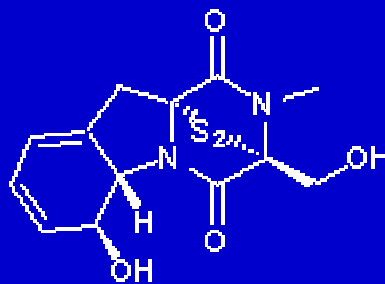


Gliotoxin



Gliotoxin—This is an unusual, highly immunosuppressive mycotoxin that belongs to a class of fungal metabolites called epipolythiodioxopiperazines. They are characterized by a disulfide group that connects across the top of the molecule. Gliotoxin was originally described because of its antifungal and other antibiotic properties.

Producing organism—Gliotoxin is produced by a wide variety of fungi including the common skin inhabitant and opportunistic pathogen, *Candida albicans*. Of considerable interest is that *Aspergillus fumigatus*, an agent of respiratory disease in humans and other animals especially poultry, produces this mycotoxin. Several *Penicillium* species and a couple of *Gliocladium* species also produce gliotoxin.

Occurrence of gliotoxin in commodities—The only known case in which gliotoxin was found to contaminate feed was a situation where camels ingested gliotoxin-contaminated hay and became intoxicated. Otherwise, gliotoxin has been associated only with the infectious agents, *Aspergillus fumigatus* and *Candida albicans*. In the latter case the human patients with *Candida albicans* induced vaginitis had gliotoxin in vaginal secretions. However, gliotoxin was found in necrotic bovine udder tissue infected with *A. fumigatus* and in peritoneal lavages from mice inoculated with this organism. Of considerable importance is that gliotoxin was found in infected tissues of turkeys experimentally infected with this same organism. Subsequently, gliotoxin was found to occur naturally in turkeys with avian aspergillosis caused by *A. fumigatus*. Of interest is that this highly immunosuppressive compound may be produced in the pathogenic state in humans as the organism, *A. fumigatus*, is a respiratory pathogen in compromised individuals especially AIDS patients. It is unknown whether this compound functions as a virulence factor for this fungal pathogen.

Toxicity impact—This compound was first isolated because of its antibiotic potential but its toxicity precluded its use clinically. Later gliotoxin was found to be immunosuppressive when it inhibited phagocytosis by macrophages in tissue culture. Since then other immunosuppressive activities have been attributed to this mycotoxin. Turkey lymphocytes in culture were inhibited from being stimulated by phytohemagglutinin with levels of gliotoxin as low as 10 ng/ml. Oral doses of gliotoxin of 7.5 mg/kg body weight killed all 1-day-old turkey poults within 24 hours. Only one of eight poults given 5 mg gliotoxin/kg body weight died in the same time period. Turkeys appear to be more sensitive to gliotoxin than rats, mice, rabbits, and hamsters. Although gliotoxin was found to occur naturally in hay and caused intoxication in camels, this route of exposure has not been significant regarding the toxicity of gliotoxin. However, its role in avian aspergillosis and possibly human candidosis and mammalian aspergillosis may be important. Its involvement in the pathogenesis of these diseases is strengthened by the fact that this mycotoxin is produced in the infected tissue of the host and has been found to do so in natural infections caused by *A. fumigatus* in turkeys and *C. albicans* in humans.

There are no regulatory limits established for this mycotoxin or the fungi that produces it.