumers. However, the milk and breast milk mycotoxin AFM₁, which is also found in milk-derived products, can concentrate on foods. As a result, the contamination of babies via breast milk (mainly AFM₁) in different parts of the world should not be underestimated. The capacity of babies for biotransformation of carcinogens is generally slower than that in adults. By comparison, foodstuffs of plant origin play a major role in the mycotoxin contamination of human beings. This mycotoxin contamination is well

documented. It is also proved by several publications, which show the presence of mycotoxins in human organs, tissues, and fluids.

Besides the above-mentioned mycotoxins, numerous other toxic fungal metabolites exist, which all pose either a minor or major danger. They are of great concern from a food perspective regarding human exposure.

This book summarizes the results of publications dealing with the natural and artificial contamination of humans and animals by mycotoxins, as well as mycotoxin experiments with animals. The major part of the book lists animal studies that investigate deposits and elimination of these toxic fungal metabolites. Furthermore, the results of articles documenting mycotoxin contamination of pets are also presented. In addition, information about detoxification products and the duration of a mycotoxin in and its clearance time from an animal are given. Moreover, the book gives advice on whether antimycotoxic substances are effective in reducing mycotoxin contamination in animals and humans.

This book provides physicians with a fast and comprehensive overview of the countries in which mycotoxin contamination of humans predominantly happens, as well as the concentration at which specific mycotoxins are found in human organs, tissues, and fluids. Veterinarians are informed about what mycotoxins, at what concentrations, can be found naturally in animals. More detailed information is presented if the index number referring to the corresponding publication at the end of the book is used.

This book may be suitable for physicians (global), pathologists (global), epidemiologists, veterinarians, nutritionists, livestock breeders, pet keepers, farmers, the food and feed industry, institutes (e.g., consumer production), ministries (global), libraries, hospitals, healthcare stations, UNO, mycologists, mycotoxicologists, microbiologists, biologists, and students of corresponding fields.

For practical use, the different mycotoxins in humans, animals, organs, tissues, or fluids are listed showing natural or artificial mycotoxin contamination. Therefore, each mycotoxin can be looked up for natural or artificial presence at the end of the book.

The book exclusively comprises articles treating concentrations of mycotoxins in humans or animals. Publications or data which express mycotoxins in % values, radioactivity or in other ways are not considered. Articles dealing with *in vitro* data are also not presented. All articles presented are available as publications of German Scientific Libraries as well as the U.S. National Library of Medicine–National Institutes of Health. The most cited publications have been included. Articles cited in this book have been selected by preference, where a declaration of a mycotoxin concentration or any advice of it is given in the title. Nevertheless, some articles containing no concentration declaration in the title, but only in the running text, are also cited.

Each declaration of the mycotoxin contamination of humans or animals comprises five main categories, e.g.:

incidence: 3/7 - three positives for aflatoxin contamination in relation to seven investigated sample

sample constitution: origin of the test people and/or composition of the sample
contamination: natural or artificial (which concentration of a mycotoxin has
been applied in an experiment)
concentration: residue values of the mycotoxin(s)
country: origin of the publication, in some cases, also origin of the test
people.

If a sample shows a “natural contamination”, information on the sample constitution is given briefly. In most cases, where a sample shows a “natural contamination”, details were not available in the corresponding article so further comments are omitted. This may not be true for human beings. In the case of an “artificial contamination”, a more precise definition of the sample constitution is presented.

Usually, the highest mycotoxin value or the highest and the lowest value of mycotoxin contamination in an experiment is given. The presented concentrations occur in the way they are presented in the published papers. If a variant of a trial is not listed, no mycotoxin contamination is recorded. However, in some cases, a variant may be stated although mycotoxin concentration is not detected. In general, HPLC values have been used for concentration declaration.

If concentration of milk mycotoxins is given, this milk more or less comes directly from cows (natural contamination). You will find additional information about natural mycotoxin contamination of milk, for example processed milk (pasteurized, UHT-milk, etc.) in *Mycotoxins in Foodstuffs*. In addition, data on the natural mycotoxin contamination of “cow milk”, “human breast milk”, “pig kidney”, “pig serum”, etc., can be found in the book *Mycotoxins in Foodstuffs*. For a comprehensive overview, these values as well as new data have also been published here.

Bonn, Germany

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Abbreviations

AC	β-apo-8'-carotenal
ACs	activated carbons
af	affected
AF(s)	aflatoxin(s)
AFB-AA	aflatoxin B ₁ -albumin adducts
AFB ₁	aflatoxin B ₁
AFB ₁ <i>endo</i> -epoxide	aflatoxin B ₁ 8,9- <i>endo</i> -epoxide
AFB ₁ <i>exo</i> -epoxide	aflatoxin B ₁ 8,9- <i>exo</i> -epoxide
AFB ₁ -FAPy	8,9-dihydro-8-(2,6-diamino-4-oxo-3,4-dihydropyrimid-5-yl-formamido)-9-hydroxyaflatoxin B ₁
AFB ₁ -FAPyr	2,3-dihydro-2-(N ⁵ -formyl-2',5',6'-triamino-4'-oxo-N ⁵ -pyrimidyl-3-hydroxyaflatoxin B ₁
AFB-N ⁷ -FAPy (minor)	8,9-dihydro-8-(2-amino-6-formamido-4-oxo-3,4-dihydropyrimid-5-yl amino)-9-hydroxyaflatoxin B ₁
AFB-N ⁷ -FAPyr (major)	8,9-dihydro-8-(2,6-diamino-4-oxo-3,4-dihydropyrimid-5-yl formamido)-9-hydroxyaflatoxin B ₁
AFB-N ⁷ -Gua	2,3-dihydro-2-(N ⁷ -guanyl)-3-hydroxyaflatoxin B ₁
AFB ₁ -N ⁷ -Gua ¹	2,3-dihydro-2-(N ⁷ -guanyl)-9-hydroxyaflatoxin B ₁
AFB ₁ -N ⁷ -Gua ²	2,3-dihydro-2-(N ⁷ -guanyl)-3-hydroxyaflatoxin B ₁
AFB ₁ -N ⁷ -Gua ³	8,9-dihydro-8-(N ⁷ -guanyl)-9-hydroxyaflatoxin B ₁
AFB ₁ -SG	aflatoxin B ₁ -glutathione conjugate
AFB-GuaI	2,3-dihydro-2-(7'-guanyl)-3-hydroxyaflatoxin B ₁
AFB-NAC	AFB ₁ -mercapturic acid
exo-AFB ₁ -NAC	exo-AFB ₁ -mercapturic acids
AFL	aflatoxicol
AFL-g	aflatoxicol-glucuronide
AFLM ₁	aflatoxicol M ₁
AFLM ₁ -g	aflatoxicol M ₁ -glucuronide
AFM ₁	aflatoxin M ₁
AF-N ⁷ -Gua	aflatoxin-N ⁷ -guanine

AFP ₁	aflatoxin P ₁
AFQ ₁	aflatoxin Q ₁
AMB	amphotericin B
avg	average
b wt	bodyweight
B-I/B-II	barley cultures of <i>Penicillium viridicatum</i>
BC	β-carotene
BEN	Balkan endemic nephropathy
BHA	2(3)- <i>tert</i> -butyl-4-hydroxyanisole
BHT	butylated hydroxytoluene
bmi	body mass index
BNF/βNF	β-naphthoflavone
BSO	D,L-buthionine-S-sulfoximine
L-BSO	L-butionine-sulfoximine
ca	case(s)
CAC1	activated charcoal
CAC2	activated charcoal
CHL	chlorophyllin
CIN	chronic interstitial nephropathy
CIT	citrinin
CMD	choline/methionine-deficient diet
CMS	complete basal diet
conc	concentration
const	constitution
CP	calcium propionate
CPA	cyclopiazonic acid
CPFA	cyclopropenoid fatty acid(s)
CPL	clinoptilolite
CPR	chromatogram poorly resolved
CX	canthaxanthin
DAS	diacetoxyscirpenol
DEDON	deepoxydeoxynivalenol
DEM	diethyl maleate
DHBV	duck hepatitis B virus
DHEA	dehydroepiandrosterone
DIOL	2,3-dihydro-2,3-dihydroxyaflatoxin B ₁
DMSO	dimethyl sulfoxide
DNA	desoxy nucleic acid
DOM/DOM-1	deepoxydeoxynivalenol = 3α,7α, 15-trihydroxytrichothec-9,12-diene-8-one
DON	deoxynivalenol (vomitoxin)

3-aDON	3-acetyldeoxynivalenol
DYP	dried yeast product
EFDV	encephalopathy and fatty degeneration of the viscera
ELISA	enzyme-linked immunosorbent assay
EN	endemic nephropathy
eq	equivalent(s)
EQ	ethoxyquin
FA	fusaric acid
FB ₁	fumonisin B ₁
FB ₂	fumonisin B ₂
FB ₃	fumonisin B ₃
FPC	fish protein concentrate
FX	fusarenon-X
Gluc	glucuronide conjugate
GSH	reduced glutathione
GTP	green tea polyphenol
GUA/Gua	guanine
HbsAg	hepatitis B virus surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HPLC-f	high-performance liquid chromatography with fluorescence detection
hr	hour(s)
HSCAS	hydrated sodium calcium aluminosilicate
hum	human(s)
I3C	indole-3-carbinol
ia	intra-aortal
IA	invasive aspergillosis
IDMS	isotope dilution mass spectrometry
ig	intra-gastric
in	intranasal
ip	intraperitoneal
it	intratracheal
iv	intravenous
ivs	intravascular
KIN	karyomegalic interstitial nephritis
LOD	limit of detection
LOQ	limit of quantification
Lys-AFB ₁ /AFB ₁ -lys	lysine-AFB ₁ /AFB ₁ -lysine

min	minute(s)
MOS	mannan oligosaccharide
MWF	micronized wheat fibers
3-MC	3-methylcholanthrene
na	not analyzed
NAC	mercapturic acid
nd	not detected
ndr	not determined
nec	no exact comment
neg	negative
NIV	nivalenol
NMB	nonmoldy barley
NMB+T	nonmoldy barley+toxin
no	number
NPC	nonparenchymal cells
NR	not reported
o	oral
OTA	ochratoxin A
OP-OTA	lactone opened ochratoxin A
OTA-OH	4-hydroxyochratoxin A
OT α	ochratoxin α
PA	penicillic acid
PB	phenobarbital/phenobarbitone
PC	parenchymal cells
PCB	polychlorinated biphenyls
peo	test people
PG	propylene glycol
PHC	primary hepatocellular carcinoma
PNA	penitrem A
pos	positive
pr	present(ed)
RBC	red blood cells
resp	respectively
rRNA	ribosomal ribonucleic acid
sa	sample(s)
sc	subcutaneous
SG	glutathione
t	topical
tr	traces
TRICHO	trichothecene

UTT	urinary tract tumors
VER	verrucarol
WHV	woodchuck hepatitis virus
wt	weight
YCW	yeast cell walls
ZEA	zearalenone
ZEA-Gluc	zearalenone-glucuronide
α -ZEAOL	α -zearalenol
α -ZEAOL-Gluc	α -zearalenol-glucuronide
β -ZEAOL	β -zearalenol
β -ZEAOL-Gluc	β -zearalenol-glucuronide
\pm	higher/lower values are reported

Notation

kg = Kilogram

mg = Milligram = 10^{-3} g; 1 mg/kg = $1:10^6$ = ppm = parts per million

μg = Microgram = 10^{-6} g; 1 μg/kg = $1:10^9$ = ppb = parts per billion

l = Liter

ml = Milliliter = 10^{-3} l; 1 ml/l = $1:10^3$

μl = Microliter = 10^{-3} ml; 1 μl/l = $1:10^6$ = ppm = parts per million

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