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Review

Natural occurrence of mycotoxins in medicinal plants: A review

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ABSTRACT

Medicinal plants are widely used as home remedies and raw materials for the pharmaceutical industries. Herbal remedies are used in the prevention, treatment and cure of disorders and diseases since ancient times. However, use of medicinal herbs may not meet the requirements of quality, safety and efficacy. During harvesting, handling, storage and distribution, medicinal plants are subjected to contamination by various fungi, which may be responsible for spoilage and production of mycotoxins. The increasing consumption of medicinal plants has made their use a public health problem due to the lack of effective surveillance of the use, efficacy, toxicity and quality of these natural products. The increase in use of medicinal plants may lead to an increase in the intake of mycotoxins therefore contamination of medicinal plants with mycotoxins can contribute to adverse human health problems and therefore represents a special hazard. Numerous natural occurrences of mycotoxins in medicinal plants and traditional herbal medicines have been reported from various countries including Spain, China, Germany, India, Turkey and from Middle East as well. This review discusses the important mycotoxins and their natural occurrences in medicinal plants and their products.

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Abbreviations: AF, aflatoxin; OTA, ochratoxin A; FB, fumonisins; ZEA, zearalenone; DON, deoxynivalenol.

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1. Introduction

Fungi are a large group of diverse eukaryotic organisms which include yeasts and moulds. Moulds (filamentous fungi) are widely distributed in nature. Due to their versatile nutritional requirements, they are common contaminants and under favorable conditions of humidity and temperature, propagate on different commodities and beverages and produce mycotoxins (Brera et al., 1998). Medicinal plants are frequently contaminated with toxigenic fungi originating in the soil. Numerous natural occurrences of mycotoxins in medicinal plants and traditional herbal medicines have been reported from various countries. Data from India suggest that higher levels of mycotoxins are present in locally available medicinal plants. Studies from Turkey reveal that dried figs are highly contaminated with aflatoxins, ochratoxin A and fumonisin B_1. One area of concern is high levels of ochratoxin A contamination in licorice roots and products. Traditional Chinese medicines are also reported to contain exceeding levels of aflatoxins and ochratoxin A.

2. Mycotoxins

Mycotoxins are toxic secondary metabolites produced by moulds such as *Aspergillus*, *Penicillium*, *Fusarium* and *Alternaria* (Zain, 2011). Mycotoxins can be defined as "fungal metabolites that when ingested, inhaled or absorbed through the skin cause illness or human and animal death" (Pitt, 1996). Mycotoxins cause variety of toxic effects. They are carcinogenic, neurotoxic, teratogenic and immunotoxic (FAO, 2001; Petzinger and Ziegler, 2000).

Currently 400 different mycotoxins have been recognized (Zinedine and Mañes, 2009). The most important mycotoxins from human and domestic animal health point of view are aflatoxins ochratoxin A, fumonisins, zearalenone and deoxynivalenol (Miller, 1995; Santos et al., 2009). These are commonly present as contaminants in different commodities including cereals, nuts, herbal teas and spices. Crops that are stored for more than a few days become susceptible to mould growth and mycotoxin production. Contamination can occur pre-harvest or post-harvest stage (EMAN, 2003). Tropical climate and poor storage are the suitable environmental conditions that support mould growth and mycotoxin production. Mycotoxin production can be enhanced by ecological conditions like drought or damage by insects or mechanical harvesting during cultivation and storage (Tassaneeyakul et al., 2004).

3. Aflatoxins

Aflatoxins (AFs) are a class of mycotoxins produced mainly by toxigenic strains of *Aspergillus flavus* and *Aspergillus parasiticus* and rarely by *Aspergillus nomius* which can grow on various kinds of foods, beverages and medicinal plants. Aflatoxins are the most important human mycotoxins (WHO, 1998) and are among the most toxic mycotoxins (Passone et al., 2010; Sardiñas et al., 2011). There are nearly 20 different types of aflatoxins of which the four major ones are aflatoxins B_1, B_2, G_1 and G_2. Aflatoxin B_1 (AFB_1) and aflatoxin B_2 (AFB_2) are produced by *Aspergillus flavus*, while all four isoforms (B_1, B_2, G_1, G_2) are produced by *Aspergillus parasiticus* (Bennett and Klich, 2003). Aflatoxin B_1 is the most toxic of the aflatoxins and most potent naturally occurring hepatocarcinogen (IARC, 1993; Squire, 1989).

3.1. Environmental factors affecting aflatoxin production

Aflatoxin production is affected by several factors. Major factors are the fungal strain, substrate potential, moisture content, temperature and relative humidity. The minor factors that affect aflatoxin production include inoculum's potential, crop variety, oxygen supply, insect interaction and storage conditions (Bhatnagar et al., 2003). Warm and moist conditions of tropical and subtropical countries are favorable for aflatoxin production and it is enhanced by poor crop storage (Busby and Wogan, 1984).

3.2. Medical implications of aflatoxins

Aflatoxins are amongst the most powerful mutagens and carcinogens known (FAO, 1997). The International Agency of Research on Cancer (IARC) has classified AFs as Group 1 human carcinogen (IARC, 1993). Aflatoxins and hepatitis B virus (HBV) infection synergistically develop approximately thirty-fold higher hepatocellular carcinoma risk in aflatoxin-exposed, HBV-positive individuals, as compared to HBV-negative persons (Groopman and Kensler, 1996). Other toxic effects of aflatoxins include genotoxicity, teratogenicity and immunosuppressive activity. Aflatoxin B_1 LD_{50} values for most animal species ranges from 1 to 50 mg/kg body weight (Leeson et al., 1995).

3.3. Permissible limits of aflatoxins

The aflatoxin contamination of foodstuff and animal feed is controlled by legal limits. Worldwide accepted range of the total aflatoxin in foodstuffs is 1–20 ppb and in the feed the permissible limit range is 0–50 ppb. The limits for the aflatoxin M_1 in the milk for human consumption are 0.05–0.5 ppb (FAO, 2003). Maximum limits of 2 μg/kg for AFB_1 and 4 μg/kg for total aflatoxins in herbal drugs have been set by the European Pharmacopoeia (EP, 2011). However due to the fact that most herbs are processed before consumption, Liu et al. (2012) proposed higher maximum limits of 5 μg/kg and 10 μg/kg for AFB_1 and total aflatoxins respectively.

4. Ochratoxin

Ochratoxins are another family of mycotoxins produced by many species of *Aspergillus* and *Penicillium*. The family of ochratoxins consists of three members, A, B, and C. Ochratoxin A (OTA) is the most abundant and the most toxic of the three while ochratoxin B (OTB) and ochratoxin C (OTC) are less important and less common (Li et al., 1997; Van der Merwe et al., 1965). OTA is mainly produced by *Penicillium verrucosum*, *P. nordicum*, *Aspergillus niger*, *A. ochraceus* and *A. carbonarius* under diverse environmental