Review Article

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POISONOUS PLANTS AFFECTING HEART FUNCTION OF CATTLE IN BRAZIL[1]

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1.0. São apresentados alguns aspectos da intoxicação por plantas que afetam o funcionamento do coração. Estas plantas podem ser agrupadas da seguinte maneira:

1.1. *Plantas que causam "morte súbita"*, uma intoxicação superaguda sem alterações significativas do coração. Esse é o grupo de plantas tóxicas mais importantes e mais numeroso no Brasil. Das aproximadamente 60 plantas tóxicas de interesse pecuário conhecidas no Brasil, 11 pertencem a este grupo. As plantas deste grupo são, estimativamente responsáveis por 60% das mortes em bovinos causadas por plantas tóxicas no Brasil. Sob condições naturais são afetados principalmente bovinos. As plantas deste grupo causam uma intoxicação que pode ser reproduzida pela administração de doses únicas pequenas (0,6 a 2 g/kg) ou médias (5 a 20 g/kg) e que se caracteriza por evolução superaguda. Os animais aparentemente sadios subitamente caem ao chão, especialmente quando movimentados, morrendo em questão de minutos. Os achados de necropsia são praticamente negativos. Os exames histopatológicos revelam lesões agudas sob forma de alterações regressivas e circulatórias não muito constantes no coração e fígado e uma alteração regressiva mais constante no rim na forma de degeneração hidropico-vacuolar das células epiteliais dos túbulos contornados distais. O quadro clínico-patológico sugere que essas plantas têm princípios tóxicos que interferem no funcionamento do coração; os animais morrem aparentemente de uma insuficiência cardíaca aguda. Só em relação a uma dessas plantas, *Palicourea marcgravii* (fam. Rubiaceae) sabemos que o princípio tóxico é o ácido monofluoroacético. É a planta tóxica mais importante deste grupo. Sabe-se que o ácido monofluoroacético interfere no ciclo energético das células, tendo efeito marcado no funcionamento do coração e no sistema nervoso central. Nos bovinos o efeito tóxico é predominantemente sobre o coração. As plantas deste grupo pertencem a 3 famílias botânicas diferentes – 4 pertencem à família das rubiáceas, 3 à das bignoniáceas e 4 à das malpighiáceas.

1.2. *Plantas que causam uma intoxicação subaguda a crônica com severa necrose de fibras cardíacas e fibrose do miocárdio.* No Brasil conhecemos somente duas plantas com capacidade de provocar esse tipo de intoxicação. São *Tetrapterys acutifolia* Cav. e *Tetrapterys multiglandulosa* Adr. Juss. (fam. Malpighiaceae), plantas tóxicas importantes em algumas áreas da Região Sudeste. A ação dessas plantas é bem diferente das plantas que causam "morte súbita". Em bovinos elas geralmente causam, ingeridas durante períodos prolongados em doses médias (5 g/kg/dia durante 60 dias) uma intoxicação de evolução subaguda a crônica, com sintomatologia cardíaca bastante característica: veia jugular engurgitada, pulsando e edema da região esternal; à necropsia, encontram-se sobretudo lesões cardíacas bem visíveis sob forma de áreas e feixes esbranquiçados ocupando boa parte da superfície de corte do miocárdio. Freqüentemente o fígado apresenta aspecto de noz-moscada e há edemas generalizados, inclusive ascite e hidrotórax. Histologicamente, estas lesões caracterizam-se por necrose severa das fibras cardíacas e fibrose do miocárdio. Pelo exercício só raramente pode se provocar a morte dos animais, quando a doença já está muito adiantada. O princípio tóxico destas plantas ainda não é conhecido. Históricos e dados patológicos sugerem fortemente de que *Tetrapterys* spp. também sejam responsáveis por abortos em bovinos.

2.0. É feita uma comparação das plantas tóxicas brasileiras que afetam o funcionamento do coração com plantas de ação semelhante de outras partes do mundo, isto é Africa e Austrália.

3.0. Compara-se os quadros clínico-patológicos da intoxicação por *Palicourea marcgravii* e por ácido monofluoroacético.

TERMOS DE INDEXAÇÃO: Intoxicação por planta, plantas cardiotóxicas, bovinos, patologia, "morte súbita", necrose e fibrose cardíacas.

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ABSTRACT.- An analysis of important aspects of poisoning by plants affecting heart function of cattle in Brazil is presented (1.0). These plants can be grouped in the following way :(1.1) Plants causing "sudden death", a peracute poisoning without significant heart lesions, and (1.2) plants causing a subacute to chronic poisoning with necrosis of heart fibres and fibrosis of the myocardium. Moreover (2.0) a comparison of the action of these plants with plants of similar action from Africa and Australia is made, and also (3.0) the clinical-pathological pictures of poisoning by *Palicourea marcgravii* (Rubiaceae) and monofluoroacetic acid are compared.

INDEX TERMS: Plant poisoning, cardiotoxic plants, cattle, pathology, "sudden death", necrosis and fibrosis of the heart muscle.

1.0. Poisoning by Plants Affecting Heart Function of Cattle in Brazil

1.1. *Plants causing "sudden death"*

General considerations

The most important and numerous group of poisonous plants in Brazil is the one which causes "sudden death" in cattle. Of the 60 poisonous plant species of interest to animal husbandry known in this country, 11 belong to this group. These plants causing "sudden death" are estimated to be responsible for about 60% of the losses due to toxic plants in Brazil. Under natural conditions mainly cattle are affected.

The plant poisoning resulting in "sudden death" can be reproduced by administration of single small (0.6 to 2 g/kg) or medium (5 to 20 g/kg) doses and mostly has a peracute course. The animals, generally without previous symptoms, suddenly fall to the ground, especially when moved, and die within a few minutes. There are practically no post-mortem findings. Histopathological changes sometimes consist of slight regressive and circulatory alterations in heart and liver, and a frequent quite characteristic regressive lesion in the kidney in the form of a hydropic-vacuolar degeneration of the epithelial cells of the distal convoluted tubules.

The clinical-pathological picture suggests that these plants have toxic principles which interfere with heart function; the animals apparently die of acute heart insufficiency. Only the poisonous principle of *Palicourea marcgravii* (fam. Rubiaceae) is known, and is monofluoroacetic acid (Oliveira 1963, Hall 1972). It is the most important plant of this group. It is well known that monofluoroacetic acid interfers with the energetic cycle of the cells, with severe effect on cardiac function and the central nervous system, causing ventricular fibrillation and tetanic convulsions (Hall 1972). In bovines the toxic effect involves mainly the heart (Allcroft & Jones 1969).

The plants of this group, in Brazil, belong to 3 different botanic families; they are:

Rubiaceae: *Palicourea marcgravii* St. Hil.,
Palicourea aeneofusca (M. Arg.) Standl.,
Palicourea juruana Krause,
Palicourea grandiflora (H.B.K.) Standl.;

Bignoniaceae: *Arrabidaea bilabiata* (Sprague) Sandw.,
Arrabidaea japurensis (DC.) Bur. & K. Schum.,
Pseudocalymma elegans (Vell.) Kuhlm.;

Malpighiaceae: *Mascagnia rigida* (Juss.) Griseb.,
Mascagnia elegans Griseb.,
Mascagnia pubiflora (Juss.) Griseb.,
Mascagnia aff. *rigida* (Juss.) Griseb.

Palicourea marcgravii is the most important poisonous plant in Brazil; it occurs all over Brazil with exception of the South of the country and Mato Grosso do Sul (Pacheco & Carneiro 1932, Döbereiner & Tokarnia 1959, Tokarnia & Döbereiner 1986). *Palicourea aeneofusca* has its distribution limited to the "zona da mata" of Pernambuco where it is the most important poisonous plant (Tokarnia et al. 1983). *Palicourea juruana* and *Palicourea grandiflora* are less important poisonous plants of the Amazon Region (Tokarnia et al. 1981, Tokarnia et al. 1982).

Arrabidaea bilabiata is the second most important poisonous plant of the Amazon Region; whilst *Palicourea marcgravii* occurs only on "terra firme", never flooded areas, *Arrabidaea bilabiata* grows only in temporarly flooded areas (Döbereiner et al. 1983). *Arrabidaea japurensis* is the most important poisonous plant of the State of Roraima and is also a plant of temporarily flooded areas (Tokarnia & Döbereiner 1981). *Pseudocalymma elegans* is a poisonous plant of low importance because of its limited distribution to slopes in hills in the State of Rio de Janeiro (Mello & Fernandes 1941, Tokarnia et al. 1969).

Mascagnia rigida is the most important poisonous plant of the large dry Norteastern Region of Brazil (Tokarnia et al. 1961), and occurs also in the northeast of Minas Gerais and the north of Espírito Santo. *Mascagnia elegans* is of little importance because of its limited distribution in the dry areas of Pernambuco (Couceiro et al. 1976). *Mascagnia pubiflora* is the most important poisonous plant of Mato Grosso do Sul; it occurs also in nearby areas in the States of São Paulo, Goiás and Minas Gerais (Fernandes & Macruz 1964, Tokarnia & Döbereiner 1973). *Mascagnia* aff. *rigida* is a poisonous plant of some importance in the north of the State of Espírito Santo (Tokarnia et al. 1985)

Distinguishing features

Although this group of plants has this common characteristic of causing "sudden death", there are many distinguishing features within the group. Some of these will be discussed below.

Toxic doses.Experiments showed that single doses of these plants are sufficient to cause death, but vary somewhat. In regard to the Rubiaceae, these doses are always small, and are for cattle between 0,6 and 2 g/kg (Tokarnia & Döbereiner 1982, 1986, Tokarnia et al. 1981, 1983).

In regard to the Bignoniaceae, similar doses sometimes have been sufficient to cause death in cattle, but there is

a great variation, up to 10 fold in the toxicity of the plants. In the case of *Pseudocalymma elegans,* experimentation in bovines showed that the younger the leaves, the more toxic is the plant (Tokarnia et al. 1969). For *Arrabidaea bilabiata* it was not possible, by experimentation in cattle, to elucidate the cause of the variation of its toxicity (Döbereiner et al. 1983); but through experiments made in rabbits (Döbereiner et al. 1984), where there occurred also a great variation in the toxicity of the plant, there were indications that the young leaves are more toxic, and that the origin of the plant material may have an influence.

Regarding *Arrabidaea japurensis,* in spite of all experiments with the fresh plant being made with young leaves, there was also a great variation in toxicity (Tokarnia & Döbereiner 1981). In experiments with the dried plant, also in bovines, in which young and mature leaves were used, the mature leaves had half the toxicity. In experiments on rabbits (Döbereiner & Tokarnia 1983), all performed with the dried young leaves, there was no significant variation in toxicity. Thus, regarding *A. japurensis,* it was not possible to obtain any indication of the cause of the variation of its toxicity.

Regarding the Malpighiaceae, there were great differences in the toxicity among the different plant species. *Mascagnia* aff. *rigida* can be compared to the Rubiaceae; there was little variation in its toxicity to bovines (0.625 to 2.5 g/kg) (Tokarnia et al. 1985). *Mascagnia pubiflora,* in spite of being less toxic, can be compared, regarding the variation of its toxicity due to its growing stage, with *Pseudocalymma elegans* of the Bignoniaceae family; the lethal dose of the young leaves is 5 g/kg and of the mature leaves 20 g/kg (Tokarnia & Döbereiner 1973).

Mascagnia rigida showed a very large variation in its toxicity in the experiments made in bovines; according to field observations (Tokarnia et al. 1961), it is possible that the deaths caused by this plant are more frequent after repeated ingestions. Experimentally fatal poisoning was observed after single and repeated administrations of the plant (Tokarnia et al. 1961, Tokarnia & Figueiredo 1979, Tokarnia et al. 1982, Santos 1975), but there was a very great variation of the doses needed to poison animals. Due to the fact that in these experiments no data were registered on the growing stage of the plant, and also due to its different origin, it is not possible to come to conclusions regarding the cause of the great variation in the toxicity of *M. rigida.* In experiments with rabbits (Tokarnia et al. 1987), the plant, which was collected from only one location, showed a constant toxicity; the rabbits died after receiving a single dose of 4 g/kg of the dried plant. Regarding *Mascagnia elegans* only 2 experiments consisting in repeated administrations of the plant to bovines were performed (Couceiro et al. 1976); no efforts were made to establish the lethal dose of the plant.

Cumulative effect. Through experiments is was shown that some of the plants of this group have a cumulative effect. *Palicourea marcgravii* has a cumulative effect when given in daily doses of 1/5 to 1/10 of the lethal dose (Tokarnia & Döbereiner 1986). With *Palicourea grandiflora* a similar cumulative effect was observed (Tokarnia et al. 1981). *Mascagnia* aff. *rigida* has only a slight cumulative effect (Tokarnia et al. 1985). Regarding the other plants of this group, the existence of a cumulative effect in cattle has not yet been sufficiently studied.

Excercise. This is an important factor in the poisoning by the plants of this group. However the importance of exercise varies according to the plant species and the amount eaten. Thus, with *P. marcgravii,* in spite of the fact that death of the animals can be caused or precipitated by exercise, the majority of the experimental bovines died without exercise (Tokarnia & Döbereiner 1986). But regarding *Mascagnia* aff. *rigida* it was seen, that - with the exception of the bovine, which received the largest dose (10 g/kg of the fresh plant), all other experimental animals which received smaller lethal doses, showed symptoms only during or soon after the animals had been exercised; thus, in these animals, death was caused or precipitated by exercise (Tokarnia et al. 1985). Also with *Palicourea grandiflora* and *Arrabidaea japurensis* a similar effect was observed. The 3 bovines which received the larger doses of *P. grandiflora* died without exercise, the other 3 bovines which received smaller doses died after exercise (Tokarnia et al. 1981). With *Arrabidaea japurensis,* 2 of the 4 bovines which ingested 10 g/kg or more, died without exercise, the other 2 animals and those which received less than 10 g/kg, died after exercise (Tokarnia & Döbereiner 1981). With the data obtained on the other plants of this group, no precise interpretation of the influence of exercise can yet be made.

Histological alterations. In Table 1, 2 and 3 the incidence of the main microscopic alterations seen in the experimental poisoning by the plants wich cause "sudden death" in Brazil, is given.

Experiments with fresh leaves given in a single dose (Table 1): In the *heart,* only slight, not very frequent, regressive alterations, in the form of intracellular edema and increase in the eosinofilia of the cytoplasm without or with picnosis of the nuclei of heart muscle fibers, always in focal distribution, occurred in poisoning by the plants of the 3 families. Only in the single experiment, with the fresh leaves with *Palicourea juruana,* well established areas of necrosis were observed in the heart; this was an exceptional case of long duration (72 hours).

In the *liver,* cloudy swelling and vacuolization of the hepatocytes was sometimes seen. *Mascagnia* aff. *rigida* caused an especially high incidence of vacuolization of the cytoplasm in the hepatocytes, in 83.3% of the animals. Necrosis of hepatocytes was seen only in poisoning by *Arrabidaea bilabiata* and *A. japurensis.* Congestion, dissociation of the hepatic cords and edema

Table 1. *Incidence of histologic changes in experimental poisoning of cattle by the fresh leaves of plants causing "sudden death" (Single doses)*

Plant	Heart						Liver					Kidney			Number of animals studied histologically
	Intracel-lular edema	Increase of eosino-philia without picnosis (focal)	Increase of eosino-philia with picnosis (focal)	Areas of necrosis	Mono-nuclear infil-tration	Prolifera-tion of fibroblasts and/or fibrosis	Swelling of liver cells	Vacuoliza-tion of liver cells	Centro-lobular necrosis	Conges-tion	Dissocia-tion of hepatic cords[a]	Edema of Disse's space	Hydropic-vacuolar degeneration: Of distal convoluted tubules	Hydropic-vacuolar degeneration: In the medul-lary zone	Albuminous granular degeneration in the cortex	
Palicourea marcgravii	5/25 20%	3/25 12%	2/25 8%	0/25 0%	9/25 36%	0/25 0%	12/26 46,1%	12/26 46,1%	0/26 0%	10/26 38,4%	6/26 23%	11/26 42,3%	18/27 66,6%	6/27 22,2%	0/27 0%	27[b]
Palicourea aeneofusca	0/2 0%	0/2 0%	0/2 0%	0/2 0%	0/2 0%	0/2 0%	1/2 50%	1/2 50%	0/2 0%	0/2 0%	0/2 0%	1/2 50%	1/2 50%	1/2 50%	0/2 0%	2
Palicourea juruana	0/1 0%	1/1 100%	1/1 100%	1/1 100%	0/1 0%	0/1 0%	0/1 0%	1/1 100%	1/1[c] 100%	0/1 0%	0/1 0%	0/1 0%	0/1 0%	0/1 0%	0/1 0%	1
Palicourea grandiflora	0/6 0%	0/6 0%	1/6 16,6%	0/6 0%	1/6 16,6%	0/6 0%	1/6 16,6%	2/6 33,3%	0/6 0%	2/6 33,3%	1/6 16,6%	3/6 50%	4/6 66,6%	1/6 16,6%	0/6 0%	6
Arrabidaea bilabiata	1/9 11,1%	0/9 0%	0/9 0%	0/9 0%	2/9 22,2%	0/9 0%	6/9 66,6%	1/9 11,1%	1/9 11,1%	3/9 33,3%	2/9 22,2%	7/9 77,7%	4/9 44,4%	0/9 0%	1/9 11,1%	9
Arrabidaea japurensis	0/8 0%	0/8 0%	0/8 0%	0/8 0%	5/8 62,5%	0/8 0%	2/8 25%	2/8 25%	0/8 0%	0/8 0%	0/8 0%	5/8 62,5%	7/8 87,5%	2/8 25%	0/8 0%	8
Pseudocalyxma elegans	2/8 25%	0/8 0%	0/8 0%	0/8 0%	2/8 25%	0/8 0%	1/8 12,5%	1/8 12,5%	0/8 0%	4/8 50%	1/8 12,5%	4/8 50%	3/8 37,5%	2/8 25%	0/8 0%	8
Mascagnia rigida	2/7 28,5%	0/7 0%	1/7 14,2%	0/7 0%	0/7 0%	0/7 0%	3/7 42,8%	1/7 14,2%	0/7 0%	1/7 14,2%	0/7 0%	2/7 28,5%	3/7 42,8%	1/7 14,2%	0/7 0%	7
Mascagnia pubiflora	6/15 40%	0/15 0%	0/15 0%	0/15 0%	1/15 6,6%	0/15 0%	8/15 53,3%	4/15 26,6%	0/15 0%	2/15 13,3%	2/15 13,3%	4/15 26,6%	10/15 66,6%	3/15 20%	4/15 26,6%	15
Mascagnia aff. *rigida*	1/6 16,6%	0/6 0%	1/6 16,6%	0/6 0%	2/6 33,3%	0/6 0%	2/6 33,3%	5/6 83,3%	0/6 0%	0/6 0%	0/6 0%	4/6 66,6%	3/6 50%	3/6 50%	1/6 16,6%	6

[a] Dissociation of hepatic cords means separation of the trabecules due to dilation of the sinusoids;
[b] The heart of 2 animals and the liver of 1 were not examined histologically. The percentage was calculated always over the organs which were examined;
[c] There is also some necrosis of the intermedian zone.

of Disse's space were also seen, with very variable frequency for the plants of the 3 families. The *kidney* showed the most characteristic histological lesion caused by all plants of this group, in the form of a hydropic-vacuolar degeneration of the epithelial cells of the distal convoluted tubules (Fig. 1). The degeneration is severe with nuclear picnosis and disappearance of the cytoplasm. It is not known how this lesion is related to the clinical picture, but it is possible that it occurs through the elimination of the toxin or its

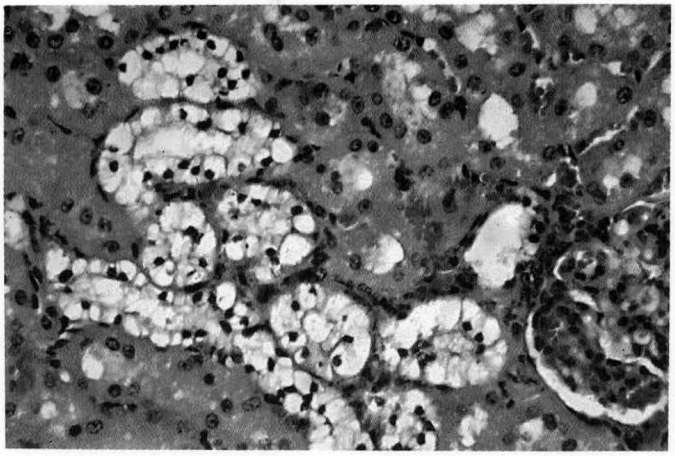


Fig. 1. *Hydropic-vacuolar degeneration of the epithelial cells of the distal convoluted tubules in the kidney, in experimental poisoning by* P. marcgravii. *The degeneration is severe, as can be seen by the nuclear picnosis and disappearance of the cytoplasm (Bov. 956, SAP 15286). HE. obj. 25.*

metabolites by the kidney. The lesion is not seen in all cases, which would help even more in the diagnosis of the poisoning. The lesion is seen in about 50% of the cases of poisoning by the fresh leaves of the plants which cause "sudden death". In poisoning by *Arrabidaea japurensis* the occurrence of this lesion is exceptionally high (87.5%).

Experiments with the dried leaves given in a single dose (Table 2): In the experiments with 6 plants of the group, slight regressive alterations in the heart were occasionally observed. Necrosis of hepatocytes was not observed. There was no hydropic-vacuolar degeneration of the epithelial cells of the distal convoluted kidney tubules due to the administration of the Rubiaceae and the one Bignoniaceae tested, but it was present in the poisoning by the 2 Malpighiaceae used.

Experiments with the dried leaves given in repeated

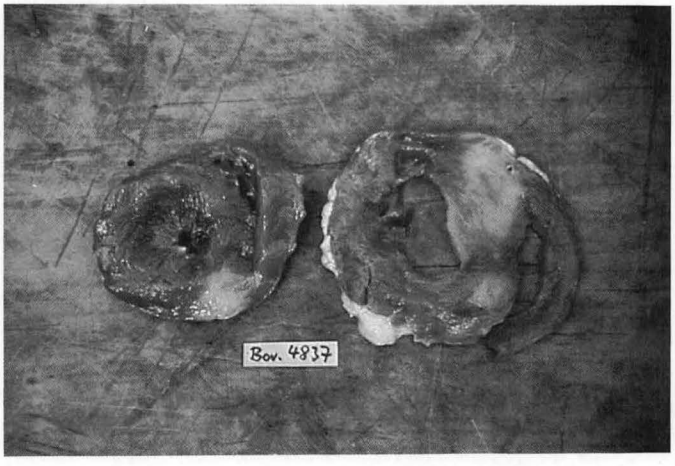
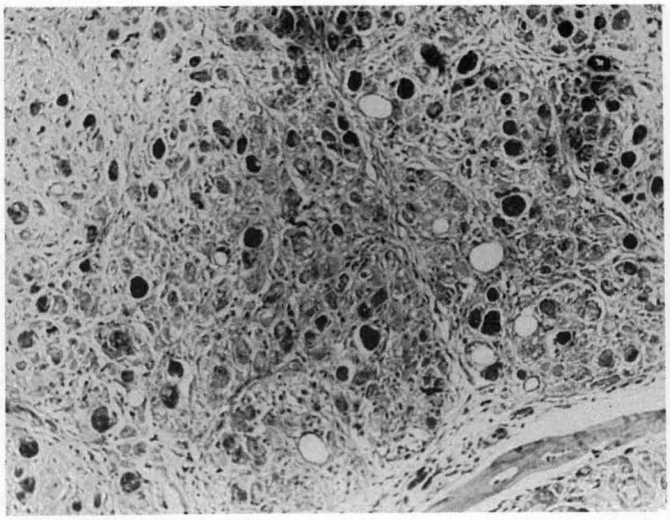


Fig. 2. *Sharp whitish areas due to fibrosis of the myocardium in experimental poisoning by* T. multiglandulosa; *the animal had received 2,5 g/kg/day of the fresh sprouts during 125 days (Bov. 4837).*

Table 2. *Incidence of histologic changes in experimental poisoning of cattle by the dried leaves of plants causing "sudden death" (Single doses)*

Plant	Heart						Liver						Kidney			
	Intracelular edema	Increase of eosinophilia without picnosis (focal)	Increase of eosinophilia with picnosis (focal)	Areas of necrosis	Mononuclear infiltration	Proliferation of fibroblasts and/or fibrosis	Swelling of liver cells	Vacuolization of liver cells	Centrolobular necrosis	Congestion	Dissociation of hepatic cords[a]	Edema of Disse's space	Hydropic-vacuolar degeneration: Of distal convoluted tubules	Hydropic-vacuolar degeneration: In the medullary zone	Albuminous granular degeneration in the cortex	Number of animals studied histologically
Palicourea marcgravii	2/3 66,6%	0/3 0%	0/3 0%	0/3 0%	1/3 33,3%	0/3 0%	2/3 66,6%	2/3 66,6%	0/3 0%	0/3 0%	1/3 33,3%	2/3 66,6%	0/4 0%	0/4 0%	0/4 0%	4[a]
Palicourea juruana	1/3 33,3%	1/3 33,3%	1/3 33,3%	0/3 0%	2/3 66,6%	0/3 0%	0/3 0%	3/3 100%	0/3 0%	0/3 0%	0/3 0%	2/3 66,6%	0/3 0%	0/3 0%	0/3 0%	3
Palicourea grandiflora	1/2 50%	0/2 0%	0/2 0%	0/2 0%	2/2 100%	0/2 0%	1/2 50%	2/2 100%	0/2 0%	0/2 0%	0/2 0%	1/2 50%	0/2 0%	0/2 0%	0/2 0%	2
Arrabidaea japurensis	0/5 0%	0/5 0%	0/5 0%	0/5 0%	1/5 20%	0/5 0%	1/5 20%	3/5 60%	0/5 0%	3/5 60%	3/5 60%	4/5 80%	0/5 0%	0/5 0%	0/5 0%	5
Mascagnia pubiflora	1/4 25%	0/4 0%	0/4 0%	0/4 0%	0/4 0%	0/4 0%	1/4 25%	2/4 50%	0/4 0%	1/4 25%	1/4 25%	1/4 25%	2/4 50%	0/4 0%	1/4 25%	4
Mascagnia aff. *rigida*	1/3 33,3%	0/3 0%	1/3 33,3%	0/3 0%	1/3 33,3%	0/3 0%	2/3 66,6%	3/3 100%	0/3 0%	0/3 0%	1/3 33,3	2/3 66,6%	1/3 33,3%	0/3 0%	0/3 0%	3

[a] The heart and the liver of 1 animal were not examined histologically.
The percentage was calculated always over the organs which were examined.



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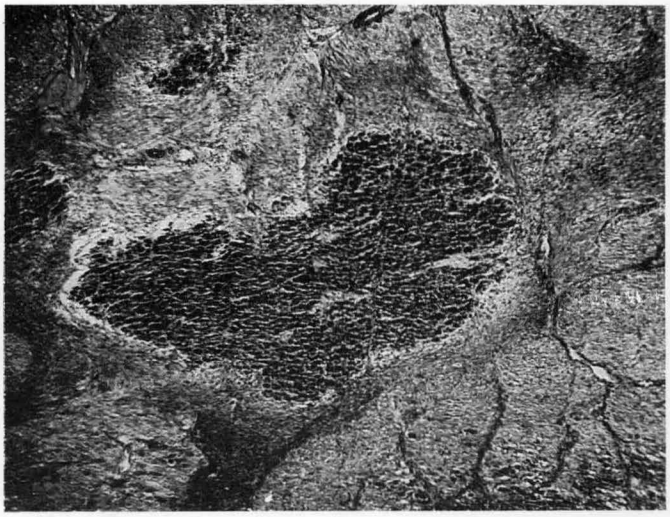

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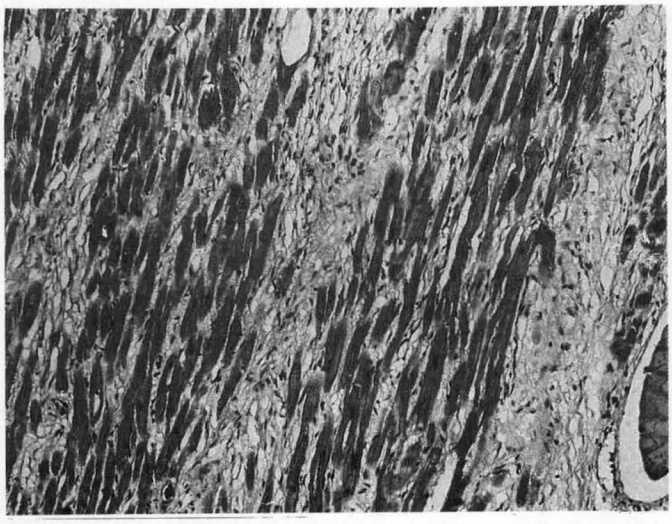

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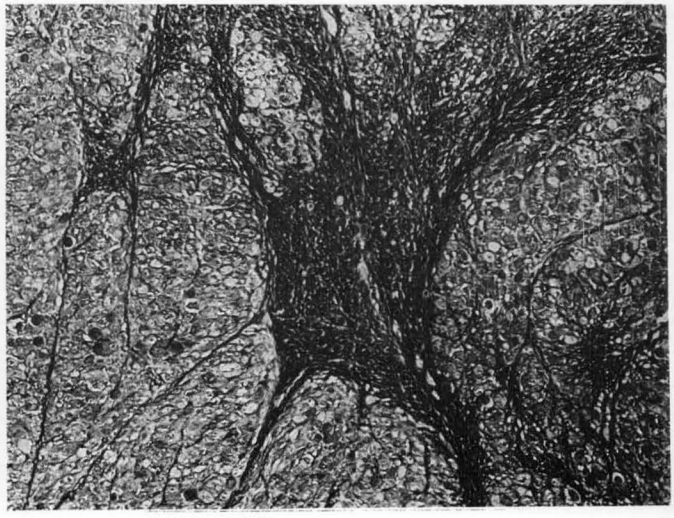

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Fig. 3. *Great number of cardiac fibres with apoptosis in an area of atrophy and fibrosis; vacuolization of some fibres. Natural poisoning by* T. multiglandulosa (Bov. 7373, SAP 23695).

Fig. 4. *Area of massive necrosis of heart fibres surrounded by fibrous connective tissue, in natural poisoning by* T. multiglandulosa *(Bov. 351/71, SAP 20472). Masson, obj. 2,5.*

Fig. 5. *Intersticial fibrosis in the myocardium with slight extracelular edema, in natural poisoning by* T. acutifolia *(Bov. 4773, SAP 23695). HE, obj. 6,3.*

Fig. 6. *Large area of fibrosis in the myocardium in natural poisoning by* T. multiglandulosa *(Bov. 351/71, SAP 20472). Masson, obj. 6,3.*

Table 3. *Incidence of histologic changes in experimental poisoning of cattle by the dried leaves of plants causing "sudden death" (Repeated small doses)*

Plant	Heart						Liver						Kidney			Number of animals studied histologically
	Intracellular edema	Increase of eosinophilia without picnosis (focal)	Increase of eosinophilia with picnosis (focal)	Areas of necrosis	Mononuclear infiltration	Proliferation of fibroblasts and/or fibrosis	Swelling of liver cells	Vacuolization of liver cells	Centrolobular necrosis	Congestion	Dissociation of hepatic cords[a]	Edema of Disse's space	Hydropic-vacuolar degeneration: Of distal convoluted tubules	Hydropic-vacuolar degeneration: In the medullary zone	Albuminous granular degeneration in the cortex	
Palicourea marcgravii	2/3 66,6%	0/3 0%	0/3 0%	0/3 0%	1/3 33,3%	0/3 0%	3/3 100%	3/3 100%	1/3 33,3%	2/3 66,6%	3/3 100%	3/3 100%	3/3 100%	1/3 33,3%	2/3 66,6%	3
Palicourea grandiflora	2/3 66,6%	0/3 0%	1/3 33,3%	0/3 0%	2/3 66,6%	0/3 0%	0/4 0%	2/4 50%	0/4 0%	3/4 75%	2/4 50%	2/4 50%	2/5 40%	1/5 20%	0/5 0%	5[a]
Mascagnia aff. *rigida*	3/4 75%	0/4 0%	2/4 50%	2/4 50%	3/4 75%	4/4 100%	1/4 25%	3/4 75%	0/4 0%	0/4 0%	0/4 0%	3/4 75%	1/4 25%	0/4 0%	1/4 25%	4

[a] The heart of 2 animals and the liver of one were not examined histologically. The percentage was calculated always over the organs which were examined.

small doses (Table 3): Such experiments were made with only 3 plants. Of interest is that in the experiments with *Mascagnia* aff. *rigida* well established areas of necrosis were observed in the heart restricted to the pilar muscle of 2 animals, and fibrosis at the same site in all 4 animals to which repeated small doses were given. In the liver *P. marcgravii* caused regressive and circulatory changes more frequently than when leaves were given in single doses. In the kidney the incidence of hydropic-vacuolar degeneration was about the same as seen in the experiments with single doses of the fresh leaves.

1.2. *Plants causing a subacute to chronic poisoning with necrosis of heart fibres and fibrosis of the myocardium*

In Brazil only 2 plants which cause this type of lesion are known. These are *Tetrapterys acutifolia* Cav. and *Tetrapterys multiglandulosa* Adr. Juss. (fam. Malpighiaceae), important poisonous plants in some areas of the Southeastern Region of Brazil. The action of these two plants is very different from those which cause "sudden death". In cattle these plants, eaten over long periods in medium doses (5 g/kg during 60 days), generally cause a subacute or chronic poisoning, with quite characteristic symptomatology: a pulsing prominent jugular vein and edema of the brisket. The main post-mortem findings are well seen cardiac lesions, in the form of sharp whitish areas and streaks across most of the cut surface of the myocardium (Fig. 2) which may be harder than normal. Nut-meg appearance of the liver and internal edemas are frequently found. Histological examination of the heart reveals severe necrosis of heart fibres (Fig. 3, 4) and fibrosis of the myocardium (Fig. 5, 6). Exercise only exceptionally causes the death of the animal when the disease is in its advanced stage. The toxic principle is not known yet. (Tokarnia et al. 1989)

Informations collected from farms and the pathological data suggest strongly that *Tetrapterys* spp. are also the cause of abortion in cattle.

2.0. Comparison of the Brazilian Poisonous Plants Affecting Heart Function with Plants of Similar Action from Africa and Australia (Table 4)

In Africa and Australia there are toxic plants which can be compared with the plants affecting heart function in Brazil. These are plants that cause an acute to peracute poisoning; symptoms and death can be precipitated by exercise. They can be divided into two groups.

The first one is that of plants which do not cause significant heart lesions. They need to be ingested only once. In Africa these plants are *Dichapetalum* spp., of the Dichapetalaceae family (Steyn 1928, 1934, Marais 1944, Vickery & Vickery 1973, Nwude et al. 1977, Kamau et al. 1978), and in Australia, *Gastrolobium* spp. (Gardner & Bennetts 1956, McEwan 1964, Eversit 1974) and *Oxylobium* spp. (Gardner & Bennetts 1956, Everist 1974), both of the Leg. Papilionaceae family. The toxic principle of these plants is monofluoroacetic acid.

A second group of plants in Africa and Australia cause severe cardiac lesions of regressive and inflammatory-proliferative nature. These have to be eaten by cattle in large amounts during long periods. In Africa, where this kind of poisoning is called "gousiekte" (quick disease), these plants are: *Pachystigma (Vangueria) pygmaeum* (Theiler et al. 1923, Pretorius & Terblanche 1967, Prozesky et al. 1988), *Pachystigma (Vangueria) thamnus* (Adelaar & Terblanche 1967), *Pavetta harborii* (Uys & Adelaar 1957, Pretorius & Terblanche 1967), *Pavetta schumaniana* (Naudé 1966) and *Fadogia monticola* (Hurter et al. 1972), all of the Rubiaceae family. In Australia only one plant which belongs to this second group has been described, *Acacia georginae* (Bell et al. 1955, Barnes 1958, Whittem & Murray 1963, Oelrichs & McEwan 1962), of the Fabaceae family. The poisonous principle of *Acacia georginae* is also monofluoroacetic acid (Oelrichs & McEwan 1962); the poisonous principle of the "gousiekte" producing plants has not been described yet.

Considering the heart lesions, which are certainly the most important aspect, the Brazilian plants causing "sudden death" can be compared with the plants of the 1st African-Australian group (*Dichapetalum* spp., *Gastrolobium* spp and *Oxylobium* spp.), whilst *Tetrapterys* spp can be compared with the plants of the 2nd group, that is *Acacia georginae* and the plants which cause "gousiekte"

But regarding the course of the disease and the influence of exercise, *Tetrapterys* spp. is different to the plants of the 2nd group, because the poisoning by them has a subacute or chronic course, and there is no

Table 4. *Comparison of the Brazilian poisonous plants affecting heart function with plants of similar action from Africa and Australia*

Plants	Heart lesions			Doses	Course	Influence of exercise	Poisonous principle
	Regr. changes	Round cell infiltr.	Fibrosis				
Plants of Brazil							
1. Without significant heart lesions (Plants causing "sudden death")	(+)[a]	–	–	Single	Peracute	+++	*In P. marcgravii* monofluoroacetic acid (MFAA), in the others not known
Palicourea marcgravii							
Palicourea aeneofusca							
Palicourea juruana							
Palicourea grandiflora							
Arrabidaea bilabiata							
Arrabidaea japurensis							
Pseudocalymma elegans							
Mascagnia rigida							
Mascagnia elegans							
Mascagnia pubiflora							
Mascagnia aff. *rigida*							
2. With severe heart lesions	+++	(+)	+ to +++	Repeated	Subacute to chronic	(+)	Not known
Tetrapterys acutifolia	The lesions are focal, but affect large areas of the miocardium						
Tetrapterys multiglandulosa							
Plants of Africa and Australia[b]							
1. Without significant heart lesions	(+)	(+)	(+)	Single	Peracute to acute	+++	In all plants of this group MFAA
Dichapetalum spp.	Lesions are multifocal in nature						
Gastrolobium spp.							
Oxylobium spp.							
2. With severe heart lesions	++	++	++	Repeated	peracute	+++	In *Acacia georginae* MFAA, in the others not known
Pachystigma (Vangueria) pygmaeum	Lesions tend to be more diffuse						
Pachystigma (Vangueria) thamnus							
Pavetta harborii							
Pavetta schumaniana							
Fagodia monticola							
Acacia georginae	Lesions tend to be multifocal in nature						

[a] (+) discrete, + slight, ++ moderate, +++ severe or intense;
[b] The data on the histological lesions of the African and Australian plants were taken from the papers by Theiler et al. (1923), Hurter et al. (1972), Whittem & Murray (1963), Newsholme & Coetzer (1984) and Schultz et al. (1982).

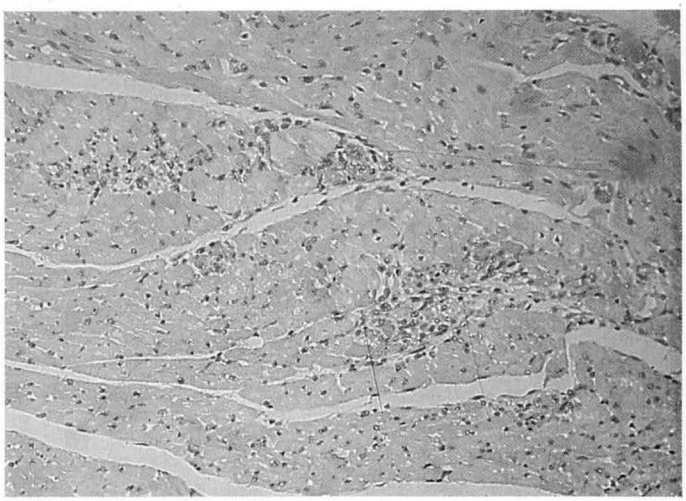

Fig. 7. *Proliferation of fibroblasts and necrosis of heart fibres in experimental poisoning (with repeated small doses) by* P. marcgravii *(Ovine 4483, SAP 23228). HE, obj. 10.*

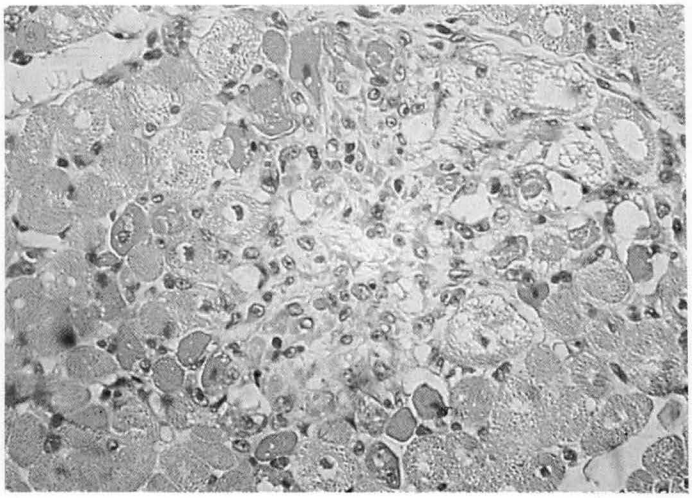

Fig. 8. *Same lesion as shown in Fig. 7. HE, obj. 25.*

Table 5. *Comparison of the clinical-pathological pictures of poisoning by* Palicourea marcgravii *and monofluoroacetic acid*

Poisoning	Animal species	Heart lesions (always focal)			Course	Influence of exercise
		Regr. changes	Round cell infiltr.	Fibroplasia/fibrosis		
Palicourea marcgravii						
(a) Single doses:	cattle (1)[a]	(+)[b]	–	–	Peracute (1-10 min.), in few cases 19-85 min.	Most aimals died without exercise, but exercise caused/precipitated death
	sheep (2)	(+)	–	–	Peracute (3-8 min.)	Most animals, dying or not, showed symptoms only with exercise
	rabbits (3)	(+)	–	–	Peracute (1-5 min.), in few cases up to 3h 45min.	The animals never were exercised
(b) Repeated sublethal doses:	cattle (1)	(+)	–	–	Peracute (1 min.) to acute (12h, 55h)	In not fatal cases symptoms only were seen when animals were exercised; in fatal cases the animals died without exercise
	sheep (2)	+	+	+	Peracute (5-7 min., 49 min.), once acute (9h)	The animals died only when exercised; in not fatal cases symptoms only were seen when animals were exercised
(c) Repeated sublethal and finally lethal doses:	sheep (2)	+	+	+	Peracute (up to 59 min.) and acute (7 h)	Death occurred with or without exercise
Monofluoroacetic acid or fluoroacetate						
(a) Single doses:	cattle (4)	?	?	?	Peracute (3-20 min.)	The animals never were exercised
	sheep (5)	–	–	–	Peracute (15 min. to 1h 45min.)	The animals never were exercised
	sheep (6)	+	–	–	Acute (hours)	The animals never were exercised
(b) Repeated doses:	sheep (6)	+(+)	+	+	Subacute and chronic	Symptoms only were seen when the animals were driven; finally they were killed

[a] (1) Tokarnia & Döbereiner 1986, (2) Tokarnia et al. 1986, (3) Peixoto et al. 1987, (4) Robison 1970, (5) Jensen et al. 1948, (6) Schultz et al. 1982;
[b] (+) discrete, + slight, +(+) slight to moderate, ++ moderate, +++ severe lesions.

necessity for exercise to cause death, although occasionally exercise will precipitate death.

It is interesting to report that of the Brazilian plants causing "sudden death", when experimentally given in daily repeated small doses, i.e. *Mascagnia* aff. *rigida* to cattle (Tokarnia et al. 1985) and *Palicourea marcgravii* to sheep (Tokarnia et al. (1986) (Fig. 7,8), cause more pronounced histological lesions in the myocardium including inflammatory and proliferative alterations than when eaten only once and when only slight regressive heart lesions are observed. Even in theses cases the histological alterations in the heart can not be compared to those seen in the poisoning by *Tetrapterys* spp.

It is also necessary to report here that in the spontaneous poisoning of cattle by *Mascagnia rigida* (Tokarnia et al. 1961) slightly more pronounced inflammatory changes in the heart were found than usually seen in spontaneous and experimental poisoning by the plants causing "sudden death". However it was not possible to reproduce these changes by single or repeated administrations of the plant to bovines. Hurter et al. (1972) suggest that a detailed comparison between "gousiekte" of Africa and the poisoning by *Mascagnia rigida* in Brazil should be very interesting. But the data available on the poisoning by *M. rigida* indicate that this plant probably belongs to the Brazilian plants which cause "sudden death" comparable to that of the African and Australian plants of the 1st group (*Dichapetalum* spp., *Gastrolobium* spp. and *Oxylobium* spp.).

3.0. Comparison of the Clinical-Pathological Pictures of Poisoning by *Palicourea marcgravii* and Monofluoroacetic Acid (Table 5)

The clinical picture and the course of the experimental poisoning with single doses of *P. marcgravii* observed in bovines (Tokarnia & Döbereiner 1986), ovines (Tokarnia et al. 1986) and rabbits (Peixoto et al. 1987) are very similar to those described in the experimental poisoning by single doses of sodium monofluoroacetate in bovines, performed by Robison (1970). Unfortunately this author did not perform post-mortem and histological examinations.

In the same way, the clinical picture of poisoning by *P. marcgravii* is very similar to that described by Jensen et al. (1948) in the experimental poisoning with single doses of sodium fluoroacetate in sheep. In the experiments by Jensen et al. (1948), the course was slightly longer (it varied from 15 min. to 1h 45min.) than in the experiments in which single doses of *P. marcgravii* (references as above) were given to bovines (a course of generally 1 to 10 min., rising in a few cases to between 19 and 85 min., mostly without exercise), ovines (a course of 3 to 8 min., mostly only after exercise), and rabbits (course of generally 1 to 5 min.,

exceptionally up to 3h 45min., with no exercise). Jensen et al. (1948) also found no important lesions at post-mortem examination and no constant histological alterations.

Schultz et al. (1982) performed experiments with fluoroacetate in sheep. They concluded to have produced acute, subacute and chronic poisoning; the acute poisoning by the administration of single and the latter by giving repeated small doses. The authors conclude that the fluoroacetate did not act as cumulative poison.

The clinical picture in the experiments of single and repeated administrations of fluoroacetate by Schultz et al. (1982) is similar to that observed in the experiments with *P. marcgravii* (references as above) in bovines (single and repeated administrations), ovines (single and repeated administrations) and rabbits (single administrations). But there are small differences in the course and outcome of the poisoning. In the experiments with single administrations of fluoroacetate (Schultz et al. 1982), death occurred after hours, whilst only minutes were usually required with single doses of *P. marcgravii* in bovines, ovines and rabbits. In these experiments the bovines died without exercise, but exercise precipitated death; most of the ovines, showed symptoms or died only after exercise; the rabbits were not excercised. In the experiments with single doses of monofluoroacetate (Schultz et al. 1982) the animals were not exercised. In the experiments with repeated small doses (Schultz et al. 1982), the animals showed symptoms only when driven; finally they were killed. In the experiments with repeated small doses of *P. marcgravii* (references as above) in bovines, the animals that did not die only showed symptoms when exercised. In the 3 fatal cases, symptoms and death occurred without exercise after 1 minute, 12 hours and 55 hours. Sheep which received repeated small doses, only showed symptoms after being exercised briefly for a few minutes; in the 6 fatal cases, death of 4 animals occurred after 5 to 7 minutes, and the other two after 49 min. and 9 hours. Of the 5 sheep which had received repeated small doses and survived, 3 died later without and 2 with exercise, after a lethal dose. Signs of poisoning lasted for 38 min., 59 min. and 7 hours in the 3 sheep in which symptoms could be observed.

Post-mortem findings in the experiments with fluoroacetate in sheep performed by Schultz et al. (1982) were rare and similar to those described in *P. marcgravii* poisoning in cattle, sheep and rabbits. They described histological alterations mainly in the heart. In the acute cases, lesions varied from slight regressive alterations with cloudy swelling, hydropic degeneration and steatosis, to more severe lesions with Zenker degeneration and necrosis; in the cases classified as subacute and chronic, necrotic areas infiltrated by lymphocytes, macrophages and small number of neutrophiles, and sometimes fibroplasia with proliferation of cells from the sarcolemma, were observed.

Regressive lesions in the heart similar to these were also found, but in a much milder form, in the experiments with single administrations of *P. marcgravii* in bovines, ovines and rabbits (references as above). On the other hand, additionally to more severe regressive alterations, focal proliferative lesions were found in the experiments with repeated administrations of small doses of *P. marcgravii* in sheep (Figs. 7, 8); however these alterations were not found in the few experiments with repeated small doses of *P. marcgravii* in cattle (Tokarnia & Döbereiner 1986).

Cumulative effect: Unlike Schultz et al. (1982), Annison et al. (1960) had previously concluded that sodium fluoroacetate showed a cumulative effect in their experiments with ovines. Rowley (1963) came to similar conclusion after showing that repeated sublethal doses of sodium fluoroacetate can accumulate and cause the death of rabbits. McEwan (1978) affirmed that monofluoroacetate has a cumulative effect when administered in repeated small doses over a short period.

Vickery & Vickery (1973), on the other hand, concluded that little has been done to determine if sublethal doses of monofluoroacetic acid have either a cumulative effect or confer tolerance to a higher dose which would otherwise be lethal.

In their experiments with *Palicourea marcgravii* in cattle, Tokarnia & Döbereiner (1986) concluded that the plant had a cumulative effect when administered daily, and that this effect was strong with doses of 1/5 of the lethal dose, and still could be shown with doses of 1/10 of the lethal dose. However, doses of 1/5 of the lethal dose, when given weekly, or smaller doses (1/20 of the lethal dose) given daily, did not cause symptoms. Costa et al. (1984) also observed a cumulative effect with *P. marcgravii*. Two bovines which received daily doses of 0.1 g/kg of the fresh plant, died on the 12th and 22nd day of the experiment.

In their experiments in sheep, Tokarnia et al. (1986) concluded that *P. marcgravii* had a cumulative effect, which in one of the experimental series was weak, but in the second one was similar to that observed in cattle They also concluded that the plant did not induce tolerance, nor did the animals become more sensitive to the toxic properties of the plant.

REFERENCES

Adelaar T.F. & Terblanche M. 1967. A note on the toxicity of the plant *Pachystigma thamnus*, Robyns. J.S. Afr. Vet. Med. Assoc. 38(1):25-26.

Allcroft R. & Jones J.S.L. 1969. Fluoroacetamide poisoning. Vet. Rec. 84:399-402.

Annison E.F., Hill K.J., Lindsay D.B. & Peters R.A. 1960. Fluoroacetate poisoning in sheep. J. Comp. Pathol. 70:145-155.

Barnes J.E. 1958. Georgina poisoning of cattle in the Northern Territory. Aust. Vet. J. 34:281-290.

Bell A.T., Newton L.G., Everist S.L. & Legg J. 1955. *Acacia georginae* poisoning of cattle and sheep. Aust. Vet. J. 31:249-257.

Costa M.V., Nascimento E.F., Pessoa J.M. & Costa W.R. 1984. Lesões em bovinos intoxicados pela *Palicourea marcgravii* St. Hil. Arq. Bras. Med. Vet. Zootec. 36(5):571-580.

Couceiro J.E.M., Silva A.C.C. & Silva J.A. 1976. Observações e ensaios

sobre a alegada intoxicação de bovinos por plantas, no Estado de Pernambuco. Anais XV Congr. Bras. Med. Vet., Rio de Janeiro, p. 45-46. (Resumo)

Döbereiner J., Peixoto P.V. & Tokarnia C.H. 1984. Intoxicação experimental por *Arrabidaea bilabiata* (Bignoniaceae) em coelhos. Pesq. Vet. Bras. 4(3):89-96.

Döbereiner J. & Tokarnia C.H. 1959. Intoxicação de bovinos pela "erva de rato" (*Palicourea marcgravii* St. Hil.) no vale do Itapicuru, Maranhão. Arqs Inst. Biol. Animal, Rio de J., 2:83-91.

Döbereiner J. & Tokarnia C.H. 1983. Intoxicação experimental por *Arrabidaea japurensis* (Bignoniaceae) em coelhos. Pesq. Vet. Bras. 3(3):95-97.

Döbereiner J., Tokarnia C.H. & Silva M.F. 1983. Intoxicação por *Arrabidaea bilabiata* (Bignoniaceae) em bovinos na região amazônica do Brasil. Pesq. Vet. Bras. 3(1):17-24.

Everist S.L. 1974. Poisonous Plants of Australia. Angus and Robertson Publ., Sidney.

Fernandes N.S. & Macruz R. 1964. Toxicidade da "corona", *Mascagnia pubiflora* (Juss.) Griseb. (Malpighiaceae). Arqs Inst. Biológico, S. Paulo, 31:1-4.

Gardner C.A. & Bennetts H.W. 1956. The Toxic Plants of Western Australia. Western Australian Newspapers, Perth.

Hall R.J. 1972. The distribution of organic fluorine in some toxic tropical plants. New Phytol. 71:855-871.

Hurter L.R., Naudé T.W., Adelaar T.F., Smit J.D. & Codd L.E. 1972. Ingestion of the plant *Fadogia monticola* Robyns as an addicional cause of gousiekte in ruminants. Onderstepoort J. Vet. Res. 39(1):71-82.

Jensen R.J., Tobiska J.W. & Ward J.C. 1948. Sodium fluoroacetate (compound 1080) poisoning in sheep. J. Vet. Res. 9:370-372.

Kamau J.A., Gachuhi D.M., Gyrd-Hansen N. & Gathuma J.M. 1978. A study of the toxicity of *Dichapetalum ruhlandii* (Ludi). Indian Vet. J. 55:626-630.

Marais J.S.C. 1944. Monofluoroacetic acid, the toxic principle of "gifblaar" *Dichapetalum cymosum* (Hook) Engl. Onderstepoort J. Vet. Sci. Anim. Ind. 20(1):67-73.

McEwan T. 1964. Isolation and identification of the toxic principle of *Gastrolobium grandiflorum*. Queensl. J. Agric. Sci. 21(2):1-14.

McEwan T. 1978. Organo-flluorine compounds in plants, p. 147-158. In: Keeler R.F., Van Kampen K.R. & James L.F. (ed.) Effects of Poisonous Plants on Livestock. Academic Press, New York.

Mello E.M.M. & Fernandes J.S. 1941. Contribuição ao estudo de plantas tóxicas brasileiras. Serv. Inf. Agrícola, Min. Agricultura, Rio de Janeiro. 106 p.

Naudé T.W. 1966. Unpublished data. (Cit. Pretorius & Terblanche 1967)

Newsholme S.J. & Coetzer J.A.W. 1984. Myocardial pathology of domestic ruminants in Southern Africa. J. South African Vet. Assoc. 55:89-96.

Nwude N., Parsons L.E. & Adaudi A.O. 1977. Acute toxicity of the leaves and extracts of *Dichapetalum barteri* (Engl.) in mice, rabbits and goats. Toxicology 7:23-29.

Oelrichs P.B. & McEwan T. 1962. The toxic principle of *Acacia Georgiane*. Queensl. J. Agric. Sci. 19:1-16.

Oliveira M.M. 1963. Chromatographic isolation of monofluoroacetic acid from *Palicourea marcgravii* St. Hil. Experientia 19:586.

Pacheco G. & Carneiro V. 1932. Estudos experimentais sobre plantas tóxicas. 1. Intoxicação dos animais pela "herva de rato da mata" *Palicourea marcgravii* St. Hil. (*Psychotria marcgravii* Spreng.). Revta Soc. Paulista Med. Vet. 2(2-3):23-46.

Peixoto P.V., Tokarnia C.H., Döbereiner J. & Peixoto C.S. 1987. Intoxicação por *Palicourea marcgravii* (Rubiaceae) em coelho. Pesq. Vet. Bras. 7(4):117-129.

Pretorius P.J. & Terblanche M. 1967. A preliminary study on the symptomatology and cardiodynamics of gousiekte in sheep and goats. J. S. Afr. Vet. Med. Assoc. 38(1):29-53.

Prozesky L., Fourie N., Neser J.A. & Nel P.W. 1988. A field outbreak in Ile-de-France sheep of a cardiotoxicosis caused by the plant *Pachystigma pygmaeum* (Schltr.) Robyns (Rubiaceae). Onderstepoort J. Vet. Res. 55:193-196.

Robison W.H. 1970. Acute toxicity of sodium monofluoroacetate to cattle. J. Wildl. Manage. 34(3):647-648.

Rowley I. 1963. The effect on rabbits of repeated sublethal doses of sodium fluoroacetate. CSIRO Wildl. Res. 8(1):52-55.

Santos H.L. 1975. Aspectos clínicos, laboratoriais e anatomo-histopatológicos, na intoxicação experimental de bovinos pela *Mascagnia rigida* (Juss.) Gr. Tese, Belo Horizonte. 36p. (Resumo em Arqs Esc. Vet. UFMG, Belo Horizonte, 27(3):398-399, 1975)

Schultz R.A., Coetzer J.A.W., Kellerman T.S. & Naudé T.W. 1982. Observations on the clinical, cardiac and histopathological effects of fluoroacetate in sheep. Onderstepoort J. Vet. Res. 49:237-245.

Steyn D.G. 1928. Gifblaar poisoning. A summary of our present konwledge in respect of poisoning by *Dichapetalum cymosum*. 13th and 14th Rep. Dir. Vet. Education and Research, Pretoria, S. Afr.:187-194.

Steyn D.G. 1934. The Toxicology of Plants in South Africa. Central News Agency, South Africa.

Theiler A., Du Toit P.J. & Mitchell D.T. 1923. Gousiekte in sheep. 9th and 10th Rep. Dir. Vet. Education and Research, Pretoria, S. Afr.:9-105, 4 p. figs.

Tokarnia C.H., Canella C.F.C. & Döbereiner J. 1961. Intoxicação por um "tingui" (*Mascagnia rigida* Griseb.) em bovinos no nordeste do Brasil. Arqs Inst. Biol. Animal, Rio de J., 4:203-215.

Tokarnia C.H. & Döbereiner J. 1973. Intoxicação por *Mascagnia pubiflora* em bovinos no Estado de Mato Grosso. Pesq. Agropec. Bras., Sér. Vet., 8:61-68.

Tokarnia C.H. & Döbereiner J. 1981. Intoxicação por *Arrabidaea japurensis* (Bignoniaceae) em bovinos em Roraima. Pesq. Vet. Bras. 1(1):7-17.

Tokarnia C.H. & Döbereiner J. 1982. Intoxicação experimental por *Palicourea juruana* (Rubiaceae) em bovinos e coelhos. Pesq. Vet. Bras. 2(1):17-26.

Tokarnia C.H. & Döbereiner J. 1986. Intoxicação por *Palicourea marcgravii* (Rubiaceae) em bovinos no Brasil. Pesq. Vet. Bras. 6(3):73-92.

Tokarnia C.H., Döbereiner J. & Canella C.F.C. 1987. Intoxicação experimental por *Mascagnia rigida* (Malpighiaceae) em coelhos. Pesq. Vet. Bras. 7(1):11-16.

Tokarnia C.H., Döbereiner J., Canella C.F.C. & Guimarães D.J. 1969. Intoxicação experimental por *Pseudocalymma elegans* (Vell.) Kuhlm. em bovinos. Pesq. Agropec. Bras. 4:195-204.

Tokarnia C.H., Döbereiner J., Couceiro J.E.M. & Silva A.C.C. 1982. Plantas tóxicas para bovinos na zona do agreste de Pernambuco. 1º Congr. Permambucano Med. Vet., Recife, 8-11 set.

Tokarnia C.H., Döbereiner J., Couceiro J.E.M. & Silva A.C.C. 1983. Intoxicação por *Palicourea aeneofusca* (Rubiaceae), a causa de "mortes súbitas" em bovinos na zona da mata de Pernambuco. Pesq. Vet. Bras. 3(3):75-79.

Tokarnia C.H., Döbereiner J. & Peixoto P.V. 1985. Intoxicação por *Mascagnia* aff. *rigida* (Malpighiaceae) em bovinos no norte do Espírito Santo. Pesq. Vet. Bras. 5(3):77-91.

Tokarnia C.H., Döbereiner J. & Silva M.F. 1981. Intoxicação por *Palicourea grandiflora* (Rubiaceae) em bovinos no Território de Rondônia. Pesq. Vet. Bras. 1(3):85-94.

Tokarnia C.H. & Figueiredo L. 1979. Relatório de viagem de estudo ao Estado da Bahia no período de 10 jan. a 2 fev. 1979. 5 p. e 2 quadros.

Tokarnia C.H., Peixoto P.V. & Döbereiner J. 1986. Intoxicação experimental por *Palicourea marcgravii* (Rubiaceae) em ovinos. Pesq. Vet. Bras. 6(4):121-131.

Tokarnia C.H., Peixoto P.V., Döbereiner J., Consorte L.B. & Gava A. 1989. *Tetrapterys* spp. (Malpighiaceae), a causa de mortandades em bovinos caracterizadas por alterações cardíacas. Pesq. Vet. Bras. 9(1/2):23-44.

Uys P.L. & Adelaar T.F. 1957. A new poisonous plant. J. S. Afr. Vet. Med. Assoc. 28(1):5-8.

Vickery B. & Vickery M.L. 1973. Toxicity for livestock of organofluorine compounds present in *Dichapetalum* plant species. Vet. Bull. 43(10):537-542.

Whittem J.H. & Murray L.R. 1963. The chemistry and pathology of Georgina river poisoning. Aust. Vet. J. 39:168-173.