Mycotoxins in milk for human nutrition: cow, sheep and human breast milk

Abstract

Mycotoxins are produced pre harvest by some molds and secreted into various food items of plant origin, such cereals, vegetables, spices, coffee and nuts. If the food items are not stored under adequate conditions, a post harvest contamination may also occur. Animals and humans take them up by food items and some of them are stored and accumulated in different tissues and organs, so that food of animal origin may be contaminated, too. Especially aflatoxin and ochratoxin are secreted into milk by consumers of contaminated food. Since milk represents the major food source of newborns and infants, they are notably exposed to these mycotoxins. This health risk for these individuals may be of particular importance, because their ability to metabolize these fungal toxic agents is not yet fully developed at this stage.

Keywords: mycotoxins, aflatoxin, ochratoxin, cow milk, human breast milk

Introduction

In principle, fungi are able to challenge human health by various ways, namely by inducing infection, by triggering allergy or by intoxication (Table 1).

The role of some pathogenic fungi as causative agents of infections is wellknown [1]. The allergenic potential of fungi is rather widely noted as well [2]. The pathogenic role of toxic effects of fungi [3], however, is highly underestimated.

There are at least 400 defined mycotoxins generated by certain toxigenic fungal species; but not every strain out of a toxigenic species will be able to produce toxins, which are secondary metabolites produced predominantly in the late-logarithmic phase of growth dependent on certain environmental conditions such as nutrient supply and temperature [3]. In addition, some volatile organic compounds from fungi may also be toxic for humans [4]. The effects of these biologically active substances may be quite different; some will be immunosuppressive [5] others carcinogenic, mutagenic, teratogenic as well as organ toxic for example for liver, kidney and nervous system; some mycotoxins exert rather hormone-like effects [3].

Only few of these fungal toxins are taken up by inhalation; the majority is ingested by various food items such as cereals, nuts, meat, spices, coffee, beer, wine as well as fresh fruit juices [6]. Acute signs of intoxication in humans are rare, because in general the amounts of toxins in the consumed food items are too low. But by accumulation the fungal agents may achieve gradually relevant concentrations in a human consumer, so that the detrimental effects will become manifest only after a certain lag-phase – sometimes after long periods. These chronic toxicities may be even accentuated by a cocktails of various mycotoxins present in food. Furthermore, the consequences may be aggravated by synergistic actions of other noxious agents such as chemicals (for example carcinogenic agents) or infectious organisms inducing chronic inflammatory reaction (for example Hepatitis B virus) [6].

To provide maximum security for public health the EU [7] has published regulations. Food items destined for human use are in general controlled by governmental authorities; at least some aliquots are examined. Furthermore, there are regulations by EU authorities for certain mycotoxins in animal foodstuff [8]. Since the standards for animal nutrition are lower than for human use, animals ingest often feed with high levels of mycotoxins. Because the degradation of mycotoxins in the animals is limited, there is a carry over to humans by consumption of meat for example. Hence, the daily intake of various mycotoxins by such as deoxynivalenol, ochratoxin, zearalenone, fusonisin and patulin is considerable in an adult consumer. Especially in countries with low food hygiene the burden can be rather excessive [6], [9].

Some mycotoxins will be transferred into certain compartments of the consumer [10]. Of particular interest is the presence of mycotoxins in milk especially of aflatoxin and ochratoxin, so that already newborns may be exposed to these harmful agents [11].

The tricky problem is, that the consumer may not be able to recognize the risk, because mycotoxin producing fungi do not multiply in the milk itself and therefore the appearance is not different from innocuous samples; furthermore, the mycotoxins do not alter the taste of the food item. Hence, the content of mycotoxins in milk product should be assessed regularly in the laboratory or rules for the handling should be worked out.
The special role of aflatoxin

Aspergillus flavus (Figure 1A) as well as other Aspergilli such as Aspergillus parasiticus (Figure 1B) are able to produce aflatoxin B₁ as well as several other chemically related derivatives. Aflatoxin B₁ is generally found in various legumes and cereals, i.e. corn, wheat, rey, and barley. Especially under wet and warm environmental conditions the production increases; the contamination with mycotoxins may occur pre-harvest as well as post-harvest, when the storage conditions are favorable for fungal growth. In principle, the burden of aflatoxin is higher in tropical areas than in countries with moderate climate. Hence, the aflatoxin content in animal food grown in Europe is relatively low, i.e. under the limit of 4 µg/kg. Until recently, contamination was generally confined to imported foods. In 2013, however, because of the global warming, maize elevated in South-East Europe also contained considerable amounts [12]. Nuts, especially pistachios, almonds and hazelnuts, are often highly contaminated, so that the tolerable limit had to be raised to 10 µg/kg for ready to eat items [13]. In other food items, such as eggs and meat, the aflatoxin content is only low [10].

Aflatoxin B₁ (Figure 2A) is highly carcinogenic and in addition immunosuppressive, mutagenic and teratogenic. In the liver it is converted through enzymatic hydroxylation by means of cytochrome P450-associated enzymes into aflatoxin M₁ (Figure 2B), which about 10-fold less active
than aflatoxin B₁. It has been classified as a group 1 human carcinogen [14]. This derivative is then excreted into the milk. The European Commission has determined the tolerable limit for aflatoxin M₁ in raw milk, treated milk, and dairy products at 50 ng/kg. The concentrations in infant formulae, infant milk, and special food products should not exceed 25 ng/kg. Exposure of infants to aflatoxin M₁ is worrisome, because their capacity for biotransformation of carcinogens is generally lower than that of adults and consequently they are more susceptible to adverse effects of mycotoxins [15].

The special role of ochratoxin

Aspergillus ochraceus together with many other Aspergilli, and Penicillium verrucosum produce ochratoxins. Several derivatives have been described with ochratoxin A as the major agent. This fungal product is present in many food items of plant origin, i.e. cereals, legumes, nuts, spices, raisins, beer, wine and coffee. Since ochratoxin is not degraded in the intestine by a human consumer after ingestion, it can be found also in meat of pork and poultry. Consequently, this mycotoxin is generally present in many food items in large amounts. It is one of the the major mycotoxins in food. Furthermore, it has to be kept in mind that in most instances ochratoxin is detected together with other mycotoxins such as deoxynivalenol and zearalenone in the same food item [3].

Ochratoxin is accused to be carcinogenic, immunotoxic, neurotoxic and in particular nephrotoxic [6]. The metabolisation of this agent in humans is rather limited, so that it will be accumulated in the body. Its role in pregnant women has been assessed quite recently [16]. EFSA [17] fixed the “tolerable weekly intake” of ochratoxin A at 120 ng/kg equivalent to a tolerable daily intake of 14 ng/kg. (Other organizations have established even lower limits for intake of ochratoxin A). According to the consumption habits of a certain population this arbitrary limit can be often exceeded, for example by strong coffee drinkers [16]. For instance, in the so-called “mediterranean diet” one can find an 8-fold higher content of mycotoxins including ochratoxin [11].

Mycotoxins in cow as well as ovine milk

At least some mycotoxins such as aflatoxin and ochratoxin are secreted into the milk, so that relatively high levels can be achieved. In contrast, other mycotoxins such as deoxynivalenol and zearalenone, are found in milk only in low concentrations [18]. This applies also to gliotoxin [19].

Dependent on the mycotoxin burden of animal food the concentrations of aflatoxin and ochratoxin found in cow milk may surpass in certain countries the tolerance limits [20], [21], [22], [23]. The maximum levels of aflatoxin exceeded the safety limits given by the EU, namely 0.05 µg/kg, in up to 75% [24]. Ochratoxin also may be present in concentrations much higher than the tolerable limits [25]. Since most of these fungal metabolites are highly temperature resistant [26], they may survive pasteurization and may be present in active form also in dairy products such as cheese and yogurt. In ovine milk lower but not negligible amounts are found [27].

Mycotoxins in human breast milk

In some regions of the world, the burden of food items with mycotoxins is substantial and therefore the oral intake of some mycotoxins by women notable. The content of mycotoxins in milk is related to the maternal dietary habits.

Especially in habitual consumers of bread, bakery products and cured pork meat ochratoxin is found often in breast milk even in considerable levels [25], [28], [29], [30], [31], [32], [33]. In Italy 74% of human breast milk samples yielded high amounts of ochratoxin; in certain samples very high concentrations of up to 405 ng/l have been detected [30] reaching almost the limits of 500 ng/kg proposed by the EU authorities [7]. The yield of aflatoxin M₁ varies definitely. In tropical countries the burden seems to be very high in the majority of samples with levels far beyond the tolerated limits [34], [35], [36]. In some European and other countries aflatoxin M₁ could not be detected or only in very few samples of human breast milk [15], [29], [37]. Furthermore, several other mycotoxins such as deoxynivalenol and zearalenone as well as some their metabolites could be found in human breast milk [38].

Consequences

After birth, breast milk or infant formulae constitute an important or often sole food source for infants during their first months of life. It is evident that breast milk as well as infant formula diets represent a relevant source of mycotoxins for neonates and infants, since their presence in samples collected in several European countries has been documented. Therefore, the presence of mycotoxins in human milk is considered to cause certain risks for infant health [15]. In developing countries especially in countries with tropical climate, food for animals as well as humans is highly contaminated with mycotoxins; hence, the mycotoxin levels in breast milk as well as in infant formulas are in general definitely higher and hence proved to be a health risk for newborns and infants [9]. Because of the climate warming, it can be expected, that this risk may increase in the future in Europe, too. At least the exposition of animals to food contaminated with aflatoxin has become a relevant problem [12].

Form the various mycotoxins present in food aflatoxin and ochratoxin play the major role, because these fungal products are secreted into the milk of animals and...
women. Ochratoxin is the most abundant mycotoxin in milk. In European countries aflatoxin is still of minor importance. In general, aflatoxins included aflatoxin M \textsubscript{1} \cite{14} may exert adverse health effects for the exposed infant, namely growth retardation and jaundice \cite{39}. Consequently, for the sake of protection of the consumers the risk assessment as well as the risk management of mycotoxins in milk products should be refined. The information about the various noxious agents and their respective health risks is the first step.

Notes

Competing interests

The authors declare that they have no competing interests.

References

1. Hof H, Heinz W, editors. Kompendium medizinische Mykologie. Ein Ratgeber für Klinik, Praxis und Labor. Linkenheim-Hochstetten: Aesopus Verlag; 2010. ISBN 978-3-936993-50-9. (Blau Reine)
2. Horner WE, Helbling A, Salvaggio JE, Lehrer SB. Fungal allergens. Clin Microbiol Rev. 1995 Apr;8(2):161-79.
3. Bennett JW, Klich M. Mycotoxins. Clin Microbiol Rev. 2003 Jul;16(3):497-516. DOI: 10.1128/CMR.16.3.497-516.2003
4. Bennett JW, Inamdar AA. Are Some Fungal Volatile Organic Compounds (VOCs) Mycotoxins? Toxins (Basel). 2015 Sep;7(9):3785-804. DOI: 10.3390/toxins7093785
5. Herter I, Geginat G, Hof H, Kupfahl C. Modulation of innate and antigen-specific immune functions directed against Listeria monocytogenes by fungal toxins in vitro. Mycotoxin Res. 2014 May;30(2):79-87. DOI: 10.1017/s12505-014-0191-5
6. Hof H, Medizinische Relevanz der Mykotoxine [Medical relevance of mycotoxins], Dtsch Med Wochenschr. 2008 May;133(20):1084-8. DOI: 10.1055/s-2008-1077222
7. European Union, Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (Text with EEA relevance). OJ. 2006 Dec 20;L364:5-24. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32006R1881
8. European Union. 2013/165/EU: Commission Recommendation of 27 March 2013 on the presence of T-2 and HT-2 toxin in cereals and cereal products (Text with EEA relevance). OJ. 2013 Apr 03;L 091:12-5. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2013.091.01.0012.01.ENG&toc=OJ:L:2013:091:TOC
9. Lombard MJ. Mycotoxin exposure and infant and young child growth in Africa: what do we know? Ann Nutr Metab. 2014;64 Suppl 2:42-52. DOI: 10.1159/000365126
10. Bundesinstitut für Risikobewertung. Übergang von Aflatoxinen in Milch, Eier, Fleisch und Innereien. Stellungnahme des BfR Nr. 009/2013 vom 4. März 2013. 2013. Available from: http://www.bfr.bund.de/cm/343/uebergang-von-aflatoxinen-in-milch-eier-fleisch-und-innereien.pdf
11. Hof H. Ernährung in der Schwangerschaft. MikrobioLOGische Aspekte. Risiken durch Infektionen und mikrobielle Toxine. Linkenheim-Hochstetten: Aesopus Verlag; 2015. ISBN 978-3-936993-65-3.
12. Perrone G, Gallo A, Logrieco AF. Biodiversity of Aspergillus section Flavi in Europe in relation to the management of aflatoxin risk. Front Microbiol. 2014;5:377. DOI: 10.3389/fmicb.2014.00377
13. European Union, Commission Regulation (EU) No 165/2010 of 26 February 2010 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs as regards aflatoxins (Text with EEA relevance). OJ. 2010 Feb 27:L 50:9-12. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=14645462190113&uri=CELEX:32010R0165
14. International Agency for Research on Cancer (IARC). Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene. Lyon: IARC Press; 2002. p. 171-230. (IARC Monographs on the evaluation of carcinogenic risks to humans; 82). Available from: https://monographs.iarc.fr/ENG/Monographs/vol82/mono82.pdf
15. Jafarian-Dehkordi A, Pourradi N. Aflatoxin M1 contamination of human breast milk in Isfahan, Iran. Adv Biomed Res. 2013;2:86. DOI: 10.4103/2277-9175.122503
16. Hof H. Ochratoxin in Nahrungsmitteln: ein Risiko für Schwangere? Der Gynäkologe. 2015;48(6):477-82. DOI: 10.1007/s00129-015-3709-9
17. European Food Safety Authority. Opinion of the Scientific Panel on contaminants in the food chain on a request from the commission related to ochratoxin A in food, Question N° EFSA-Q-2005-154, Adopted on 4 April 2006. EFSA J. 2006:365:1-56. Available from: http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/365.pdf
18. Winkler J, Kersten S, Valenta H, Meyer U, Engelhardt UH, Dänicke S. Development of a multi-toxin method for investigating the carryover of zearalenone, deoxynivalenol and their metabolites into milk of dairy cows. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2015;32(3):371-80. DOI: 10.1080/19440049.2015.1011714
19. Pellegrino M, Alonso V, Vissio C, Larriestra A, Chiacchiera SM, Bogni C, Cavagliari L. Gliotoxinoageneric Aspergillus fumigatus in the dairy herd environment. Mycotoxin Res. 2013 May;29(2):71-8. DOI: 10.1017/s12505-013-0162-2
20. Sefidgar SA, Azizi G, Khoasravi AR, Roudabar-Mohammadi S. Presence of Aflatoxin M1 in raw milk at cattle farms in Babol, Iran. Pak J Biol Sci. 2008 Feb;11(3):484-6. DOI: 10.3923/pjbs.2008.484.486
21. Santini A, Raiola A, Ferrantelli V, Giangrosso G, Macaluso A, Bognanno M, Galvano F, Ritieni A. Aflatoxin M1 in raw, UHT milk and dairy products in Sicily (Italy). Food Addit Contam Part B Surveill. 2013;6(3):181-6. DOI: 10.1080/19393210.2013.780186
22. Scaglioni PT, Becker-Algeri T, Dunkler D, Badiade-Furlong E. Aflatoxin B1 and M1 in milk. Anal Chim Acta. 2014 Jun 829:69-74. DOI: 10.1016/j.aca.2014.04.039
23. Oluwafemi F, Badmos AO, Kareem SO, Ademuyiwa O, Kolapo AL. Survey of aflatoxin M1 in cows’ milk from free-grazing cows in Abeokuta, Nigeria. Mycotoxin Res. 2014 Nov;30(4):207-11. DOI: 10.1080/19393210.2013.870186
24. Torović L, Aflatoxin M1 in processed milk and infant formulae and corresponding exposure of adult population in Serbia. Food Addit Contam Part B Surveill. 2013-2014. Food Addit Contam Part B Surveill. 2013;6(3):181-6. DOI: 10.1080/19393210.2013.870186
25. Meucci V, Razzuoli E, Soldani G, Massart F. Mycotoxin detection in infant formula milks in Italy. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2010 Jan;27(1):64-71. DOI: 10.1080/02652030903207201
26. Awasthi V, Bahman S, Thakur LK, Singh SK, Dua A, Ganguly S. Contaminants in milk and impact of heating: an assessment study. Indian J Public Health. 2012 Jan-Mar;56(1):95-9. DOI: 10.4103/0019-557X.96985
27. Bognanno M, La Fauci L, Ritiieni A, Tafuri A, De Lorenzo A, Micari P, Di Renzo L, Ciappellano S, Sarullo V, Galvano F. Survey of the occurrence of Aflatoxin M1 in ovine milk by HPLC and its confirmation by MS. Mol Nutr Food Res. 2006 Mar;50(3):300-5. DOI: 10.1002/mnfr.200500224

28. Skaug MA, Helland I, Sovoll K, Saugstad OD. Presence of ochratoxin A in human milk in relation to dietary intake. Food Addit Contam. 2001 Apr;18(4):321-7. DOI: 10.1080/02652030117740

29. Turconi G, Guarcello M, Livieri C, Comizzoli S, Maccarini L, Castellazzi AM, Pietri A, Piva G, Roggi C. Evaluation of xenobiotics in human milk and ingestion by the newborn— an epidemiological survey in Lombardy (Northern Italy). Eur J Nutr. 2004 Aug;43(4):191-7. DOI: 10.1007/s00394-004-0458-2

30. Galvano F, Pietri A, Bertuzzi T, Gagliardi L, Ciotti S, Luisi S, Bognanno M, La Fauci L, Iacopino AM, Nigro F, Li Volti G, Vanella L, Giammanco G, Tanta G, Gazzolo D. Maternal dietary habits and mycotoxin occurrence in human mature milk. Mol Nutr Food Res. 2008 Apr;52(4):496-501. DOI: 10.1002/mnfr.200700266

31. Gürbay A, Girgin G, Sabuncuoğlu SA, Sahin G, Yurdakök M, Yigit S, Tekinalp G. Ochratoxin A: is it present in breast milk samples obtained from mothers from Ankara, Turkey? J Appl Toxicol. 2010 May;30(4):329-33. DOI: 10.1002/jat.1499

32. Biasucci G, Calabrese G, Giuseppe R, Carrara G, Colombo F, Mandelli B, Maj M, Bertuzzi T, Pietri A, Rossi F. The presence of ochratoxin A in cord serum and in human milk and its correspondence with maternal dietary habits. Eur J Nutr. 2011 Apr;50(4):211-8. DOI: 10.1007/s00394-010-0130-y

33. Muñoz K, Campos V, Blaszkewicz M, Vega M, Alvarez A, Neira J, Degen GH. Exposure of neonates to ochratoxin A: first biomonitoring results in human milk (colostrum) from Chile. Mycotoxin Res. 2010 May;26(2):59-67. DOI: 10.1007/s12550-009-0040-0

34. Abdulrazzaq YM, Osman N, Yousif ZM, Al-Falahi S. Aflatoxin M1 in breast-milk of UAE women. Ann Trop Paediatr. 2003 Sep;23(3):173-9. DOI: 10.1179/027249303322296484

35. Polychronaki N, West RM, Turner PC, Amra H, Abdel-Wahhab M, Mykkänen H, El-Nezami H. A longitudinal assessment of aflatoxin M1 excretion in breast milk of selected Egyptian mothers. Food Chem Toxicol. 2007 Jul;45(7):1210-5. DOI: 10.1016/j.fct.2007.01.001

36. Diaz GJ, Sánchez MP. Determination of aflatoxin M1 in breast milk as a biomarker of maternal and infant exposure in Colombia. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2015;32(7):1192-8. DOI: 10.1080/19440049.2015.1049563

37. Navas SA, Sabino M, Rodríguez-Amaya DB. Aflatoxin M1 and ochratoxin A in a human milk bank in the city of São Paulo, Brazil. Food Addit Contam. 2005 May;22(5):457-62. DOI: 10.1080/0265203050110950

38. Rubert J, León N, Sáez C, Martins CP, Godula M, Yúsà V, Mañes J, Soriano JM, Soler C. Evaluation of mycotoxins and their metabolites in human breast milk using liquid chromatography coupled to high resolution mass spectrometry. Anal Chim Acta. 2014 Apr;820:39-46. DOI: 10.1016/j.aca.2014.02.009

39. Shuaib FM, Ehrli J, Abdullahi A, Williams JH, Jolly PE. Reproductive health effects of aflatoxins: a review of the literature. Reprod Toxicol. 2010 Jun;29(3):262-70. DOI: 10.1016/j.reprotox.2009.12.005

Corresponding author:
Prof. Dr. med. Herbert Hof
MVZ Labor Limbach, Im Breitpiel 15, 69126 Heidelberg, Germany, Phone: +49 6221 34 32 342
Herbert.hof@labor-limbach.de

Please cite as
Hof H. Mycotoxins in milk for human nutrition: cow, sheep and human breast milk. GMS Infect Dis. 2016;4:Doc03.
DOI: 10.3205/id000021, URN: urn:nbn:de:0183-id0000214

This article is freely available from
http://www.egms.de/en/journals/id/2016-4/id000021.shtml

Published: 2016-06-20

Copyright
©2016 Hof. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 License. See license information at http://creativecommons.org/licenses/by/4.0/.