



# Proceedings Diseases in ruminants associated with *Pteridium aquilinum* ingestion.

Filipe Silva<sup>1,4</sup>, Andreia Garcês \*, Catarina Magalhães<sup>3</sup>, Isabel Pires<sup>4</sup>

- <sup>1</sup>Exotic and Wildlife Service University of Trás-os-Montes and Alto Douro, Vila Real, Portugal
- <sup>2</sup>CITAB, University of Trás-os-Montes and Alto Douro, Vila Real, Portugal
  - <sup>3</sup>Direção Geral de Alimentação e Veterinária
  - <sup>4</sup> CECAV, University of Trás-os-Montes and Alto Douro, Vila Real, Portugal
  - \* Correspondence: andreiamvg@gmail.com
  - + Presented at the title, place, and date.

**Abstract:** *Pteridium aquilinum* (*L.*) *Kuhn*, commonly known as bracken-fern, is a cosmopolitan plant species absent only from polar and desert regions. Worldwide, Pteridium aquilinum has been rapidly spreading due to the neglect of agricultural fields and the growing wave of forest fires. This plant has several toxic components such as thiaminases, brains, active glucosides, beta-glucopyranosides and ptaquloside in its constitution that can be lethal to animals. The animals do not normally choose it as food, except in situations of food shortage, in periods of drought, when the ferns are still green or when the animals graze in places with large amounts of the plant in question. In order to revisit the major syndromes caused by *P. aquilinum* major toxins, the authors present several cases of acute and chronic ruminant poisoning associated with ingesting *P. aquilinum* in Portugal in sheep and cattle. The primarily associated syndromes observed in animals that consume this plant were thiamine deficiency, blindness in sheep, acute or subacute poisoning with bone marrow depression, and consequently, leucopenia and bladder tumors in cattle. Given the economic impact of the diseases caused by the toxins of this plant, and possible public health implications, it is imperative to minimize the syndromes in animals and establish measures for their prevention.

Keywords: fern, pteridium, ptaquiloside, cattle, tumor, toxicity

## 1. Introduction

*Pteridium aquilinum (L.) Kuhn,* commonly referred as common fern, fento or fern of the mountains, or female fern of apothecary, is a cosmopolitan species, absent only in the polar and desert regions (Figure 1) [1–3].

There are two subspecies and, within these, several geographical races. Tyron, quoted by Page, 1976, distinguishes subspecies *Aquilinum* and *Caudatum*, each with different varieties [4].

The global presence of *Pteridium aquilinum* can be attributed to its remarkable adaptability to various environmental conditions. This plant exhibits a highly opportunistic nature and employs a range of mechanisms to sustain its dominance. One such mechanism involves the synthesis of substances that, upon release into the environment or incorporation into the soil following the fern's demise, effectively hinder the emergence and growth of other plants. This attribute grants *P. aquilinum* allelopathic characteristics. Additionally, the fern employs the production of several secondary metabolites as a survival strategy, serving as deterrents for potential predators [1,5,6].

**Citation:** To be added by editorial staff during production.

Academic Editor: Firstname Lastname

Published: date



**Copyright:** © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/license s/by/4.0/).



**Figure 1.** Geographical distribution of *Pteridium aquilinum* subspecie *aquilinum* (Adapted from Page, 1976).

The morphology of the plant can be categorized into three main parts: roots, rhizomes, and fronds, with the fronds featuring fiddleheads in their immature stage (Figure 2). As the Bracken fern (BF) develops, the fiddlehead progressively unfurls, eventually giving rise to mature fronds responsible for the dispersal of essential spores required for reproduction [7,8].



Figure 2. Bracken Fern (Illustration Andreia Garcês and photo Isabel Pires).

In order to revisit the major syndromes caused by *P. aquilinum* major toxins, the authors present several cases of acute and chronic ruminant poisoning associated with ingesting *P. aquilinum* in Portugal in sheep and cattle.

#### 2. Material and Methods

Based on the cases received at the Histology and Anatomical Pathology and at the Veterinary Hospital of UTAD (Vila Real, Portugal), the authors describe the main animal syndromes associated with the ingestion of *P. aquilinum* in ruminants, based on the literature

# 3. Results and discussion

The primarily associated syndromes observed in animals that consume this plant were thiamine deficiency, blindness in sheep, acute or subacute poisoning with bone marrow depression, and consequently, leucopenia and bladder tumors in cattle.

The plant in question possesses various toxic constituents, namely illudane and illudalane sesquiterpenes, nor-sesquiterpenes, benzoic acid derivatives, cinnamic acid derivatives, enzymes, and thiaminases, which contribute to thiamine (vitamin B1) deficiency, particularly in equines. Also, it contains flavonoid antioxidants such as quercetin and kaempferol, along with an unstable glycoside. Notably, the plant harbours a prominent carcinogenic compound known as ptaquiloside, which is primarily responsible for its carcinogenic properties **[9–12]**.

#### 3.1. Thiamine deficiency

Thiamine deficiencies are frequent, due to the type 1 thiaminase present in this plant. They are mainly affected in monogastric herbivores such as horses since the microbial flora can synthesize this vitamin from its derivatives in ruminants **[13–15]**. Typical cases of poisoning from bracken fern require relatively high doses over an extended period, such as consuming hay contaminated with 20%–25% bracken fern for at least three months or longer. In horses, the condition known as equine bracken staggers are characterized by symptoms including anorexia, weight loss, lack of coordination, a hunched posture with an arched back and neck, and a wide stance with feet apart. Trembling muscles can be observed when the affected horses are forced to move. In severe cases, tachycardia and arrhythmias may occur, and death usually follows within 2–10 days after the onset of symptoms. Prior to death, convulsions, clonic spasms, and opisthotonos may be observed. The poisoning has been linked to bracken fern thiaminases, as the clinical manifestations resemble those of vitamin B1 deficiency. Thiamine therapy is commonly employed, and most animals respond well to it **[16–18]**.

Poisoning in pigs is relatively rare and presents with less distinct symptoms. Affected pigs typically exhibit anorexia and weight loss. In the terminal phase, the condition may resemble heart failure, and sudden death can occur following recumbency (lying down) and difficulty breathing (dyspnea) (18). However, in sheep fed P. aquilinum together with other thiaminase-rich plants, polioencephalomalacia associated with thiamine deficiency has been diagnosed **[13–15]**.

#### 3.2. Blindness in sheep

In sheep, ingestion of *Pteridium aquilinum* appears to be associated with blindness due to progressive retinal atrophy (Figure 3) **[19]** 

The condition known as tapel hyperreflectivity is clinically recognized. These affected animals experience permanent blindness and remain generally alert. The responsiveness of their pupils to light is typically diminished, and advanced cases display narrowed arteries and veins during funduscopic examination. Moreover, the *tapetum nigrum*, a layer of the eye responsible for reflecting light, appears pale with fine cracks and gray spots. Histologically, the affected animals exhibit severe degeneration of retinal rods, cones, and the outer nuclear layer, which is most prominent in the tapetal portion of the retina [16,17,20]. Additionally, these animals often present with various other lesions associated with bracken fern consumption, including bone marrow suppression, hemorrhage, immunosuppression, and urinary tract neoplasia [21]



Figura 3: Sheep with blindness.

# 3.3. Acute or subacute poisoning

Ingestion of bracken fern can lead to acute poisoning and produce various clinical symptoms, including fever, apathy, drooling, haemorrhages in organs such as the gums, nostrils, and gastrointestinal tract. Hematuria and blood in the milk may also occur. Necropsy findings often include red infarcts in the liver and significant bone marrow aplasia [12,22–24].

## 3.4. Bladder tumours in cattle

Associated with fetus carcinogens are bladder neoplasms (Figure 4), usually with enzootic hematuria and upper alimentary tract neoplasms in cattle [19].

The major carcinogenic compound of *Pteridium* is known as ptaquiloside [9–12,25–27].

Ptaquiloside contains the potent carcinogen dienone 2. Studies have revealed that under weak alkaline conditions, dienone 2 exhibits significant alkylating activity, leading to the cleavage of deoxyribonucleic acid (DNA). Consumption of bracken fern in high doses can cause DNA damage, resulting in programmed cell death and cell cycle arrest even at lower doses [12,28].

PTA shows lower levels in roots and spores but higher concentrations in edible parts and crosiers [29]. Fortunately, hydrothermal methods have been discovered to degrade PTA into a stable form, potentially reducing its toxicity. However, there is a need for further research to provide specific information and evidence on the reduction of toxicity, such as conducting in vitro cytotoxicity tests, and to determine the optimal conditions for PTA degradation, including temperature and heating duration [7,30].



Figure 4: Bladder tumour.

## 4. Conclusions

*Pteridium aquilinum*, commonly known as bracken fern, has rapidly expanded its global presence, particularly in Portugal, where it poses a significant potential threat due to favorable environmental conditions. The spread of *P. aquilinum* has been facilitated by the abandonment of certain agricultural crops and the increasing occurrence of forest fires. This fern species has an extensive rhizome system that allows it to survive fires, and while it does not produce spores in shaded areas, exposed regions promote the development of sporangia, leading to the production of a large number of spores. These spores, characterized by their small size, are easily dispersed by wind. Furthermore, *P. aquilinum* is one of the first plants to colonize newly burned areas.

Bracken fern intoxication is incurable, except in cases of thiamin deficiency. Therefore, it is crucial to control and prevent exposure to this plant. Implementing improved grazing management and alternating grazing between fern-contaminated and fern-free areas at three-week intervals can help minimize the risk of poisoning. Measures to stop the growth and density of bracken fern are important and could include regular cutting of mature plants or, if suitable, deep tillage.

Climate change appears to have a favourable impact on the spread of bracken fern, particularly in Northern Europe and mountainous regions. Rising temperatures, extended growing seasons, increased humidity, and additional hours of sunlight contribute to its proliferation. However, it is important to recognize the negative consequences this fern can bring to both humans and animals. Therefore, caution must be exercised to prevent excessive exposure to its hazardous chemicals.

**Author Contributions:** Conceptualization, F.S., I.P.; methodology, F.S., I.P.; software, F.S., A.G., C.M., I.P.; validation F.S., A.G., C.M., I.P.; formal analysis, F.S., A.G., C.M., I.P.; investigation, C.M., I.P.; resources, A.C. and I.P.; data curation, A.G. and I.P.; writing—original draft preparation, C.M., I.P.; writing—review and editing, F.S., A.G., C.M., I.P.; visualization, F.S., A.G., C.M., I.P.; supervision, I.P.; project administration, I.P.; funding acquisition, I.P., F.S. All authors have read and agreed to the published version of the manuscript.

**Funding:** The participation of Pires I, Silva F. was supported by the projects UIDB/CVT/00772/2020 and LA/P/0059/2020, funded by the Portuguese Foundation for Science and Technology (FCT). (Project UIDB/CVT/0772/2020). The participation of Garcês A. was supported by National Funds from FCT Portuguese Foundation for Science and Technology, under the project UIDB/04033/2020.

Informed Consent Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

# References

- Antiquário, M. de C.-L. *Iconographia selecta florae azoricae*; Secretaria Regional da Cultura Autotoma dos Açores, 2015;
- 2. Rivera Núñez, D. La guía de Incafo de las plantas útiles y venenosas de la Península Ibérica y Baleares (excluídas medicinales); Las guías verdes; Incado: Madrid, 1991; ISBN 978-84-85389-83-4.
- 3. Durão, J. Aspectos Anatomopatológicos e Clínicos Da Hematúria Enzoótica Dos Bovinos. *Revista Portuguesa de Ciências Veterinárias* **1995**, 131–137.
- PAGE, C.N. The Taxonomy and Phytogeography of Bracken a Review. *Botanical Journal of the Linnean Society* 1976, 73, 1–34, doi:10.1111/j.1095-8339.1976.tb02010.x.
- 5. COOPER-DRIVER, G. Chemotaxonomy and Phytochemical Ecology of Bracken. *Botanical Journal of the Linnean Society* **1976**, *73*, 35–46, doi:10.1111/j.1095-8339.1976.tb02011.x.
- 6. GLIESSMAN, S.R. Allelopathy in a Broad Spectrum of Environments as Illustrated by Bracken. *Botanical Journal of the Linnean Society* **1976**, *73*, 95–104, doi:10.1111/j.1095-8339.1976.tb02015.x.
- 7. Kim, M.K.; Kang, J.S.; Kundu, A.; Kim, H.S.; Lee, B.-M. Risk Assessment and Risk Reduction of Ptaquiloside in Bracken Fern. *Toxics* **2023**, *11*, 115, doi:10.3390/toxics11020115.
- Biological Flora of the British Isles: Pteridium Aquilinum (L.) Kuhn MARRS 2006 Journal of Ecology Wiley Online Library Available online: https://besjournals.onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2745.2006.01177.x (accessed on 31 May 2023).
- 9. Soeder, R.W. Fern Constituents: Including Occurrence, Chemotaxonomy and Physiological Activity. *Bot. Rev* **1985**, 51, 442–536, doi:10.1007/BF02860970.
- Freitas, L.; Paranaíba, J.; Peréz, A.; Machado, M.; Lima, F. Toxicity of Pesticides in Lizards. *Hum Exp Toxicol* 2020, 39, 596–604, doi:10.1177/0960327119899980.
- Alonso, M.B.; Feo, M.L.; Corcellas, C.; Vidal, L.G.; Bertozzi, C.P.; Marigo, J.; Secchi, E.R.; Bassoi, M.; Azevedo, A.F.; Dorneles, P.R.; et al. Pyrethroids: A New Threat to Marine Mammals? *Environment International* 2012, 47, 99–106, doi:10.1016/j.envint.2012.06.010.
- 12. Ugochukwu, I.C.I. Bracken Fern Toxicity and Its Associated Clinicopathological Effects in Humans and Animals: A Review. *Comp Clin Pathol* **2019**, *28*, 593–597, doi:10.1007/s00580-018-2636-2.
- EVANS, W.C. Bracken Thiaminase-Mediated Neurotoxic Syndromes. *Botanical Journal of the Linnean Society* 1976, 73, 113–131, doi:10.1111/j.1095-8339.1976.tb02017.x.

- Bakker, H.J.; Dickson, J.; Steele, P.; Nottle, M.C. Experimental Induction of Ovine Polioencephalomalacia. *Vet Rec* 1980, 107, 464–466, doi:10.1136/vr.107.20.464.
- 15. Chick, B.F.; Carroll, S.N.; Kennedy, C.; McCleary, B.V. Some Biochemical Features of an Outbreak of Polioencephalomalacia in Sheep. *Aust Vet J* **1981**, *57*, 251–252, doi:10.1111/j.1751-0813.1981.tb02680.x.
- 16. Plumlee, K.H. Clinical Veterinary Toxicology; Elsevier Health Sciences Division, 2007; ISBN 978-0-323-05455-3.
- 17. Fenwick, G.R. Bracken (Pteridium Aquilinum) Toxic Effects and Toxic Constituents. *Journal of the Science of Food and Agriculture* **1989**, *46*, 147–173, doi:10.1002/jsfa.2740460204.
- 18. Caloni, F.; Cortinovis, C. Plants Poisonous to Horses in Europe. *Equine Veterinary Education* **2015**, *27*, 269–274, doi:10.1111/eve.12274.
- Smith, B.L. Bracken Fern and Animal Health in Australia and New Zealand. AIAS Occasional Publication 1990, 227– 232.
- Hirono, I.; Ito, M.; Yagyu, S.; Haga, M.; Wakamatsu, K.; Kishikawa, T.; Nishikawa, O.; Yamada, K.; Ojika, M.; Kigoshi, H. Reproduction of Progressive Retinal Degeneration (Bright Blindness) in Sheep by Administration of Ptaquiloside Contained in Bracken. J Vet Med Sci 1993, 55, 979–983, doi:10.1292/jvms.55.979.
- Stegelmeier, B.L.; Field, R.; Panter, K.E.; Hall, J.O.; Welch, K.D.; Pfister, J.A.; Gardner, D.R.; Lee, S.T.; Colegate, S.; Davis, T.Z.; et al. Chapter 40 - Selected Poisonous Plants Affecting Animal and Human Health. In *Haschek and Rousseaux's Handbook of Toxicologic Pathology (Third Edition)*; Haschek, W.M., Rousseaux, C.G., Wallig, M.A., Eds.; Academic Press: Boston, 2013; pp. 1259–1314 ISBN 978-0-12-415759-0.
- Kigoshi, H.; Niwa, M.; Ohashi, H.; Tanaka, H.; Hirokawa, J.; Ishiwata, H.; Yamada, K. Synthesis of Bracken Ultimate Carcinogen Analogues Possessing a DNA Binding Moiety and Their DNA Cleaving Activities. *Tetrahedron Letters* 1995, *36*, 5349–5352, doi:10.1016/0040-4039(95)00984-K.
- 23. Tourchi, M. Múltiples Efectos Del Helecho Macho En Condiciones in Vivo e in Vitro (En Inglés). *Asian Pacific Journal of Cancer Prevention* **2014**, 5349–5352.
- Anjos, B.L.; Irigoyen, L.F.; Fighera, R.A.; Gomes, A.D.; Kommers, G.D.; Barros, C.S.L. Intoxicação aguda por samambaia (Pteridium aquilinum) em bovinos na Região Central do Rio Grande do Sul. *Pesq. Vet. Bras.* 2008, 28, 501–507, doi:10.1590/S0100-736X2008001000010.
- Gil da Costa, R.M.; Bastos, M.M.S.M.; Oliveira, P.A.; Lopes, C. Bracken-Associated Human and Animal Health Hazards: Chemical, Biological and Pathological Evidence. *J Hazard Mater* 2012, 203–204, 1–12, doi:10.1016/j.jhazmat.2011.12.046.
- Pires, I.; Silva, F.; Queiroga, F.L.; Rodrigues, P.; Henriques, R.; Pinto, C.A.; Lopes, C. Epithelioid Hemangiosarcomas of the Bovine Urinary Bladder: A Histologic, Immunohistochemical, and Ultrastructural Examination of Four Tumors. J Vet Diagn Invest 2010, 22, 116–119, doi:10.1177/104063871002200124.
- 27. Pires, I.; Magalhães, A.; Diez, J.; Saraiva, C.; Silva, F. Enzootic Bovine Hematuria.; Academic Publications, 2020;
- 28. Pires, I.; Queiroga, F.L.; Silva, F.; Pinto, C.; Lopes, C. Kaposi-like Vascular Tumor of the Urinary Bladder in a Cow. *J Vet Med Sci* **2009**, *71*, 831–833, doi:10.1292/jvms.71.831.
- Sharma, R.; Bhat, T.K.; Sharma, O.P. The Environmental and Human Effects of Ptaquiloside-Induced Enzootic Bovine Hematuria: A Tumorous Disease of Cattle. *Rev Environ Contam Toxicol* 2013, 224, 53–95, doi:10.1007/978-1-4614-5882-1\_3.
- Chen, L.-Y.; Hu, A.; Chang, C.-J. The Degradation Mechanism of Toxic Atractyloside in Herbal Medicines by Decoction. *Molecules* 2013, *18*, 2018–2028, doi:10.3390/molecules18022018.

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.