

## Fumonisin: Historical Perspectives and Future Objectives

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Fumonisin 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<sub>1</sub> (FB<sub>1</sub>) and B<sub>2</sub> (FB<sub>2</sub>) 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<sub>1</sub> in 1990. Analytical methods for the detection of FB<sub>1</sub> and FB<sub>2</sub> in maize were developed in 1990 and naturally occurring levels reported in maize screenings associated with field outbreaks of LEM and POS. Fumonisin 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<sub>1</sub> 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 toxicokinetics of fumonisin in 1992 revealed that FB<sub>1</sub> is rapidly excreted in the faeces and urine of rats. It is still enigmatic why the fumonisin 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 fumonisin were proposed in 1996. Embryotoxicity of FB<sub>1</sub> in cultured rat embryos was demonstrated in 1996. In 1997, researchers in the USA reported that FB<sub>1</sub> 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<sub>1</sub>. 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<sub>1</sub> in maize tortillas. Experimental evidence that FB<sub>1</sub> causes NTD in mouse embryos in whole embryo culture and that folic acid prevents FB<sub>1</sub> - induced NTD was published in 2002. Future objectives include the following:

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

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

Comment [COMMENT1]:

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