Review of Literature
Early maturing bunch cultivars TMV 2, TMV 7 and J 11 are generally more susceptible to *C. personata*, than are late maturing spreading branched cultivars that exhibit various degrees of resistance (Gibbons, 1966). Hemingway (1957), suggested that bunch cultivars are more susceptible to infection because they have a higher proportion of stomata of 'penetrable size' on the adaxial leaf surface. Hassan and Beute (1977), found a wild *Arachis* species that had smaller mean stomata apertures on the adaxial leaf surface. According to Abdow et al. (1974), germ tube growth was directed toward stomata on highly susceptible *Arachis* varieties. However, no directional responses were recorded on varieties immune to *C. personata*. These workers noted that in moderately susceptible varieties, resistance after penetration was associated with cell-wall swelling and thickening in advance of and around the infection site, and in highly resistant varieties with the deposition of pectic substances on cell walls and in intercellular spaces.

**Toxins of *C. personata***:

Cercosporin was first isolated from *Cercosporina kikuchii* (Kuyama and Tamura, 1957a) since then found in other *Cercospora* species (Assente et al., 1977a; Balis and Payne, 1971; Lynch and Geoghegon, 1977; and Venkataramani, 1967).

Lynch and Geoghegon (1979b) showed that light greatly stimulated the production of cercosporin in the strains of *C. beticola* and light was an
absolute requirement for cercosporin production in some strains. Although light intensity is an important consideration in diseases incidence in the field (Calpouzos and Stalknecht, 1967), this factor did not have a significant effect on growth or cercosporin production in C. beticola cultures. The investigation of Lynch and Geoghegan (1979b) suggested that quinones might act as photoreceptor molecule in C. beticola. Cercosporin by absorbing and dissipating light energy may protect microorganisms from photodynamic injury (Lynch and Geoghegan, 1979a). The photodynamic action is associated with toxic effects on mice and bacteria (Yamazaki et al., 1975). The photodynamic effect is linked with the phytotoxic activity of cercosporin. The evidence suggests that absorbed light energy is transferred from the pigment to molecular oxygen, exciting it to the reactive single state and thereby initiating the auto-oxidation of membrane lipids (Macri and Vianello, 1979).

Dothistromin, an orange red pigment was first isolated from Dothistroma pine, the needle pathogen of Pinus radiate (Gallagher and Hodges, 1972). Dothistromin is a mixture with a small amount of deoxydothistromin (Danks and Hodges 1974). Subsequently, a substance which was recognized as a mixture of dothistromin and its 2-epimer was obtained from C. smilacia and other Cercospora species Dothistromin is a major metabolite from C. arachidicola and C. personata (Stoessl, 1981; and Ramanujam and Swamy, 1984).
Fazola (1978) demonstrated the presence of cercosporin by plants affected with *Cercospora* spp. It was partially purified and shown to be phytotoxic by inducing such symptoms as necrosis or chlorosis. These studies have established cercosporin as a vivo toxin.

Many pigments produced by fungi have toxic properties. Work with species of *Fusarium* (Kern, 1972) and *Cercospora* has provided evidence for this. Cercosporin was detected in infected soybean epidermal peels and in groundnut leaves (Venkataramani, 1967). Fazola (1978) successfully demonstrated cercosporin in *C. vicinella* new sources of resistance to *C. arachidicola* from within the cultivated species have been identified (Hasson and Beaute, 1977;) and variation in the reaction of plants to *C. personata* infection has been reported (Subramanyam et al., 1983). This review of literature covers only the human aspects of the untoward effects of mycotoxins. However, owing to the frequent non-specific effects of mycotoxin involvement, the results of animal experiments are useful for understanding possible effects on humans.

Ergot is the common name of the sclerotia of fungal species within a genus *Claviceps*, which produce ergot alkaloids. The sclerotium is the dark-coloured, hard fungal mass that replaces the seed or kernel of a plant following infestation. Ergot alkaloids are also secondary metabolites of some strains of *Penicillium*, *Aspergillus* and *Rhizopus* spp. (Fleiger M, Wurst M, Shelby R. 1997)

*Claviceps purpurea* produces ergotamine-ergocristine alkaloids, which cause the gangrenous form of ergotism because of their vasoconstrictive
activity. The initial symptoms are edema of the legs, with severe pains. Paraeszthenias are followed by gangrene at the tendons, with painless demarcation. The last-recorded outbreak of gangrenous ergotism occurred in Ethiopia in 1977-78; 140 persons were affected and the mortality was high (34%)(King B 1979).

The other type of ergotism, a convulsive form related to intoxication with clavinet alkaloids from Claviceps fusiformis, was last seen during 1975 in India when 78 persons were affected (Krishnamachari KAVR, Bhat RV 1976; Tulpule PG, Bhat R.V. 1978). It was characterized by gastrointestinal symptoms (nausea, vomiting and giddiness) followed by effects on the central nervous system (drowsiness, prolonged sleepiness, twitching, convulsions, blindness and paralysis). The onset of symptoms occurred 1-48 hours following exposure; there were no fatalities.

Ergotism is extremely rare today, primarily because the normal grain cleaning and milling processes remove most of the ergot so that only very low levels of alkaloids remain in the resultant flours. In addition, the alkaloids that are the causative agents of ergotism are relatively labile and are usually destroyed during baking and cooking.

Aflatoxins have been detected in the blood of pregnant women, in neocatal umbilical cord blood, and in breast milk in African countries, with significant seasonal variations (Coulter J.B.S., et al 1984; Lamplugh et al, 1988, Maxwell S.M. et al 1989). Levels of aflatoxins detected in some umbilical cord
bloods at birth are among the highest levels ever recorded in human tissue and fluids.

Aflatoxins have been suggested as an etiological factor in encephalopathy and fatty degeneration of viscera, similar to Reye syndrome, which is common in countries with a hot and humid climate (Olson LC et al 1971). The clinical picture includes enlarged, pale, fatty liver and kidneys and severe cerebral edema. Aflatoxins have been found in blood during the acute phase of the disease, and in the liver of affected children. However, use of aspirin or phenothiazines is also suspected to be involved in the etiology (Casteels – Van Deele M, Eggermont E, 1994).

In tropical countries, clinically recognizable jaundice is frequent during the neonatal period. In a large investigation undertaken on 327 babies with jaundice and 80 matching controls in Nigeria, it was found that the occurrence of glucose-6-phosphate dehydrogenase (G6PD) deficiency together with the presence of aflatoxins in the serum are significant risk factors for the development of neonatal jaundice (Sodeinde O et al 1995).

In several tropical countries, aflatoxins have been found more frequently and in higher concentration in liver specimens from children with kwashiorkor than in controls. Clinical investigation of aflatoxin elimination in children with kwashiorkor and marasmic kwashiorkor, who were fed an aflatoxin-free diet, proved that aflatoxins in these children are slowly eliminated (De Vries HR et al 1990). In several studies, aflatoxicol was found in the serum,
liver, urine and stools of children with kwashiorkor and marasmic kwashiorkor, in contrast to marasmic and control children where this metabolite was not found. It is not clear whether this difference is causally related to kwashiorkor or is a consequence of the disease.

In recent studies, aflatoxins were found in the brain and lungs of children who had died from kwashiorkor and in control children who had died from various other diseases (Oyelami OA et al 1995). It was suggested that the presence of aflatoxins in the brains of control children might be due to metabolic imbalance or to a failure in the excretory mechanisms of children with conditions such as measles (which in 25% of cases precedes kwashiorkor), renal failure, pyloric stenosis, gastroenteritis. Aflatoxins in the lungs were found in all children diagnosed to have pneumonia, irrespective of the presence of kwashiorkor. This could be due to a reduced clearing ability of the lungs in pulmonary diseases or to exposure via the respiratory route. In the Philippines, a study of the relationship between the presence of aflatoxin in the serum and urine of children and the outcome of acute lower respiratory infection failed to prove a correlation (Denning DW et al 1995). However, aflatoxin B₁ was found in the lungs of one textile and two agricultural workers who died from pulmonary interstitial fibrosis (Dvorackova I, Pichova V. 1986). These individuals were probably occupationally exposed to aflatoxin B₁ via the respiratory route. Aflatoxin B₁ was also detected in the lung tissue of a chemical engineer who had worked for 3 months on a method for sterilizing Brazilian peanut meal contaminated with Aspergillus flavus, and who died of alveolar cell carcinoma (Dvorackova I 1976).
Ochratoxins are secondary metabolites of *Aspergillus* and *Pencillium* strains, found on cereals, coffee and bread, as well as on all kinds of food commodities of animal origin in many countries (Speijers GJA, Van Egmond HP 1993). The most frequent is ochratoxin A, which is also the most toxic. It has been shown to be nephrotoxic, immunosuppressive, carcinogenic and teratogenic in all experimental animals tested so far.

Acute renal failure in one person, possibly caused by inhalation of ochratoxin A in a granary which had been closed for 2 years, was reported in Italy (Di Paolo N et al 1994). The symptoms developed after 24 hours of transitory epigastric tension, respiratory distress, and retrosternal burning. Acute tubular necrosis was found on biopsy, but the blood was not analysed for ochratoxin A. The presence of the mycotoxin in wheat from the granary was proved qualitatively by thin-layer chromatography.

Owing to the similarity of morphological and functional kidney lesions in ochratoxin A-induced porcine nephropathy and endemic nephropathy, this mycotoxin has been proposed as the causative agent of endemic nephropathy (Krogh P. 1974). This fatal renal disease occurs among rural population in Croatia, Bosnia and Herzegovina, Yugoslavia, Bulgaria and Romania, where it has been estimated that about 20,000 people are either suffering from or are suspected to have the disease (Plestina R. 1992). There is no acute phase of the illness; the first signs and symptoms of the disease are not specific and include fatigue, headache, loss of body weight and pale skin. A mild
low-molecular-mass proteinuria without hypertension but with either aplastic or
normochromic anaemia gradually develops over several years. The main
features of endemic nephropathy are bilateral, primary chronic lesions of the
renal cortex (tubular degeneration, intestinal fibrosis and hyalinization of the
glomeruli). In the advanced stage of the disease, the size and weight of kidneys
are remarkably reduced, with diffuse cortical fibrosis, usually without signs of

Ochratoxin A is found more frequently and in higher concentration
in the blood of inhabitants from endemic regions than control regions (Radic B. et
al 1997; Petkova – Bocharova T. Castegnaro M 1991). Many samples of locally
produced food and feed collected in the endemic area contained ochratoxin A
(Pavlovic M, Plestina R, Krogh P. 1979). It should be emphasized that the grain
analysed had been kept for many months in the inadequate food stores of
individual families.

In Tunisia, ochratoxin A has been detected in high concentrations
in the blood and food of patients with kidney impairment of unknown etiology
(Maaroufi K, et.al 1995). It has also been found in several countries, both in food
and feed (Speijers GJA, Van Egmond Hi 1993) and in humans. So far no cases
of endemic nephropathy have been recorded in these countries.

In endemic regions of Croatia, Bulgaria and Yugoslavia, the
incidence of otherwise rare urothelial tumours of the pelvis and ureter is 50, 90
and 100 times greater, respectively, than in non-endemic regions (Ceovic S et al
It has been suggested that ochratoxin A may be the causal agent for both endemic nephropathy and urothelial tumours (Castergnaro M et al 1990). IARC classified ochratoxin A as a compound possibly carcinogenic to humans (Group 2B).

Trichothecenes are mycotoxins produced mostly by members of the Fusarium genus, although their genera (e.g., Trichoderma, Trichothecium, Myrothecium and Stachybotrys) are also known to produce these compounds. To date, 148 trichothecenes have been isolated, but only a few have been found to contaminate food and feed. The most frequent contaminants are deoxynivalenol (DON), also known as vomitoxin, nivalenol (NIV), diacetoxyxyscirpenol (DAS), while T-2 toxin is rarer.

Common manifestations of trichothecene toxicity are depression of immune responses and nausea, sometimes vomiting. The first recognized trichotheccene mycotoxicosis was alimentary toxic aleukia in the USSR in 1932, the mortality rate was 60% (Gajdusek DC 1953). In regions where the disease occurred, 5-40% of grain samples cultured showed the presence of Fusarium sporotrichoides, while in those regions where the disease was absent this fungus was found in only 2-8% of samples. The severity of mycotoxicosis was related to the duration of consumption of toxic grain. Such severe trichothecene mycotoxicoses, the consequence of continuous ingestion of toxins, have not been recorded since this outbreak.
In several cases, trichothecene mycotoxicosis was caused by a single ingestion of bread containing toxic flour (Bhat. RV. et al., 1989) or rice; (Ueno Y 1971; Wang ZG, Feng JN, Tong Z 1993).

In experimental animals, trichothecenes are 40 times more toxic when inhaled than when given orally (Smoragiewicz, W. et al 1993). Trichothecenes were found in air samples collected during the drying and milling process on farms (Lappalainen S et al 1996), in the ventilation systems of private houses (Croft WA, et al 1986) and office buildings (Smoragiewicz W et. Al., 1993), and on the walls of houses with high humidity (Croft WA et al 1986; Nikulin M et al 1994). There are some reports showing trichothecene involvement in the development of “sick building syndrome” (Smoragiewicz W et al 1993; Croft WA et al 1986). The symptoms of airborne toxicosis disappeared when the buildings and ventilation systems were thoroughly cleaned (Croft WA et al 1986).

Zearalenone (previously known as F-2) is produced mainly by Fusarium graminearum and related species, principally in wheat and maize but also in sorghum, barley and compound feeds. Zearalonone and its derivatives produce estrogenic effects in various animal species (infertility, vulval oedema, vaginal prolapse and mammary hypertrophy in females and feminization of males – atrophy of testes and enlargement of mammary glands).

In Puerto Rico, zearalonone was found in the blood of children with precocious sexual development (Saenz de Rodriguez CA 1984) exposed to
contaminated food. Zearalenone was also found together with other Fusarium mycotoxins in “scabby grain toxicosis” in China, but the significance of this finding is not clear.

Fumonisins are mycotoxins produced throughout the world by Fusarium moniliforme and related species when they grow in maize. Fumonisins B₁ and B₂ are of toxicological significance, while the others (B₃, B₄, A₁ and A₂) occur in very low concentrations and are less toxic.

In India a single outbreak of acute foodborne disease possibly caused by fumonisin B₁ has been reported (Bhat RV et al 1997). In the 27 villages involved, the individuals affected were from the poorest social strata, who had consumed maize and sorghum harvested and left in the fields during unseasonal rains. The main features of the disease were transient abdominal pain, borborygms and diarrhea, which began half an hour to one hour following consumption of unleavened bread prepared from mouldy sorghum or mouldy maize. Patients recovered fully when the exposure ceased and there were no fatalities. Fumonisin B₂ was found in much higher concentrations in the maize and sorghum from the affected households than from controls (Chu FS, Li GY 1994).

Fumonisin B₂ was found more frequently and in much higher concentrations in maize in regions of Transkei (Marasas WFO et al 1981; Jaskiewicz K, Marasas WFO, Van der Walt FE 1987) China (Chu FS, Li GY 1994) and north-east Italy (Pascale M, Doke MB, Visconti A 1995) with a higher
incidence of oesophageal cancer than other regions. It was postulated that the high incidence of oesophageal cancer was related to the presence of this mycotoxin in maize, which is a staple food in these regions. The incidence and concentration of aflatoxin B₁, deoxynivalenol and fumonisins B₁, B₂ and B₃ were recently determined in maize samples from an area of China (Haimen) with a high incidence of primary liver cancer and from an area with a low incidence (Penlai) (Ueno Y et al 1997). Aflatoxin B₁ was found in low concentrations in almost all maize samples from both these areas, but the incidence and concentration of deoxynivalenol and fumonisins were much higher in the samples from the area where the incidence of primary liver cancer was high. The authors put forward the hypothesis that fumonisins, which have known cancer-promoting activity in rat liver (Gelderbloin WCA et al 1992), and deoxynivalenol promote the initial lesion caused by aflatoxin B₁.

The impact of other mycotoxins on human health was reported in persons occupationally exposed to large amounts of different mycotoxin-producing fungi (farmers, workers in sils, etc.). In such cases, exposure to spores via the respiratory tract seems to be of considerable importance.

In Norway an extensive epidemiological study was undertaken between 1967 and 1991 on 192 417 births (Kristensen P et al 1997) to test the hypotheses that perinatal death was associated with parental exposure to pesticides, Toxoplasma gondii infection from sheep or pigs, or mycotoxins found in grain. The proportion of late-term abortions (gestational age 16-27 weeks)
was higher among farmers. The risk associated with grain farming was higher after the harvest, the seasons with a poor quality harvest and in pregnancies with multiple fetuses, which suggests that mycotoxins in grain induce labour at an early stage of pregnancy.

Pulmonary mycotoxicosis has been reported in ten persons exposed to large quantities of fungal hyphae and spores during the cleaning of soils (Emanuel DA, Wenzel FJ, Lawton BR 1975). The clinical picture developed several hours afterwards, with burning eyes, throat and chest, irritating cough and fever. There was no wheezing, cyanosis or other sign of bronchospasm. In five patients, chest X-rays revealed reticular and fine nodular features compatible with intestinal pneumonitis. Histological study of a lung biopsy from one patient showed a multifocal acute process, with primary involvement of terminal bronchioles containing members of various spores. Cultures from lung biopsy material revealed at least five fungi species, including one *Fusarium* and one *Penicillium*. However, blood samples were not checked for the presence of mycotoxin. In contrast with the findings in pattern with farmer’s lung disease, these patients did not develop positive serological reactions to thermophilic actinomycetes or to extracts of fungal obtained from hay or silage. The patients were followed for periods of 1-10 years; they continued their work, avoiding massive re-exposure to fungal dust, and during the observation period there were no further incidents.