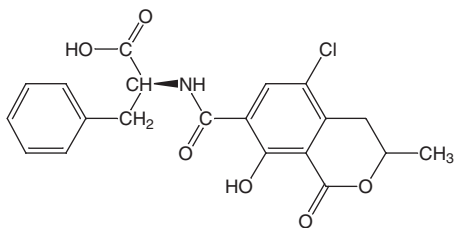


## Ochratoxin A

### CAS No. 303-47-9

Reasonably anticipated to be a human carcinogen  
First Listed in the *Sixth Annual Report on Carcinogens* (1991)



### Carcinogenicity

Ochratoxin A is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. When ochratoxin A was administered in the diet, hepatocellular tumors (designated as well-differentiated trabecular adenomas), renal-cell tumors (renal cystadenomas and solid renal-cell tumors), hepatomas (some exhibiting the trabecular structure), and hyperplastic hepatic nodules were observed in male mice. In another study, administration of ochratoxin A in the diet induced hepatocellular carcinomas and adenomas in female mice. Gavage administration of ochratoxin A to male and female rats resulted in a dose-related increase in the incidence of renal-cell adenomas and adenocarcinomas; further, metastasis of the renal-cell tumors was also observed in male and female rats. When administered by gavage, ochratoxin A increased the incidence and multiplicity of fibroadenomas of the mammary gland in female rats (IARC 1993, NTP 1989).

No adequate human studies of the relationship between exposure to ochratoxin A and human cancer have been reported. Incidence of, and mortality from urothelial urinary tract tumors have been correlated with the geographical distribution of Balkan endemic nephropathy in Bulgaria and Yugoslavia. A relatively high frequency of contamination of cereals and bread with ochratoxin A has been reported in an area of Yugoslavia where Balkan endemic nephropathy is present (IARC 1976, 1983, 1987, 1993).

### Properties

Ochratoxin A is a toxic metabolite produced primarily by *Aspergillus*, but also by *Penicillium* and other molds. It is a white crystalline powder. Recrystallized from xylene, it forms crystals that emit green (acid solution) and blue (alkaline solution) fluorescence in ultraviolet light; the melting point of these crystals is 169°C. The free acid of ochratoxin A is soluble in organic solvents (IARC 1983, 1993). The sodium salt is soluble in water. Ochratoxin A is unstable to light and air, degrading and fading even after brief exposure to light, especially under humid conditions. Ethanol solutions are stable for longer than 1 year if kept refrigerated and in the dark. Ochratoxin A is fairly stable to heat; in cereal products, up to 35% of the toxin survives autoclaving for up to 3 hours (IARC 1976).

### Use

Ochratoxin A has no known commercial use, but it is an experimental teratogen and carcinogen (IARC 1983, Sax and Lewis 1987).

### Production

Ochratoxin A is naturally produced by fungi. The most important ochratoxin A producing species is *A. ochraceus*. It is also produced by one species of *Penicillium*, *P. verrucosum*, and rare species in the *ochraceus* group (IARC 1993). Ochratoxin A is not produced commercially; however, it was previously offered for sale by one

foreign firm (HSDB 2000). Chem Sources (2001) identified nine current U.S. suppliers of ochratoxin A.

### Exposure

Ochratoxin A is a naturally occurring mycotoxin. It exists completely in particulate phase in ambient atmosphere. It is immobile in soil. Its widespread occurrence in food and animal feed results in probable human exposure. Mycotoxins may well be among the world's most significant food contaminants (Fischbach and Rodricks 1973). Ochratoxin-producing fungi are included in the *Penicillium* and *Aspergillus* genera (IARC 1976, 1993). In the colder climates, ochratoxin A is formed by *Penicillium* strains; while in tropical and subtropical areas, ochratoxin A is formed by *Aspergillus*. Ochratoxin A is a natural contaminant on corn, peanuts, storage grains, cottonseed, and decaying vegetation (Merck 1989). It has been detected in moldy cereals including wheat, maize, rye, barley, and oats; peanuts; coffee beans; bread; flour; rice; peas; and beans (IARC 1983, 1993). Detected contamination levels in cereals range from 0.03 to 27.5 ppm (Scott *et al.* 1972, Krogh *et al.* 1973). Although the carryover from barley into beer is possible, one survey of all 130 U.S. breweries failed to detect ochratoxin A (up to 10 µg/kg) in beer or malted barley (Fischbach and Rodricks 1973, IARC 1983). The malting process completely degrades the toxin in moderately contaminated barley, but 2 to 7% of the toxin were carried over to the final product from a heavily contaminated lot (Krogh *et al.* 1974, IARC 1983). Up to 28% of added toxin was detected in a final beer product (Chu *et al.* 1975).

Residues of ochratoxin A have been detected in samples of meat from animals slaughtered immediately after consuming contaminated feed (Krogh 1977, IARC 1983, 1993). It has been detected at levels of 10 to 920 µg/kg in sausage, ham, and bacon samples (IARC 1983, 1993).

No direct evidence of worker exposure has been reported. Potential worker exposure exists for all personnel handling and storing grains, nuts, corn, cereals, and animal feeds.

### Regulations

No specific regulations or guidelines relevant to reduction of exposure to Ochratoxin A were identified.

### REFERENCES

- ChemSources. 2001. Chemical Sources International, Inc. <http://www.chemsources.com>.
- Chu, F. S., C. C. Chang, S. H. Ashoor and N. Prentice. 1975. Stability of aflatoxin B-1 and ochratoxin A in brewing. *Appl Microbiol* 29(3): 313-6.
- Fischbach, H. and J. V. Rodricks. 1973. Current efforts of the Food and Drug Administration to control mycotoxins in food. *J Assoc Off Anal Chem* 56(3): 767-70.
- HSDB. 2000. Hazardous Substances Data Base. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
- IARC. 1976. Some Naturally Occurring Substances. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 10. Lyon, France: International Agency for Research on Cancer. 353 pp.
- IARC. 1983. Some Food Additives, Feed Additives and Naturally Occurring Substances. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 31. Lyon, France: International Agency for Research on Cancer.
- IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.
- IARC. 1993. Some Naturally Occurring Substances: Food Items and Constituents, Heterocyclic Aromatic Amines, and Mycotoxins. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 56. Lyon, France: International Agency for Research on Cancer. 571 pp.
- Krogh, P. 1977. Ochratoxin A residues in tissues of slaughter pigs with nephropathy. *Nord Vet Med* 29(9): 402-5.
- Krogh, P., B. Hald, P. Gjertsen and F. Myken. 1974. Fate of ochratoxin A and citrinin during malting and brewing experiments. *Appl Microbiol* 28(1): 31-4.
- Krogh, P., B. Hald and E. J. Pedersen. 1973. Occurrence of ochratoxin A and citrinin in cereals associated with mycotoxic porcine nephropathy. *Acta Pathol Microbiol Scand [B] Microbiol Immunol* 81(6): 689-95.
- Merck. 1989. The Merck Index, 11th ed. Rahway, NJ: Merck & Company, Inc.
- NTP. 1989. Toxicology and Carcinogenesis Studies of Ochratoxin A (CAS No. 303-47-9) in F344/N Rats (Gavage Studies). Technical Report Series No 358. NTIS Publication No. PB90-21947B/AS. Research Triangle Park, NC and Bethesda, MD: National Toxicology Program. 142 pp.
- Sax, N. I. and R. J. Lewis. 1987. Hawley's Condensed Chemical Dictionary, 11th ed. New York: Van Nostrand Reinhold Co.
- Scott, P. M., W. Van Walbeek, B. Kennedy and D. Anyeti. 1972. Mycotoxins (ochratoxin A, citrinin, and sterigmatocystin) and toxigenic fungi in grains and other agricultural products. *J Agric Food Chem* 20(6): 1103-9.