AFLATOXINS

These substances were considered by previous working groups, in December 1971 (IARC, 1972), October 1975 (IARC, 1976) and March 1987 (IARC, 1987a). Since that time, new data have become available, and these have been incorporated into the monograph and taken into account in the present evaluation.

Aflatoxins were first identified in 1961 in animal feed contaminated by *Aspergillus parasiticus* (Sargeant *et al.*, 1961). They are known to be produced by three species: *A. flavus*, *A. parasiticus* and the rare species *A. nomius* (Kurtzman *et al.*, 1987). It is generally considered that *A. flavus* produces aflatoxins B\_1 and B\_2, whereas *A. parasiticus* produces aflatoxins B\_1, B\_2, G\_1 and G\_2 (Dorner *et al.*, 1984).

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OCCURRENCE

The aflatoxin-producing *Aspergillus* species, and consequently dietary aflatoxin contamination, are ubiquitous in areas of the world with hot, humid climates, including sub-Saharan Africa and Southeast Asia. Exposure in those countries results from contamination of dietary staples and is therefore likely to be chronic. Since countries in colder climatic areas import foods from areas where aflatoxin levels are high, however, aflatoxins are of worldwide concern.

The relative proportions of aflatoxin B$_1$, aflatoxin G$_1$, aflatoxin B$_2$ and aflatoxin G$_2$ on crops depend on the particular *Aspergillus* species present. Aflatoxin B$_1$ is the most frequent type present in contaminated samples, and aflatoxin G$_1$ has never been reported in the absence of aflatoxin B$_1$. Aflatoxin B$_2$ and aflatoxin G$_2$ are typically present in much lower quantities. Aflatoxin M$_1$ is a metabolic hydroxylation product of aflatoxin B$_1$; it can occur in the absence of other aflatoxin.

Samples of most dietary staples have been shown to be contaminated with aflatoxins at one time or another; foodstuffs may be contaminated with aflatoxin both pre- and post-harvest. An extensive review of the levels of aflatoxins in foods and feeds from 16 countries in North America, South America, Europe, Asia and Africa was made for the period 1976–83 (Jelinek et al., 1989). Data were presented as total aflatoxins. In maize and maize products from nine countries, median levels ranged from < 0.1 to 80 µg/kg; in several countries, more than 10% of grain samples contained levels above 5 µg/kg. Data from the USA demonstrated annual and geographical fluctuations in aflatoxin levels and increased levels in maize in conditions of drought. Levels in other grains and cereal products were lower than those in maize in all the countries surveyed.

Groundnuts imported into the USA in 1981 from India, the Sudan and Brazil contained much higher levels, more than 50% of samples containing over 26 µg/kg. Other nuts, including almonds, cashews, filberts, hazel-nuts, mixed nuts, pecans and walnuts, were contaminated to a lower extent, but higher levels were occasionally seen in surveys of pistachios, pumpkin seeds and Brazil-nuts.

Rice exposed during cyclones in India had levels up to 1130 µg/kg. This commodity is otherwise rarely contaminated at levels > 20 µg/kg (Choke, 1990). High levels of aflatoxins (> 100 µg/kg) occurred in cottonseed and groundnut and in sunflower seeds. Exposure can occur due to the presence of aflatoxin and aflatoxin metabolites in milk and milk products from animals that have consumed contaminated feed (Applebaum et al., 1982). Some data on the occurrence of aflatoxin M$_1$ in the late 1960s, 1970s and 1980s in several countries are reported in Table 1. High proportions of positive samples were found in some surveys, usually at levels of less than 0.5 µg/kg.
### Table 1. Occurrence of aflatoxin M₁ in milk

<table>
<thead>
<tr>
<th>Country or region</th>
<th>Period of sampling</th>
<th>No. positive/ no. samples</th>
<th>Proportion positive (%)</th>
<th>Range of concentrations (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>1983–86</td>
<td>0/65</td>
<td>0</td>
<td>&lt; 0.03</td>
</tr>
<tr>
<td>Belgium</td>
<td>1960s, 1970s</td>
<td>42/68</td>
<td>62</td>
<td>0.02–0.2</td>
</tr>
<tr>
<td></td>
<td>1980–86</td>
<td>135/809</td>
<td>16.7</td>
<td>&lt; 0.01–0.5</td>
</tr>
<tr>
<td>China</td>
<td>1981, 1983</td>
<td>173/319</td>
<td>54.2</td>
<td>0.02–0.5</td>
</tr>
<tr>
<td>Finland</td>
<td>1982, 1986</td>
<td>0/17</td>
<td>0</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>France</td>
<td>1981–85</td>
<td>580/3634</td>
<td>16.4</td>
<td>0.02–0.5</td>
</tr>
<tr>
<td>Germany</td>
<td>1960s, 1970s</td>
<td>229/788</td>
<td>29.1</td>
<td>0.04–6.5&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>India</td>
<td>1960s, 1970s</td>
<td>3/21</td>
<td>14</td>
<td>up to 13.3</td>
</tr>
<tr>
<td>Ireland</td>
<td>1981–82</td>
<td>0/36</td>
<td>0</td>
<td>&lt; 0.015</td>
</tr>
<tr>
<td>Italy</td>
<td>1982–84</td>
<td>213/537</td>
<td>39.7</td>
<td>0.001–0.15</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1960s, 1970s</td>
<td>74/95</td>
<td>82</td>
<td>0.03–0.5</td>
</tr>
<tr>
<td></td>
<td>1985–86</td>
<td>964/1241</td>
<td>77.7</td>
<td>0.01–0.09</td>
</tr>
<tr>
<td>South Africa</td>
<td>1960s, 1970s</td>
<td>5/21</td>
<td>24</td>
<td>0.02–0.2</td>
</tr>
<tr>
<td>Spain</td>
<td>1983</td>
<td>7/95</td>
<td>7</td>
<td>0.02–0.04</td>
</tr>
<tr>
<td>Sweden</td>
<td>1983–86</td>
<td>384/647</td>
<td>59.4</td>
<td>0.005–0.3</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1986</td>
<td>0/217</td>
<td>0</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1960s, 1970s</td>
<td>85/278</td>
<td>31</td>
<td>0.03–0.52</td>
</tr>
<tr>
<td></td>
<td>1981–83</td>
<td>59/686</td>
<td>8.6</td>
<td>0.01–0.78</td>
</tr>
<tr>
<td>USA</td>
<td>1960s, 1970s</td>
<td>191/302</td>
<td>63</td>
<td>Trace–&gt; 0.7</td>
</tr>
</tbody>
</table>

Compiled from van Egmond (1989a)

<sup>a</sup> For milk powder, calculated on the basis of reconstituted milk (dilution factor, 10×)

<sup>b</sup> Western part, 0.04–0.54; eastern part, <0.1–6.5

Aflatoxins in foods are not readily degraded under normal cooking conditions (Goldblatt, 1969; Müller, 1982).

They can be completely destroyed by autoclaving in the presence of ammonia or by treatment with bleach(IARC 1976,1993).

**Spices and herbs:** the contamination of processed meat with aflatoxin was shown to correlate with the addition of spices to fresh meat (Aziz, N H : Youssef, Y A Occurrence of aflatoxins and aflatoxin-producing moulds in fresh and processed meat in Egypt, Food-Addit-Contam. 1991 May-Jun; 8(3): 321-31).

**Meat, eggs, milk, and other edible products** from animals that consume aflatoxin-contaminated feed are additional sources of potential exposure (11th report on carcinogens, 2004, III-10).
**Occupational exposure** to aflatoxins occurs by inhalation of dust generated during the handling and processing of contaminated crops and feeds. Therefore, farmers and other agricultural workers have the greatest risk of occupational exposure.

**EU regulatory framework**

The European Union introduced measures to minimise the presence of aflatoxins in different foodstuffs. Maximum levels of aflatoxins are laid down in Commission Regulation (EC) No 1881/2006. Products exceeding the maximum levels should not be placed on the market in the EU. Directive 2002/32/EC lays down maximum levels for aflatoxins B1 in feed materials. Methods of sampling and analysis for the official control of mycotoxins, including aflatoxins, are laid down in Commission Regulation No 401/2006. This ensures that the same sampling criteria intended for the control of mycotoxin content in food are applied to the same products by the competent authorities throughout the EU and that certain performance criteria, such as recovery and precision, are fulfilled. In 2008, the Codex Alimentarius set a maximum level of 10 µg/kg total aflatoxins in ready-to-eat almonds, hazelnuts, and pistachios at a level higher than that currently in force in the EU (4 µg/kg total aflatoxins). Currently the European Commission and Member States are discussing the alignment of EU legislation for these nuts with the Codex Alimentarius decision. In addition, discussions will take place to align the new proposed maximum levels for all tree nuts.

COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs


**Section 2: Mycotoxins**

<table>
<thead>
<tr>
<th>Foodstuffs (1')</th>
<th>Maximum levels (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B₁</td>
</tr>
<tr>
<td>2.1 Aflatoxins</td>
<td>8,0 (5)</td>
</tr>
<tr>
<td>2.1.1 Groundnuts to be subjected to sorting, or other physical treatment, before human consumption or use as an ingredient in foodstuffs</td>
<td>5,0 (5)</td>
</tr>
</tbody>
</table>

(1')
| 2.1.3 | Groundnuts and nuts and processed products thereof, intended for direct human consumption or use as an ingredient in foodstuffs | 2.0 (Ț) | 4.0 (Ț) | — |
| 2.1.4 | Dried fruit to be subjected to sorting, or other physical treatment, before human consumption or use as an ingredient in foodstuffs | 5.0 | 10.0 | — |
| 2.1.5 | Dried fruit and processed products thereof, intended for direct human consumption or use as an ingredient in foodstuffs | 2.0 | 4.0 | — |
| 2.1.6 | All cereals and all products derived from cereals, including processed cereal products, with the exception of foodstuffs listed in 2.1.7, 2.1.10 and 2.1.12 | 2.0 | 4.0 | — |
| 2.1.7 | Maize to be subjected to sorting or other physical treatment before human consumption or use as an ingredient in foodstuffs | 5.0 | 10.0 | — |
| 2.1.8 | Raw milk (Ț), heat-treated milk and milk for the manufacture of milk-based products | — | — | 0.050 |
| 2.1.9 | Following species of spices:  
Capsicum spp. (dried fruits thereof, whole or ground, including chillies, chilli powder, cayenne and paprika)  
Piper spp. (fruits thereof, including white and black pepper)  
Myristica fragrans (nutmeg)  
Zingiber officinale (ginger)  
Curcuma longa (turmeric) | 5.0 | 10.0 | — |
| 2.1.10 | Processed cereal-based foods and baby foods for infants and young children (1) (7) | 0.10 | — | — |
| 2.1.11 | Infant formulae and follow-on formulae, including infant milk and follow-on milk (4) | — | — | 0.025 |
| 2.1.12 | Dietary foods for special medical purposes (8)  
(10) intended specifically for infants | 0.10 | — | 0.025 |

**LEGISLATION:**

Maximum levels of aflatoxins (aflatoxins B1, B2, G1, G2 and M1) are laid down in Commission Regulation (EC) No 1881/2006.


The maximum levels established for aflatoxins in groundnuts and derived products in the Annex to Regulation (EC) 1881/2006  
Commission Regulation (EC) No 669/2009 of 24 July 2009 ...

Safeguard decisions as regards aflatoxins

Special conditions governing certain foodstuffs imported from certain third countries due to contamination risks of these products by aflatoxins are laid down in Commission Decision 2006/504/EC.

In order to assist the competent authorities on the official control of aflatoxin contamination in food products which are subject to Commission Decision 2006/504/EC, a guidance document "Guidance document for competent authorities for the control of compliance with EU legislation on aflatoxins" has been elaborated. This document is also applicable for the control of aflatoxins in food products not subject to the safeguard Decision.

Methods of sampling and analysis


Commission Regulation (EC) No 401/2006 of 23 February 2006 laying down the methods of sampling and analysis for the official control of the levels of mycotoxins in foodstuffs (Text with EEA relevance)


COMMISSION REGULATION (EC) No 152/2009 of 27 January 2009 laying down the methods of sampling and analysis for the official control of feed

This Regulation sets out provisions on the methods of sampling and analysis for the official control of feed. Sampling for the official control of feed, as regards the determination of constituents, additives and undesirable substances, with the exception of residues of pesticides and microorganisms, shall be carried out in accordance with the methods set out in Annex I. Preparation of samples for analysis and expression of results shall be carried out in accordance with the methods set out in Annex II.

CARCINOGENICITY

Human carcinogenicity data

- one cohort study of a small number of Dutch oilpress workers exposed to aflatoxin containing dusts indicated increased mortality from cancer, but no death from hepatocellular carcinoma was observed.
- a cohort study in China found significant excess mortality from liver cancer among individuals in villages where foods were heavily contaminated with aflatoxins.
- a cohort study of Danish workers exposed to aflatoxin from imported feed found an excess of hepatocellular carcinoma among those who had had major exposure to aflatoxin-contaminated feed in the period 10 or more years before diagnosis.
- a cohort study in China, a significant elevation in risk for hepatocellular carcinoma was found among people with aflatoxin metabolites in the urine, after adjustment for hepatitis B surface antigen positivity.
- case-control studies in the Philippines in which an attempt was made to evaluate exposure to aflatoxin B1, found a significantly greater risk for hepatocellular carcinoma among people whose intake of aflatoxin was estimated to be heavy than in those with light aflatoxin intake.
- the two cohort studies in China addressed combined exposure to hepatitis B virus and aflatoxins and suggested that each has an independent effect.
- several correlation studies have been performed, the majority showing a strong association between estimated aflatoxin intake and incidence of hepatocellular carcinoma.

In only a few was it possible to evaluate simultaneously any correlation with the prevalence of hepatitis infection. Of those that did so, two—one in Swaziland and one in China— showed a stronger correlation with exposure to aflatoxin B1 than with hepatitis B viral infection.

Carcinogenicity in experimental animals
Mixtures of aflatoxins and aflatoxin B1 have been tested extensively for carcinogenicity by various routes of administration in several strains of mice and rats, in hamsters, several strains of fish, ducks, tree shrews and monkeys. Following their oral administration, mixtures of aflatoxins and aflatoxin B1 caused hepatocellular and/or cholangiocellular liver tumours, including carcinomas, in all species tested except mice. In rats, renal-cell tumours and a low incidence of tumours at other sites, including the colon, were also found. In monkeys, liver angiosarcomas, osteogenic sarcomas and adenocarcinomas of the gall-bladder and pancreas developed, in addition to hepatocellular and cholangiocellular carcinomas. In adult mice, aflatoxin B1 administered intraperitoneally increased the incidence of lung adenomas. Intraperitoneal administration of aflatoxin B1 to infant mice, adult rats and toads produced high incidences of liver-cell tumours in all of these species. Subcutaneous injection of aflatoxin B1 resulted in local sarcomas in rats. Intraperitoneal administration of aflatoxin B1 to rats during pregnancy and lactation induced benign and malignant tumours in mothers and their progeny in the liver and in various other organs, including those of the digestive tract, the urogenital system and the central and peripheral nervous systems.

Aflatoxin B2 induced foci of altered hepatocytes and hepatocellular adenomas following its oral administration to rats. A low incidence of hepatocellular carcinomas was observed after intraperitoneal administration of aflatoxin B2 to rats. Oral administration of aflatoxin G1 induced foci of altered hepatocytes, hepatocellular adenomas and carcinomas and renal-cell tumours in rats and liver-cell tumours in fish. The hepatocarcinogenic effect of aflatoxin G1 was weaker than that of aflatoxin B1. Subcutaneous injection of aflatoxin G1 in rats resulted in local sarcomas, which developed at a lower incidence and at later times than those induced by aflatoxin B1.
at the same dose level and by the same route. Oral administration of aflatoxin G2 to trout had no hepatocarcinogenic effect in one experiment. Aflatoxin M1, a hydroxy metabolite of aflatoxin B1, produced fewer hepatocellular carcinomas following its oral administration to rats and fish than aflatoxin B1 given at the same dose level and by the same route.

EXPOSURE DATA

Chemical and physical data

**Synonyms, structural and molecular data**

**Aflatoxin B₁**
*Chem. Abstr. Services Reg. No.: 1162-65-8*
*Chem. Abstr. Name: (6aR-cis)(2,3,6a,9a)Tetrahydro-4-methoxycyclopenta[c]furo[3′,2′:4,5]furo[2,3-h][l]benzopyran-1,11-dione*
*Synonyms: 6-Methoxydifurcoumarone; 2,3,6α,9a α-tetrahydro-4-methoxycyclopenta[c]furo[3′,2′:4,5]furo[2,3-h][l]benzopyran-1,11-dione*

**Aflatoxin B₂**
*Chem. Abstr. Services Reg. No.: 7220-81-7*
*Chem. Abstr. Name: (6aR-cis)(2,3,6a,8,9,9a)Hexahydro-4-methoxycyclopenta[c]furo[3′,2′:4,5]furo[2,3-h][l]benzopyran-1,11-dione*
*Synonyms: Dihydroaflatoxin B₁; 2,3,6α,8,9,9α-hexahydro-4-methoxycyclopenta[c]furo[3′,2′:4,5]furo[2,3-h][l]benzopyran-1,11-dione*

**Aflatoxin G₁**
*Chem. Abstr. Services Reg. No.: 1165-39-5*
*Chem. Abstr. Name: (7aR-cis)(3,4,7a,10a)Tetrahydro-5-methoxy-1H,12H-furo[3′,2′:4,5]furo[2,3-h][l]benzopyran-1,12-dione*
*Synonym: 3,4,7α,10α-Tetrahydro-5-methoxy-1H,12H-furo[3′,2′:4,5]furo[2,3-h]pyrano[3,4-c][l]benzopyran-1,12-dione*

**Aflatoxin G₂**
*Chem. Abstr. Services Reg. No.: 7241-98-7*
*Chem. Abstr. Name: (7αR-cis)(3,4,7a,9,10,10a)Hexahydro-5-methoxy-1H,12H-furo[3′,2′:4,5]furo[2,3-h]pyrano[3,4-c][l]benzopyran-1,12-dione*
*Synonyms: Dihydroaflatoxin G₁; 3,4,7α,9,10,10α-hexahydro-5-methoxy-1H,12H-furo[3′,2′:4,5]furo[2,3-h]pyrano[3,4-c][l]benzopyran-1,12-dione*
**Aflatoxin M₁**

*Chem. Abstr. Services Reg. No.: 6795-23-9*

*Chem.Abstr.Name: 2,3,6a,9a-Tetrahydro-9a-hydroxy-4-methoxycyclopenta[c]furo[3′,2′:4,5]furo[2,3-h][1]benzopyran-1,11-dione*


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**Chemical and physical properties of aflatoxins** (from Castegnaro et al., 1980, 1991; Budavari, 1989, unless otherwise stated)

(a) **Description:** Colourless to pale-yellow crystals. Intensely fluorescent in ultraviolet light, emitting blue (aflatoxins B₁ and B₂) or yellow-green (aflatoxins G₁, G₂) fluorescence, from which the designations B and G were derived, or blue-violet
fluorescence (aflatoxin M₁)

(b) Solubility: Very slightly soluble in water (10–30 mg/mL); insoluble in non-polar solvents; freely soluble in moderately polar organic solvents (e.g., chloroform and methanol) and especially in dimethyl sulfoxide (Cole & Cox, 1981)

(c) Stability: Unstable to ultraviolet light in the presence of oxygen, to extremes of pH (< 3, > 10) and to oxidizing agents

(d) Reactivity: The lactone ring is susceptible to alkaline hydrolysis. Aflatoxins are also degraded by reaction with ammonia or sodium hypochlorite.

Analysis

The numerous methods for the determination of aflatoxins B and G in maize (known as ‘corn’ in the USA), groundnuts (peanuts) and cottonseed meal (Egan et al., 1982) and of aflatoxin M₁ in milk products (Scott, 1989) have been reviewed. Those that have been verified in collaborative studies and have been proposed as official methods by the Association of Official Analytical Chemists (Scott, 1990) are shown in Table 1.

Table 1. Analytical methods validated by the Association of Official Analytical Chemists

<table>
<thead>
<tr>
<th>Method no.</th>
<th>Aflatoxin</th>
<th>Food</th>
<th>Method&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Detection limit (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>975.36</td>
<td>All</td>
<td>Foods and feeds (screening)</td>
<td>MC</td>
<td>10</td>
</tr>
<tr>
<td>979.18</td>
<td>All</td>
<td>Maize and groundnuts (screening)</td>
<td>MC</td>
<td>10</td>
</tr>
<tr>
<td>990.31</td>
<td>All</td>
<td>Maize and groundnuts (Aflatest screening)</td>
<td>IC</td>
<td>10</td>
</tr>
<tr>
<td>990.34</td>
<td>All</td>
<td>Maize, cottonseed, groundnuts (screening)</td>
<td>ELISA</td>
<td>20–30</td>
</tr>
<tr>
<td>989.06</td>
<td>B₁</td>
<td>Cottonseed products and mixed feed (screening)</td>
<td>ELISA</td>
<td>15</td>
</tr>
<tr>
<td>990.32</td>
<td>B₁</td>
<td>Maize and groundnut (screening)</td>
<td>ELISA</td>
<td>20</td>
</tr>
<tr>
<td>968.22</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Groundnuts and groundnut products</td>
<td>TLC</td>
<td>5</td>
</tr>
<tr>
<td>970.45</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Groundnuts and groundnut products</td>
<td>TLC</td>
<td>10</td>
</tr>
<tr>
<td>971.23</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Cocoa beans</td>
<td>TLC</td>
<td>10</td>
</tr>
<tr>
<td>971.24</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Coconut, copra and copra meal</td>
<td>TLC</td>
<td>50</td>
</tr>
<tr>
<td>972.26</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Maize</td>
<td>TLC</td>
<td>5</td>
</tr>
<tr>
<td>980.20</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Cottonseed products</td>
<td>TLC, HPLC</td>
<td>10, 5</td>
</tr>
<tr>
<td>970.46</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Green coffee</td>
<td>TLC</td>
<td>25</td>
</tr>
<tr>
<td>974.16</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Pistachio nuts</td>
<td>TLC</td>
<td>15</td>
</tr>
<tr>
<td>972.27</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Soya beans</td>
<td>TLC</td>
<td>10</td>
</tr>
<tr>
<td>990.33</td>
<td>B₁, B₂, G₁, G₂</td>
<td>Maize and groundnut butter</td>
<td>HPLC</td>
<td>5</td>
</tr>
<tr>
<td>978.15</td>
<td>B₁</td>
<td>Eggs</td>
<td>TLC</td>
<td>0.1</td>
</tr>
<tr>
<td>982.24</td>
<td>B₁ and M₁</td>
<td>Liver</td>
<td>TLC</td>
<td>0.1</td>
</tr>
<tr>
<td>974.17</td>
<td>M₁</td>
<td>Dairy products</td>
<td>TLC</td>
<td>0.1</td>
</tr>
<tr>
<td>980.21</td>
<td>M₁</td>
<td>Milk and cheese</td>
<td>TLC</td>
<td>0.1</td>
</tr>
<tr>
<td>986.16</td>
<td>M₁ and M₂</td>
<td>Fluid milk</td>
<td>HPLC</td>
<td>0.1</td>
</tr>
</tbody>
</table>

From Scott (1990)

<sup>a</sup>MC, minicolumn; IC, immunoaffinity column, ELISA, enzyme-linked immunosorbent assay; TLC, thin-layer chromatography; HPLC, high-performance liquid chromatography
A number of approaches have been used to analyse for aflatoxins and their metabolites in human tissues and body fluids. These include immunoaffinity purification, immunoassay (Wild et al., 1987), high-performance liquid chromatography with fluorescence or ultraviolet detection and synchronous fluorescence spectroscopy (Groopman & Sabbioni, 1991). Molecular biomarkers, such as urinary markers, metabolites in milk and parent compounds in blood, are used for determining exposure to aflatoxins (Groopman, 1993).

**Production and use**

**Production**

In the USA and Africa, *A. flavus* and *A. parasiticus* are widely distributed; in Southeast Asia, *A. flavus* occurs to the virtual exclusion of the other species (Pitt et al., 1993).

Aflatoxins are produced, in small quantities for use in research only, by large-scale fermentation on solid substrates or liquid media, from which the aflatoxins are extracted and purified by chromatography. Total annual production probably does not exceed 100 g.

**Use**

Aflatoxins are not used commercially other than in research.

**Regulations and guidelines**

It is probably not possible to eliminate completely exposure of humans to aflatoxins. In 1987, at least 50 countries had existing or proposed regulations for aflatoxins in foodstuffs (van Egmond, 1989b, 1992; Stoloff et al., 1991). The maximum limits range from none detectable to 50 µg/kg of food for either the sum of aflatoxins B<sub>1</sub>, B<sub>2</sub>, G<sub>1</sub> and G<sub>2</sub> or for aflatoxin B<sub>1</sub> alone; 5 µg/kg is the commonest maximal limit.

Aflatoxins were reviewed by a joint FAO/WHO Expert Committee on Food Additives in 1987 (WHO, 1987). No acceptable daily intake was given; it was recommended that human intake be reduced to the lowest practicable level (ALARA=as low as reasonably achievable).

**Evaluation**

There is sufficient evidence in humans for the carcinogenicity of naturally occurring mixtures of aflatoxins.

There is sufficient evidence in humans for the carcinogenicity of aflatoxin B1.

There is inadequate evidence in humans for the carcinogenicity of aflatoxin M1.

There is sufficient evidence in experimental animals for the carcinogenicity of naturally occurring mixtures of aflatoxins and aflatoxins B1, G1 and M1.

There is limited evidence in experimental animals for the carcinogenicity of aflatoxin B2.

There is inadequate evidence in experimental animals for the carcinogenicity of aflatoxin G2.

Naturally occurring aflatoxins are carcinogenic to humans (Group 1).

Aflatoxin M1 is possibly carcinogenic to humans (Group 2B).
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