Fumonisins: Historical Perspectives and Future Objectives

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Fumonisins were first isolated in South Africa in 1988 from cultures of *Fusarium verticillioides* (previously known as *F. moniliforme*) strain MRC 826 and the structures of fumonisin B_1 (FB_1) and B_2 (FB_2) were elucidated. During 1989/1990, maize screenings of the 1989 USA maize crop caused widespread outbreaks of leukoencephalomalacia (LEM) in horses and pulmonary oedema syndrome (POS) in pigs in the USA. Both of these syndromes were proven to be caused by FB_1 in 1990. Analytical methods for the detection of FB_1 and FB_2 in maize were developed in 1990 and naturally occurring levels reported in maize screenings associated with field outbreaks of LEM and POS. Fumonisins were also found to occur naturally in home-grown maize in a high-incidence area of oesophageal cancer (OC) in the Transkei region of South Africa. During 1991, FB_1 was shown to cause liver cancer in rats and to inhibit sphingolipid biosynthesis by researchers in South Africa and the USA, respectively. The latter finding indicated the use of changes in the sphinganine : sphingosine ratio as a biomarker of fumonisin exposure in animals. Initial studies on the toxicokineties of fumonisins in 1992 revealed that FB_1 is rapidly excreted in the faeces and urine of rats. It is still enigmatic why the fumonisins have such an array of pathological effects while they are excreted so rapidly, mostly unmetabolised. Risk assessment parameters, ie tolerable daily intake (TDI) and probable daily intake (PDI), for fumonisins were proposed in 1996. Embryotoxicity of FB_1 in cultured rat embryos was demonstrated in 1996. In 1997, researchers in the USA reported that FB_1 inhibits folic acid transport by the folate receptor. Folic acid deficiency causes neural tube defects (NTD) and the authors postulated that some NTD in humans may be related to dietary exposure to FB_1. This hypothesis was taken a step further when the high incidence of NTD in Mexican American women along the Texas - Mexico border was associated with FB_1 in maize tortillas. Experimental evidence that FB_1 causes NTD in mouse embryos in whole embryo culture and that folic acid prevents FB_1 - induced NTD was published in 2002. Future objectives include the following:

- Mouse model: dose- effect and structure-activity relationships
- Primate model for NTD
- Fumonisins in OC and NTD
- Epidemiology and case-control studies
- Effect of folic acid supplementation
- Effect of implementation of maximal tolerable levels for fumonisins

In conclusion, the solution to the problem of fumonisins in maize is not regulation, but prevention of *Fusarium* infection and fumonisin contamination in the field.