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RESEARCH COMMUNICATION

A COMPARATIVE STUDY OF THE TOXICITY OF *FUSARIUM VERTICILLIOIDES* (=*F. MONILIFORME*) TO HORSES, PRIMATES, PIGS, SHEEP AND RATS

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ABSTRACT

KRIEK, N. P. J., KELLERMAN, T. S. & MARASAS, W. F. O., 1981. A comparative study of the toxicity of *Fusarium verticillioides* (=*F. moniliforme*) to horses, primates, pigs, sheep and rats. *Onderstepoort Journal of Veterinary Research*, 48, 129–131 (1981).

An isolate of *Fusarium verticillioides* (MRC826) that induced experimental leukoencephalomalacia, also caused acute toxicity when fed to pigs and administered per rumen fistula to sheep. Pigs developed severe pulmonary oedema while sheep manifested severe nephrosis and hepatosis. A less toxic isolate (*F. verticillioides* MRC602), fed to baboons, resulted in acute congestive heart failure or hepatic cirrhosis, depending on the dose. Both isolates were toxic to rats and caused similar lesions, namely, hepatic cirrhosis and intraventricular cardiac thrombosis.

Résumé

UNE ÉTUDE COMPARATIVÉ DE LA TOXICITÉ DU FUSARIUM VERTICILLIOIDES (=F. MONILIFORME) *CHEZ LES CHEVAUX, LES PRIMATES, LES PORCS, LES MOUTONS ET LES RATS*

Un isolat de Fusarium verticillioides (*MRC*826) *qui produisit une leuko-encephalomalacia, causa aussi une toxicité aiguë quand il était administré au porc d'une manière alimentaire ou encore, administré par des fistules du rumen au mouton. Les porcs développèrent un oedème pulmonaire sévère tandis que le mouton manifesta une néphrose et une hepatose sévères. Un isolat moins toxique* (F. verticillioides *MRC*602) *donné en alimentation aux baboins résulta en syncope congestive cardiaque ou en cirrhose hépatique, selon la dose. Les deux isolats furent toxiques pour les rats et causèrent des lésions similaires, à savoir cirrhose hépatique et thrombose cardiaque intraventriculaire.*

INTRODUCTION

Fusarium verticillioides (Sacc.) Nirenberg [=*F. moniliforme* (Sheldon)] is among the most prevalent fungi on maize in most of the maize-producing areas of the world (Booth, 1971; C.M.I. Distribution Maps of Plant Disease, Map No. 102, Ed. 4, 1972), including South Africa (Doidge, 1938). In spite of its having been implicated as a causal agent in a number of of diseases of both man and animals since the turn of the century (Pienaar, Kellerman & Marasas, 1981), *F. verticillioides* has only recently been shown to be responsible for natural outbreaks of the mycotoxicosis, equine leukoencephalomalacia (LEM) (Wilson & Maronpot, 1971; Marasas, Kellerman, Pienaar & Naudé, 1976).

Field outbreaks of LEM following the ingestion of *F. verticillioides*-infested maize are sporadic but not uncommon, and they have been recorded in a number of countries (Pienaar *et al.*, 1981).

Little is known about the toxigenic potential of *F. verticillioides*. As yet, moniliformin is the only known mycotoxin elaborated by certain North American isolates of *F. verticillioides* (Cole, Kirksey, Cutler, Doupnik & Peckham, 1973; Springer, Clardy, Cole, Kirksey, Hill, Carlson & Isidor, 1974). Toxigenic, but non-moniliformin-producing, strains of this fungus were isolated from various maize-producing areas of southern Africa (Kriek, Marasas & Thiel, 1981). On the basis of their toxicity to ducklings, 21 of these isolates were selected and fed to rats. Sixteen of these isolates proved to be toxic to rats in varying degrees, although they all caused hepatic cirrhosis, acute haemorrhagic or proliferative endocardial lesions, and intraventricular cardiac thrombosis as their main toxic effects (Kriek *et al.* 1981).

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MATERIALS AND METHODS

One of the most toxic of the above isolates of *F. verticillioides*, namely MRC826, was propagated on maize in bulk as previously described (Kriek *et al.*, 1981). After being ground to a fine meal, this culture material was stored at 4 °C until administered to rats, horses, pigs and sheep (Table 1). A less toxic isolate (MRC602), prepared in a similar way, was fed to rats and baboons as indicated in Table 1.

Clinical signs and body mass during the course of the experiments were recorded. All of the experimental animals were autopsied immediately after death or the termination of experiments, and specimens were collected in 10% buffered formalin for the preparation of paraffin-embedded, haematoxylin and eosin-stained sections for light microscopy.

RESULTS

The results of the various experiments are recorded in Table 1.

DISCUSSION

Over and above the very marked variation in toxigenic potential reported for the various isolates of *F. verticillioides* (Kriek *et al.*, 1981), there is also a very prominent variation in the localization of lesions and target organs in the various species examined. Although certain organs appear to be constantly affected to a greater or lesser degree, in all the animals the main target organ was different in each species, namely, the brain in horses, the liver and heart in rats, the liver in baboons, the lung in pigs and the kidney and liver in sheep.

It is thus apparent that certain isolates of *F. verticillioides* capable of inducing experimental leukoencephalomalacia in horses are also toxic to other species under experimental conditions. Furthermore, the time from initiation to death in this experiment for leukoencephalomalacia is comparable to that reported for horses under field conditions (Pienaar *et al.*, 1981). Considering the toxicity of the same

TABLE 1 Toxicity of *F. verticillioides* to horses, pigs, sheep, rats and baboons

Species	Initial live mass (kg)	Age (years)	Dosing regimen					Duration of experiment (days)	Fate	Principal lesions
			Isolate	Route of administration	Dose (g/kg × n)	Period dosed (days)	Total dose (g)			
Horse 1...	245	8	MRC826	Stomach tube	2,5 × 5 5,0 × 1	7	4 287	8	Died	Brain oedema; early leukoencephalomalacia; toxic hepatosis; nephrosis
Horse 2...	254	5	MRC826	Stomach tube	2,5 × 6	11	3 810	14	Died	Leukoencephalomalacia; nephrosis
Pig 1.....	64	0,6	MRC826	Fed in ration	*c.* 5,0 × 3	2	960	6	Died	Pulmonary oedema
Pig 2.....	11	0,3	MRC826	Fed in ration	*c.* 5,0 × 3	5	165	6	Died	Pulmonary oedema
Pig 3.....	11,5	0,25	MRC826	Fed in ration	*c.* 2,5 × 19 *c.* 5,0 × 24	89	*c.* 2 176	92	Killed	Cachexia (feed refusal)
Sheep 1...	48	1	MRC826	Rumen fistula	5,0 × 8	8	1 920	10	Died	Acute nephrosis & hepatosis
Sheep 2...	45	2	MRC826	Rumen fistula	5,0 × 11	10	2 475	12	Died	Acute nephrosis & hepatosis
Rat*.....	*c.* 0,075	0,1	MRC826	Fed in ration	*c.* 10 × 62	62	*c.* 50	77	Died or killed	Cirrhosis & intraventricular cardiac thrombosis; nephrosis
Rat*.....	*c.* 0,075	0,1	MRC826	Fed in ration	*c.* 40 × 44	44	*c.* 140	77	Died or killed	Cirrhosis & intraventricular cardiac thrombosis; nephrosis
Rat*.....	*c.* 0,075	0,1	MRC602	Fed in ration	*c.* 20 × 78	78	*c.* 100	161	Died	Cirrhosis & intraventricular cardiac thrombosis; nephrosis
Rat*.....	*c.* 0,075	0,1	MRC602	Fed in ration	*c.* 40 × 49	49	*c.* 140	161	Died	Cirrhosis & intraventricular cardiac thrombosis; nephrosis
Baboon 1.	13,6	Young adult	MRC602	Fed in ration	*c.* 0,74 × 32 *c.* 1,48 × 57 *c.* 1,66 × 31 *c.* 2,39 × 30 *c.* 2,96 × 20 *c.* 3,30 × 13 *c.* 3,68 × 65	248	*c.* 7 920	248	Died	Acute congestive heart failure
Baboon 2.	12,7	Young adult	MRC602	Fed in ration	*c.* 0,39 × 13 *c.* 0,78 × 24 *c.* 1,18 × 6 *c.* 1,57 × 7 *c.* 1,96 × 93	143	*c.* 2 860	143	Died	Acute congestive heart failure
Baboon 3.	13,0	Young adult	MRC602	Fed in ration	*c.* 0,38 × 13 *c.* 0,77 × 707	720	*c.* 7 135	720	Killed	Cirrhosis

* Six and 20 BDIX rats per treatment for MRC826 and MRC602, respectively. Initial live mass and period dosed are means for the group (Kriek *et al.* 1981)

isolate (MRC826) to particularly sheep and pigs, and the natural occurrence of toxigenic LEM-inducing strains under field conditions, it is not unlikely that natural outbreaks of these experimental, non-equine mycotoxicoses will also be encountered.

In view of the above and previously published results (Kriek *et al.,* 1981) and because of their consistent reaction to these isolates, rats are considered to be the best available system to screen toxigenic isolates of *F. verticillioides* capable of inducing the lesions described in the various mammalian species.

References

BOOTH, C., 1971. The genus *Fusarium*. Commonwealth Mycological Institute, Kew, England, p. 237.

COLE, R. J., KIRKSEY, J. W., CUTLER, H. G., DOUPNIK, B. L. & PECKHAM, J. C., 1973. Toxin of *Fusarium moniliforme:* Effects on plants and animals. *Science*, 179, 1324–1326.

DOIDGE, E. M., 1938. Some South African fusaria. *Bothalia*, 3, 331–483.

KRIEK, N. P. J., MARASAS, W. F. O. & THIEL, P. G., 1981. Hepato- and cardiotoxicity of *Fusarium verticillioides* (=F. *moniliforme*) isolates from southern African maize. *Food and Cosmetics Toxicology*, 19. (In press).

MARASAS, W. F. O., KELLERMAN, T. S., PIENAAR, J. G. & NAUDE, T. W., 1976. Leukoencephalomalacia: A mycotoxicosis of equidae caused by *Fusarium moniliforme* Sheldon. *Onderstepoort Journal of Veterinary Research*, 43, 113–122.

PIENAAR, J. G., KELLERMAN, T. S. & MARASAS, W. F O., 1981. Field outbreaks of leukoencephalomalacia in horses consuming maize infected by *Fusarium verticillioides* in South Africa. *Journal of the South African Veterinary Association*, 52, 21–24.

SPRINGER, J. P., CLARDY, J., COLE, R. J., KIRKSEY, J. W. HILL, R. K., CARLSON, R. M. & ISIDOR, J. L., 1974. Structure and synthesis of moniliformin, a novel cyclobutane microbial toxin. *Journal of the American Chemical Society*, 96, 2267–2268.

WILSON, B. J. & MARONPOT, R. R., 1971. Causative fungal agent of leucoencephalomalacia in equine animals. *Veterinary Record*, 88, 484–486.