

A nervous disorder in cattle, caused by the plants *Ficus ingens* var. *ingens* and *Ficus cordata* subsp. *salicifolia*

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ABSTRACT

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Two outbreaks of neurotoxicoses are reported in cattle browsing on the leaves of *Ficus* spp. In the first outbreak, three animals died and one became ill. A sheep developed severe nervous signs, including tetanic spasms, when dosed with the leaves of *Ficus ingens* var. *ingens* from the toxic camp where the cattle had died.

The second outbreak resulted in the death of 12 heifers within 48 h of ingestion of the leaves of *F. cordata* subsp. *salicifolia*. Clinical signs included hyperaesthesia, ataxia, muscle tremors and paddling motions while in lateral recumbency. Similar signs were reproduced by drenching the incriminated leaves to a steer. The sheep dosed with *F. ingens* var. *ingens* and two cattle, one of which had died during the second outbreak and the steer drenched with *F. cordata* subsp. *salicifolia*, were necropsied. Light microscopical examination consistently revealed oedema of the central nervous system. In the steer, focal demyelination was evident in localized areas of the brain and spinal cord. Liver lesions ranged from mild degeneration to focal disseminated necrosis of hepatocytes.

INTRODUCTION

Ficus spp. are known in both human and animal medicine for their therapeutic effects. For instance, the latexes of various species have been used since ancient times as anthelmintics, mainly because of the proteolytic enzyme, ficin, isolated from a number of South American species (Watt & Breyer-Brandwijk 1962). The pharmacological and anthelmintic proper-

ties of ficin have been the subject of considerable study, and the toxicity of this enzyme has been found to be largely dose dependent. Sublethal doses produce vomiting, haemorrhagic diarrhoea and prostration, accompanied by gross lesions such as severe irritation of the gastro-intestinal tract and occasional erosion of the mucosa. Parenteral administration or topical application of ficin to a wound, broken skin or to conjunctival surface, results in severe tissue irritation. Intravenous injection of small doses of ficin lowers the erythrocyte count and markedly prolongs the blood-clotting time (Watt & Breyer-Brandwijk 1962).

Ficus cordata subsp. *salicifolia* (synonyms *F. pretoriae* and *F. salicifolia*) is used by people in Zimbabwe as a remedy for sterility, the root being chewed with water. The Zulus give an infusion of the root, bark and leaves to cows to increase the milk supply. This is possibly a superstition linked with the milky latex produced by the trees (Drummond & Coates Palgrave 1973).

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Although more than 20 spp. of wild fig trees occur commonly in southern Africa (Von Breitenbach 1986), poisoning by these plants has not previously been recorded in this area (Steyn 1949; Kellerman, Coetzer & Naudé 1988). In India, *Ficus tsiela* was shown to be toxic when the leaves were fed to cattle during a feed shortage (Divakaran Nair, Valsala, Ramachandran & Rajan 1985; Rajan, Divakaran Nair, Valsala, Maryamma & Ramachandran 1986).

In this study, a recent field outbreak of *Ficus cordata* subsp. *salicifolia* poisoning in cattle, and subsequent dosing trials with the plant material are described. Details are also given of an outbreak of poisoning of cattle that occurred during 1970 with *F. ingens* var. *ingens* and the dosing trials that followed.

DESCRIPTION OF FIELD OUTBREAKS

The first outbreak of *Ficus* poisoning occurred early in May 1970 on a farm (farm 1) near Naboomspruit in the northern Transvaal. A bull became sick and three heifers died after supposedly having eaten the leaves of a small tree growing amongst rocks. The leaves were said to contain a caustic latex which "burnt" the mouths and noses of the affected animals which also developed severe "strychnine-like jerks".

The second outbreak occurred in 1992 and involved a group of Friesland heifers on a dairy farm (farm 2) near Brits in the central Transvaal. During a period of fodder shortage in August the farmer fed the leaves of an indigenous fig tree growing near his house as

roughage to his heifers. Roughly 40 kg of wet leaves and terminal branches were fed to a group of 15 heifers, 6–24 months old. Twelve of the heifers started showing signs of intoxication within 24 h of eating the leaves, and all died within a further period of 24 h. The farmer first noticed depression, muscle stiffness and salivation, followed by ataxia and muscle tremors. The animals became laterally recumbent, made paddling movements, salivated and showed fasciculation of the lips and nystagmus, while a few showed a serous nasal discharge and severe congestion of the mucous membranes. Some heifers remained in lateral recumbency for up to 24 h before dying. The owner's dog also developed similar nervous signs and died. The owner had noticed it consuming some of the meat and rumen contents from a carcass. A group of mature cows and calves managed on the farm semi-intensively, and not fed the leaves, remained clinically normal.

MATERIALS AND METHODS

Ficus ingens var. *ingens* and *Ficus* spp.

Dosing trials

The entire stripling suspected of poisoning the cattle on farm 1 was submitted to the Onderstepoort Veterinary Institute for toxicological examination. Within 4 d of receiving it, fresh green leaves from the plant were macerated in a blender and drenched at the rate of 9 g/kg live mass to a milk-tooth wether (sheep 1; Table 1). A further two consignments of plant material

TABLE 1 Dosing of *Ficus* spp. to ruminants

Animal			Dosing regimen					Results	
No.	Live mass (kg)	Age m-t* 4-t*	Species	Stored (d)	Dose (g/kg)	Days on which dosed	Total dose (g)	Clinical signs	Gross pathology
Sheep 1	21.5	mt	<i>F. ingens</i> var. <i>ingens</i>	4.0	9	0	193.5	Lateral recumbency, tetanic spasms, galloping and chewing motions, nystagmus, opisthotonus, bloat (day 1–2), death (day 2)	Degeneration of the liver, subepicardial petechiae, oedema and congestion of lungs, mild splenomegaly, oedema of lymph nodes
Sheep 2	26.0	4-t	<i>Ficus</i> sp.	4.0	10	0	260.0	No signs	No lesions
Sheep 3	27.0	4-t	<i>Ficus</i> sp.	1.0 5.0 14.0 17.0	5 10 10 10	0 8 14 20	945.0	No signs	No lesions
Sheep 4	45.0	4-t	<i>F. cordata</i> subsp. <i>salicifolia</i>	0.5	15	0	675.0	No signs	No lesions
Steer	144.5	mt	<i>F. cordata</i> subsp. <i>salicifolia</i>	0.5	15	0	2167.0	Hypersensitivity, ataxia, circling, falling, recumbency (day 1)	No lesions

m-t* = milk tooth

4-t* = 4-tooth

arrived from the same farm 10–14 d after the first. Leaves from this material were prepared as before and dosed once (10 g/kg x 1) and 4 times (5 g/kg x 1, 10 g/kg x 3) to two four-tooth wethers, respectively (sheep 2 and 3; Table 1).

Ficus cordata subsp. *salicifolia*

Field outbreak

From farm 2, a heifer showing clinical signs was euthanased for necropsy, and the brain, liver, kidney, lung and myocardium were fixed in 10% buffered formalin, routinely processed and stained with haematoxylin and eosin (HE) for light microscopy. Brain smears were prepared from the hippocampus, stained with Giemsa and examined for the presence of *Cowdria ruminantium* colonies. Ruminal contents from the heifer were tested for pesticides containing chlorinated hydrocarbon, carbamate and organophosphor compounds, and ruminal contents and muscle for prussic acid. Stomach contents from the poisoned dog were also analyzed for pesticides.

Dosing trials

Freshly collected terminal branches including the syconia (fruit) from the incriminated tree were chopped in a hammer-mill and dosed to a 9-months-old steer and an adult sheep (sheep 4; Table 1). The steer was given 15 g/kg plant material as a single dose by means of a stomach tube. Sheep 4 was given 15 g/kg of the plant material per rumen fistula as a single dose. The steer was euthanased by an intravenous injection of pentobarbitone sodium. The brain, spinal cord, brachial and sciatic nerves and specimens from a range of other tissues and organs were fixed in formalin and prepared for light microscopy. Transverse and longitudinal blocks were taken from each spinal segment. In addition, samples of the cerebral cortex, thalamus, medulla oblongata and cerebellum were fixed in 2.5% gluteraldehyde and stained with uranyl acetate and lead citrate according to standard procedures for transmission electron microscopy.

RESULTS

Ficus ingens var. *ingens* and *Ficus* spp.

Plant identification

The stripling from farm 1 was identified as the red-leaved fig, *Ficus ingens* (Miq.) Miq. var. *ingens* (Jordaan 1993) by the National Botanical Institute (NBI), Pretoria. Trees are deciduous, usually low-growing shrubs when occurring on rock faces, but may reach heights of 15 m or more in the western Transvaal. Syconia measure 9–12 mm in diameter and they are pink when ripe (Van Greuning 1990). The distribution of the tree is illustrated in Fig. 1. Plants from the second batch from farm 1 were identified merely as *Ficus* spp.

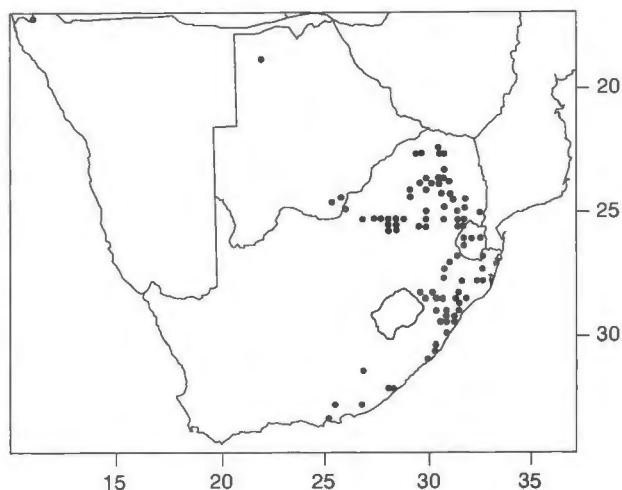


FIG. 1 Distribution of *Ficus ingens* var. *ingens* in southern Africa, excluding Zimbabwe and Mocambique (Courtesy of J.V. van Greuning, Department of Botany, University of Pretoria)

Clinical signs

Sheep 1 dosed with *F. ingens* var. *ingens* from farm 1 was found in lateral recumbency, having tetanic spasms on the morning of day 1 (18 h after dosing). The head was thrown back, it made galloping and chewing motions, foamed at the mouth, showed nystagmus, and urinated frequently. It was also apparently blind and tympany was so severe that the gas had to be released by trochar. Other clinical signs included cyanosis, tachycardia (heart rate 280/min), polypnoea (40/min) and an elevated body temperature. The animal died approximately 2 h after the clinical signs were first noticed. Sheep 2 and 3 in the trial showed no ill effects despite having been dosed respectively with 260 g/kg and 945 g/kg of the unidentified *Ficus* spp. (Table 1).

Gross pathology

In sheep 1, dosed with *F. ingens* var. *ingens*, the liver was slightly swollen and light brown, and the parenchyma had a friable consistency. The lungs were moderately congested and oedematous and the spleen was mildly swollen. The myocardium had a parboiled appearance and multiple subepicardial petechiae were present. Several lymph nodes were oedematous and some contained petechiae.

Light microscopy

Mild to moderate oedema of the central nervous system was noticed in sheep 1. Changes in the liver comprised mild degeneration of hepatocytes. In the kidneys moderate nephrosis accompanied by congestion was present. Muscle fibres throughout the myocardium had a more eosinophilic and granular appearance than normal and the interstitium contained accumulations of small numbers of mononuclear cells, predominantly lymphocytes.

Ficus cordata subsp. *salicifolia*

Plant identification

The tree from farm 2 was identified as the Wonderboom fig, *Ficus cordata* Thunb. subsp. *salicifolia* (Vahl) C.C. Berg [synonym *F. pretoriae* (Burt Davy) or *F. salicifolia* (Vahl)] (Jordaan 1993), by the NBI, Pretoria. This fig is an evergreen, low-growing shrub when present against slopes and rocky hills, and may reach up to 20 m on deep loamy soil as was the case on farm 2. Syconia are 5–8 mm in diameter (Fig. 2) and red when ripe (Van Greuning 1990). A map showing the distribution of this species is shown in Fig. 3.



FIG. 2 *Ficus cordata* subsp. *salicifolia* branchlet and syconia from farm 2

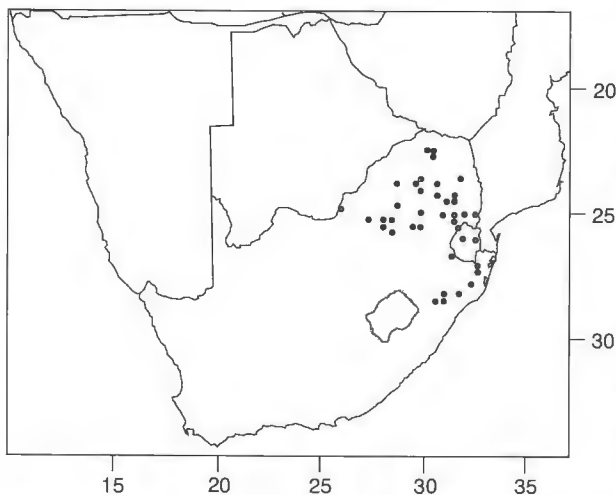


FIG. 3 Distribution of *Ficus cordata* subsp. *salicifolia* in southern Africa, excluding Zimbabwe and Mozambique (Courtesy of J.V. van Greuning, Department of Botany, University of Pretoria)

Clinical signs

Clinical signs noted on the morning of day 1 in the steer dosed with *F. cordata* subsp. *salicifolia*, included anxiety, a bewildered expression, dilated pupils, continual movements of the ears and salivation. The animal was also ataxic and tottered around, taking short steps and lifting the legs high. Occasionally, it fell down and would lie on the ground for 1–2 min before rising, appearing to be disorientated. Later the signs became more severe and the steer went into lateral recumbency, unable to regain its feet, and it was euthanased on the same day.

Sheep 4 did not develop clinical signs of intoxication.

Gross pathology

Macroscopical changes in the heifer from farm 2 were limited to moderate meningeal congestion and oedema of the brain. No significant changes were observed on macroscopical examination in the steer.

Light microscopy

In the heifer from farm 2, moderate oedema of the brain, involving the white and grey matter, was evident. Multiple foci of coagulative necrosis, often infiltrated by small numbers of neutrophils and macrophages, were randomly distributed throughout the liver (Fig. 4). The remainder of the hepatocytes were moderately degenerated. The kidneys showed mild nephrosis and congestion. In the lungs the alveolar walls were moderately distended by infiltrations of neutrophils and macrophages and by congestion. The myocardium contained groups of degenerated myofibres and focal accumulations of macrophages and lymphocytes, predominantly in perivascular locations.

Light microscopy of the steer dosed with *F. cordata* subsp. *salicifolia* revealed moderate to marked oedema

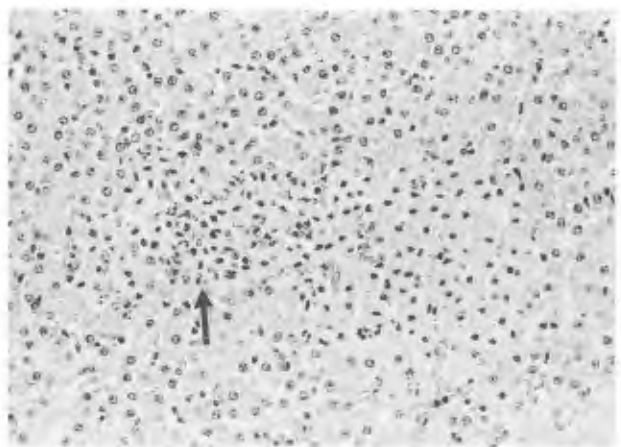


FIG. 4 Focus of coagulative necrosis infiltrated by inflammatory cells in the liver (arrow). Heifer poisoned by *Ficus cordata* subsp. *salicifolia*. HE X 200

of the white and grey matter in the brain, especially of the white matter in the midbrain, medulla oblongata and cerebellum. The white matter appeared loosely textured and perivascular spaces were often distended, sometimes containing small eosinophilic droplets. Myelin sheaths in these areas were dilated and occasionally contained swollen axons or foamy macrophages and myelin debris. In the spinal cord, dilated myelin sheaths and focal Wallerian demyelination were noted peripherally in the lateral and ventral funiculi (Fig. 5). The peripheral nerves showed focal swelling of the myelin sheaths. In the liver mild hepatocellular degeneration and small infiltrations of neutrophils were found. A mild nephrosis was also present. No colonies of *C. ruminantium* were present in the brain smears.

Electron microscopy

Electron microscopy confirmed widened perivascular and extracellular spaces in the steer. Astrocytic processes about vessels were watery and electron-lucent and showed dispersal of cytoplasmic organelles. Changes were not seen in neurons, axons or other tissue elements and there was no evidence of myelin breakdown in the sections that were examined.

Toxicology

No pesticides nor prussic acid could be demonstrated in the respective samples.

DISCUSSION

The clinical signs observed during the field cases, namely hypersensitivity, muscle tremors, convulsions and nystagmus, were indistinguishable from those manifested by the sheep and steer dosed respectively with *F. ingens* var. *ingens* and *F. cordata* subsp. *salicifolia*. These signs also closely resembled those described in bovine *F. tsiella* poisoning in India (Divakaran Nair *et al.* 1985; Rajan *et al.* 1986).

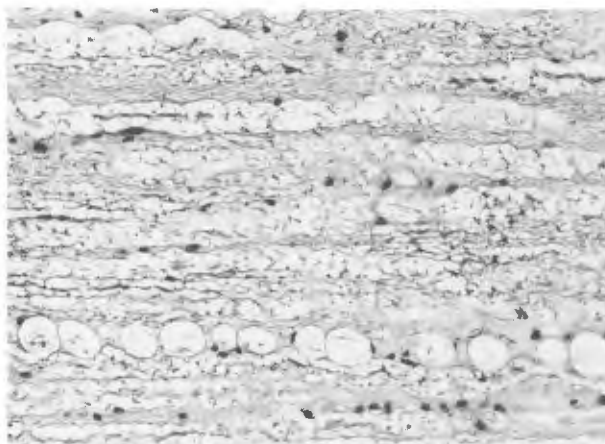


FIG. 5 Dilated myelin sheaths and focal demyelination in the spinal cord of a steer dosed with *Ficus cordata* subsp. *salicifolia*. HE X 200

The clinical signs in cattle could be confused with heartwater, rabies, the nervous form of malignant catarrhal fever, cerebral babesiosis, cerebral theileriosis, and meningitis and encephalitis caused by various bacteria (Van de Pypekamp & Prozesky 1987). Other differential diagnoses include poisoning by chlorinated hydrocarbon, carbamate or organophosphor compounds, lead (Van de Pypekamp & Prozesky 1987), urea and ammonified hay, and by several plants, namely *Albizia versicolor*, *A. tangangicensis*, *Sarcostemma viminale*, *Solanum kwebense*, *Cynanchum* spp. and *Euphorbia mauritanica* (Van de Pypekamp & Prozesky 1987; Kellerman *et al.* 1988).

Indications are that *Ficus* spp. could cause a drop in the glucose levels (Augusti 1973; Ghosh & Gupta 1980) and it may be worth while to investigate whether lowering of the blood sugar in this intoxication can cause nervous signs in cattle. This characteristic feature of *Ficus* spp. has been utilized as a traditional remedy in the treatment of people with high blood-sugar levels in India. Cups are carved from the wood of *Ficus* trees and water is allowed to stand in these cups for 24 h before being consumed (I. Moosajee, Faculty of Veterinary Science, Medunsa, personal communication 1993). The effects of ficin, the toxic principle isolated from a number of South American *Ficus* spp., have been reported (Watt & Breyer-Brandwijk 1962). The acute course of the intoxication and nature of the lesions in the cases described in this paper, suggested that these effects were probably not caused by ficin.

In contrast to the steer, the sheep dosed with *F. cordata* subsp. *salicifolia* developed no clinical signs, despite having received the same dosage. Although only one animal per species was used, this suggests a species difference in the susceptibility to *Ficus* spp. which needs further investigation. No symptoms developed in sheep 2 and 3 dosed with the *Ficus* spp., suggesting that these plants were probably not toxic to sheep.

The cause of death of the dog (farm 2) that died after eating meat and rumen content from the carcass of an animal poisoned by *F. cordata* subsp. *salicifolia*, has not been established. As far as plant poisonings are concerned, only krimpsiekte, a toxicosis of goats, sheep, cattle and horses, caused by the ingestion of plakkies (members of the genera *Cotyledon*, *Tylecodon* and *Kalanchoe*), is known to elicit secondary poisoning in animals. Dogs are particularly susceptible and can be poisoned by eating the meat of sheep and goats that have died of krimpsiekte (Kellerman *et al.* 1988).

Oedema of the brain is a consistent lesion in cases of *Ficus tsiella* poisoning (Divakaran Nair *et al.* 1985; Rajan *et al.* 1986), and in the steer in the present study, was more conspicuous in the white matter. Electron microscopy in this animal confirmed that the oedema was localized in extracellular spaces without significant involvement of glial cells. This indicates vasogenic oedema resulting from damage to vascular endothelium,

and increased permeability with subsequent leakage of plasma constituents (Jubb & Huxtable 1993). Moderate to severe demyelination of the brain white matter was reported by Divakaran Nair *et al.* (1985) in experimental *F. tsiela* poisoning in calves. In the present study, demyelination was noted in the steer dosed with *F. cordata* subsp. *salicifolia*; however, the mild and focal nature of these lesions may have been related to the short course of the intoxication.

The liver lesions in *Ficus* poisoning range from mild degeneration to focal disseminated necrosis of hepatocytes, as seen in the present cases, to centrilobular necrosis reported previously (Divakaran Nair *et al.* 1985; Rajan *et al.* 1986).

The two outbreaks described in this paper confirm the danger of feeding leaves from any *Ficus* spp. to livestock. As the toxic *F. cordata* subsp. *salicifolia* and *F. ingens* var. *ingens* are taxonomically closely related to each other as well as to *F. cordata* subsp. *cordata* and *F. verruculosa* (Van Greuning 1990; F. von Breitenbach and A.E. van Wyk, personal communication 1992), this group, in particular, should be considered potentially toxic.

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