



Spontaneous and experimental poisoning by *Myrocarpus frondosus* in cattle¹

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ABSTRACT. Tineli T.R., Ogliari D., Raldi D., Menegatt J.C.O., Melchiorreto E. & Gava A. 2024. **Spontaneous and experimental poisoning by *Myrocarpus frondosus* in cattle.** *Pesquisa Veterinária Brasileira* 44:e07237, 2024. Laboratório de Patologia Animal, Centro de Ciências Agroveterinárias, Universidade do Estado de Santa Catarina, Av. Luís de Camões 2090, Conta Dinheiro, Lages, SC 88520-000, Brazil. E-mail: aldo.gava@udesc.br

An outbreak of photosensitization in Holstein and Jersey cattle occurred after the passage of an extratropical cyclone in Southern Brazil. On that occasion, several trees fell, including some of the species *Myrocarpus frondosus* (Fabaceae family) popularly known as “gabreúva”, “cabriúna” or “gabriúna”. Five heifers consumed the leaves of this plant, and all of them became ill. The main clinical signs were decreased appetite, permanence in the water, decreased ruminal movements, dry stools, congested and icteric sclera and conjunctivae, dark urine and restlessness when exposed to the sun. One heifer showed circling, incoordination, restlessness and death six days after the onset of clinical signs. From the seventh day, three heifers showed improvement; one remained apathetic, with jaundiced mucous membranes, ulceration, and scaling on the tongue, increased respiratory rate, and fever, and died 18 days after ingestion of the plant. At necropsy, photosensitivity lesions were observed on the depigmented skin, snout, teats, and ear tip, characterized by discontinuity of the skin with the formation of crusts, inflammatory exudate associated with redness of the skin, in addition to ulceration in the mouth, snout and ventral portion of the tongue and jaundice and edema in the submandibular region. The liver was enlarged, with an orange color, full gallbladder, and wall edema. Through microscopy, liver lesions were characterized by moderate and diffuse necrosis of hepatocytes, vacuolar and centrilobular degeneration, bilirubin retention and proliferation of biliary epithelium. The literature shows no reports of *M. frondosus* toxicity in cattle. Experiments were carried out in cattle to clarify the possible clinical-pathological picture produced by this plant. A survey of the epidemiological data of the diagnosed spontaneous outbreak was carried out, and subsequently, three cattle received the plant’s green leaves, and a fourth received the dried leaves. After administering the plant, blood samples were collected daily for blood count, measurement of liver enzymes (gamma glutamyl transferase, alkaline phosphatase, alanine aminotransferase, aspartate transferase), bilirubin, measurement of vital parameters and liver biopsy from the onset of signs. In case of death, a necropsy was performed with collection of viscera samples for macro and microscopic evaluation. The experimental part was developed at the Laboratory of Animal Pathology, CAV-UDESC. The single dose of 33g/kg of green leaves caused severe clinical signs, while the administration of 22g/kg and 11g/kg caused mild to moderate signs of the disease. The supply of desiccated leaves in a single dose did not cause clinical manifestations. *M. frondosus* can be blamed as a cause of spontaneous hepatogenous photosensitization in cattle. Experimentally, the ingestion of green leaves of this plant, in doses greater than 11g/kg can lead to clinical changes, with subsequent recovery, or progress to death with severe liver damage.

INDEX TERMS: Hepatotoxic plant, liver necrosis, photosensitization, toxic plants, poisoning, *Myrocarpus frondosus*, cattle.

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RESUMO.- [Intoxicação espontânea e experimental por *Myrocarpus frondosus* em bovinos.]

Um surto de fotossensibilização em bovinos da raça Holandesa e Jersey foi observado após a passagem de um ciclone extratropical no Sul do Brasil, quando houve queda de diversas árvores, dentre elas *Myrocarpus frondosus* (família Fabaceae), popularmente conhecida como “gabreúva, cabriúna ou gabriúna”. Cinco novilhas consumiram folhas dessa planta, e todas adoeceram. Os principais sinais clínicos foram diminuição do apetite, permanência dentro da água, diminuição dos movimentos ruminais, fezes ressecadas, esclera e conjuntivas congestionadas e ictericas, urina escura e inquietação quando expostas ao sol. Uma novilha apresentou andar em círculos, incoordenação e inquietação e morte seis dias após início dos sinais clínicos. A partir do sétimo dia, três novilhas apresentaram melhora e uma permaneceu apática, com as mucosas ictericas, ulceração e descamação na língua, aumento da frequência respiratória, febre e morreu 18 dias após ingestão da planta. Na necropsia foram observadas lesões de fotossensibilização na pele despigmentada, focinho, tetos, ponta da orelha, caracterizadas por descontinuidade da pele com formação de crostas, exsudato inflamatório associado a vermelhidão da pele além de ulceração na boca, focinho e porção ventral da língua e icterícia acentuada e edema, na região submandibular. O fígado estava aumentado de volume, de cor laranja, vesícula biliar repleta e com edema de parede. Através da microscopia foram observadas, lesões hepáticas, caracterizadas por necrose de hepatócitos, moderada e difusa, degeneração vacuolar, centrolobular, retenção de bilirrubina e proliferação de epitélio biliar. Na literatura, não há relatos da toxicidade de *M. frondosus* para bovinos. Com o objetivo de esclarecer o possível quadro clínico-patológico produzido por essa planta foram conduzidos experimentos em bovinos. Foi realizado um levantamento dos dados epidemiológicos do surto espontâneo diagnosticado e, posteriormente, três bovinos receberam as folhas verdes da planta e um quarto recebeu as folhas dessecadas. Após a administração da planta, foram coletadas amostras de sangue diariamente para hemograma, dosagem de enzimas hepáticas (gama glutamil transferase, fosfatase alcalina, alanina aminotransferase, aspartato transferase), bilirrubina, aferição dos parâmetros vitais e biópsia hepática a partir do surgimento dos sinais clínicos. Em caso de morte, foi realizada necropsia com coleta de amostras de vísceras para avaliação macro e microscópica. A parte experimental foi desenvolvida nas dependências do Laboratório de Patologia Animal, CAV-UDESC. A dose única de 33g/kg de folhas verdes causou graves sinais clínicos, enquanto a administração de 22g/kg e 11g/kg causou sinais leves a moderados da doença. O fornecimento de folhas dessecadas em dose única não causou manifestações clínicas. *M. frondosus* pode ser responsabilizada como causa de fotossensibilização hepatogênica espontânea em bovinos. A ingestão de folhas verdes dessa planta em doses superiores a 11g/kg pode levar a alterações clínicas, com posterior recuperação, ou evoluir para morte com lesões hepáticas graves.

TERMOS DE INDEXAÇÃO: Plantas hepatotóxicas, necrose hepática, fotossensibilização, plantas tóxicas, intoxicação, *Myrocarpus frondosus*, bovinos.

INTRODUCTION

The term photosensitization refers to an increase in the sensitivity of the superficial layers of the skin to light due to photodynamic agents, whose chemical configuration can absorb certain wavelengths of ultraviolet light that can cause cell damage when depigmented skin is exposed to intense light (Tokarnia et al. 1999). The causes of photosensitization can be of primary origin: Type I – caused by plant pigments; Type II – associated with genetic disorders, which result in the accumulation of hematoporphyrins; Type III – hepatogenic photosensitization due to the accumulation of phytoporphyrin (phyloerythrin), resulting from liver dysfunction (Rech et al. 2021).

Hepatogenic photosensitization in cattle is frequently caused by plants that produce liver lesions, such as *Lantana* spp., *Brachiaria* spp., *Myoporum* spp., *Stryphnodendron* spp., *Enterolobium* spp. and the fungus *Pithomyces chartarum* (Tokarnia et al. 2012).

In the Southern Brazilian state of Santa Catarina, the most significant photosensitizing plants are *Lantana* spp. and *Brachiaria* spp. Outbreaks of photosensitization have also been observed in cattle grazing on *Avena sativa* pastures, but the etiology was not defined. Subsequently, an outbreak of photosensitization and death in cattle occurred in July-August 2020, in which suspicion fell on the ingestion of leaves of a plant popularly known locally as “gabreúva, cabriúna, orgabriúna” (*Myrocarpus frondosus*). This tree of the Fabaceae family, deciduous and up to 35 meters tall, occurs mainly in the Southern and Southeastern states of Brazil, as well as in Argentina and Paraguay (Carvalho 2003). There are no reports in the literature on the toxicity of this plant to cattle.

The objective of the present study was to describe the clinical-pathological and epidemiological aspects of a photosensitization outbreak in cattle and to experimentally reproduce the disease in this species through the administration of *M. frondosus* leaves.

MATERIALS AND METHODS

Animal Ethics. The execution of the experiment followed a procedure analyzed and approved by the Ethics Committee on the Use of Animals of the “Universidade do Estado de Santa Catarina” (CEUA-UDESC) under protocol No. 4187091220.

Spontaneous illness. Information on an outbreak of photosensitization in cattle, which occurred in the municipality of Videira (27°00'30" S, 51°09'06" W) in Midwestern Santa Catarina, was obtained through a visit to the property, with collection of epidemiological and clinical data, liver biopsy in five sick cattle, and later necropsy of two cattle. Samples from the liver, kidneys, lungs, heart, lymph nodes, spleen, skeletal muscle, stomachs, intestines, bone marrow, bladder, and central nervous system were collected, fixed in 10% formalin, and processed for histological evaluation with hematoxylin and eosin (HE) staining.

Experimental study. For experimental verification of *Myrocarpus frondosus* toxicity, fresh leaves of the plant were collected from the property where the spontaneous outbreak occurred. The leaves were kept at room temperature and then fed orally to three cattle in single doses of 11, 22, and 33g/kg, and one cattle, desiccated leaves in a single dose of 11g/kg. The cattle were submitted to clinical examinations before the administration of the plant and daily afterward. Respiratory and heart rates, ruminal movements, rectal

temperature, appetite, and behavior were evaluated. Daily blood samples were collected from either the jugular or the coccygeal artery or both to evaluate possible hematological alterations and ascertain liver enzymes (gamma-glutamyl transferase – GGT, alkaline phosphatase – AP, alanine aminotransferase – ALT, and aspartate transferase – AST) and total bilirubin. Liver biopsy was carried out daily for 15 days using the technique described by Braga et al. (1985). One animal was euthanized due to the advanced stage of the disease and necropsied. Viscera samples were collected, fixed in 10% formalin, routinely processed, and stained by the HE technique at the “Laboratório de Patologia Animal” of the “Centro de Ciências Agroveterinárias” (CAV) of UDESC.

RESULTS

Spontaneous illness

The outbreak was observed in Holstein and Jersey cattle in August 2020, after the passage of an extratropical cyclone, when several trees fell, including *Myrocarpus frondosus* (Fig.1-2 and 3), popularly known as “gibreúva”. The trees were still seen in the paddock on the day of the visit, with signs of consumption of the leaves confirmed by the owner, who saw some animals consuming the plant.

On this property, four Holstein heifers and one Jersey heifer consumed leaves of this plant, and all of them became ill, with clinical manifestations. The paddock consisted of native pasture, and the heifers were supplemented with corn silage. No other plants were known to be toxic in the access paddock of heifers that fell ill. On the 1st day after ingestion of the plant, the heifers showed decreased appetite (5/5). On the 2nd day, they were found in the water, had inappetence and marked apathy (5/5). On the 3rd day, the previous signs persisted, in addition to decreased ruminal and bowel movements (5/5), abdominal breathing (5/5), and dry stools (2/5). On the 4th day, the sclera and conjunctiva were congested and jaundiced (2/5), with a jaundiced and dry snout (1/5). On the 5th day, all animals presented polydipsia, and one heifer presented behavior of walking in circles, incoordination, and restlessness, progressing to death. On the 6th day, dry stools (2/4) were observed, along with concentrated urine (2/4), jaundiced mucous membranes (3/4), and restlessness when exposed to the sun (4/4). From the 7th day on, three heifers showed improvement, and one remained apathetic, with jaundiced mucous membranes, ulcerations with scaling, increased respiratory rate, and fever, progressing to death 18 days after ingesting the leaves of the plant.



Fig.1-2. *Myrocarpus frondosus*.

In the necropsy of the two heifers that died naturally, photosensitization lesions were observed on depigmented skin, snout, teats, and ear tip, characterized by skin discontinuity with crusting, associated inflammatory exudate and redness of the skin, in addition to ulcerations in the mouth, snout, and ventral portion of the tongue. Marked jaundice was observed in the subcutaneous tissue, the inner wall of the large-caliber vessels, and edema in the submandibular region. The liver was enlarged and orange in color; the gallbladder was full and showed wall edema. The most significant microscopic lesions were observed in the liver and ranged from moderate to severe intensity, characterized by necrosis and centrilobular vacuolar degeneration of hepatocytes, bilirubin retention, and proliferation of biliary epithelium (Fig.4).

Experimental disease

A 33g/kg dose of fresh *M. frondosus* leaves fed to Animal 3 caused severe clinical signs. In contrast, 11 and 22g/kg administration to Animals 1 and 2, respectively, caused signs of mild to moderate intensity. The supply of desiccated leaves in a single dose of 11g/kg to Animal 4 did not cause clinical manifestations of poisoning.

Clinical signs were observed from the second day after ingestion of the plant, with maximum intensity varying according to the dose ingested. The main clinical signs are shown in Table 1. The animals sought shade and water daily. Photosensitization skin lesions were observed in Animals 1 and 3, which took part in the experiment on sunny days. The experimentation with Animal 2 took place on cloudy days and did not present skin clinical signs or lesions.



Fig.3. Details of alternate pinnate leaves of *Myrocarpus frondosus*.

The necropsy findings of Animal 3 included diffuse jaundice of subcutaneous tissue associated with edema. Marked diffuse desquamation and exudation were observed on the snout (Fig.5) and on the ventral portion of the tongue, the focal area of desquamation. The liver was orange in color with rounded edges, and the gallbladder was enlarged (Fig.6).

Microscopy of the superficial region of the snout showed diffuse, severe necrosis and moderate hemorrhage. In the liver, there was moderate swelling and vacuolization of hepatocytes, more intense in the intermediate zone, coagulative necrosis in the central zones of the lobules, and proliferation of fibroblasts and bile ducts in the portal spaces.

Animal 1, which ingested fresh leaves in a single dose of 11g/kg, showed signs of moderate photosensitization, and the liver lesions observed in the biopsies were mild, showing clinical improvement about 20 days after ingestion of the plant. Animal 2, which received a single dose of 22g/kg, showed mild clinical signs and absence of liver lesions in the evaluation of the biopsies until 10 days after ingestion of the plant. Animal 3, which ingested 33g/kg in a single dose, presented marked clinical signs and severe liver damage in the evaluation of the biopsies. The clinical signs worsened, and the animal was euthanized.

Alterations were found in the biochemical tests of the three cattle that manifested clinical alterations and liver lesions observed through biopsy, with a significant increase in ALT, AST, GGT, and total bilirubin. AP did not increase compared to the reference values.

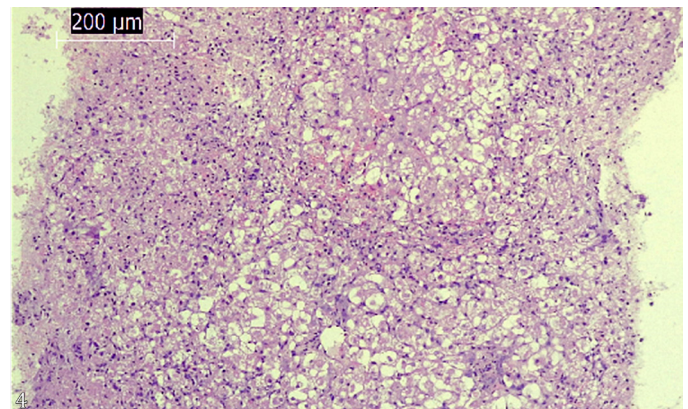


Fig.4. Cattle, female, Holstein. Spontaneous poisoning by *Myrocarpus frondosus*. Liver, centrilobular necrosis associated with vacuolar degeneration and proliferation of the biliary epithelium. HE, obj.10x.

Table 1. Clinical behavior of cattle fed with *Myrocarpus frondosus* at different doses

| Animal | Sex | Age (months) | Dose (g/kg) | Clinical signs | Outcome |
|--------|--------|--------------|-------------|--|---|
| 1 | Male | 18 | 11 | Inappetence, apathy, peeling of skin and muzzle, progressive weight loss | Recovery 20 days after ingestion of the plant |
| 2 | Female | 18 | 22 | Constipation, progressive weight loss | Recovery 10 days after ingestion of the plant |
| 3 | Female | 24 | 33 | Inappetence, apathy, constipation, jaundice, peeling of skin and muzzle, progressive weight loss, corneal opacity, and edema | Euthanasia 17 days after ingestion of the plant |
| 4 | Female | 12 | 11 | None | — |

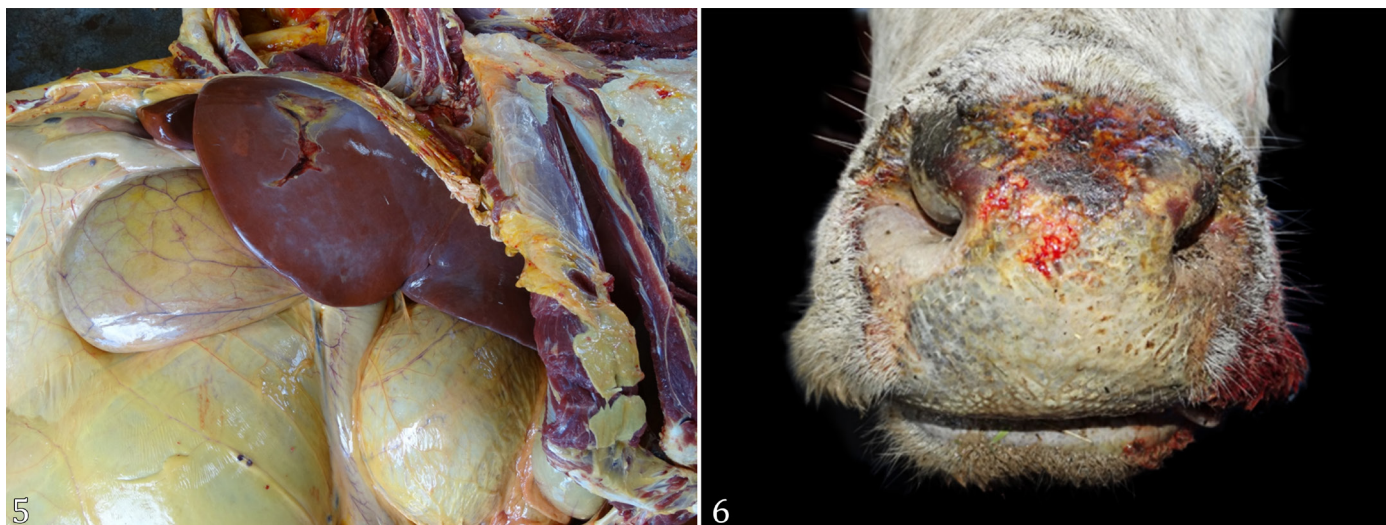


Fig.5-6. Cattle, female, Charolais. Spontaneous poisoning by *Myrocarpus frondosus*. (5) Hepatomegaly associated with hemorrhage and fibrin deposition (biopsy lesion) and gallbladder with increased volume. (6) Muzzle, Ulceration and fibrinous exudation.

DISCUSSION

The diagnosis of hepatogenic photosensitization in cattle produced by the ingestion of *Myrocarpus frondosus* was made from epidemiological data, clinical signs, macroscopic and microscopic findings, biochemical alterations, and experimental reproduction of the disease.

In major outbreaks of photosensitization reported in cattle, cases are mainly attributed to ingestion of *Lantana camara* (Tokarnia et al. 1999), *Lantana glutinosa* (Riet-Correa et al. 1984), and *Brachiaria* spp. (Döbereiner et al. 1976, Lemos et al. 1996, Driemeier et al. 1998). The reproduction of hepatogenic photosensitization with *M. frondosus* leaves includes this plant in the differential diagnosis with other photosensitizing plants.

The clinical, necropsy, and histological findings of *M. frondosus* poisoning are similar to those of other photosensitizing plants observed in Southern Brazil, where this spontaneous outbreak occurred. Attention should be paid to poisoning by *Lantana* spp., which presents marked jaundice and secondary hepatogenic photosensitization, very similar to poisoning by *M. frondosus*. In addition to epidemiology and histological analyses, multinucleated hepatocytes can be observed in *Lantana* spp. poisoning (Tokarnia et al. 2012), which was not observed in the cases of *M. frondosus* poisoning described here.

Another important differential diagnosis is poisoning by *Brachiaria* spp., which has been described in several countries, including Brazil (Lemos et al. 1996), especially in this country's Central-West region. These plants contain hepatotoxic steroidal saponins, which are associated with the deposition of crystalloid material in the biliary system, cholangitis, and foam cells (Mendonça et al. 2008). In *M. frondosus* poisoning, no foam cells were observed, and this may be a criterion to differentiate the two diseases when it is not possible to identify the presence of photosensitizing plants in the area where an outbreak is occurring. The clinical and pathological findings of *M. frondosus* poisoning described here are also very similar to those observed in hepatogenic photosensitization by *Pithomyces chartarum* (Döbereiner et al. 1976), *Enterolobium* spp. (Tokarnia et al. 1999), *Stryphnodendron* spp. (Tokarnia et al. 1999), and

chronic poisoning by *Senecio* spp, which produces chronic liver lesions, mainly fibrosis and megalocytosis (Tokarnia et al. 2012). Photosensitization in cattle is also described to occur from the ingestion of *Panicum* spp. (Bridges et al. 1987), *Tribulus terrestris* (Kellerman et al. 1989), and *Agave lechuguilla* (Miles et al. 1991), but these plants do not occur in Brazil. The differential diagnosis of poisoning by *M. frondosus* should be based mainly on epidemiological data and observation of plants with signs of consumption.

Hepatogenic photosensitization in cattle may also have other causes, such as anaplasmosis and liver neoplasms, but these diseases rarely produce photosensitization, and the lesions are specific.

Dried leaves of *M. frondosus* at a dose of 11g/kg did not produce clinical changes. This suggests that the desiccated leaves of the plant have no toxic effect on cattle.

CONCLUSION

Myrocarpus frondosus can be blamed as a cause of spontaneous hepatogenic photosensitization in cattle. Experimentally, the ingestion of green leaves of this plant in doses higher than 11g/kg can lead to clinical changes that can progress either to subsequent recovery or severe liver damage and death.

Conflict of interest statement.- The authors declare that there are no conflicts of interest.

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