



Review Article

Bracken Fern (*Pteridium Aquilinum*) -Toxic And Carcinogenic Effects On Human And Animals

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ABSTRACT

The fern (*Pteridium aquilinum* L Kuhn) is one of the most victorious plants in the world. It covers approximately 700,000 hectares in England and is expanding its area by 1-3% each year. Not only does the fern limit marginal land use, but toxins in the plant can cause serious illness or death in animals that eat the plant's rhizomes or ponds¹. Significant impacts on biodiversity, animal health and human health are due to the presence of ptaquiloside and related compounds in milk, meat and water as well as the global increase of *P. aquilinum* and its development in acidic environments, rapid colonization of soil and fire area². Fern (*Pteridium aquilinum*) eaten by cattle has been shown to cause bladder and intestinal infections in cattle and various diseases in other livestock³. Bracken poisoning is mainly caused by ptaquiloside, a norsesquiterpene that is also a potent carcinogen and can cause many types of cancer in experimental animals¹.

INTRODUCTION

Pteridium aquilinum, commonly known as "fern", is eaten as a vegetable. The fern (*Pteridium aquilinum*) is the fifth most common plant species in the world. Its ecological distribution is quite wide and the plant can easily grow and spread in many soil types. Sometimes the canopy of *P. aquilinum* is attacked (e.g. in the UK). Bracken has different chemical compounds: some cyanogenic glycosides, those that work with anti-

inflammatory substances (thermostable thiamine enzymes and other thermostable compounds), and those that work with carcinogenic substances (mainly ptaquiloside) high work poison⁴. While the sprouts are used to treat cancer, the herb decoction is used to treat tuberculosis. The leaves and a poultice made from the leaves are used to treat pain and bind broken bones. Its leaves are used in baths to treat arthritis. The main botanical characteristics of this plant include high

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reproduction, regrowth, rapid adaptation to ecological conditions and spreading speed. Secondary metabolites of fern can cause different and serious problems in different animal and human species. Its major and most dangerous metabolite is ptaquiloside, which can be consumed by humans directly or directly from milk⁵.



Figure1:- Bracken Fern(Pteridium Aquilinum)

Botanical aspects of plant:-

Bracken fern belongs to the phylum Pteridophyta and the family Dennstaedtiaceae (formerly the family Polypodiaceae)⁶. According to recent statistics, this species has nine subspecies and is a cosmopolitan plant (there is another species, *P. esculentum*, in New Zealand and Australia; Fern is the common name for all subspecies. Fossil evidence suggests the plant is at least 55 million years old. It has a powerful rhizome and alternate branches up to 2-2.5 cm in diameter, which serve as a warehouse for carbohydrate accumulation. Long branches form the trunk of the plant and have several lateral buds. The second type is leaves that grow from long branches, producing ring-shaped leaves and many dormant leaves. Thin black roots start from the rhizome and can penetrate more than 50 cm into the soil. The leaves of the fern are generally 30 to 60 centimeters long.



Figure2

The leaves are divided into auricles, the base of which is sometimes large enough (so that it can be seen as a three-part leaf). Pinnae are divided into smaller parts called pinnae. Fertile leaves produce spores in structures called sporangia, which are found on the surface of the leaves. Fern seedlings can usually produce spores (up to 300 million spores per year) by the end of their third or fourth growing season. In good ecological conditions (temperature: 15-30°C, pH: 5.5-7.5), new seedlings can be seen 6-7 weeks. Large production of stomatal cells allows it to live in a dry environment, which is not characteristic of most ferns. Prehistoric people often ate ferns (rhizome in winter, young leaves in spring). The plant is widely distributed from the equator to northern Europe, Central Asia, China and Japan, and from central South America to arctic Canada. For example, the area under cultivation in England is approximately 1,300,000 hectares. The plant is abundant in different Quercus and Scots pine gardens. In Hungary, fern is a species of fern found in different tree communities: mainly in the western Danube region and Nilsegg⁴.

NAMES AND TAXONOMY

Preferred scientific name

Pteridium aquilinum (L.) Kuhn

Taxonomic position

Domain:	Eukaryota
Kingdom:	Viridiplantae

Phylum:	Pteridophyta
Class:	Pteridopsida
Order:	Myrtales
Family:	Dennstaedtiaceae

Other scientific names

Pteris aquilina L.

Pteridium esculentum (Forst.) Nakai

Pteridium revolutum (Bl.) Nakai

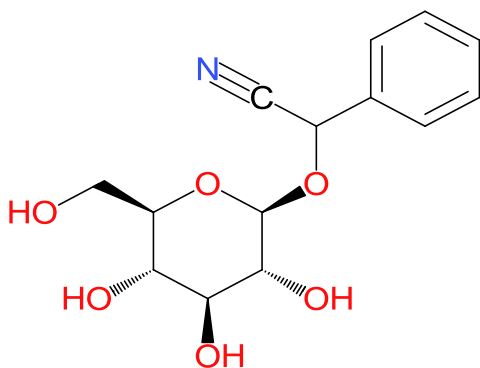
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PTEAQ (*Pteridium aquilinum*)

PTERE (*Pteridium revolutum*)⁷

Chemical constituents of bracken fern:

Cyanogen glycosides: The main cyanide component of this plant is prunasin. According to Alonso-Amelot and Oliveros (2000), prunasin concentration is 10.4- 61.3 mg/g fresh tissue. Gametophytes and sporophytes from the same spore source have been reported to secrete different concentrations of HCN. Cyanide can be found in both the gametophytic and sporophytic generations of the fern; Young leaves produce more cyanide than older leaves. Cyanide is common in herbivore conservation strategies.



Chemical Structure Of Prunasin

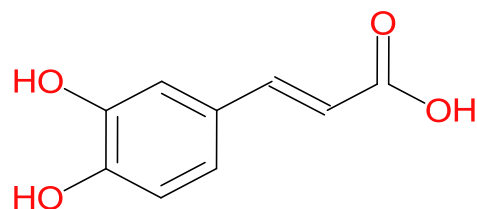
Content of thiamine enzymes:

Early studies have shown that there are two groups of thiamine enzymes:

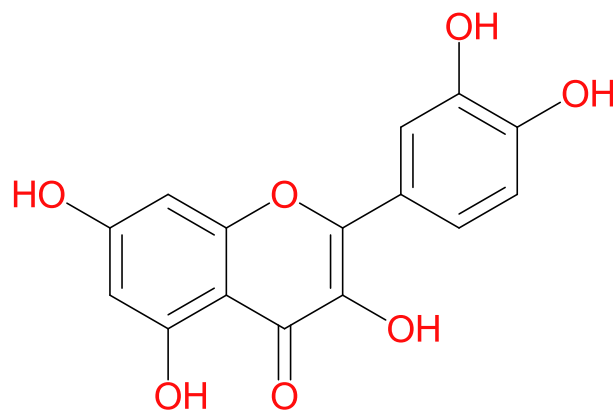
- Thiamine enzymes and
 - Enzymes that undergo chemical reactions. thiamine Thermally stable compound with the properties of thiamine.
- Thiaminase. Bracken has been known to cause vitamin B1 deficiency in some animals

since the mid-1940s. Two types of thiamine enzymes (1 and 2) with significant activity have been isolated (Meyer, 1989). Thiaminase activity (content) is highest in rhizomes.

- Other, thermostable antithiamine factors. Experiments with horses have documented the occurrence of these conditions (Konishi and Ichijo, 1984). Thiamine levels decreased in horses' blood and urine, blood pyruvate and lactate increased, and one horse showed signs of fern poisoning. Identify stable energy products with antiinflammatory properties, including caffeic acid (Figure a), astragalalin and isoquercetin (Figure a,b)



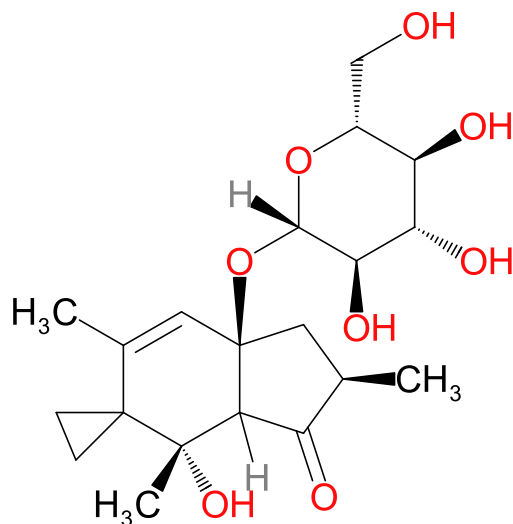
A. Caffeic acid



B. Quercetin

In 1983, two groups of scientists from Japan and the Netherlands isolated a carcinogenic, mutagenic and clastogenic source. The name of the drug is ptaquiloside (PT). It has a norsesquiterpene skeleton. Pterin B is produced under acidic conditions, and under alkaline conditions, an unstable binary compound is formed that can be aromatized to produce pterin B. PT-induced tumors of the esophagus and bladder are associated with pH values of 8.1-8.2 (blue) and 7.5-8.5 (urine),

respectively. Determination of PT involves aqueous extraction after washing of the polyamide resin column, and PT content is determined by high-performance liquid chromatography (HPLC) isolated PT from freeze-dried soil material, and the previously proposed structure was confirmed by multiple pulse and 2D NMR techniques.



Chemical structure of Ptaquiloside

High but variable PT levels (0–12,945 $\mu\text{g PT/g}$ dry matter, DM) are found in ferns grown in Australia (Smith et al., 1994). 15% of the samples had more than 5000 $\mu\text{g PT/g DM}$, and 57% had more than 1000 $\mu\text{g PT/g DM}$. The actual amount of PT a fern contains varies by plant material, depending on the species and age (maturity) of the plant. There is a negative correlation between PT concentration and the growth stage of *P. aquilinum* leaves. The rhizome or tissue contains almost no PT. Another unstable iluca-type sesquiterpene glycoside (Ptaquiloside Z) was fractionated by reverse-phase HPLC from *P. Aquilinum* var. tail. This new component of fern has been shown to have toxicity similar to PT for brine shrimp. *P. aquilinum* spores do not have PT, but their carcinogenic properties are indisputable. This can be explained by the occurrence of one or more other carcinogenic or mutagenic compounds. Bracken fern contains other illudane type β -glucosides, isoptaquiloside

and caudatoside, which have structural similarities to PT. Ecotoxicological aspects of PT. Investigation of the properties and toxicology of PT in the soil is a relative new project. In Denmark, PT levels detected in the soil were 0.008–40.6 $\mu\text{g PT/g}$ dry soil in the autumn and 1.56–212 $\mu\text{g PT/g}$ dry soil in late winter. The risk of PT leaching is high if the soil pH is slightly acidic to neutral, the clay content is high, and microbial degradation of PT is slow.

Other components:

Recently, different substances with steroid properties have been found in fern): α - and β -ecdysone were identified⁴.

Toxicity on animals:-

Bracken is believed to be toxic and carcinogenic, according to initial reports more than 50 years ago. It has been revealed in many animal tests to be highly carcinogenic and causes many health problems in pets worldwide. In addition, Charles Evans, in Aberystwyth, UK, found that fern caused thiamine-deficiency "distress" in horses and cancer-related leukopenia and cancer in cattle and mice. It was independently validated by Charles and Antice Evans working in Bangor, UK, and different fractions were analyzed testing not only for mutagenicity but also for carcinogenicity. This led to the discovery of ptaquiloside (PTQ), a member of the illudanes, a subclass of sesquiterpenes, first isolated from *P. aquilinum* subsp. *latiusculum* was prepared by Japanese and Dutch chemists⁸.

Primary Evidence of Bracken-Cancer :-

Known as "bracken poisoning", the toxicity of fern to cattle, goats and horses has been known for more than a century. In the acute phase, it can cause the death of the animal within a few days, but long-term sublethal consumption can cause complex diseases such as bone marrow hypoplasia, thrombocytopenia, leukopenia, decrease in polymorphonuclear white blood cells. For immunity, it reduces intestinal iron absorption,

vitamin B1 deficiency and heavy bleeding. The most obvious symptoms for the veterinarian are; weakness, lack of coordination in the hind legs and neck, tendency to infection, shortness of breath, bleeding from the nose, anus and urethra. The last one, known as bovine endemic hematuria (BEH), is the most important for our current discussion because it is not only an incurable disease with major economic impact, but also causes cancer. Vascular sacs in the lining rupture and blood flows into the urine. These processes include telangiectasia, hemangioma lumen formation, and vascularized proliferation of the stroma and epithelium, with most of the bladder consisting of papillary carcinomas, transitional epithelial carcinomas, angiosarcomas, and fibromas. This disease has occurred in many countries around the world and is always associated with cattle fed on ferns. To avoid financial loss, many farmers kill diseased animals before the emergency⁹. Bovine endemic hematuria (BEH) is a condition characterized by permanent anemia and bleeding due to hemorrhagic cystitis and/or bladder tumors. BEH is caused by consuming ferns (*Pteridium* spp) over a period of 2 to 3 years¹⁰.

Toxicological Studies on Bracken Fern including Carcinogenicity:-

Toxicity tests on experimental animals and HeLa strains were performed on young leaves of the fern *Pteridium aquilinum* var. *latiusculum* focused on behavioral carcinogens and bovine toxicants. Dried leaves and rhizomes of ferns have been shown to be carcinogenic when fed to mice¹¹. We attempted to isolate carcinogens from fern (*Pteridium aquilinum*), a naturally occurring poison that can cause long-term carcinogens. Endemic hematuria and bladder cancer in cattle and carcinogenicity of various target organs in different species. The hot methanol extract of Bracken fern was dissolved in water and extracted with chloroform followed by an n-butanol-butane mixture (1:1). The residue was dried and

trituated with ether-methanol (4:1), n-butanol and finally ethanol. The insoluble residue is dissolved in 10% aqueous methanol and passed through Dowex 1 OH-, Dowex 50 H+ or Dowex' 1 OH- and Dowex 50 H+ ion exchange resins. The concentrated tannins isolated from some parts are the same as those isolated from ferns by the caffeine process used to isolate tannins from other plants. Three systems were used for

Bioassays:

Cholesterol-containing fern was implanted into the bladder lumen of mice to induce cancer; Fern components were injected intraperitoneally into rats to induce toxicity; and growth inhibition of *E. coli*. The following substances cause more urinary tract infections compared to cholesterol alone: tannins, Dowex 50 H+, residues, n-butanol and methanol. Tiliroside, a fern component that enters the bladder cavity of mice; Neither cinnamon nor quercetin is carcinogenic. Tannins are the most toxic (average

Lethal dose:

0.16 mg/g) and carcinogenic. No carcinogenic substance inhibits the growth of *E. coli*¹². A further test on the carcinogenicity of June fern leaves were dried, ground and placed into the diet of 7-week-old non-inbred Lister rats (20 of all sexes) based on 33% dry weight. The duration of consumption of the fern is only 64 days, but this is sufficient time for all experimental animals to develop multiple ileal adenocarcinoma within 7 months to a year after starting to consume the fern. Out of 40 checks nothing happened. In fact, intestinal tumors are rare in mice, so this finding has additional significance. Subsequent experiments confirmed these results and showed age-related injuries for which young animals were at risk. The possibility of malignancy resulting from a non-specific diet will be eliminated because the leaf residue after extraction is not carcinogenic¹³. Bracken Fern toxicity on Humans:- Human exposure to fern poison can

occur in three main ways: eating the plant, making physical contact with it or especially its spores, and eating the milk of animals. Eating this plant is common in Japan, and although pretreatment with boiling water or soda ash reduces carcinogenicity, the risk of esophageal cancer increases by 2.1 in men and 3.7 in women. Young fern is like that in Japan. Since they are used as human food, a significant part of the research in the country focuses on the effects of traditional practices on plants. In water boiled for 5-10 minutes, the rate of ileal tumors is reduced to 75% (long incubation time and no sarcoma), but the number of bladder tumors increases. Therefore, boiling the fern in plain water eliminates carcinogens only to a certain degree, but when wood ash, sodium bicarbonate or added salt is used, as is often the case, the process will reduce the carcinogenic activity to a lower level (3/12 for wood ash, 1 for others /10), but that doesn't eliminate it completely. Today's storage methods, such as canning and the use of sealed containers, allow the fern to be eaten all year round, as demonstrated by Hodge (1973) and tested in an experiment on mice, because the new system will be different from the old and there are fewer. potentially carcinogenic³.

Human cancer and the possible connection with bracken :-

Cancer is still the leading cause of death. If the fern is to some extent responsible for cancer, it must be related to two groups of organs:

1. Respiratory diseases caused by inhalation of carcinogenic bacteria that the fern scales produce and carry in large quantities. It contributes greatly to the entry of airborne particles into the lungs.

2. In intestinal diseases, ingested carcinogens and fern leaf illudanes often form material containing epithelial cells before being destroyed by acidic

and/or alkaline environments middle digestive system. While lung cancer and colon cancer are the leading causes of cancer deaths among men in developed and developing regions of the world, and among women gastric cancer is second⁹. Industrial pollution and smoking have been linked to cancer, and spores can cause stress. In fact, no epidemiological studies have been conducted to establish a link between spores and cancer in ferns. Bracken can be viewed as a cause of cancer from two perspectives: people who eat fern products directly, and people who do not eat fern products directly but live with fern infestation space for long-term residents. There are significant epidemiological studies focusing on two areas that allow evaluation of the fern's role as an environmental carcinogen⁹.

Control of Bracken Fern:-

Pteridium aquilinum is a troublesome, perennial, worldwide invasive species that causes serious problems¹⁴. Manipulated fern control field trials were carried out simultaneously at six different sites in the UK. The effectiveness of (1) cutting and (2) antibiotics (asulam) as a control treatment was evaluated for three years based on seasonality of leaf activity and rhizome biomass. Cutting combination with Asulam is also included¹⁵.

Suitable ways for complete treatment are:-

- (i) No treatment,
- (ii) Cutting once a year,
- (iii) Cutting twice a year
- (iv) 1 spray asulam every year,
- (v) One slaughter in the 1st year / asulam in the 2nd year,
- (vi) Asulam in the 1st year / slaughter in the 2nd year. Annual cutting is stopped after 9/10 years¹⁴.

CONCLUSION:-

This review mainly explores the various properties of fern (*Pteridium aquilinum*), delving into its global impact and chemical availability. However,



it should be noted that *P. aquilinum* is also associated with the presence of ptaquiloside, a substance with carcinogenic potential. It contains a threat both to animals that penetrate plants and to humans who may ingest compounds derived from contaminated food, especially milk and meat. Besides ptaquiloside, which has a good study, attention should be paid to other compounds that cause whole plant toxicity, such as thiamine enzymes and prunasin. Thiamine enzymes are known for their anti-thiamine properties and induce short- and medium-term health benefits in monogastric animals. It is important to investigate all interventions and mitigation strategies, especially when they pose a risk to rhizomes and young leaves. Similarly, prunasin (cyanogenic glycoside) adds another layer of determination, as hydrogen cyanide is released when tissue is damaged. Preparation and cooking of fern has a clear effect on the concentration of these compounds. Various studies have shown that heat treatment or special cooking techniques (such as boiling or steaming) can reduce or eliminate ptaquiloside and thiaminase. In general, *P. aquilinum* as a medicinal plant has both positive and negative aspects. It is exciting to understand the ecological impact of its growth, develop new management strategies, and explore its medicinal potential. Additionally, a better understanding of ptaquiloside metabolism and the development of methods to reduce its presence in food and water may change safety practices. Essentially, the aim of this review is not only to provide connections between existing knowledge but also to stimulate future research. It is important to focus on the development of sustainable management to effectively control the spread of fern infestation and reduce its negative impacts. This will include removing ferns in ecologically sensitive areas, encouraging the growth of native plants and using biological control methods. Additionally, raising public awareness of the health risks associated

with the consumption of *P. aquilinum*, especially in livestock and products, is important to reduce human exposure to harmful compounds such as ptaquiloside. Consideration of the strengths and weaknesses of the literature touched upon in the previous review reveals the need for continued research and reform in this dynamic field. Periodic analysis of the ecological impact, medicinal potential and toxicity of ferns will provide a better understanding and guide management strategies.

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