



Bracken fern toxicity and its associated clinicopathological effects in humans and animals: a review

Iniobong Chukwuebuka Ikenna Ugochukwu¹

Received: 9 August 2017 / Accepted: 2 January 2018 / Published online: 2 February 2018
© Springer-Verlag London Ltd., part of Springer Nature 2018

Abstract

Bracken fern is a delicacy consumed by humans and serves as animal forage around the world. It is said to be the 5th most common plant, an important toxic plant and the only higher plant known to cause cancer in animals. Occurrence of urinary bladder neoplasia is extremely high in cattle and it is associated with the continuous consumption of bracken fern. Animals are affected by bracken toxic active components, leading to huge economic losses. Bracken fern toxicity in cattle presents the following clinical signs of pyrexia, epistaxis, melena, chronic weight loss, dysphagia, incoordination and haemorrhagic lesions on the udder. The thiaminase content in bracken fern causes anorexia and incoordination in horses while the signs of bracken fern toxicity in ovines generally lead to retinal neuroepithelium degeneration. In bovines, bracken fern toxicity is a known aetiology in the depression of bone marrow haematopoietic activity characterised by anaemia, leucopenia, thrombocytopenia and haematuria which are cardinal haematopathology associated with bracken poisoning. Significant elevations in serum enzymes like aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), urea and creatinine levels were seen in animals exposed to bracken fern. Diagnosis of bracken toxicity is based on evidence of ingestion with appropriate clinical and postmortem findings, histopathological examination, polymerase chain reaction and immunohistochemistry are also very important tools in diagnosis. In conclusion, special attention should be given to this plant by toxicologists, botanists, veterinarians, toxicopathologists, oncologists and public health specialists. The human populace, farmers inclusive, should be educated about the public health significance of this plant.

Keywords Anaemia · Bracken fern · Haematuria · Ptaquiloside · Urinary bladder neoplasia

Introduction

Bracken fern (*Pteridium aquilinum*) as shown in Fig. 1 is a delicacy consumed as food by humans and serves as animal forage in many areas of the world (Bryan and Pamukcu 1979). It grows everywhere in the world except the continent Antarctica. It is reportedly the 5th most common plant (Freitas et al. 2001; Rasmussen et al. 2003). Bracken fern is well known as a problem species (Pakeman et al. 1996). It has been reported as an important toxic plant in different areas of the globe (Anjos et al. 2008; Bischoff and Smith 2011). It is the only known higher plant that is carcinogenic in animals when ingested (Norton 2008).

Toxic plants may produce toxic effects as a result of inadvertent exposure on contact or their accidental ingestion (Norton 2008). Another source of toxicity may be from intentional ingestion of some herbs, especially when they are taken chronically (Norton 2008).

Most poisonous plants are not palatable and livestock will normally avoid them; thus, plant poisonings are often pointers to other management problems, such as inadequate forage, overstocking, poor pasture management, heavy contamination of hay, silage, grain, or other feedstuffs with toxic plants, or careless disposal of clippings from poisonous ornamental plants (Bischoff and Smith 2011).

Bracken has for a very long time been used by man (Gil da Costa et al. 2012). Bracken has been used for animal bedding, soap production (Sanderson 2002) and for medicinal uses (Gil da Costa et al. 2012). Bracken fern rhizomes were used as food in times of draught (Smith and Seawright 1995; Alonso-Amelot and Avendaño 2002). The human population could be directly or indirectly exposed to bracken toxicity by

✉ Iniobong Chukwuebuka Ikenna Ugochukwu
iniobongugochukwu@unn.edu.ng

¹ Department of Veterinary Pathology and Microbiology, University of Nigeria Nsukka, Nsukka, Nigeria

Fig. 1 Bracken fern



direct consumption, its spore inhalation or ingestion of bracken-contaminated water, milk and meat (Tourchi 2014). Humans in some areas of Japan, in the Ouro Preto area in Brazil and in Canada eat bracken crosiers as a delicacy, known as warabi, as broto de samambaia and as fiddleheads, respectively (Hirono 1993; Marlière et al. 1998; Hojo-Souza et al. 2010). Public health risks associated with this ornamental plant have been long identified and studied, especially since the discovery of its carcinogenic active component, ptaquiloside (Niwa et al. 1983) and its carcinogenic properties (Gil da Costa et al. 2012).

Bracken fern has for a long time been known as a plant of toxicological interest (Gil da Costa et al. 2012). During periods of reduced food availability, for example, during the periods of tropical dry season and draught, domestic animals readily consume bracken fern (Shahin et al. 1999). The toxic effects of bracken ingestion are diverse, depending on the animal involved and on the dose(s) consumed (Gil da Costa et al. 2012). Bracken fern ingestion is linked with tumourigenesis in animals (Lucena et al. 2011; Masuda et al. 2011). For example, in various areas of the world, occurrence of urinary bladder cancer of the cattle is very high and it is linked with a long period of eating the bracken fern (Carvalho et al. 2006). Animals are affected by the active component toxins found in bracken fern leading to serious livestock losses annually. In addition to this, the human populations are directly and indirectly exposed through multi-routes (Gil da Costa et al. 2012).

This plant contains some toxic components which include the following: illudane and illudalane sesquiterpenes and nor-sesquiterpenes, benzoic acid derivatives, cinnamic acid derivatives, the enzyme and thiaminases, which cause deficiency of thiamine (vitamin B₁) especially in the equines, flavonoid antioxidants such as quercetin, kaempferol and an unstable glycoside, ptaquiloside, which is the main carcinogenic compound present in bracken fern (Soeder 1985; Freitas et al. 2001; Alonso-Amelot 2002; Panter et al. 2007; Gil da Costa et al. 2012).

Ptaquiloside, contains the ultimate carcinogen, the dienone 2, which under weak alkaline conditions, has been reported to have a potent alkylating action against amino acids and nucleic acid bases and, thus, leading to deoxyribonucleic acid (DNA) cleavage (Kigoshi et al. 1995). DNA damage due to cleavage and its programmed cell death occurs when bracken is consumed in high doses and may cause cell cycle arrest at mild doses (Tourchi 2014). Bracken extracts or ptaquilosides acting alone could induce hazardous effects on animals and humans, they could produce both genotoxic and cytotoxic effects in experimental conditions. (Somvanshi et al. 2006; Tourchi et al. 2012). Apart from the carcinogenicity of bracken fern, acute poisoning due to its ingestion could lead to the following clinical manifestations: fever, apathy, drooling, haemorrhages of varying degrees in several organs like the gums, nostrils, and gastrointestinal tract as shown in Fig. 2, haematuria and blood in the milk (Anjos et al. 2008). At necropsy, red infarcts in the liver and marked bone marrow aplasia could be seen (Anjos et al. 2008).



Fig. 2 Haemorrhages in the mesentery of a 6-year-old cow with suspected bracken fern poisoning (DAFM, 2009).

Clinical signs, gross and histopathologic lesions associated with bracken fern toxicity

The toxic clinical manifestations triggered by ingestion of huge quantity of bracken are diverse in different domestic animals (Evans et al. 1982). Cattle feeding on bracken fern was reported to show clinical signs of pyrexia, epistaxis (Fig. 3), melena, cutaneous bleeding, severe cachexia, dysphagia, drooling, regurgitation of ruminal contents through the nares, a stiffly gait and haemorrhagic lesions on the mammary gland (Lucena et al. 2011; Plessers et al. 2013). The enzyme constituent of bracken fern, thiaminase, induces anorexic conditions and incoordination in horses. However, bracken toxicity in sheep generally leads to neuroepithelial degeneration of the retina leading to bright blindness. In cattle, bracken poisoning also causes depression of haematopoietic activity of the bone marrow characterised by leucopenia, thrombocytopenia and haematuria (Shahin et al. 1998; Perez-Alenza et al. 2006). In addition to these, Perez-Alenza et al. (2006) recorded anaemia, extremely high monocytosis, hypergammaglobulinemia, microhaematuria and proteinuria.

According to Shahin et al. (1998), experimental rats fed on feed containing bracken fern developed macroscopic lesions like multiple ileal, urinary bladder and mammary gland adenocarcinomas. Ptaquiloside can be transferred to humans when bracken is used for food and could be the cardinal aetiology for the increased incidence of stomach cancer observed in Japan among people using bracken fern for food (Bischoff and Smith (2011). Ptaquiloside has also been identified in the milk produced by bracken-fed cows (Alonso-Amelot et al. 1996). The concentration of ptaquiloside in milk has been found to be about 8.5% of the total amount ingested by the cow (Potter and Baird 2000). Most certainly,



Fig. 3 Epistaxis in a 3-year-old Belgian blue cow suffering from coagulation disorders due to acute bracken fern poisoning (Plessers et al. 2013)

ptaquiloside in milk is responsible for the connection between bracken infestation and the incidence of gastric cancer in populations of farmers inhabiting cattle-range areas in Costa Rica and other countries where bracken vegetation is dense (Potter and Baird 2000).

Haemangiosarcoma, haemangioma, transitional cell epithelial carcinoma of the urinary bladder and chronic cystitis were diagnosed in the urinary bladder of six captive fallow deer (*Dama dama*); these were reported by Scala et al. (2014). Other gross lesions like haematuria and severe body wasting were also observed in the chronic cases. These findings were compatible with chronic bovine enzootic haematuria and were suspected to have been induced by chronic ingestion of bracken fern present on the premises (Scala et al. 2014), hydronephrosis and renal carcinoma were also seen in some cases (Scala et al. (2014). Squamous cell carcinomas of the upper digestive tract of bovines have also been associated with continuous bracken fern ingestion over a long period of time (Borzacchiello and Roperto 2008; Masuda et al. 2011).

Polypoid and follicular cystitis, both of which caused deformation of the bladder wall architecture, were common macroscopic lesions seen in cattle exposed to bracken fern, other lesions observed include multifocal neoplasia in the urinary bladder wall and haemorrhages in the bladder mucosa, giving rise to bovine enzootic haematuria (Carvalho et al. 2006).

Histopathological findings seen were mostly surface epithelial growths, which varied in diameter from some millimetres to several centimetres, had an attachment to the urinary bladder wall which was either pedunculated or broad, and a smooth or branch-like surface (Carvalho et al. 2006). Non-neoplastic epithelial abnormalities included hyperplasia, von Brunn's nests, cystitis cystica, cystitis glandularis and intestinal metaplasia, although these histopathological lesions are often associated with neoplasia (Carvalho et al. 2006). In the digestive tract, the following lesions could be seen microscopically, epithelial neoplastic keratinocytes of the oesophagus, there was also ulceration of the oesophageal mucosal epithelium. All tumours were highly invasive, projecting into the inner tissue layers. Areas of necrosis, keratin aggregation and mineralisation surrounded by multinucleated giant cells were a common histopathological finding (Masuda et al. 2011). Eosinophilic and lymphoplasmacytic infiltrations were also seen (Masuda et al. 2011).

In rabbits exposed to bracken fern toxicity, mild to moderate lesions were seen in the blood vessels of most of the visceral organs, hepatocellular vacuolar degeneration changes, hypersecretory activity in the intestines, presence of renal tubular casts and degenerative changes in renal tubular lining cuboidal epithelial cells (Gounalan et al. 1999). Shahin et al. 1998 also reported ischemic tubular necrosis in the kidneys and type II pneumocyte proliferation in the lungs of rats experimentally exposed to bracken fern. There were mild vascular changes in lungs, degenerative changes in testes, hepatocytic focal

necrosis and villous atrophy or hyperplasia of lining epithelial cells (Kataria et al. 1998).

Haematological and serum biochemical observations in bracken fern toxicity

Haematological changes seen in bracken fern toxicity are always associated with acute toxicity (Gil da Costa et al. 2012). These haematological changes result from depression of the haematopoietic activity of the bone marrow, with consequent reduction in thrombocytopoiesis, erythropoiesis and leukopoiesis, thus resulting in severe thrombocytopenia which leads to widespread ecchymotic and petechial haemorrhages (Gil da Costa et al. 2012).

Haematological parameters of animals exposed to bracken fern revealed severe pancytopenia and blood coagulation disorders (Plessers et al. 2013). Fern-fed rabbits and cattle showed severe non-regenerative anaemia, leucopenia, lymphopenia and relative heterophilia (Gounalan et al. 1999; Di Loria et al. 2012). These haematological findings were also seen in ruminants exposed to bracken fern (Prakash et al. 1996; Gil da Costa et al. 2012). Prakash et al (1996), in addition to the above findings, also reported reduced haemoglobin levels and Gil da Costa et al. (2012) reported neutropenia and lymphopenia in ruminants. Observed leucopenia in cases of bracken toxicity will result in increased susceptibility to infections (Gil da Costa et al. 2012).

Significant elevations in serum enzymes like serum glutamate oxaloacetate transaminase (SGOT) presently referred to as aspartate aminotransferase (AST), serum glutamate pyruvate transaminase (SGPT) which is now referred to as alanine aminotransferase (ALT), alkaline phosphatase (ALP), urea and creatinine levels were all elevated. These were seen in animals exposed to bracken fern (Gounalan et al. 1999; Huang et al. 2006). Shahin et al. (1998) reported serum elevations of the levels of tumour necrosis factor alpha (TNF α) in cases of bracken fern toxicity in experimental animal models. Moderate hypoproteinemia and hypoalbuminemia were also observed in affected cattle (Di Loria et al. 2012).

Diagnosis of bracken fern toxicity

Few veterinary diagnostic laboratories test for plant toxins. Diagnosis is usually based on evidence of ingestion with appropriate clinical and postmortem findings (Bischoff and Smith 2011). Some phytotoxins, such as pyrrolizidine alkaloids, have chronic effects and animals often do not show clinical signs for weeks or months, after the plant is no longer present on pasture or in the current batch of hay (Bischoff and Smith 2011). Histopathological examination, polymerase chain reaction and immunohistochemistry are also very important tools in diagnosis (Freitas et al. 2002; Masuda et al. 2011).

Conclusion

Bracken fern from times past has been used by man as a delicacy and for animal forage. It grows everywhere in the world except Antarctica so it is a very common plant. It is, however, a toxic plant that is associated with tumour formation, ovotoxicity, genotoxicity, bone marrow depression, blindness, etc. Blood examination of animals exposed to bracken fern usually reveals severe pancytopenia and blood coagulation disorders. Ingestion of bracken fern is usually associated with poor management and leads to enormous economic losses due to deaths associated with bracken fern toxicity.

Therefore, particular attention should be given to this plant by toxicologists, botanists, veterinarians, toxicopathologists, oncologists and public health specialists. The human populace, farmers inclusive, should be educated about the public health significance of this plant and, in this way, curtail the unpleasant effects of this plant on humans and their livestock.

Acknowledgements A special thanks goes to Profs CN Chineme and C.O. Njoku for exposing, mentoring and guiding me in the field of Veterinary Oncology. I am also grateful to Profs NDG Ibrahim and KAN Esievo for their helpful contributions and suggestions.

Compliance with ethical standards

Conflict of interest The author declares that there is no conflict of interest.

Ethical approval This review article does not contain any studies with animals or human participants performed by the author.

References

- Alonso-Amelot ME (2002) The chemistry and toxicology of bioactive compounds in bracken fern (*Pteridium* spp.) with special reference to chemical ecology and carcinogenesis. *Stud Nat Prod Chem* 26: 685–673. [https://doi.org/10.1016/S1572-5995\(02\)80017-5](https://doi.org/10.1016/S1572-5995(02)80017-5)
- Alonso-Amelot ME, Avendaño M (2002) Human carcinogenesis and bracken fern: a review of the evidence. *Curr Med Chem* 9(6):675–686. <https://doi.org/10.2174/0929867023370743>
- Alonso-Amelot ME, Castillo U, Smith BL, Lauren DR (1996) Bracken ptaquiloside in milk. *Nature* 382(6592):587. <https://doi.org/10.1038/382587a0>
- Anjos BL, Irigoyen LF, Figuera RA, Aline D, Gomes AD, Gláucia D et al (2008) Intoxicação aguda por samambaia (*Pteridium aquilinum*) em bovinos na Região Central do Rio Grande do Sul. *Pesq Vet Bras* 28(10):501–507. <https://doi.org/10.1590/S0100-736X2008001000010>
- Bischoff K, Smith MC (2011) Toxic plants of the northeastern United States. *Vet Clin North Am Food Anim Pract* 27(2):459–480. <https://doi.org/10.1016/j.cvfa.2011.02.001>
- Borzacchiello G, Roperto F (2008) Bovine papillomaviruses, papillomas and cancer in cattle. *Vet Res* 39(5):45–74. <https://doi.org/10.1051/vetres:2008022>
- Bryan GT, Pamukcu AM (1979) Bracken fern (BF) a natural urinary bladder carcinogen. In: Deichmann WB (ed) *Toxicological and occupational medicine, developments in toxicology and*

- environmental science, vol 4. Elsevier North Holland Inc, New York, pp 311–336. <https://doi.org/10.1016/B978-0-444-00288-4.50026-8>
- Carvalho T, Pinto C, Peleteiro MC (2006) Urinary bladder lesions in bovine enzootic haematuria. *J Comp Pathol* 134(4):336–346. <https://doi.org/10.1016/j.jcpa.2006.01.001>
- Department of Agriculture, Food and the Marine (DAFM). August 2009 RVL Monthly Report 2009; www.agriculture.gov.ie, retrieved 27th January, 2017; 6:15pm
- Di Loria A, Piantedosi D, Cortese L, Roperto S, Urraro C, Paciello O, Guccione J, Britti D, Ciaramella P (2012) Clotting profile in cattle showing chronic enzootic haematuria (CEH) and bladder neoplasms. *Res Vet Sci* 93(1):331–335. <https://doi.org/10.1016/j.rvsc.2011.07.011>
- Evans WC, Patel Y, Kooh Y (1982) Acute bracken fern poisoning in monogastric and ruminant animals. *Proc R Soc Edinb* 81:29–64
- Freitas RN, O'Connor PJ, Prakash AS, Shahin M, Povey AC (2001) Bracken (*Pteridium aquilinum*)-induced DNA adducts in mouse tissues are different from the adduct induced by the activated form of the bracken carcinogen ptaquiloside. *Biochem Biophys Res Commun* 281(2):589–594. <https://doi.org/10.1006/bbrc.2001.4388>
- Freitas RN, Brasileiro-Filho G, Silva ME, Pena SDJ (2002) Bracken fern-induced malignant tumors in rats: absence of mutations in *p53*, *H-ras* and *K-ras* and no microsatellite instability. *Mutat Res* 499(2):189–196. [https://doi.org/10.1016/S0027-5107\(01\)00275-5](https://doi.org/10.1016/S0027-5107(01)00275-5)
- Gil da Costa RM, Bastos MMSM, Oliveira PA, Lopes C (2012) Bracken-associated human and animal health hazards: chemical, biological and pathological evidence. *J Hazard Mater* 203–204:1–12. <https://doi.org/10.1016/j.jhazmat.2011.12.046>
- Gounalan S, Somvanshi R, Kataria M, Bisht GS, Smith BL, Lauren DR (1999) Effect of bracken (*Pteridium aquilinum*) and dryopteris (*Dryopteris juxtaposita*) fern toxicity in laboratory rabbits. *Ind J Exp Biol* 37(10):980–985
- Hirono I (1993) Edible plants containing naturally occurring carcinogens in Japan. *Jpn Cancer Res* 84(10):997–1006. <https://doi.org/10.1111/j.1349-7006.1993.tb02791.x>
- Hojo-Souza NS, Carneiro CM, Santos RC (2010) *Pteridium aquilinum*: what we know and what is yet to be learnt. *Biosci J* 26:798–808
- Huang X, Choi Y, Im H, Yarimaga O, Yoon E, Kim H (2006) Aspartate aminotransferase (AST/GOT) and alanine aminotransferase (ALT/GPT) detection techniques. *Sensors (Basel)* 6(7):756–782. <https://doi.org/10.3390/s6070756>
- Kataria M, Somvanshi R, Dash S (1998) Biochemical and histological changes in blood, erythrocytes and tissue of rats on feeding *Dryopteris juxtaposita* fern. *Ind J Exp Biol* 36(5):510–513
- Kigoshi H, Niwa M, Ohashi H, Tanaka H, Hirokawa J, Ishiwata H, Kiyoyuki Y (1995) Synthesis of bracken ultimate carcinogen analogues possessing a DNA binding moiety and their DNA cleaving activities. *Tetrahedron Lett* 36(30):5349–5352. [https://doi.org/10.1016/0040-0399\(50\)0984K-](https://doi.org/10.1016/0040-0399(50)0984K-)
- Lucena RB, Rissi DR, Kommers GD, Piezezan F, Oliveira-Filho JC, Macedo JTSA, Flores MM, Barros CSL (2011) A retrospective study of 586 tumours in Brazilian cattle. *J Comp Pathol* 145(1):20–24. <https://doi.org/10.1016/j.jcpa.2010.11.002>
- Marlière CA, Santos RC, Galvao MAM, Soares JF (1998) Ingestão de broto de samambaia e risco de cancer de esôfago e estômago na região de Ouro Preto, MG. *Rev Bras Cancerol* 44:225–229
- Masuda EK, Kommers GD, Martins TB, Barros CSL, Piazer JVM (2011) Morphological factors as indicators of malignancy of squamous cell carcinomas in cattle exposed naturally to bracken fern (*Pteridium aquilinum*). *J Comp Pathol* 144(1):48–54. <https://doi.org/10.1016/j.jcpa.2010.04.009>
- Niwa H, Ojika M, Wakamatsu K, Yamada K, Hirono I, Matsushita K (1983) Ptaquiloside a novel norsesquiterpene glycoside from bracken *Pteridium aquilinum* var. *latiusculum*. *Tetrahedron Lett* 24(38):4117–4120. [https://doi.org/10.1016/S0040-4039\(00\)88276-3](https://doi.org/10.1016/S0040-4039(00)88276-3)
- Norton S (2008) Toxic effects of plants. In: Klassen CD (ed) Cassarett and Doull's toxicology, basic science of poison, 7th edn. McGraw Hill, San Francisco, pp 1103–1104
- Pakeman RJ, Marrs RH, Howard DC, Barr CJ, Fuller RM (1996) The bracken problem in Great Britain: its present extent and future changes. *Appl Geogr* 16(1):65–86. [https://doi.org/10.1016/0143-6228\(95\)00026-7](https://doi.org/10.1016/0143-6228(95)00026-7)
- Panther KE, Gardner DR, Lee ST, Pfister JA, Ralphs MH, Stegelmeier BL, James LF (2007) Important poisonous plants of the United States. In: Gupta RC (ed) Veterinary toxicology: basic and clinical principles. New York: Academic Press, New York, pp 825–872. <https://doi.org/10.1016/B978-012370467-2/50163-2>
- Perez-Alenza MD, Blanco J, Sardon D, Sanchez Moreiro MA, Rodriguez-Bertos A (2006) Clinico-pathological findings in cattle exposed to chronic bracken fern toxicity. *New Zeal Vet J* 54(4):185–192. <https://doi.org/10.1080/00480169.2006.36693>
- Plessers E, Pardon B, Deprez P, De Backer P, Croubels S (2013) Acute hemorrhagic syndrome by bracken poisoning in cattle in Belgium. *Vlaams Diergen Tijd* 82:31–37
- Potter DM, Baird MS (2000) Carcinogenic effects of ptaquiloside in bracken fern and related compounds. *Br J Cancer* 83(7):914–920. <https://doi.org/10.1054/bjoc.2000.1368>
- Prakash AS, Pereira TN, Smith BL, Shaw G, Seawright AA (1996) Mechanism of bracken fern carcinogenesis: evidence for H-ras activation via initial adenine alkylation by ptaquiloside. *Nat Toxins* 4:221–227
- Rasmussen LH, Kroghsbo S, Frisvad JC, Hansen HCB (2003) Occurrence of the carcinogenic bracken constituent ptaquiloside in fronds, topsoils and organic soil layers in Denmark. *Chemosphere* 51(2):117–127. [https://doi.org/10.1016/S0045-6535\(02\)00694-X](https://doi.org/10.1016/S0045-6535(02)00694-X)
- Sanderson HDV (2002) Prendergast, commercial uses of wild and traditionally managed plants in England and Scotland. Kew (UK); Centre for Economic Botany, Royal Botanic Gardens (UK), pp 53–6
- Scala C, Ortiz K, Catinaud J, Lemberger K (2014) Hematuria and urinary bladder lesions compatible with bracken fern (*Pteridium aquilinum*) intoxication in captive fallow deer (*Dama dama*). *J Zoo Wildl Med* 45(2):380–385. <https://doi.org/10.1638/2013-0274R1.1>
- Shahin M, Moore MR, Worrall S, Smith BL, Seawright AA, Prakash AS (1998) H-Ras activation is an early event in the ptaquiloside-induced carcinogenesis: comparison of acute and chronic toxicity in rats. *Biochem Biophys Res Commun* 250(2):491–497. <https://doi.org/10.1006/bbrc.1998.9341>
- Shahin M, Smith BL, Prakash AS (1999) Bracken carcinogens in the human diet. *Mutat Res* 443(1-2):69–79. [https://doi.org/10.1016/S1383-5742\(99\)00011-3](https://doi.org/10.1016/S1383-5742(99)00011-3)
- Smith BL, Seawright AA (1995) Bracken fern (*Pteridium* spp.) carcinogenicity and human health—a brief review. *Nat Toxins* 3(1):1–5. <https://doi.org/10.1002/nt.2620030102>
- Soeder RW (1985) Fern constituents: including occurrence chemotaxonomy and physiological activity. *Bot Rev* 51(4):442–536. <https://doi.org/10.1007/BF02860970>
- Somvanshi R, Lauren DR, Smith BL, Dawra RK, Sharma OP, Sharma VK, Singh AK, Gangwar NK (2006) Estimation of the fern toxin, ptaquiloside, in certain Indian ferns other than bracken. *Curr Sci* 91(11):1547–1555
- Tourchi RM (2014) Multiple effects of bracken fern under in vivo and in vitro conditions. *Asian Pac J Cancer Prev* 15(18):7505–7513. <https://doi.org/10.7314/APJCP.2014.15.18.7505>
- Tourchi RM, Bahrami AR, Dehghani H (2012) Bracken-fern extracts induce cell cycle arrest and apoptosis in certain cancer cell lines. *Asian Pac J Cancer Prev* 13:6047–6053