IN VIVO CYTOGENETIC EFFECT OF AFLATOXIN IN EXPERIMENTAL ANIMALS

Thesis

Submitted For Partial Fulfilment Of The Master Degree

In

Medical Environmental Sciences

By

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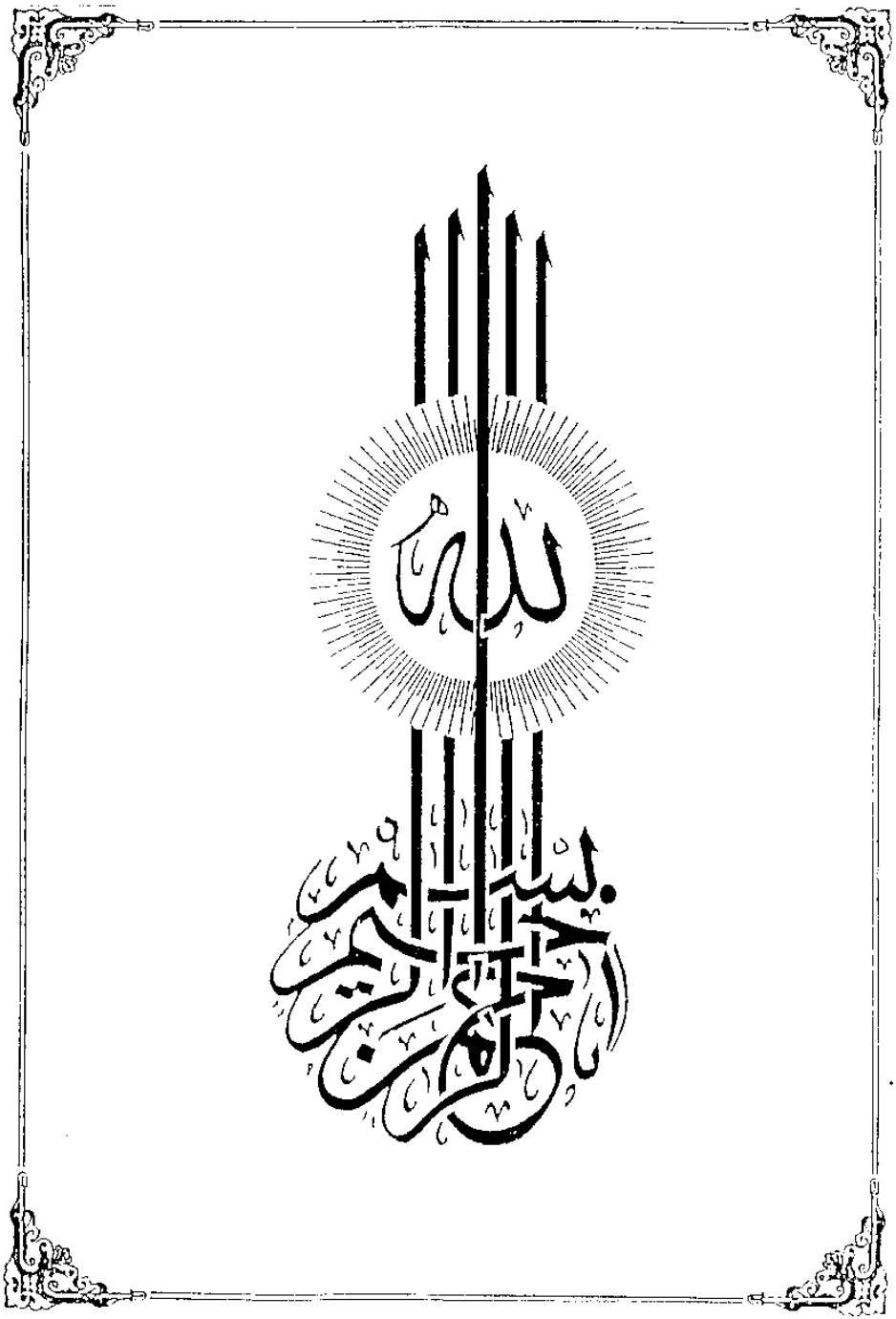

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INTRODUCTION

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Mycotoxins are secondary metabolites of certain fungal species. They are found in a large variety of food especially in mold-damaged agricultural seeds such as corn, barly, wheat, peanuts, cotton seeds and others.

Mycotoxin production can occur in damaged seeds and grains, before harvest, during the time between harvesting and drying, storage, processing, shipment and even feeding. The chemical composition, pH, and moisture content of the substrate form the favorable media for the development of mycotoxins. The mycotoxin production can easily occur when the environmental factors, such as high humidity and high temperature, are favorable. Mycotoxins can enter the food chain directly when an animal eats food contaminated with mycotoxins, which is known as primary mycotoxicosis. Secondary mycotoxicosis occurs when an individual consumes animal products from an animal which had ingested mycotoxins.

On the basis of structure, mycotoxins are classified into four classes:-

* Aflatoxins produced by Aspergillus flavus and A. parasiticus, where the principal target organ in aflatoxicosis is the liver (Wogan et al., 1967).

* Ochratoxins produced by Penicillium sp. and Aspergillus ochreus. Ochratoxin A has a long half-life in the body and is one of the mycotoxins which may have residue problems in animal tissues or body fluids (Hult et al., 1989). Ochratoxin A causes kidney damage in rats, dogs and swine.

* Trichothecenes produced by a number of genera of fungi including Fusarium, Trichoderma, Trichothecium, Stachybotrys. Trichothecenes produced by Fusarium species include deoxynivalenol, T-2 toxin, nivalenol and diacetoxyscipenol. Several of trichothecences are skin irritant of which T-2 is the most potent (Ueno, 1984).

* Zearolenone produced by Fusarium graminearum. It is estrogenic and affects the urogenital system. Swine are the most commonly affected animals, with cattle and poultry being affected to a lesser extent (Council For Agriculture Science and Technology, 1979).

Several other mycotoxins including luteoskyin, cyclochlortine, rugulosi (Enomoto and Ueno, 1977), patulin (Ciegler, 1977), penicillic acid (Cole and Cox, 1981), and sterigmatocystin have been reported to be carcinogen.

The mycotoxins that have received the most attention are aflatoxins. The four major mold-produced aflatoxin are aflatoxin B_1, aflatoxin B_2, aflatoxin G_1 and aflatoxin G_2.

Mutagenicity and carcinogenicity of compartively high doses of aflatoxins have been well established by studies in laboratory mammals (Chattopadhyaya and Nandi, 1988), prokaryotes (Goze et al., 1975; Jorgensen et al., 1987) and in cells in culture (Gabliks et al., 1965; Bhattacharya et al., 1987).

Dutton, (1988) found that sterigmatocystin is an important precursor for the biosynthesis of AFB_1 and it has reported that the acute toxicity of aflatoxin B_1 (AFB_1) was 100 times as potent as that of sterigmatocystin.

Aflatoxin B_1 (AFB_1), the most abundant and the most active of the aflatoxin compounds, has been shown to produce chromosome aberrations in plant root-tip cells (Lilly, 1965) and human leucocytes cultures (Dolimpio et al., 1968); (Garner, 1973) and fungal test systems (Matzinger and Ong, 1976).

Aflatoxin B_1 (AFB_1), one of mycotoxins, is a typical natural toxicant in food. It has not only an acute toxic activity but also a potent hepato-carcinogenic activity (Newberne and Butler, 1969; Wogan and Newberne, 1970).

AFB_1 is one of the most known potent hepatocarcinogen; it has been classified by International Agency for Research on Cancer (IARC) as a group I carcinogen. It has also been found to induce cancer in other organs in experimental animals, depending on the species and route of administration (IARC Mon., 1987). A positive correlation has been established between estimated aflatoxin intake determined from the level of aflatoxin of either market food samples or cooked food samples and the incidence of liver cancer in a number of studies in African and Asian countries (Sun and Chu, 1984 and Van Rensburg et al., 1985).

In Kenya and Swaziland, Peers and Linsell (1973) and Peers et al., (1976) demonstrated that the rise in liver cancer incidence with increasing aflatoxin intake was greater for men than women. Moreover, in a study in different parts of Uganda (Alpert et al., 1971), it was found that the aflatoxin contamination of food samples (range 10.8 - 43%) were associated with an increase in the incidence of primary liver cancer (range 1.4 -15.0 cases per 100,000 total population per year).

Hepatitis B infection is common in countries with a high incidence of primary liver cancer. So, hepatitis B virus and aflatoxins may be cofactors in the etiology of the liver cancer disease.

Hendrickse and Maxwell, (1989) proved a relationship between exposure to aflatoxins and kwashiorkor especially in developing countries where aflatoxins had been detected more frequently and at higher concentrations in the sera of kwashiorkor patients than in other children, and autopsy liver samples, from individuals died with kwashiorkor, contained AFB_1.

Sinha et al., (1987) ; Sinha and Prasad (1990) found that a dose as small as 0.05 ug when administered in concentration of 50 ppb/animal/day, could induce damage in both mitotic and meiotic chromosomes in mice (Mus musculus). On the other hand, the first observation of a disease in animals and birds, which are exposed to aflatoxin, was characterised by rapid deterioration in the condition of the birds, sub-

cutaneous hemorhages and death. The liver of these birds was pale and fatty and showed extensive necrosis and biliary proliferation. Administration of AFB_1 to lactating rats resulted in a transfer of AFB_1 metabolites to the offspring, and the metabolites were distributed to many different tissues. Binding to DNA in these tissues could not be detected but binding to proteins and RNA was observed (Allameh et al., 1989).

It is possible to remove the mycotoxins or to degrade them into less or non toxic compounds. Chemical methods are widely used to minimize mould growth in food. Various food additives such as benzoic acid, sodium chloride and antibiotics (Rusul and Marth, 1988; Lebron et al., 1989) and spices (Salmeron et al., 1990) have been shown to inhibit the growth of toxigenic fungi. The use of ammonia to detoxify aflatoxin-containing foodstuffs has been investigated (Coker et al., 1985) and shown to result in a hundred-fold reduction in the level of AFB_1 contamination. Ammonia treatment of aflatoxin-contaminated corn flour (Smith, 1985) and groundnut meal (Manson and Neal, 1987) is now being used in the United States, but only for animal feed, because the ammoniation process lowers the protein efficiency rate values of the product and produces off-flavour and off-odour.