TOXIC PLANTS FOR RUMINANTS IN BRAZIL AND URUGUAY: ECONOMIC IMPACT, CONTROL MEASURES AND PUBLIC HEALTH IMPLICATIONS

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Economic impact

Livestock poisoning by plants in Brazil and Uruguay has been a problem since the Spanish and Portuguese pioneers first grazed cattle on their natural pastures. Economic losses due to livestock poisoning by plants can be defined as direct and indirect losses. Direct losses are caused by death of animals, lower reproductive performance (abortions, infertility, malformations), reduced production of surviving animals and other alterations due to transitory illness, subclinical diseases with decreased production of milk, meat or wool, and increased susceptibility to other diseases due to suppressed immunological response. Indirect losses include cost of controlling poisonous plants in the pastures, management measures to prevent poisoning such as use of fences and alternative grazing, reduction in the value of the forage due to delayed or deferred grazing, reduced land value, cost of replacement of the breeding stock lost by plant poisoning, and the cost associated with diagnosis and treatments of the affected animals (Riet-Correa et al. 1993, James 1994). The economic loss by plant poisoning is difficult to estimate because reliable data are not available for many components of the cost, but losses due to deaths are easy to measure if there are data from diagnostic laboratories related with the frequency of different causes of death.

In Rio Grande do Sul, southern Brazil, it is estimate that annually 5% of the cattle are lost. With a cattle population of 13 millions, these losses represent 650,000 deaths per year. Data of the Regional Diagnostic Laboratory at Pelotas University from 1978 to 1998 showed that an average of 10.6% of the cases diagnosed in cattle were due to plant poisoning, varying annually from 5% to 25%.

Data from the Diagnostic Laboratory of Santa Maria University showed that approximately 14% of the deaths in cattle are caused by toxic plants (Claudio Barros; personal communication). Assuming that, in Rio Grande do Sul, 10% to 14% of deaths in cattle per year are due to toxic plants, one can estimate that the annual death rate due to toxic plants in this State varies from 64,000 to 90,000 animals. Considering a mean price of US$ 200 for a head of cattle, it can be assumed that US$ 12.8 to 18 millions are annually lost due to cattle deaths caused by toxic plants.

In the State of Santa Catarina, southern Brazil, with a cattle population of 2.960.343 heads, catlle mortality is also approximately 5%. Data from the University of Santa Catarina Veterinary Diagnostic Laboratory, showed that deaths caused for toxic plants represent, in the last 12 years, 13.9% of the cattle deaths, with an annual variation from 8.5% to 24,3% (Aldo Gava; personal communication). The mean annual cattle mortality due to toxic plants is estimated in 20.574 heads.

Because almost no reliable data on the losses of cattle due to toxic plants are available in other Brazilian States, the losses of cattle deaths due to toxic plants are difficult to estimate. But, assuming that the annual death losses are similar to those in Rio Grande do Sul and Santa Catarina, cattle deaths in Brazil, with a cattle population of 160 millions, will represent 800,000 to 1,120,000 heads.

Data from the Regional Diagnostic Laboratory in Pelotas University show that in Rio Grande do Sul, deaths of sheep due to toxic plants represent 7.2% of the deaths of this animal species. Considering a sheep mortality of 15% to 20% and a population of 5 million sheep, toxic plant losses due to mortality in this species can be estimated in 54,000 to 72,000.

In Uruguay data from the Regional Diagnostic Laboratories at Treinta y Tres and Paysandú (Fernando Dutra and Rodolfo Rivero; personal communications) showed that plant poisoning in cattle represents approximately 14% of the field diagnostic cases. With a cattle population of 14 millions and a mortality of 5%, deaths caused by toxic plants can be estimated in 98,000 heads annually.

In Brazil there are numerous toxic plants, the number of which is still increasing. Actually about 88 species belonging to 50 genera have been reported as toxic for ruminants or horses. In Uruguay toxic plants include 31 species and 26 genera. Despite this large number of toxic plants, those identified as really important are relatively few. In Rio Grande do Sul, southern Brazil, *Senecio* spp. are responsible for 50.7% of the cattle deaths caused by toxic plants from 1978 to 1998 (Data from the Regional Diagnostic Laboratory, Pelotas University). In sheep, in this State, poisoning by *Nierembergia veitchii* represents 77.8% of the plant intoxications (Data from the Regional Diagnostic Laboratory, Pelotas University). *Ateleia glazioviana*, a tree that causes abortion in ruminants and horses and cardiac fibrosis in cattle, is a very important poisonous plant in Santa Catarina and northern Rio Grande do Sul. *Pteridium aquilinum* is one of the more troublesome Brazilian plants causing an acute pancytopenic hemorrhagic syndrome, chronic hematuria, and squamous cell carcinomas of the upper digestive tract. It causes severe losses in cattle in the South and the Southeast of Brazil and also causes intoxication in the other Brazilian regions. In the state of Santa Catarina, tumours of the upper digestive tract are the most important cause of death in adult cattle (Aldo Gava; personal communication). *Palicourea marcgravii*, which contains fluoracetate, is probably the most important Brazilian toxic plant for cattle. It causes severe losses in the whole Country, except in the three states of the Southern Region. Other three plants that cause “sudden death” are important: *Arrabidaea bilabiata* and *Arrabidaea japurensis* in the Northern Region, the Amazon (Tokarnia et al. 1979), and *Mascagnia rigida* in the Northeast of Brazil. Tokarnia et al (1990) estimated that plants causing “sudden death” are responsible for approximately 60% of the losses due to toxic plants in the Country. Severe economic losses are produced in cattle and sheep, mainly in the Southeastern and Central-western Regions, by *Brachiaria decumbens* and other *Brachiaria* species that cause photosensitization. In the states of Rio de Janeiro and Espírito Santo, Southeastern Brazil, the most important toxic plant is *Cestrum laevigatum* (Carlos H. Tokarnia; personal communication).

In Uruguay bloat caused mainly by *Trifolium repens* and *T. pratense* is the most important cause of death in adult cattle (Rodolfo Rivero; personal communication). *Baccharis coridifolia* is also a very important cause of death in animals transferred from areas free of the plant to areas were it exists. Recently, weeds such as *Nierembergia hippomanica* and *Anagallis arvensis* caused many outbreaks of intoxication in sheep and cattle in cultivated pastures (Rodolfo Rivero; personal communication). In areas of non cultivated pastures the intoxication by *Senecio* spp. is the most important cause of intoxication in cattle (Fernando Dutra; personal communication).

Control measures

Research with toxic plants in Brazil and Uruguay has been concerned mainly with the identification of hazardous plants and definition of the clinical signs, pathology and some aspects of the epidemiology of the intoxications. Few efforts have been made to identified the toxins of these plants and to define the biochemical mechanisms of their actions.

Prevention and control of plant poisoning in Brazil and Uruguay have been based mainly on the knowledge factors related to the plant, the diseased animal, and the environment and management variables that contribute to the occurrence of intoxications. Such measures are: 1) the management of pastures and animals including prevention of overgrazing, use of livestock not susceptible to the toxic plants present, and avoidance of turning hungry and/or thirsty animals onto pastures with toxic plants; 2) the use of fences to isolate areas with toxic plants; 3) the elimination of toxic plants by spraying, grubbing, plowing, burning, mowing or pulling, 4) the use of controlled seeds using only those free of contamination by weeds; 5) avoidance of contamination by toxic plants during hay or silage production; 6) the use of techniques that induce aversion, as in the case of intoxication by *Baccharis coridifolia* (Riet-Correa et al. 1993).

The efficiency of such preventive and control measures in the control of plant intoxications in Brazil and Uruguay has been limited, and the more important plants mentioned before still produce severe economical impact. To control some of these poisonings it is necessary to develop research programs regarding the different aspects of the plant poisoning. First of all, it is necessary to identify the active principles of many Brazilian toxic plants and to define their biochemical mechanisms of action. As mentioned by Molyneux et al. (1994), the isolation and characterization of toxic natural products is the first step in preventing livestock losses due to poisonous plants. Actually the toxic principle is unknown in at least 32 of the 88 species of toxic plants reported in Brazil. This knowledge is necessary to develop more efficient techniques for the control of poisonous plants, which are summarized as follows:

1) Vaccination. Attempts to develop vaccines against low molecular weight plant toxins had been developed in Australia in the last 25 years. Inmunogens are prepared by covalent conjugation of these molecules to an antigen protein. Some of these vaccines, including those against *Lantana* active principles, pyrrolizidine alkaloids and phytoestrogens, were not successful to control the diseases (Edgar 1994); but more recently, efficient vaccines have been developed to protect against lupinosis (Edgar et al. 1998) and intoxication by corynetoxins (Than et al. 1998). It is possible to achieve a good protection against a plant intoxication if the toxin is susceptible to degradation by the immune system. Vaccines produced with non degradable toxins, like pyrrolizidinic alkaloids, will be redistributed in the organism, and the vaccination leads to higher levels of retention of the drug (Edgar 1994).

2) Biologic control. Many plants have been successfully controlled by the use of biologic enemies including insects or other plant pathogens. *Senecio jacobea* was controlled in USA by releasing three insects: *Tyria jacobeae, Longitarsus jacobeae* and *Pegohylemia seneciella* (Coombs et al. 1997). *Xanthium pungens* has been controlled in Queensland through the release of the gall moth *Epiblema strenuana* and the fungus *Puccinia xanthii* (Dowling & Mckenzie 1993). *Hypericum perforatum*

has been successfully controlled in California and Oregon by two beetles, *Chrysolina gemellata* and *G. hyperici* (Cheeke 1998).

3) Microbial detoxification in the rumen. This is a mechanism of natural resistance to poisoning. Ruminants that ingest gradually increased amounts of oxalate containing plants became resistant to the toxin due to detoxification by ruminal microbes (Craig & Blythe 1994). Detoxifying bacteria have been used successfully to control intoxication by *Leucaena leucocephala*. The plant contains the aminoacid mimosine which is metabolized in the rumen to a toxic metabolite. The resistance to the toxin was transferred from Hawaiian goats to Australian goats and cattle by transferring detoxifying ruminal bacteria (Craig & Blythe 1994). Ruminal detoxification has been used also for the detoxification of nitrotoxins (Anderson et al. 1998). The possibility to prevent fluoracetate intoxication in cattle by use of ruminal bacteria genetically manipulated by the transference of a gene encoding fluoracetate dehalogenase has been investigated (Edgar 1998, Mayer & Van Rooyen 1994). In Brazil at least 12 plant species cause "sudden death" but only *Palicourea marcgravii* is known to contain fluorinated organic compounds. The possibility to use microbial detoxification for the prevention of "sudden deaths" caused by plants containing fluorinated organic compounds should be one of the main objectives for future research in Brazilian toxic plants.

4) Toxic binding agents. Activated charcoal has a considerable capacity to adsorb some substances in the gastrointestinal tract (Edgar 1998) and has been used to treat some intoxications including those caused by *Baccharis coridifolia* and *Lantana camara.* The problem with this substance is the large amount necessary to save poisoned stock. Hydrated sodium calcium aluminosilicates have been used in feeds for binding aflatoxins and reduce their absorption in the gastrointestinal tract. More recently, host molecules such as cyclodextrins and callixarenes, that molecularly encapsulate guest molecules, were evaluated for the treatment and prevention of some intoxications (Edgar 1998). Cyclodextrins are able to bind corynetoxins and protect sheep against this toxin which is produced

by *Clavibacter toxicus* and responsible for annual rye grass toxicity (Stewart et al. 1998).

5) Conditioned food aversion. Ruminants can be trained to avoid toxic plants through the process of food aversion. Food aversion was induced in cattle fed with tall larkspur (*Delphynium barbeyi*) or locoweeds (*Astragalus* spp. and *Oxytropis* spp.) and then treated with lithium chloride (LiCl, 200mg/kg body weight) through a rumen catheter or by gavage (Ralph 1994, Lane et al. 1990). Aversion can be maintained up to 2 years in the field if averted animals graze separatly from other non averted animals. However, if averted animals are placed with non averted cohorts that are eat readily the plant, they start to graze the plant and aversion is extinguished. This behavior, called social facilitation, is the most important factor preventing widespread application of aversion conditioning (Ralphs & Olsen 1998). Natural food aversion seems to be the mechanism, because ruminants and horses raised in areas where *Baccharis coridifolia* occurs do not ingest it. *B. coridifolia* is a toxic plant from Uruguay, Argentina and southern Brazil, that causes intoxication in cattle sheep and horses transferred from areas free of the plant to areas in which it exists. Animals raised in areas where the plant occurs do not ingest it, except lambs in the first month of age which occasionally are affected by the intoxication. Food aversion, induced by different ways, has been used by farmers to prevent the intoxication by *B. coridifolia* in animals that are transferred from areas free of the plant.

6) Use of plant breeding and selection programs to obtain non toxic or less toxic forages or crops. One of the best examples of these programs was the selection and breeding of *Trifolium subterraneum* cultivars with low estrogenic activity in Australia for the control of infertility caused by phytoestrogens (Cox 1978). Control of bloat caused by alfalfa is in progress by the selection of varieties with reduced rate of release of a bloat-producing cytoplasmatic protein fraction in the rumen (Cheeke 1998). In Brazil, *Brachiaria decumbens*, one of the most important toxic plants in some regions, should be controlled by the selection and breeding of

varieties with low content of steroidal saponins or by its substitution by other non toxic *Brachiaria* spp. with similar productivity.

Another important issue to be considered in the control of plant intoxications in South America is the development of good reporting systems to improve the information related to diseases affecting livestock. We also must acquire a better information regarding the phenology of the more important toxic plants; this knowledge will be necessary for correct management practices to prevent intoxications.

Public health implications

An important aspect of the ingestion of toxic plants by animals is that toxins can be transferred to humans by way of the consumption of milk, meat, eggs, honey or other animal products. There are few descriptions of human intoxications by the consumption of animal products. It is well known that the consumption of milk from cows grazing on *Eupatorium rugosum* infested pastures causes a disease known as milksickness, that can produce death in humans (James et al. 1994). Other milk transfer plant toxins are pyrrolizidine alkaloids. No human disease has been reported from the consumption of these alkaloids from milk, but we must consider the risk of their mutagenic and teratogenic effects. In Brazil, milk from goats fed with *Crotalaria spectabilis* was toxic for rats (Medeiros et al. 1999), and litters from rats fed with *C. spectabilis* or monocrotaline were also intoxicated via milk (Medeiros & Górniak, 1995, Medeiros et al. 1998). Ptaquiloside, the carcinogenic toxic principle of *Pteridium aquilinum*, passes through the milk and can cause lesions in lactating rats, mice and calves (James et al. 1994). Swansonine, a toxin present in *Ipomoea carnea* and *Ipomoea asarifolia* from Brazil (Molineaux and Medeiros, 1999; unpublished data), is excreted in milk and can cause lesions in suckling calves and lambs (James et al. 1994). The observation of photosensitization in calves, younger than 30 days old, from cows grazing *Brachiaria decumbens*, strongly suggest that the steroidal saponins contained in this plant are also excreted in toxic amounts with the milk (Lemos et al. 1998). In developed countries, the risk of human intoxication by natural toxins in milk is very remote, because blending of milk associated with processing and marketing dilutes any toxin that may enter milk products (James et al 1984). However, in Brazil where many people still drinking unprocessed milk from small farms, the risk of intoxications still present. In this aspect, goats, which are common in several Brazilian regions, would be more likely a source of contaminated milk than dairy cattle (Cheeke 1998).

An example for the presence of residues of plant toxins in meat is the secondary poisoning reported in dogs fed with meat from horses intoxicated by *Indigofora linnaei* containing the toxic aminoacid indospecine (Hegarty et al. 1988). In Australia, dogs were apparently intoxicated by the consumption of bone marrow from pigeons that ingested seeds of fluoracetate containing plants. In that country some native animals have evolved with plants containing high levels of fluoracetates and have a high degree of tolerance to this substance (Seawright 1994). In Brazil, *Palicourea margravii* which contains fluoracetate is the most important toxic plant, and another 11 species, of the genera *Palicourea*, *Mascagnia*, *Arrabidaea* and *Pseudocalymma*, which also cause "sudden death" (Tokarnia et al. 1990), probably contain fluoracetate derived compounds. In many areas of Brazil some people use to eat meat from cattle which died suddenly. Another example of secondary intoxication is that caused by the bufadienolides cardiac glycosides in humans and dogs consuming meat from intoxicated cattle (Kellerman, 1990).

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