

# *Phytolacca Americana*

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## Botany

*Phytolacca americana* L. (syn. *P. decandra* L.) belongs to the Phytolaccaceae [1]. English vernacular names include poke, pokeweed, pokeroot, pokeberry, inkberry, pigeon berry, American nightshade, scoke, pocan, red ink, and garget [2–5]. The plant is known as Kermes in German and as phytolaque in French [2].

## Chemistry

In the 19th century, the roots of *P. americana* were believed to contain an alkaloidal substance named “phytolaccine”, together with phytolaccic acid, tannin, resin, gum and fixed oil [6]. However, later researchers were unable to confirm the presence of any alkaloid [7–9]. Although this makes “phytolaccine” a confusing concept, the term still is occasionally encountered in modern toxicological literature [10,11].

After the presence of alkaloids had been disproved, phytochemical research on the roots of *P. americana* focused primarily on the presence of saponins. Ahmed et al. [8] reported the isolation of a toxic acidic steroidal saponin. Stout et al. [12] designated this material as phytolaccatoxin, and obtained from it, by acid hydrolysis, a triterpene aglycone named phytolaccagenin. Woo and co-workers [13–15] subsequently demonstrated that the roots also yielded the closely related aglycone phytolaccagenic acid. They isolated seven different triterpene saponins, which were designated as phytolaccosides A, B, D, E, G, F and D<sub>2</sub>. In addition, several sterols were identified [16].

Johnson and Shimizu [17] obtained, from the fresh berry juice of *P. americana*, 0.6% of a crude saponin mixture. This fraction afforded, on acid hydrolysis, the triterpene aglycones phytolaccagenin (the major aglycone), desmethylphytolaccagenin (= jaligonic acid), and phytolaccinic acid (= phytolaccagenic acid). Oleanolic acid, the major aglycone in berries of *P. dodecandra*, was detected only in a trace amount. The presence of

phytolaccagenin, jaligonic acid, and phytolaccagenic acid in the hydrolysate was confirmed by Kang and Woo [18]. These researchers also detected the structurally related pokeberrygenin and esculentic acid, together with a trace of acinosolic acid [18]. The berries of *P. americana* contain a considerable amount of red pigment, phytolaccanin, which is identical to the betanin pigment of beetroot (*Beta vulgaris*) [19,20].

The leaves and seeds of *P. americana* yield proteins which have been designated as pokeweed antiviral proteins (PAPs) because of their antiviral activity [21–24]. A pokeweed antiviral protein also occurs in the seeds of the related *P. acinosa* [25]. The seeds of *P. americana* also contain lignans that are known as americanin A, americanin B, and americanin D [26].

### Pharmacology and Uses

The root of *P. americana* was at one time described as an alterative, cathartic, emetic, a narcotic, and a gargle, as well as a remedy for conjunctivitis, cancer, dyspepsia, glandular swelling, chronic rheumatism, ringworm, scabies, and ulcers. There is no satisfactory evidence, however, that it has any therapeutical usefulness [2,11,27,28].

Poke root has also been used in non-western folk medicine for treating edema and rheumatism, and it is alleged that its saponins have anti-inflammatory activity [14]. A Chinese text book recommends the roots of *P. americana* and *P. acinosa* internally for oliguria, edema and ascites, and externally for trauma, hemorrhage, carbuncle, and pyogenic skin infections [29].

Poke berries have also been employed in folk medicine for the treatment of rheumatism and arthritis [28], and their purple juice has reputedly been used to color food and wine [19,27]. Similar to the fruit of *P. dodecandra*, which yields a potent molluscicidal substance known as “endod”, the fruit of *P. americana* has been shown to contain one or more molluscicidal principles [17,30].

The sprouts of the young poke plant are sometimes eaten as potherbs after being boiled in two changes of water [3].

The pokeweed antiviral proteins occurring in the leaves and seeds of *P. americana* exhibit antiviral activity and inhibit protein synthesis in cell-free systems [21,22,25,31]. The seed protein was shown to have immunomodulatory activity in experimental animals [23].

### Adverse Reaction Profile

The toxicity of *P. americana* is generally believed to reside in its triterpene saponins and its mitogenic proteins [8,28,32,33]. The toxicology of the related *P. dodecandra* has been reviewed by Duncan [34]. According to an

early source, death has occurred following the administration of 10 to 15 g of the juice of raw fresh leaves of *P. dodecandra* [35].

## General Animal Data

Macht [27] studied the toxicity of fluid alcoholic extracts of poke root and poke berries in experimental animals. The extracts were administered as such or in the form of saline suspensions obtained by evaporating the alcohol and replacing it by physiological saline. The saline suspensions proved to be very irritating, and their intraperitoneal lethality for mice, rats, and guinea pigs was found to be quite high. Intravenous injection into anesthetized cats markedly depressed respiratory and circulatory functions. Administration of diluted poke root extract by stomach tube to cats produced violent vomiting. Large oral doses of fluid extracts did not impair the kidney function of rabbits, but liver function was markedly impaired by this treatment.

Goldstein et al. [7] observed the following sequence of symptoms in cats following intraperitoneal administration of a hydroalcoholic extract, corresponding to 1.0 g of poke root per kg body weight: discomfort, retching and sometimes emesis; gradual loss of the use of hind and front legs; stupor, somnolence and diminished perception of pain; profound narcosis; slower and weaker heart beat and shallower respiration; and ultimately death from respiratory failure.

Ahmed et al. [8] tested the toxicity of an acidic steroidal saponin obtained from the root of *P. americana* in mice. Its intraperitoneal LD<sub>50</sub> was computed as 0.065 mg/kg. With lethal doses, the substance showed marked depressant activity, especially on circulation and respiration, and it acted as a potent convulsant in relatively larger doses.

Experimental studies of the toxicity of poke berries in poultry have produced conflicting results. In one feeding study, they were harmless to some chickens and a duck [36], whereas in another study the administration of berries to turkey poults produced a reduction of growth rate, ataxia, inability to walk and death [37].

Accidental poisoning in animals is rare, partly because the root (which is generally considered to be the most toxic part of the plant) is underground, and partly because the plant is not particularly palatable [38].

## General Human Data

Human intoxication by *P. americana* commonly involves an initial burning sensation in the mouth and throat, followed within a few hours by nausea, protracted vomiting, sometimes with hematemesis, salivation, profuse diaphoresis, severe abdominal cramps and pain, watery or bloody diarrhoea,

generalized weakness, headache, dizziness, hypotension and tachycardia [5,33,38–42]. Urinary incontinence, confusion, unconsciousness, and gross tremors of the hands may also occur [5], and sometimes melena, visual disturbances, weakened respiration, lethargy, stupor, and convulsions have been observed [10,38,42]. All recently described patients recovered within 24–48 hours, often with the aid of supportive care [5,33,40–42], but fatalities have occurred in the 19th century [33,42].

Several case reports specified that the plant had been used inappropriately, viz. by chewing the root without boiling it prior to consumption [42], by eating the raw leaves [40], or by drinking a herbal tea prepared by extracting the leaves and stems [5] or the powdered root [33] with boiling water. These comments can be retraced to a widespread belief that the young green shoots or leaves can be consumed safely as vegetables after boiling them in water, discarding the cooking water and then reboiling them [3,10,28,38,40,43]. Moreover, a Chinese text states that the toxicity of Shanglu (the root of *P. acinosa* or *P. americana*) may be greatly reduced by boiling the drug for two hours [29]. It should be noted, however, that an outbreak of 21 cases of pokeweed poisoning occurred in a group of campers, who had taken a pokeweed salad prepared by boiling, draining, and re-boiling the young leaves. Contrary to claims that this preparation ensures harmlessness, the campers experienced the typical symptoms of pokeweed intoxication, and four of them required hospitalization because of protracted vomiting and dehydration. The camp counselor had been preparing pokeweed salad for many years without apparent ill effects, and it remained unexplained, why his latest salad resulted in an outbreak of gastrointestinal illness [41]. So long as the factors which govern the toxicity of pokeweed preparations remain unknown, abstinence from any preparation seems the only course of action which is guaranteed to be absolutely safe.

Secondary sources generally agree that the root is the most toxic part and that toxicity increases with plant maturity, the only exception being that green berries are considered to be more toxic than mature red berries [10,28,41,42]. Unfortunately, such secondary statements are not supported by primary references, and controversy exists about the relative toxicity of poke berries [28]. It is sometimes alleged that ten berries, if eaten uncooked by a preschool child, are very toxic [10], whereas other sources feel that references to the poisoning of children by the berries are not conclusive [38]. A two-year-old child died after eating berries that were undisputedly pokeweed berries. An original report about this case has never been presented in the literature, however, because the hospital staff members involved disagreed over etiology and the autopsy findings. The hospital pathologist was convinced that the child died from a viral infection, but he noted enlarged lymphocytes, apparently showing mitotic activity, in the brain sections, which eventually led to the discovery of the mitotic capacity (see the section on hematological reactions) [43]. It is sometimes claimed that the berries are edible if cooked [10], but primary information on this

subject is quite limited. There is a recent report about a group of boy scouts and their leader, who ate pokeberry pancakes (prepared by stirring mashed pokeberries into pancake batter and frying the mixture over wood fire). No apparent side effects occurred other than mild or moderate diarrhoea [11].

In 1979, the American Herb Trade Association issued a policy statement that pokeroot should not be sold as a herbal beverage or food because of its toxicity. The Association recommended that no part of the mature plant should be sold for ingestion and that all poke products, except immature leaves, should be withdrawn from sale in the United States [33].

### Cardiovascular Reactions

Tachycardia and hypotension are commonly noted in intoxications by *P. americana* (see the section on general human data). In one case, ECG-abnormalities suggestive of ischemia were observed [42].

### Dermatological Reactions

The green plant and root often produce inflammation of the skin, and topical preparations derived from these parts can result in smarting and burning [44]. Early researchers claimed that this irritant action of poke root is not due to its toxic alcohol-soluble principle, but to one or more water-soluble principles [7].

According to a preamble of a Directive of the European Communities regarding cosmetic products, it is necessary to prohibit the use of *Phytolacca* spp. to protect public health [45].

### Gastrointestinal Reactions

Poisoning by *P. americana* is characterized by nausea, vomiting, abdominal cramps and pain, and diarrhoea (see the section on general human data). The latter effect explains, why pokeweed is reputed to be a cathartic (see the section on pharmacology and uses). It should be added, however, that saline suspensions, obtained by evaporating the alcohol from fluid alcoholic extracts of *P. americana* and replacing it by physiological saline, were shown to paralyze *in vitro* intestinal loops from cats and rabbits [27].

### Hematological Reactions

The roots of *P. americana* yield five physiochemically distinct proteins with mitogenic properties [46], whereas two mitogenic proteins have been found in the root of the related *P. octandra* [47,48].

*In vitro*, extracts of *P. americana* have mitogenic effects on human peripheral blood cells in dilutions up to 1:1 000 000 [49,50]. *In vivo*, large immature basophilic lymphocytes and typical plasma cells appeared in the peripheral blood of two adults shortly after accidental exposure to a root extract (one through the conjunctiva and the other through a subcutaneous puncture wound). An extensive search revealed no mitotic cells, and all other hematological findings were within normal limits [51]. Barker et al. [50] reported a significant increase in the number of plasmacytoid lymphocytes in the peripheral blood of children, who had either ingested the berries of *P. americana* or handled the berries with freshly cut or abraded hands. No distinctive clinical features were seen in association with this peripheral blood plasmacytosis.

The peripheral plasmacytosis may persist for two or more months [4,42].

### Ocular Reactions

Since pokeroor has been described as a remedy for conjunctivitis (see the section on pharmacology and uses), it should be noted that the dust of dried poke root is irritant to the eye and that occupational exposure to the fresh plant may result in serious inflammation of the eye lids [7]. Instillation of saline suspensions (obtained by evaporating the alcohol from fluid alcoholic extracts of *P. americana* and replacing it by physiological saline) into rabbit eyes resulted in marked reddening and irritation of the conjunctivae [27].

### Respiratory Reactions

Ahmed et al. [8] studied the effect of an acidic steroidal saponin obtained from the root of *P. americana* on the respiratory tract. Inhalation of the substance caused an extreme sternutatory effect, followed by rhinitis, pharyngitis, sore throat, cough with pains in the chest, and persistent headache.

Due to the potent irritant action of poke root, occupational exposure to its dust may cause severe complications. Two subjects, who were engaged in the milling of poke root and accidentally inhaled the dust, developed respiratory irritation and gastroenteritis, which were so severe that one subject required hospitalization. Several other occupants of the same building were also forced to discontinue their work because of rhinitis and gastroenteritis [7].

### Fertility, Pregnancy and Lactation

According to secondary sources, abortion in cows has been described as a result of pokeberry toxicity [18,37]. Yeung et al. [52] reported that acetone-

precipitated powders obtained from the related *P. acinosa* showed mid-term abortifacient activity in mice, when given in intraperitoneal doses corresponding to 4.76 g of the fresh leaves, 4.35 g of the fresh roots, or 0.55 g of the fresh seeds per kg body weight. As the abortifacient activity could be destroyed by heat and by the proteolytic enzyme pepsin, the suggestion was raised that the active principle was most likely a protein. Stolzenberg et al. [53] observed antifertility activity of a butanolic extract from the related *P. dodecandra*, when given by intrauterine injection to the rat. In contrast, oral treatment of mice with an aqueous extract of *P. dodecandra* had no significant effects on reproduction [54], and subcutaneous treatment with an aqueous extract of *P. esculenta* for 5 days did not affect the fertility of female mice [55].

Saponins from *P. americana* [56], *P. dodecandra* [57,58], and *Phytolacca* plants used in Chinese medicine [29] have all been shown to possess spermicidal properties.

No data have been recovered from the literature about the teratogenicity of *P. americana* or about its effects on the suckling child, when used by a breast-feeding mother.

## Mutagenicity and Carcinogenicity

Butanol extracts from the seeds or fruit of *P. americana* did not demonstrate mutagenic activity in *Salmonella typhimurium* strain TM677 either in the presence or absence of a metabolic activating system [30].

Data about the carcinogenicity of *P. americana* have not been recovered from the literature.

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