The cover features a photograph of a forest floor. A large, weathered log lies diagonally across the upper half. In the foreground, two white bloodroot flowers with yellow centers are in bloom, surrounded by green leaves and moss. The background is dark and filled with fallen leaves and twigs.

Bloodroot
Sanguinaria canadensis
An Annotated Bibliography

MARY L. PREDNY AND
JAMES L. CHAMBERLAIN

Bloodroot (*Sanguinaria canadensis*)

is an important herbal medicinal plant collected from the hardwood forests of the Southern United States.



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Bloodroot (*Sanguinaria canadensis*): An Annotated Bibliography

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Statements made by authors cited in this document concerning medicinal uses and properties may not have been evaluated by the Food and Drug Administration, and are included for educational purposes only. Discussion of medical uses is not intended for diagnoses, treatment, cure, nor prevention of disease. Bloodroot is toxic and should not be ingested. Information in this publication about medicinal uses is intended for educational purposes only and is not a substitute for the advice of qualified healthcare professionals. Material presented in this document is for reader information only and does not imply endorsement by the U.S. Department of Agriculture.

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Abstract

Bloodroot (*Sanguinaria canadensis*) is a spring-blooming herbaceous perennial found mainly in rich woods throughout the Appalachian Mountain regions and across the Eastern United States. The common name bloodroot and scientific name *Sanguinaria* denote the blood-red sap found throughout the plant, particularly in the roots. This sap contains the alkaloids that make this plant so valuable. Native Americans used bloodroot as a dye, love charm, and medicine. European colonists adopted Native American medicinal uses to suit their own needs. Bloodroot was described in pharmacopoeias as early as the 1800s, with detailed descriptions of the plant, constituents, therapeutics, and case studies. The popular use of herbal remedies declined in the 1920s with the development of the pharmaceutical industry, though there has been a renewed interest in herbal medicine as research confirms the efficacy of some traditional uses. Bloodroot is still wildcrafted in the United States for domestic and international uses. This report describes the characteristics and growth habits of bloodroot, summarizes the various uses of the herb, reviews the global market and trade, examines the conservation status of the plant, and identifies needs for future research.

Keywords: Bloodroot, conservation, dental products, medicinal herbs, nontimber forest products, *Sanguinaria*.

Nomenclature

Bloodroot (*Sanguinaria canadensis*), a member of the Papaveraceae family, is known by several common names. According to Sanders (2002), the various common names refer to the many uses or properties of the plant. Bloodroot and red root are two names that refer to the dark-red sap found throughout the plant, particularly in the roots. Puccoon is a Native American term for a red dye; the names puccoon, paucon, pauson, red puccoon, coonroot, and Indian paint are all references to the Native American use of the plant to color skin, clothes, and baskets. Tetter is an Old English word for skin disease; the name tetterwort refers to the external use of bloodroot to treat warts, benign skin tumors, eczema, and other afflictions of the skin. The name sweet slumber denotes the use of the plant to induce sleep, and snakebite indicates the plant's poisonous elements, which have been known to be fatal when ingested in large amounts.

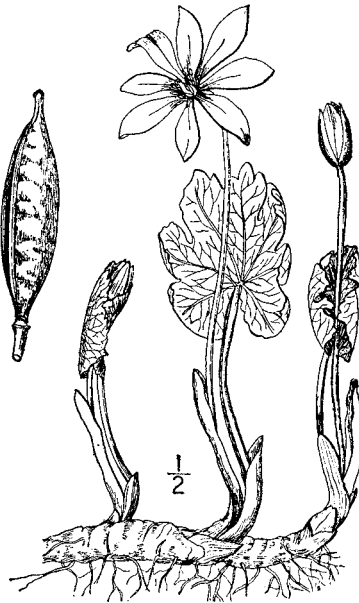


Figure 1—Bloodroot plant (Britton and Brown 1913).

Botany and Ecology

Bloodroot is one of the first herbaceous perennials to emerge in early spring (Reed 1999–2002). Plants reach a height of 6 to 12 inches at maturity, though they are typically only half that height at the time of bloom (Foster and Duke 2000). Each plant consists of a single leaf wrapped tightly around a flower bud; the leaf opens to expose the flower as it blooms (Missouri Botanical Garden 2002, Sievers 1930) (fig. 1).

Bloodroot leaves are kidney shaped, with five to nine rounded lobes arranged palmately and covered with a whitish-gray down (Grieve 1931, Harding 1936, Sievers 1930). The pale underside of the leaf is prominently veined (Grieve 1931, Harding 1936). Once the flowers have faded, the basal leaves persist until August, when they turn a deeper green and reach their maximum size of 6 to 10 inches (Harding 1936, Missouri Botanical Garden 2002, Sievers 1930).

Each waxy, white flower grows on a single stem up to 8 inches in height, blooming around late March and early April (Harding 1936, Sievers 1930). Flowers are roughly 2 inches in diameter, with gold-colored stamens in the center (Foster and Duke 2000, Harding 1936, Miller 1988). Whereas other

members of the Papaveraceae family have flowers with 4 petals, bloodroot flowers have 8 to 10 petals arranged in 2 to 4 rows. Lehmann and Sattler (1993) state that in the genus *Sanguinaria*, the extra petals replace some of the stamens in a process known as homeosis, where one structure either partially or completely replaces another.

Bloodroot flowers typically bloom for only a few days, opening during the day and closing each night (Hendershot 2002). Two mechanisms controlling this are temperature and sunlight. Flowers do not open when temperatures are under 8 °C (46 °F) (Lyon 1992). As temperatures rise, flowers open earlier and close later; though on cloudy days when the sun is obscured, they will open later and close earlier.

Bloodroot flowers are hermaphroditic, with both male and female organs (Fern 1997–2000). According to Lyon (1992), this makes it possible for the plants to be facultatively xenogamous, with the ability to either self-pollinate or be cross-pollinated. The initial female phase lasts 1 to 3 days. Self-pollination cannot occur during this time, because the stamens are positioned to avoid contacting the stigma even when the flower closes at night. The main pollinators during this phase are bees (members of the Adrenidae, Apidae, and Halictidae), but can also include other insects such as Hymenoptera, Hemiptera, and Coleoptera (Judd 1977, Lyon 1992). If flowers have not been pollinated in the initial 3 days due to cold temperatures, rain, or lack of pollinator visitation, the stamens bend down to contact the stigma and self-pollination occurs (Lyon 1992).

Bloodroot seeds produce a lipid-rich appendage called an elaiosome, a nutritious food source for ants (Hendershot 2002). Ants collect bloodroot seeds and carry them back to their nest, where they consume the elaiosome and discard the intact and viable seeds in old galleries or refuse tunnels. These refuse areas tend to be high in organic matter, phosphorus, potassium, and nitrogen—ideal for germinating bloodroot seeds. This mutually beneficial relationship between the bloodroot plant and native ants is known as “myrmecochory” or ant farming (Beattie and Culver 1982, Hendershot 2002). The ants benefit from the nutritious food source, while the seeds that are “planted” in ant nests are safe from predation by rodents, avoid competition with parent plants, and have access to the essential nutrients present in the underground nests (Heithaus 1981, Pudlo and others 1980).

The native range of bloodroot extends from Nova Scotia south to northern Florida, and west to Manitoba, western South Dakota, and eastern Texas (fig. 2) (Foster and Duke 2000; Miller 1988; U.S. Department of Agriculture, Natural Resources Conservation Service 2001). Bloodroot is

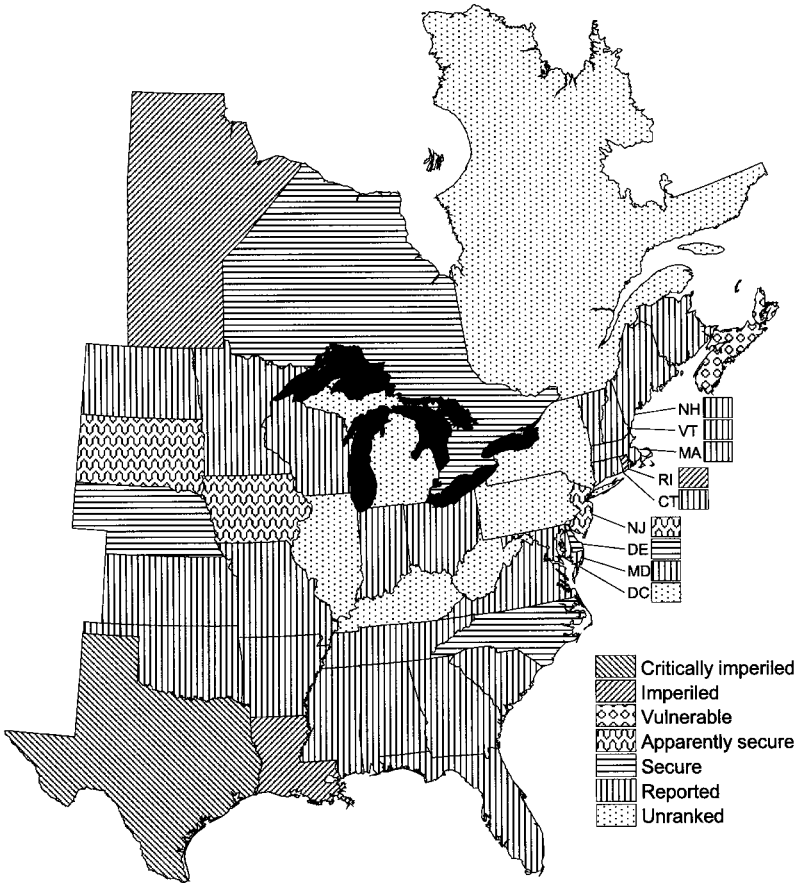


Figure 2—Bloodroot range and distribution [adapted from NatureServe Explorer (2002) and U.S. Department of Agriculture, Natural Resources Conservation Service (2001)].

mostly found in rich woodlands or on sunny-to-shady edges of wooded areas (Fern 1997–2000), on slopes (Reed 1999–2002), or on bottomlands along shaded streams (Miller 1988). The global heritage status rank is G5 and the national heritage status rank is N5, indicating that bloodroot is currently secure within its range (NatureServe Explorer 2002).

Bloodroot prefers light-to-medium well-drained soils with a sandy-to-loamy texture (Fern 1997–2000). Though most often found in semi- to full-shaded conditions, research has shown that in areas with sufficient soil nutrients, increased light levels from openings in the forest canopy due to fallen trees

or other causes can activate vegetative spread and increase local populations (Marino and others 1997). Bloodroot can tolerate a range of pH, but does best in soils with a pH of 5 to 7 or higher (Fern 1997–2000, Miller 1988). Soils with a layer of leaf cover in cool areas under deciduous trees are optimal (Fern 1997–2000). Bloodroot is an indicator species for birch-maple-basswood (*Betula* spp., *Acer* spp., and *Tilia americana*) hardwood forests (Sutherland 1999). Dormant plants can tolerate temperatures down to $-20\text{ }^{\circ}\text{C}$ ($-4\text{ }^{\circ}\text{F}$) (Fern 1997–2000), and are hardy in U.S. Department of Agriculture zones 4A to 9A (Horticopia, Inc. 2001).

Bloodroot can be propagated by seed, root division, or leaf cuttings (Fern 1997–2000). Seeds can be sown in outdoor beds in the spring or summer, or in a cold frame in winter. A cold stratification period is required for the seed to produce a root, then another warm and cold period to produce a shoot (Fern 1997–2000). Rhizomes can be divided by breaking them into small pieces, each of which should contain one bud. This is typically done in late summer or early fall after the leaves die back (Miller 1988). Leaf cuttings can be taken from shoots in late spring and set in a protected cold frame until the plants are established (Fern 1997–2000).

Chemical Constituents

Bloodroot exudes a bright orange-red sap from all parts when cut, with the highest concentrations found in the rhizome where the juices are stored. The sap contains isoquinoline alkaloids, red resin, and an abundance of starch (Foster and Duke 2000). Sanguinarine is the predominant alkaloid, making up 50 percent of the total alkaloid content (Bennett and others 1990). The alkaloids in the sap contribute to the medicinal properties of the herb, though they can also be poisonous in large doses, causing nausea, vomiting, dizziness or fainting, dilated pupils, and heart failure (Russell 1997).

Studies on environmental variables that affect the concentration of alkaloids in bloodroot rhizomes have shown that favorable environmental conditions result in higher concentrations of active constituents (Bennett and others 1990, Salmore and Hunter 2001b). Sources have indicated that alkaloid levels in roots are higher during and just after bloom (Bennett and others 1990, Farwell 1915); however, the rhizomes are traditionally harvested in autumn after dieback to allow plants the opportunity to disperse seeds (Grieve 1931, Harding 1936, Sievers 1930).

Uses

Medicinal

Native Americans used bloodroot as a dye, love charm, and potent medicine (Moerman 1999). European colonists learned of the Native American medicinal uses for the herb and adopted them to suit their own needs. Bloodroot was described in pharmacopoeias as early as the 1800s, with detailed descriptions of the plant, constituents, therapeutics, and case studies (Cook 1869, Ellingwood 1919, Felter 1922, Felter and Lloyd 1898, Petersen 1905, Potter 1902, Winterburn 1882–1883).

The alkaloids in bloodroot have strong antibiotic and anti-inflammatory properties (Godowski 1989). The herb has also been described as having antiseptic, cathartic, diuretic, emetic, emmenagogue, escharotic, expectorant, febrifuge, sedative, spasmolytic, stimulant, and tonic properties (Fern 1997–2000, Grieve 1931, Haughton 2001). In small doses, bloodroot is relaxing and soothing, particularly on the bronchial muscles. In moderate doses, the herb has stimulating and emetic properties. Large doses can cause irritation of the mucus membranes (Grieve 1931, Haughton 2001).

Bloodroot is currently used to cause expectoration and to clear the respiratory pathways of mucus. The herb can be taken internally to treat a variety of ailments such as asthma, emphysema, laryngitis, bronchitis, pharyngitis, sore throats, and croup (Fern 1997–2000, Haughton 2001). Cough lozenges are made by mixing fresh sap from roots with maple syrup or sugar (Miller 1988, Sanders 2002). A homeopathic remedy containing bloodroot has also been used to treat migraines (Fern 1997–2000, Haughton 2001).

Fresh bloodroot sap or an infusion of the root can be applied externally to treat warts, benign skin tumors, ulcers, eczema, chilblains, or ringworm (Fern 1997–2000, Foster and Duke 2000, Grieve 1931). The dried powder can be sniffed to treat nasal polyps (Fern 1997–2000, Haughton 2001).

Of particular note is the use of bloodroot to treat skin cancers (Fern 1997–2000, Foster and Duke 2000, Grieve 1931). In the mid-19th century at the London Middlesex Hospital, Dr. J. Weldon Fell experimented with the use of bloodroot to treat skin cancers. Although used extensively at that time, the treatment eventually fell out of use until its revival in the 1960s for minor skin tumors, particularly those in the nose and ears (Sanders 2002). From the 1920s up to 1960, Harry Hoxsey operated a medical practice—with clinics in several States—treating cancer patients with a formula

containing bloodroot and several other herbs. In the 1950s, however, the American Medical Association called Hoxsey's tonics and salves to the attention of the U.S. Food and Drug Administration (FDA). Claiming that Hoxsey used herbs not approved for human consumption, the FDA forced him to shut down his clinics. Hoxsey reopened his clinic in Tijuana, Mexico, where it continues to operate today. Most of the herbs in Hoxsey's formulas, such as bloodroot, have been found to have antitumor properties in recent scientific research. Several biographies and articles have been written about Harry Hoxsey and the conflict between natural homeopathic treatment and conventional medicine (Center for Alternative Medicine Research, University of Texas 1999; Phillips 2001; Walters 1993). Researchers are currently studying the ability of bloodroot alkaloids to selectively fight cancer cells without harming normal cells. Although it has experimentally shown antiproliferative potential towards human carcinoma cells, current *in vitro* studies are not conclusive and more research is needed before bloodroot is considered for development as a commercial anticancer drug (Ahmad and others 2000).

Dental

Sanguinarine, the medicinally valuable alkaloid found in bloodroot sap, is purported to have antibacterial and anti-inflammatory properties that inhibit the formation of plaque and reduce gingival inflammation and bleeding (Foster and Duke 2000, Miller 1988, Sanders 2002). Research has shown that the alkaloid is retained in the mouth for long periods after brushing, providing longer resistance to plaque and gingival inflammation (Godowski 1989). Sanguinarine has been used in toothpaste and oral rinses; one of the most widely available dental products containing the alkaloid was Viadent[®], a Colgate-Palmolive product originally formulated by Vipont Pharmaceutical, Inc.

During the 1980s and 1990s, clinical studies on both animals and humans debated the safety and effectiveness of dental products containing sanguinarine (reviewed in Frankos and others 1990, Munro and others 1999, Schwartz 1986). Some studies found the sanguinarine regimen to be significantly effective in controlling plaque, gingival inflammation, and/or bleeding (Hannah and others 1989; Harper and others 1990; Klewanski and Roth 1986; Koczyk and others 1991; Southard and others 1984, 1987; Tenenbaum and others 1999; Wennstron and Lindhe 1985), whereas others found no significant difference from toothpastes or oral rinses that did not contain sanguinarine (Cullinan 1997, Drisko 1998, Mallatt and others 1989, Mauriello and Bader 1988, Polson and others 1996). After years of debate, several sources conceded that the differing results of these studies were

probably due to variations in research design, and studies that combined both toothpaste and oral rinse containing sanguinarine showed significant reduction in plaque and gingivitis compared to placebos (Kopczyk and others 1991, Kufnec and others 1990).

In the preceding studies, only a few individuals had adverse reactions to the products. The observed negative side effects were either a burning or stinging sensation in the mouth, or a sloughing of the epithelium cells (Frankos and others 1990, Kopczyk and others 1991). In 1990, a panel of experts was hired by Vipont Pharmaceutical, Inc. to thoroughly review the literature and published research on sanguinarine to determine the potential danger of the products containing the alkaloid. The panel concluded that the appropriate safety research had been completed; none of the studies found the level of sanguinarine present in Viadent[®] products to be of any potential danger to consumers, even under exaggerated use conditions (Frankos and others 1990). In 1999, however, Damm and others (1999) published a study that indicated an association between Viadent[®] usage and the presence of a precancerous disease of the mouth known as leukoplakia. Leukoplakia appears as a white patch on the tongue, gums, or inside of the mouth that cannot be rubbed off, and cannot be diagnosed clinically or histopathologically as any other condition (Allen and others 2001). Leukoplakia lesions are often associated with tobacco use, though they occasionally appear ideopathically. Because most of the previous studies on sanguinarine concluded after just 6 months, the association of leukoplakia with long-term use of sanguinarine products had not been identified (Damm and others 1999).

In the following years, several additional studies concluded that the development of oral leukoplakia of the maxillary vestibule was significantly higher in Viadent[®] users than in nonusers, and sanguinarine was removed from the Viadent[®] product formula (Allen and others 2001, Eversole and others 2000, Mascarenhas and others 2001, Wagner 2001). Results of these additional studies concluded that:

- Viadent[®] users were 10 times more likely to develop lesions than nonusers
- Risk was highest with use of both toothpaste and oral rinse, followed by use of oral rinse alone, and lowest for users of toothpaste only
- There was a dose-response reaction (increased incidence of lesions with increased duration or intensity of use)
- Risk of developing lesions increased with age

- A percentage of lesions resolved after discontinued use of the products
- Few lesions showed severe dysplasia or developed carcinoma (although because of the recent discovery of this association the long-term evaluation of these lesions has not yet been determined) (Allen and others 2001, Eversole and others 2000, Mascarenhas and others 2001, Wagner 2001)

Other Uses

Feed additive—Bloodroot can be used as a botanical dewormer for cattle and sheep (Duval 1997). A German company, Phytobiotics GmbH, is using bloodroot to produce livestock feed that fattens animals naturally; in 2000, the company purchased 40 metric tons of bloodroot from the Southern Appalachians, which was less than a third of what they needed (Clark 2002). Bloodroot is not grown commercially anywhere in the world; this new use of the herb as a feed additive puts added pressure on wild populations. Yellow Creek Botanical Institute in Graham County, NC, recently began experimentally cultivating bloodroot under forest canopy to help meet this high demand without threatening the sustainability of wild resources (Clark 2002). Successful cultivation would mean new income opportunities for area landowners.

Pesticide—Previous uses of bloodroot have implied insecticidal and phototoxic properties for the herb, though the compounds responsible for these effects were not isolated or studied until recently. Tuveson and others (1989) found that sanguinarine chloride, when irradiated with near ultraviolet light in the presence of a catalyst, produces hydrogen peroxide. The photoionization of sanguinarine also produces hydrated electrons, which are very reactive towards numerous biological targets such as amino acids and DNA bases. Tuveson and others (1989) also found sanguinarine chloride to be significantly toxic to certain strains of bacteria, but not to cabbage looper larvae (*Trichoplusia* spp.). Arnason and others (1992) expanded this research to test sanguinarine's toxicity to mosquito larvae (*Aedes atropalpus*) at varying concentrations; they found phototoxic qualities similar to those found by Tuveson and others (1989), with significant mortality of mosquitoes in the larval stage. The exact mechanisms causing these reactions are still uncertain.

Market Trends

In the early 1990s, the estimated domestic market for bloodroot was 200 tons annually, while the estimated world market was 2,000 tons (Miller

1988; U.S. Department of Agriculture, Forest Service 1993). In 2002, retail prices for common preparations of bloodroot included: \$0.15 to \$0.22/g or \$3.25 per ounce of powdered wildcrafted root; \$3.35 per ounce of cut dried wildcrafted root; \$13.99 to \$14.33 per ounce of liquid extract; \$2.44 to \$3.05 per ounce of cut and sifted wildcrafted root; and \$0.54 per seed for propagation (Green Canyon, n.d.; Herbal Wise, n.d.; HerbTrader, n.d.).

Conservation

Bloodroot is listed as “At-Risk” by the United Plant Savers organization. Often collected from the wild and marketed domestically and internationally, the plants on the “At-Risk” list have experienced pressure due to overcollection or habitat loss. This pressure, combined with the innate sensitivity and rarity of the plants listed, has led to the rapid decline of wild populations in their native ranges (United Plant Savers, n.d.).

Several recent publications have evaluated ecological issues that may affect the conservation and future proliferation of bloodroot. Fritz and Merriam (1993) studied the ability of several forest species to survive in the fence-row habitats that connect isolated patches of plants. They concluded that bloodroot could persist in these exposed conditions, but that new populations are unlikely to become established.

Pudlo and others (1980) studied the dispersal of bloodroot seeds by ants in areas with varying degrees of disturbance. In highly disturbed sites, the diversity of ant populations decreased, resulting in a decrease in seed dispersal and an increase in asexual reproduction. Without a means of seed dispersal, the advantages a species such as bloodroot gains through sexual reproduction and adaptation are lost. In areas colonized by invasive fire ants (*Solenopsis invicta*), native ant species have decreased by as much as 70 percent (Porter and Savignano 1990). This decrease of native ant species has had a strong negative impact on myrmecochorous species such as bloodroot. Fire ants also collect seeds with elaiosomes, but often damage the seeds while consuming the appendage, or deposit them in areas that are unfavorable to germination and establishment. As the range of fire ants continues to spread throughout the Southeastern United States, so does the threat of vulnerability to the obligate myrmecochorous bloodroot (Zettler and others 2001). Heithaus (1981) showed that with decreasing numbers of native ant species, bloodroot seeds are not as likely to be distributed as far from the parent plants and are also more susceptible to predation by rodents.

Discussion

As one of the earliest and most beautiful spring flowers, bloodroot has received a lot of attention, with an abundance of literature describing its botanical properties. The unique flowers and myrmecochorous seeds of the plant have also made bloodroot the subject of numerous ecological studies. With a long history of medicinal use, clinical research on the herb's effectiveness and safety is readily available. Ongoing research into other applications for bloodroot, particularly in animal feeds or as a botanical pesticide, may lead to additional markets for the plant. Conservation issues caused by habitat loss and decreasing numbers of seed dispersing ants can be speculated about, but without more information on the plant's ability to adapt and regenerate after harvest, the projected outlook on sustainability remains incomplete.

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Annotated Bibliography

Research Literature

Ahmad, N.; Gupta, S.; Husain, M.M. [and others]. 2000. Differential antiproliferative and apoptotic response of sanguinarine for cancer cells versus normal cells. *Clinical Cancer Research*. 6: 1524-1528.

Explores the cancer-fighting abilities of sanguinarine in a clinical setting. For both human epidermal carcinoma and normal human epidermoid keratinocytes, sanguinarine has shown dose-dependent antiproliferative and apoptotic (cell death) potential, without harming normal cells. Research materials, methods, results, and a discussion are presented.

Keywords: Cancer, medicinal uses, research, sanguinarine.

Allen, C.L.; Loudon, J.; Mascarenhas, A.K. 2001. *Sanguinaria*-related leukoplakia: epidemiologic and clinicopathologic features of a recently described entity. *General Dentistry*. 49(6): 608-614.

Describes the oral mucosa leukoplakias associated with Viadent® use. Leukoplakias are premalignant white patches that cannot be rubbed off or diagnosed clinically or histopathologically as any other condition. These lesions are usually idiopathic or associated with tobacco use. Although the bloodroot extract used in dental products was initially considered to be harmless, the mixture of benzophenanthridine alkaloids in the extract have shown to interact with DNA *in vitro*, indicating mutagenic potential. The case study presented in this article shows that Viadent® usage increased the risk of developing these lesions by 10 times, with a dose-dependent response. Because the harmful effects of dental products containing bloodroot have only recently been discovered, the understanding and knowledge of treatment is limited.

Keywords: Alkaloids, cancer, case studies, oral leukoplakia, research, Viadent®.

Arnason, J.T.; Guerin, B.; Kraml, M.M. [and others]. 1992. Phototoxic and photochemical properties of sanguinarine. *Photochemistry and Photobiology*. 55(1): 35-38.

Examines the photochemical properties of sanguinarine. Sanguinarine was phototoxic to mosquito larvae in the presence of near-ultraviolet light at concentrations as low as 0.05 parts per million (ppm). This toxic effect

proved chronic over time, with 100 percent mortality within 5 days at concentrations of 0.15 ppm and higher. Once surviving larvae reached the pupal and adult stages, the phototoxic effects were no longer observed. The chemical processes are discussed.

Keywords: Pesticide use, phototoxicity, research, sanguinarine.

Beattie, A.; Culver, D.C. 1982. Inhumation: how ants and other invertebrates help seeds. *Nature*. 297(5868): 627.

Describes the mutual benefits of inhumation, where ants and other invertebrates disperse seeds of certain plants and aid in germination. An example of this is myrmecochory—where ants collect seeds, carry them to their nest to consume the nutritious appendage called an elaiosome, and discard the viable seeds in old chambers that are perfect for germination. Ants benefit from the nutritious elaiosome, and seeds benefit from ant dispersal and nutritious soil for germination. When ants are absent, bloodroot can propagate vegetatively by the rhizome; however, plant populations benefit from increased density and seed dispersion from the presence of ants. Seeds that are relocated to ant nests are also protected from predators.

Keywords: Ants, elaiosome, myrmecochory, seed dispersal.

Bennett, B.C.; Bell, C.R.; Boulware, R.T. 1990. Geographic variation in alkaloid content of *Sanguinaria canadensis* (Papaveraceae). *Rhodora*. 92(870): 57-69.

Compares the alkaloid content of bloodroot plants in various habitats. Populations in the Southern Appalachians had higher alkaloid levels than populations found north of West Virginia and Pennsylvania. The plants found in the North Carolina Coastal Plain had lower alkaloid levels than those in the western part of the State. Ecological conditions with a positive correlation to alkaloid content included soil clay content, soil structure, slope, and leaf litter depth. The highest alkaloid concentrations were found in populations growing in mature, undisturbed deciduous forest in mountain-like habitats. Other related factors include light, pH, moisture, soil chemistry, temperature, altitude, successional status, geographical location, plant tissue, tissue age, cell age, and herbivory. A correlation between the weight and volume of rhizomes and sanguinarine indicated an accumulation of the alkaloid over time. Leaf size was not correlated with alkaloid content. The concentration of alkaloids in the rhizome peaks in early spring, and gradually decreases throughout the summer.

Keywords: Alkaloids, ecology, habitat, range, research, sanguinarine.

Cullinan, M.P.; Powell, R.N.; Faddy, M.J.; Seymour, G.J. 1997. Efficacy of a dentifrice and oral rinse containing *Sanguinaria* extract in conjunction with initial periodontal therapy. *Australian Dental Journal*. 42(1): 47-51.

Investigates the effectiveness of a toothpaste and oral rinse that contain a bloodroot extract for reducing gingival inflammation in patients with periodontal disease. A randomized, double-blind study divided 34 patients into 2 groups: 1 group used toothpaste and rinse with bloodroot and zinc chloride, while the other group used a placebo toothpaste and rinse. Patients were examined for gingival index, plaque index, and probing pocket depths (bleeding upon probing) at the time of initial therapy, then 2 and 6 weeks later. Although the results showed significant improvement for both groups after the initial therapy, there was no significant difference between the treatment with the bloodroot extract and the placebo.

Keywords: Clinical studies, dental uses.

Damm, D.D.; Curran, A.; White, D.K.; Drummond, J.F. 1999. Leukoplakia of the maxillary vestibule – an association with Viadent®? *Oral and Maxillofacial Pathology*. 87(1): 61-66.

Uses dental case studies to identify an association between regular Viadent® use and a type of oral precancer known as leukoplakia. A review of 88 patients with leukoplakia of the maxillary vestibule showed that 84.1 percent were regular users of Viadent®; only 3 percent used other dental products. The lesions were confined to a specific area in the anterior of the mouth that is not adjacent to any major salivary gland ducts. Materials in this section of the mouth remain more concentrated and are less likely to be diluted by saliva. The appearance and characteristics of the leukoplakia lesions are specific, and are described. Previous research on the safety of bloodroot in dental products generally concluded at 6 months, which is not sufficient time to observe negative effects.

Keywords: Case studies, dental uses, leukoplakia, research, Viadent®.

Drisko, C.H. 1998. The use of locally delivered doxycycline in the treatment of periodontitis. Clinical results. *Journal of Clinical Periodontology*. 25(11, pt 2): 947-952.

Compares the effectiveness of locally delivered doxycycline to sanguinarine chloride, scaling and root planing, and a vehicle control for the treatment of

adult periodontitis in a multicenter, randomized, parallel-design controlled clinical trial. Results showed that the doxycycline treatment was comparable to scaling and root planing and superior to sanguinarine chloride and the vehicle control for reducing signs of adult periodontitis.

Keywords: Clinical studies, dental uses.

Duval, J. 1997. The control of internal parasites in cattle and sheep. *Ecol. Agric. Proj. Publ.* - 70. http://www.eap.mcgill.ca/general/home_frames.htm. [Date accessed: March 8, 2004].

Lists bloodroot as a plant with deworming properties when ingested by cattle or sheep.

Keywords: Animal feed additive, dewormer.

Dzink, J.L.; Socransky, S.S. 1985. Comparative *in vitro* activity of sanguinarine against oral microbial isolates. *Antimicrobial Agents and Chemotherapy*. 27(4): 663-665.

Shows that dental products with sanguinarine effectively decrease the formation of plaque, and are held in the mouth in high concentrations for several hours after use. Methods of action are discussed in detail.

Keywords: Clinical studies, dental uses, sanguinarine.

Eversole, L.R.; Eversole, G.M.; Kopick, J. 2000. *Sanguinaria*-associated oral leukoplakia. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics*. 89: 455-464.

Characterizes the maxillary gingival leukoplakia lesions associated with the use of dental products containing bloodroot. Biomarkers and ploidy data were compared and contrasted for leukoplakias and other forms of benign and premalignant oral cancers believed to be caused by dental products containing sanguinarine. The analysis and findings are described in detail. The lesions associated with dental products containing bloodroot appear in the anterior maxillary gingiva/mucobuccal fold region, which is usually pouched during forced rinsing. This area is not a common site for other forms of leukoplakia. The lesions do not show evidence of severe dysplasia, nor have any cases of carcinoma been reported; therefore, the progression to squamous cell cancer is unknown.

Keywords: Clinical studies, dental uses, leukoplakia.

Farwell, O.A. 1915. The proper time to collect *Sanguinaria*. American Journal of Pharmacy. 87: 97-98.

Reviews previous research, adding more datasets for the year-round evaluation of alkaloid content in bloodroot rhizomes. The authors conclude that the flowering period, when the alkaloid concentration is highest, is the best time to collect roots.

Keywords: Alkaloids, harvest, research.

Frankos, V.H.; Brusick, D.J.; Johnson, E.M. [and others]. 1990. Safety of *Sanguinaria* extract as used in commercial toothpaste and oral rinse products. Journal of the Canadian Dental Association. 56(7): 41-47.

Presents the results of an evaluation of clinical safety studies on Viadent® dental products containing sanguinarine. The expert panel conducting the evaluation concluded that data from previous research sufficiently demonstrated the safety and effectiveness of these products. The panel also concluded that the clinical study findings of adverse effects such as reproductive, cardiovascular, or ocular toxicity or carcinogenicity were unfounded, anecdotal, not sufficiently corroborated, nor consistent enough to substantiate concern. Provides a thorough review of research literature and discussion.

Keywords: Adverse reactions, clinical studies, dental uses, research reviews, toxicity, Viadent®.

Fritz, R.; Merriam, G. 1993. Fencerow habitats for plants moving between farmland forests. Biological Conservation. 64(2): 141-148.

Tests the ability of several woodland herbs to survive and proliferate along fencerow habitats. Fragmentation of forested areas has decreased habitat and increased isolation of many plant species. The ability of a plant species to survive in a fencerow, riparian strip, hedgerow, or roadside habitat determines the genetic and demographic flow and links to other forested populations. In order for plants to survive as a population, they must find the environment suitable to grow and reproduce repeatedly in increments over a period of years. Plants must be able to thrive under increased exposure to light and wind, with increased temperatures and decreased humidity. The studies found that although bloodroot could survive in these conditions, plant populations were ephemeral and unlikely to establish themselves in numbers suitable for incremental movement.

Keywords: Ecology, habitat, research.

Godowski, K.C. 1989. Antimicrobial action of sanguinarine. *Journal of Clinical Dentistry*. 1(4): 96-101.

Summarizes the antimicrobial properties of sanguinarine, with a focus on its effectiveness in reducing plaque and gingivitis when used in dental products. Sanguinarine is antibacterial for both gram-positive and gram-negative bacteria, antifungal against *Candida* and dermatophytes, antiprotozoal against *Trichomonas*, and anti-inflammatory. Clinical safety research has shown that sanguinarine is not absorbed orally, does not induce mucosal irritation or sensitization in exaggerated doses, and does not induce mutagenicity *in vitro* or *in vivo*. Sanguinarine is effective in preventing the adhesion of plaque to the salivary pellicle covering the tooth, and is contained in the mouth in effective concentrations for long periods after use. A table of clinical studies on dental products containing sanguinarine is included. It is concluded that the combined use of dentifrice and oral rinse containing sanguinarine significantly reduces plaque, gingivitis, and bleeding indexes. Mechanisms of action are discussed.

Keywords: Clinical studies, dental uses, research reviews, sanguinarine.

Hakim, S.A.E. 1968. Sanguinarine, a carcinogenic contaminant in Indian edible oils. *Indian Journal of Cancer*. 10: 183-197.

Describes cases of food poisoning in India caused by adulteration of edible oils with seeds from the weed argemone (*Argemone mexicana*), which contains the alkaloid sanguinarine. Adulteration of oils with argemone is associated with high incidence of dropsy, heart disease, abortions, glaucoma, diarrhea, and death. This publication describes epidemics caused by argemone food poisoning, the alkaloid sanguinarine which causes the poisoning, clinical animal studies demonstrating the detrimental effects of sanguinarine, the metabolism of sanguinarine into carcinogenic substances, the causes and hazards of adulteration of edible oils, and cancers that have been attributed to consumption of related substances throughout the world.

Keywords: Cancer, research, sanguinarine.

Hannah, J.J.; Johnson, J.D.; Kuftinec, M.M. 1989. Long-term clinical evaluation of toothpaste and oral rinse containing *Sanguinaria* extract in controlling plaque, gingival inflammation, and sulcular bleeding during orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*. 96: 199-207.

Evaluates the effectiveness of a toothpaste and oral rinse containing bloodroot for reducing plaque, gingival inflammation, and sulcular bleeding for orthodontic patients. After an initial oral hygiene period, subjects were divided into two groups—one receiving Viadent® products and the other receiving products with the same base formula, but without bloodroot. Results showed that the bloodroot products were significantly better than placebos at reducing plaque, gingival inflammation, and sulcular bleeding.

Keywords: Clinical studies, dental uses, Viadent®.

Harkrader, R.J.; Reinhart, P.C.; Rogers, J.A. [and others]. 1990. The history, chemistry, and pharmacokinetics of *Sanguinaria* extract. Journal of the Canadian Dental Association. 56(7): 7-12.

Presents the sources, historical uses, chemical analysis, biochemistry, and pharmacokinetics of benzophenanthridine and related alkaloids derived from bloodroot extract, particularly as they are used in dental products. A list of products and manufacturers is included.

Keywords: Alkaloids, dental uses, history, products.

Harper, D.S.; Mueller, L.J.; Fine, J.B. [and others]. 1990. Effect of 6 months use of a dentifrice and oral rinse containing *Sanguinaria* extract and zinc chloride upon the microflora of the dental plaque and oral soft tissues. Journal of Periodontology. 61(6): 359-363.

Supports previous research findings that dental products containing *Sanguinaria* extract are clinically effective at reducing plaque and gingivitis. Sixty gingivitis patients were divided into 2 groups—with 30 receiving the treatment (Viadent® products) and 30 receiving comparable placebo products in a randomized, double-blind, parallel-design study. After the 6-month trial period, participants receiving the Viadent® treatment showed a significant reduction in plaque accumulation, gingivitis, and bleeding. Four individuals in the placebo group dropped out of the study due to scheduling conflicts, two individuals in the active group dropped out because they didn't like the taste of the products, and one individual in the active group dropped out due to an intra-oral condition not related to the study. No adverse side effects were reported.

Keywords: Clinical studies, dental uses.

Heithaus, E.R. 1981. Seed predation by rodents on three ant-dispersed plants. Ecology. 62(1): 136-145.

Examines the loss of seeds to predation by rodents such as squirrels, chipmunks, mice, and some birds. A detailed methods section describes the process used to record and observe data in the field. Results showed that the seeds of spring-flowering plants are a major source of food for rodents. In areas with fewer ant populations, loss of seeds to rodents was increased. This decreases local genetic variability, and plant sexual reproduction efforts are wasted.

Keywords: Ecology, research, seeds.

Judd, W.W. 1977. Insects associated with flowering bloodroot, *Sanguinaria canadensis* L., at Fanshawe Lake, Ontario [pollinators]. Entomological News. 88(1/2): 13-17.

Observes pollinators of bloodroot at Fanshawe Lake in Ontario in 1975. Insects in Hemiptera, Coleoptera, and Hymenoptera were collected. The most dominant pollinators were bees in the Andrenidae, Halictidae, and Apidae.

Keywords: Pollinators, research.

Karlowsky, J.A. 1991. Bloodroot: *Sanguinaria canadensis* L. Canadian Pharmaceutical Journal. 124: 260, 262-263.

Provides details on the harvest and drying of bloodroot, chemical constituents and their physiological actions, historical and present-day uses, products and dosage, dental uses, side effects, and toxicity. Reviews of clinical research are included.

Keywords: Alkaloids, chemical constituents, medicinal actions, research reviews, toxicity.

Keller, K.A.; Meyer, D.L. 1989. Reproductive and developmental toxicology evaluation of *Sanguinaria* extract. The Journal of Clinical Dentistry. 1(3): 59-66.

Evaluates the toxicity of bloodroot extracts in rats and rabbits. No effects were observed on fertility, reproduction, or fetal development.

Keyword: Toxicity.

Klewanski, P.; Roth, D. 1986. *Sanguinaria* in the control of bleeding in periodontal patients. Compendium, Supplement. 7: S218-S221.

Compares the effectiveness of dental toothpastes containing bloodroot and zinc chloride, bloodroot alone, zinc chloride alone, and a placebo. After the conclusion of the 10-week study, the groups using bloodroot products alone showed the most significant reduction in plaque and bleeding.

Keywords: Clinical studies, dental uses.

Kopczyk, R.A.; Abrams, H.; Brown, A.T. [and others]. 1991. Clinical and microbiological effects of a *Sanguinaria*-containing mouth rinse and dentifrice with and without fluoride during 6 months of use. *Journal of Periodontology*. 62: 617-622.

Uses American Dental Association guidelines to test the safety and efficacy of dental products containing bloodroot. The study involved 120 patients in a 6-month, double-blind, placebo controlled, parallel investigation. Products containing bloodroot and zinc chloride produced significant results, with less plaque, gingival inflammation, and bleeding. The group using products with bloodroot, zinc chloride, and fluoride showed slightly better scores than the group using products with bloodroot and zinc chloride alone. One subject experienced a burning sensation when using the products and was excluded from the study—about 1 percent of the population has adverse reactions to constituents in dental products. It was concluded that the use of dentifrice and rinse containing bloodroot is safe and significantly more effective than placebos.

Keywords: Adverse reactions, clinical studies, dental uses.

Kuftinec, M.M.; Mueller-Joseph, L.J.; Kopczyk, R.A. 1990. *Sanguinaria* toothpaste and oral rinse regimen: clinical efficacy in short- and long-term trials. *Journal of the Canadian Dental Association*. 56(7): 31-33.

Evaluates previous studies on the effectiveness of dental products containing bloodroot. Both positive and negative results have been reported from short- and long-term studies. Research that combined both toothpaste and rinse containing bloodroot for a period of 6 months consistently showed positive results for reducing plaque, gingival inflammation, and bleeding. Of the 260 subjects tested, no adverse hard tissue effects were observed. Only one negative soft tissue effect was observed, and was reversed upon discontinuation of use.

Keywords: Adverse reactions, clinical studies, dental uses, research reviews.

Laster, L.; Lobene, R.R. 1990. New perspectives on *Sanguinaria* clinicals: individual toothpaste and oral rinse testing. *Journal of the Canadian Dental Association*. 56(7): 19-30.

Reviews previous studies on the effectiveness of dental products containing sanguinarine in preventing plaque, gingival inflammation, and bleeding. Inconsistencies and varying methods have produced conflicting results. However, all studies that combine the dentifrice with oral rinse, use parallel instead of crossover designs, select appropriate subjects, use significant numbers of subjects to increase statistical power, use proper statistical evaluation, and ensure intrarater or interrater reliability prior to the onset of the research consistently show significant results. Guidelines for effective clinical testing are included. Numerous studies are summarized and critiqued.

Keywords: Clinical studies, dental uses, research reviews, sanguinarine.

Lehmann, N.L.; Sattler, R. 1993. Homeosis in floral development of *Sanguinaria canadensis* and *S. canadensis* "Multiplex" (Papaveraceae). *American Journal of Botany*. 80(11): 1323-1335.

Describes the evolutionary process of homeosis and the variations that result in bloodroot flowers. Other members of the Papaveraceae (poppy) family have four petals, whereas bloodroot has eight. The four additional petals, which are morphologically distinct from the first four petals, arise where the first four stamens are positioned in other members of the poppy family; it is thus concluded that the additional petals in bloodroot are homeotic. Homeosis is the process where one plant structure either completely or partially replaces another. It is believed that the bloodroot cultivar "Multiplex," which has numerous additional petals, also displays this characteristic.

Keywords: Cultivars, flowers, homeosis, Papaveraceae family.

Lyon, D.L. 1992. Bee pollination of facultatively xenogamous *Sanguinaria canadensis* L. *Bulletin of the Torrey Botanical Club*. 119(4): 368-375.

Observes conditions for bee pollination and self-pollination of bloodroot. If bloodroot flowers are not successfully pollinated by insects, they are capable of self-pollinating after a period of 3 days. During the first 2 days of blooming, flowers are protogynous, with a female phase. At this time, stigmas are receptive to pollination, but the stamens are positioned close to the petals to avoid contact with the stigmas both when the flower is opened

during the day and closed at night. On the third day of blooming, the anthers are positioned upright so that the filaments bend inward to pollinate the stigmas. Of the insect pollinators, the most important are the Andrenidae, who are capable of carrying pollen on the underside of the thorax and abdomen, enabling effective pollination. Pollinator activity is dependent upon weather. Flowering is also dependent upon sunlight and temperature, with blooms opening earlier and staying open later on warm and sunny days. Bloodroot is one of the earliest spring blooms; facultative self-pollination is an adaptive process that enables flowers to set fruit when insect pollinators are absent due to cold temperatures or rain.

Keywords: Flowers, pollination, pollinators.

Mallatt, M.E.; Beiswanger, B.B.; Drook, C.A. [and others]. 1989.

Clinical effect of a *Sanguinaria* dentifrice on plaque and gingivitis in adults. *Journal of Periodontology*. 60(2): 91-95.

Describes a clinical trial to compare a bloodroot extract-zinc chloride dentifrice, a sodium fluoride dentifrice, and a sodium fluoride oral rinse for reducing plaque and gingival inflammation. After 21 days all subjects returned to a twice-daily brushing and flossing regimen. Post-test evaluations after 2 weeks showed significant improvement for both groups using dentifrice compared to the rinse, but no significant differences between the two dentifrices.

Keywords: Clinical studies, dental uses.

Marino, P.C.; Eisenberg, R.M.; Cornell, H.V. 1997. Influence of sunlight and soil nutrients on clonal growth and sexual reproduction of the understory perennial herb *Sanguinaria canadensis* L. *Journal of the Torrey Botanical Society*. 124(3): 219-227.

Examines the differences in leaf size, seedpod size, and clonal growth for bloodroot plants in high and low light, and with or without added soil nutrients. At the completion of the study, plants that received fertilizer in high-light areas had fewer small leaves and more large leaves than unfertilized plants. Fertilization did not affect leaf size on plants in low-light areas. Fertilized plants in both high- and low-light areas had more leaves per plant than the unfertilized plants; but both fertilized and unfertilized plants in high-light areas had more leaves than all plants in the low-light areas. Increased fertilization in low light had no effect or a detrimental effect on plants. Increased light and nutrient levels resulted in plants with more abundant and larger leaves. Plants responded more positively to increased

light than to increased fertilizer. Seedpod length was unaffected by light or fertilizer, though plants in high-light areas produced more seeds. The authors state that the 12-month duration of the research may not have been long enough to observe changes in reproductive efforts. The increased vegetative production following increased light levels indicates that disturbances in the forest canopy from fallen trees can result in larger colonies of plants.

Keywords: Ecology, fertilization, research, seeds, soil, sun requirements.

Mascarenhas, A.K.; Allen, C.M.; Loudon, J. 2001. The association between Viadent® use and oral leukoplakia. *Epidemiology*. 12(6): 741-743.

Investigates the association between Viadent® use and the development of oral leukoplakia lesions in a case-controlled study. A questionnaire was given to 148 cases and controls. Results of logistic analysis showed that patients who used Viadent® products were 8 to 11 times more likely to develop lesions than nonusers. Risk increased with age, and with frequency and duration of use. Individuals using both the paste and rinse were most likely to develop lesions, followed by users of the rinse only, and finally by users of the paste only. Other variables investigated that did not show a correlation included gender, use of a dental prosthesis, alcohol use, and tobacco use.

Keywords: Leukoplakia, research, Viadent®.

Mauriello, S.M.; Bader, J.D. 1988. Six-month effects of a sanguinarine dentifrice on plaque and gingivitis. *Journal of Periodontology*. 59: 238-243.

Compares the effectiveness of a sanguinarine dentifrice to a placebo in a double-blind clinical trial of 6 months duration. Statistical analysis showed no significant differences between the two groups.

Keywords: Clinical studies, dental uses, sanguinarine.

Morales, M.A.; Heithaus, E.R. 1998. Food from seed-dispersal mutualism shifts sex ratios in colonies of the ant *Aphaenogaster rudis*. *Ecology*. 79(2): 734-739.

Investigates the benefits of myrmecochory for ant populations. Ants collect seeds that have an elaiosome, or nutritious appendage. The seeds are carried back to the nests where larvae consume the appendage. The remaining seed,

which is still viable, is discarded in old tunnels or refuse piles that are rich in nutrients and perfect for germination. The benefits of this mutualism have been well documented for plants—parent-offspring competition, seed predation by rodents, and damage from fire are reduced; and ant nests offer a fertile site for germination. Ants benefit from the nutritious food source, but other ecological benefits have not been previously studied. In this study, *Aphaenogaster rudis* ants were fed bloodroot seeds, and ant population dynamics recorded. Ant colony fitness is measured by the number of reproductives, or gynes. Gynes are winged ants that are capable of becoming queens after mating. Colonies that received bloodroot seeds produced significantly more gynes than control colonies. The numbers of workers and males, and queen size were comparable for both groups. The increased production of reproductive ants shows that myrmecochory is a true mutualism.

Keywords: Ecology, elaiosome, myrmecochory, seeds.

Munro, I.C.; Delzell, E.S.; Nestmann, E.R.; Lynch, B.S. 1999. Viadent® usage and oral leukoplakia: a spurious association. *Regulatory Toxicology and Pharmacology*. 30: 182-196.

Responds to the initial study by Damm and others (1999) suggesting an association between Viadent® use and oral lesions. Weaknesses in the initial study include lack of proof that Viadent® use preceded the onset of leukoplakia lesions, no dose response or biological plausibility, and selective information bias. Numerous studies demonstrating the safety of dental products containing bloodroot are summarized and critiqued.

Keywords: Leukoplakia, research reviews, Viadent®.

Nikiforuk, G. 1990. The *Sanguinaria* story – an update and new perspectives. *Journal of the Canadian Dental Association*. 56(7): 5-6.

Summarizes research on the safety and effectiveness of bloodroot.

Keywords: Research reviews, safety.

Polson, A.M.; Stoller, N.H.; Hanes, P.J. [and others]. 1996. Two multi-center trials assessing the clinical efficacy of 5% sanguinarine in a biodegradable drug delivery system. *Journal of Clinical Periodontology*. 23(8): 782-788.

Compares the effectiveness of dental products containing sanguinarine extract to scaling and root planing, supragingival plaque control, and a vehicle control for treating adult periodontitis in two controlled clinical trials. All treatments showed significant reduction of plaque and bleeding after 90 days. Scaling and root planing was the most effective treatment for all study parameters. Results from the sanguinarine treatment, supragingival plaque control, and vehicle control varied. Analysis showed that the form of sanguinarine used in the study was not potent enough to provide significant results.

Keywords: Clinical studies, dental uses, sanguinarine.

Porter, S.D.; Savignano, D.A. 1990. Invasion of polygyne fire ants decimates native ants and disrupts arthropod community. *Ecology*. 71: 2095-2106.

Discusses changes in the abundance and diversity of ants and other arthropods caused by the invasion of polygyne fire ants (*Solenopsis invicta*) in Texas. In areas where the invasive ants had colonized, native ant species decreased by 90 percent and total species richness declined by 70 percent. The total number of ants in infested sites increased 10 to 30 times, with 99 percent of the ants being the invasive species. Several factors contribute to the ability of invasive ants to displace native species: (1) polygyne fire ant colonies produce multiple reproductive queens, enabling them to establish large communities that can outcompete native species; (2) the average size of fire ant workers is smaller than native ants, allowing for larger colonies to be supported by the same energy base; (3) fire ants may utilize more diverse food sources; and (4) invasive ants have fewer pathogens and parasites compared to native species. Data from this study indicates that invasive polygyne fire ants are a significant threat to natural biodiversity in areas where they have colonized.

Keywords: Ants, myrmecochory.

Pudlo, R.J.; Beattie, A.J.; Culver, D.C. 1980. Population consequences of changes in an ant-seed mutualism in *Sanguinaria canadensis*. *Oecologia*. 146: 32-37.

Compares ant-seed mutualisms for three populations of bloodroot in different habitats with varying degrees of disturbance. High levels of disturbance decreased the number and variety of ant colonies. In the undisturbed habitat, bloodroot seeds were removed more frequently and distributed greater distances. Plant populations showed few clones and more

sparse populations. There was less seed production, yet seeds that were produced were often carried outside the boundaries of the parent population. The plant populations in the highly disturbed site showed both high density and high numbers of clones. Although seed production rates were high, seed removal rates by ants were low. The site with some disturbance showed intermediate results. This study shows that habitat disturbance reduces the number of ant populations, and in turn has direct consequences on plants. Bloodroot is capable of propagating asexually through the rhizome, but without ants to disperse seeds, the benefits of sexual propagation are lost.

Keywords: Ecology, habitat, myrmecochory, research, seeds.

Rho, D.; Chauret, N.; Archambault, J. 1992. Growth characteristics of *Sanguinaria canadensis* L. cell suspensions and immobilized cultures for production of benzophenanthridine alkaloids. *Applied Microbiology and Biotechnology*. 36: 611-617.

Describes tissue culture of bloodroot.

Keywords: Propagation, tissue culture.

Robbins, C. 1999. Medicine from U.S. wildlands: an assessment of native plant species harvested in the United States for medicinal use and trade and evaluation of the conservation and management implications. Prepared by TRAFFIC North America for the Nature Conservancy. <http://www.nps.gov/plants/medicinal/pubs/traffic.htm>. [Date accessed: March 8, 2004].

Summarizes conservation issues and concerns. In 1995, 35 permits for bloodroot collection were sold in the Hoosier National Forest (Indiana); in 1996, 105 permits were sold in the Hoosier National Forest, 62 in the Wayne National Forest (Ohio), and 1 in the Daniel Boone National Forest (Kentucky); and in 1997, 97 permits were sold in the Hoosier National Forest, 57 in the Wayne National Forest, and 1 in the Daniel Boone National Forest.

Keywords: Conservation, harvest, permits.

Rockwood, L.L.; Lobstein, M.B. 1994. The effects of experimental defoliation on reproduction in four species of herbaceous perennials from northern Virginia. *Castanea*. 59(1): 41-50.

Examines the effects of defoliation on reproduction. In the first year of the study, with 50 percent defoliation, bloodroot reproduction was not greatly reduced, though the mean number of undeveloped embryos increased. In the following 2 years of the study, herbivores such as deer and ground hogs caused 100 percent defoliation and greatly reduced plant reproduction.

Keywords: Defoliation, research.

Salmore, A.K.; Hunter, M.D. 2001a. Elevational trends in defense chemistry, vegetation, and reproduction in *Sanguinaria canadensis*. *Journal of Chemical Ecology*. 27(9): 1713-1728.

Evaluates the variability in alkaloid content, reproduction, and vegetative growth of bloodroot as related to environmental conditions. Benzophenanthridine concentrations decreased with increasing elevation, whereas protopine, sanguinarine, and chelerythrine concentrations were unchanged. Water content of roots also declined with increasing elevation, which may affect nutrient absorption. Alkaloid content either increased or remained the same with increasing vegetative or reproductive growth; the lowest alkaloid concentrations were observed at the time of seed set. Sanguinarine levels increased with seed and elaiosome size and seed weight. All alkaloids increased with root size. Hypotheses and chemical mechanisms are discussed.

Keywords: Alkaloids, ecology, research, sanguinarine.

Salmore, A.K.; Hunter, M.D. 2001b. Environmental and genotypic influences on isoquinoline alkaloid content in *Sanguinaria canadensis*. *Journal of Chemical Ecology*. 27(9): 1729-1747.

Evaluates environmental influences on alkaloid levels in bloodroot. As light and fertilizer levels increase, alkaloid levels decrease.

Keywords: Alkaloids, fertilization, research, sun requirements.

Schwartz, H.G. 1986. Safety profile of sanguinarine and *Sanguinaria* extract. *Compendium, Supplement*. 7: S212-S217.

Evaluates the safety of bloodroot extract, sanguinarine, and dental products containing them, in accordance with the U.S. Food and Drug Administration guidelines for toxicological testing. Several safety studies on animals are summarized. Results show that a human would have to consume a vast amount of the dental products to experience toxicity. Even with exaggerated

use patterns, no mucosal membrane irritation or sensitization was observed in human or animal studies. No mutagenic potential was observed, nor any effects on blood pressure, heart rate, cardiac output, or respiration. The authors concluded that sanguinarine dental products are safe for human use.

Keywords: Dental uses, research reviews, sanguinarine, toxicity.

Southard, G.L.; Boulware, R.T.; Walborn, D.R. [and others]. 1984.

Sanguinarine, a new antiplaque agent: retention and plaque specificity. *Journal of the American Dental Association.* 108(3): 338-341.

Discusses the antiplaque effects of bloodroot and retention of the compounds in plaque and saliva after use. Bloodroot was identified for possible dental use because it contains alkaloids similar to those found in *Fagara zanthoxyloides*, a species used for tooth-cleaning sticks in Africa. Methods of analysis are described in detail. Results show that bloodroot has both a preventive and therapeutic effect on plaque. Bloodroot is retained in the mouth at high levels for several hours after rinsing, extending its plaque-fighting abilities.

Keywords: Clinical studies, dental uses, sanguinarine.

Southard, G.L.; Parsons, L.G.; Thomas, L.G. [and others]. 1987. Effect of *Sanguinaria* extract on development of plaque and gingivitis when supragingivally delivered as a manual rinse or under pressure in an oral irrigator. *Journal of Clinical Periodontology.* 14(7): 377-380.

Compares the effects of a sanguinarine oral rinse and supragingival irrigation to a placebo rinse and supragingival irrigation. The study was designed as a repeated measure, single-blind crossover, where patients utilized either the active or placebo rinse or supragingival irrigator without brushing for 2 weeks. Results showed no significant difference between the oral rinse and supragingival irrigation method of application, though the products containing sanguinarine showed significantly greater ability to control plaque and gingivitis compared to placebos.

Keywords: Clinical studies, dental uses.

Tenenbaum, H.; Dahan, M.; Soell, M. 1999. Effectiveness of a sanguinarine regimen after scaling and root planing. *Journal of Periodontology.* 70(3): 307-311.

Describes a study on the effectiveness of sanguinarine in a follow-up treatment for adults with periodontitis. Sixty patients received initial

periodontitis treatment, followed by a 2-week treatment with chlorhexidine, and 14 weeks of treatment with dental products with or without sanguinarine. The group using sanguinarine dental products showed significant inhibition of gingivitis and bleeding compared to control. It was concluded that sanguinarine optimized the effectiveness of chlorhexidine without side effects.

Keywords: Clinical studies, dental uses, sanguinarine.

Tin-Wa, M.; Farnsworth, N.R.; Fong, H.H.S.; Trojanek, J. 1970.

Biological and phytochemical evaluation of plants. VIII: Isolation of a new alkaloid from *Sanguinaria canadensis*. *Lloydia*. 33(2): 267-269.

Identifies a new alkaloid in bloodroot rhizomes.

Keyword: Alkaloids.

Tuveson, R.W.; Lawson, R.A.; Marley, K.A. [and others]. 1989.

Sanguinarine, a phototoxic H_2O_2 -producing alkaloid. *Photochemistry and Photobiology*. 50(6): 733-738.

Investigates the phototoxicity of sanguinarine chloride. In the presence of near-ultraviolet light, sanguinarine chloride produced hydrogen peroxide (H_2O_2). Sanguinarine chloride was phototoxic to catalase-deficient strains of *Escherichia coli*, but not to *Trichoplusia ni*, a cabbage looper moth larvae which maintains a high level of catalase activity.

Keywords: Pesticide use, phototoxicity, research, sanguinarine.

Walker, C. 1990. Effects of sanguinarine and *Sanguinaria* extract on the microbiota associated with the oral cavity. *Journal of the Canadian Dental Association*. 56(7): 13-18.

Summarizes clinical studies on the safety and effectiveness of bloodroot in dental products.

Keywords: Clinical studies, dental uses, research reviews, sanguinarine.

Wennstrom, J.; Lindhe, J. 1985. Some effects of a sanguinarine-containing mouth rinse on developing plaque and gingivitis. *Journal of Clinical Periodontology*. 12(10): 867-872.

Assesses the effectiveness of a sanguinarine mouth rinse in reducing plaque and gingivitis. The study was set up as a blind crossover with a sanguinarine

rinse and a placebo rinse. After a baseline examination, subjects refrained from brushing for 2 weeks, rinsing twice daily instead. Clinical examinations of plaque and gingivitis were conducted at various points in the study. During the second test phase, subjects who had rinsed with the placebo were switched to the active compound and vice versa. The results showed that the sanguinarine mouth rinse was significantly effective in reducing plaque and development of gingivitis.

Keywords: Clinical studies, dental uses, sanguinarine.

Zettler, J.A.; Spira, T.P.; Allen, C.R. 2001. Ant-seed mutualisms: can red imported fire ants sour the relationship? *Biological Conservation*. 101(2001): 249-253.

Discusses the impact that red imported fire ants (*Solenopsis invicta*) have on natural ant-seed mutualisms. Bloodroot is one of an estimated 70 plant species that benefit from ant mutualism. The specific benefits for ants and plants are summarized. The red imported fire ant established colonies in the United States in the 1930s, and has continued to spread throughout the Southeastern States. After fire ants become established, native ant species richness decreases by as much as 70 percent; this decrease in the number of beneficial ants disrupts the dispersal of seeds. Red imported fire ants can also damage elaiosome-bearing seeds making them nonviable, or discard them in areas that are not fit for germination. These issues and the conservation implications are discussed in detail.

Keywords: Conservation, myrmecochory.

Popular Press

The following articles and websites have not been peer reviewed, but are included to indicate popular views and perceptions.

Baldia, C.M. 2002. The cultural significance of bloodroot (*Sanguinaria canadensis*). *Ancient Textiles*. <http://home.columbus.rr.com/ancienttextiles/sanguinariacanadensis.htm>. [Date accessed: May 24, 2004].

Highlights general information on bloodroot, with a focus on the use of the herb as a dye for fabrics. Definitions for *Sanguinaria canadensis* from dictionaries and encyclopedias are offered, along with a brief botanical and ecological description. The alkaloids in bloodroot are related to opium, and can be poisonous. Bloodroot is not grown commercially, so all of the roots

in commercial trade are harvested from the wild. Native Americans used the roots to dye baskets, clothing, and their skin.

Keywords: Alkaloids, dye uses, Native American uses.

Center for Alternative Medicine Research, University of Texas. 1999.

Hoxsey. The University of Texas-MD Anderson Cancer Center. <http://www.mdanderson.org/departments/CIMER/display.cfm?id=35F65FD9-F06A-11D4-810200508B603A14&method=displayFull&pn=6EB86A59-EBD9-11D4-810100508B603A14>. [Date accessed: May 12, 2004].

Examines the cancer-fighting effects of a formula used by Harry Hoxsey in the early and mid-1900s. The American Medical Association and the U.S. Food and Drug Administration forced Hoxsey to close his clinics in 1960 and prevented him from treating patients in the United States. Hoxsey and his nurse, Mildred Nelson, reopened the clinic in Mexico in 1963 and continue to treat patients there. Two studies are cited—a study from the clinic’s pamphlet describing best-case scenarios, and a follow-up study with no controls that observed patients from the clinic after treatment. Plants used in the formula are identified and their cancer-fighting capabilities discussed.

Keywords: Cancer, Harry Hoxsey.

Clark, P. 2002. Scientists hope bloodroot plant could be new crop for farmers. Asheville Citizen-Times. May 19. <http://www.goldenleaf.org/n20020519.html>. [Date accessed: March 8, 2004].

Describes the cultivation of bloodroot at the Yellow Creek Botanical Institute located in Graham County, NC, and summarizes the use and market for roots both domestically and internationally. One German company, Phytobiotics GmbH, uses 120 to 150 metric tons of bloodroot per year, adding the herb to animal feeds as an alternative to synthetic antibiotics. Bloodroot is not currently cultivated on any scale; all sources are wildcrafted. Research on the cultivation of various medicinal herbs by the Yellow Creek Botanical Institute is presented.

Keywords: Animal feed additive, cultivation, market, Phytobiotics GmbH, Yellow Creek Botanical Institute.

Hendershot, D. 2002. The naturalist’s corner. Smoky Mountain News. April 3. http://www.smokymountainnews.com/issues/09_04/09_15_04/out_naturalist.html. [Date accessed: October 8, 2004].

Summarizes the identification, ecology, and uses of bloodroot. Even though bloodroot flowers do not produce nectar, they attract several insects that spread pollen. If insect pollinators are not present, the bloodroot plant can self-pollinate. When seeds are ripe the seedpod “pops,” dispersing the seeds. Ants are attracted to an appendage on the seed called an elaiosome; the insects carry the seeds back to their nests, depositing them in chambers where they can germinate and grow. Bloodroot can also reproduce vegetatively by the rhizome. Native Americans used the rhizomes for various medicinal purposes and as a dye. Colonists who practiced the doctrine of signatures (the belief that herbs contained signs to indicate their uses) used bloodroot to treat illnesses associated with blood, such as ulcers, hemorrhages, and wounds. The medicinal properties of the plant are attributed to the alkaloids sanguinarine, chelerythrine, and protopine. These alkaloids can be toxic, and high doses may be fatal. The main commercial use for bloodroot in the 1980s and 1990s was as an additive to toothpastes and mouth rinses, particularly Viadent®. When research identified a link between Viadent® and oral precancerous lesions in 1999, sanguinarine was removed from the Viadent® formula. Several other brands of dental products containing bloodroot have since reentered the market.

Keywords: Alkaloids, dental uses, dye uses, flowers, medicinal uses, Native American uses, pollination, toxicity, Viadent®.

Phillips, G. 2001. The cancer racket. <http://cancerinform.org/article.html>. [Date accessed: October 8, 2004].

Offers a brief biography of Harry Hoxsey and the story of his herbal cancer remedy, which was banned in the United States in the 1960s. Bloodroot was one of the many plants used in the formula.

Keywords: Cancer, Harry Hoxsey, medicinal uses.

Sanders, J. 2002. A bloody early bloomer. <http://www.acorn-online.com/hedge/blood.htm>. [Date accessed: October 8, 2004].

Provides general information on bloodroot from a naturalist. Bloodroot is one of the earliest plants to emerge in the spring, with a single white flower protected by a small leaf. A member of the poppy family (Papaveraceae), *Sanguinaria canadensis* is the only plant of this genus. The common name, bloodroot, comes from the dark-red color of the sap, which will stain anything it touches. The sap was used by Native Americans as a dye. Other common names include coonroot, snakebite (due to poisonous characteristics), sweet-slumber (medicinally used to induce sleep), red root,

corn root, turmeric, and tetterwort (tetter = skin disease). Bloodroot was traditionally used to treat ringworm, ulcers, general debility, and skin diseases such as cancer. In the mid-19th century, a physician in London used bloodroot in a cancer treatment at the Middlesex Hospital. The cancer treatment fell out of use for a period, but was revived in the 1960s for minor cancers and polyps. Bloodroot sap was mixed with maple sugar to soothe sore throats. It was used to treat influenza, whooping cough, scarlet fever, catarrh, menstrual problems, and as an additive in toothpastes and dental rinses. The plant is poisonous and can cause skin irritation or death if ingested in large quantities. Plants can be propagated from seed. Flowers contain no nectar, but are pollinated by bees and other insects.

Keywords: Cancer, common names, dye uses, medicinal uses, Papaveraceae family, toxicity.

Sutherland, Z. 1999. Zen's WNC nature notebook plant index. <http://main.nc.us/naturenotebook/plants/bloodroot.html>. [Date accessed: May 24, 2004].

Provides a general overview of bloodroot. Includes botanical and habitat descriptions, and medicinal applications. Bloodroot is mainly found near streams with other early spring flowers, and is an indicator for birch-maple-basswood (*Betula* spp., *Acer* spp., and *Tilia americana*) hardwood forests. The plant is poisonous, with overdose symptoms such as intense thirst, burning stomach, vomiting, faintness, vertigo, prostration, and dim sight.

Keywords: Habitat, medicinal uses, toxicity.

Wagner, H. 2001. Dentists see legacy of discontinued ingredients in patients' mouths. Ohio State University research. <http://www.osu.edu/units/research/archive/viadent.htm>. [Date accessed: March 8, 2004].

Summarizes the results of studies on the association between the white lesions known as leukoplakias and the use of Viadent® dental products containing bloodroot. Viadent® has since changed its formula and no longer contains bloodroot; however, some patients have either developed lesions or had existing lesions persist even after discontinued use.

Keywords: Leukoplakia, research reviews.

Walters, R. 1993. Options: the alternative cancer therapy book. Garden City Park, NY: Avery Publishing Group. 396 p.

Provides a biography of Harry Hoxsey, with details about his cancer-fighting remedy, which contained bloodroot. The cancer treatment was a mixture of various anticancerous herbs combined in a formula developed by Hoxsey's grandfather. In 1960, the Hoxsey Cancer Clinic in Dallas, TX was supported by branches in 17 States. Hoxsey did not have a medical license however, and pressure from the American Medical Association and the U.S. Food and Drug Administration forced him to close his clinics. He reopened his clinic in Mexico with the help of one of his nurses, who continued to direct the clinic after his death.

Keywords: Cancer, Harry Hoxsey, medicinal uses.

Other Information Sources

The following are general materials that provide background and reference information. Included are encyclopedias, fact sheets, historical documents, planting guides, herbal manuals, and other miscellaneous information.

Britton, N.L.; Brown, A. 1913. An illustrated flora of the Northern United States, Canada, and the British Possessions. In: U.S. Department of Agriculture, Natural Resources Conservation Service. 2001. The PLANTS database. Version 3.1. National Plant Data Center, Baton Rouge, LA. Vol. 2. <http://plants.usda.gov>. [Date accessed: March 8, 2004].

[No abstract].

Keywords: Botanical description.

Cook, W. 1869. The physiomedical dispensatory. Scanned version by J. Medical Herbalism, 2001. http://www.ibiblio.org/herbmed/eclectic/cook/SANGUINARIA_CANADENSIS.htm. [Date accessed: May 24, 2004].

Summarizes historical information on the medicinal uses of bloodroot. A brief botanical description is provided. Roots are used medicinally, acting upon the mucus membranes, gall ducts, and secreting organs. Specific uses are summarized, with detailed instructions for various preparations.

Keywords: History, medicinal uses, preparations.

Ellingwood, F. 1919. The American materia medica, therapeutics and pharmacognosy. Scanned version by M. Moore, 2001–2002. <http://www.ibiblio.org/herbmed/eclectic/ellingwood/sanguinaria.html>. [Date accessed: May 24, 2004].

Summarizes historical uses for bloodroot. Includes chemical constituents and physiological actions. The herb has been used to treat lung congestion, bronchial coughs, stridulous laryngitis, membranous croup, atonic conditions, hepatization, otitis media, ulcers, irregular menstruation, nasal catarrh, lupus, and more.

Keywords: History, medicinal uses.

Felter, H.W. 1922. The eclectic materia medica, pharmacology and therapeutics. Scanned version by M. Moore, 2001–2002. <http://www.ibiblio.org/herbmed/eclectic/felter/sanguinaria.html>. [Date accessed: May 24, 2004].

Provides historical information on the medicinal use of bloodroot. Chemical constituents include chelerythrine, sanguinarine, gamma-homochelidilone, protopine, sanguinarinic acid, and resin. Preparations, indications, and medicinal uses are described. Bloodroot is used externally to treat nasal polyps, frozen feet or chilblains, eczema, ringworm, warts, and tinea. An extract from the roots is used internally as an emetic and stomach cleanser, expectorant, and treatment for hepatitis, atonic dyspepsia, duodenal catarrh, nasal catarrh, amenorrhea, dysmenorrhea, impotence, bronchitis, pharyngitis, laryngitis, whooping cough, and croup.

Keywords: Chemical constituents, history, medicinal uses, preparations, sanguinarine.

Felter, H.W.; Lloyd, J.U. 1898. King's American dispensatory. 18th ed., 3rd rev. Scanned version by H. Kress, 2000–2001. <http://www.ibiblio.org/herbmed/eclectic/kings/sanguinaria.html>. [Date accessed: May 24, 2004].

Offers extensive historical information on bloodroot, including common names, botanical description, ecology, distribution, chemical constituents, medicinal uses, indications, preparations, and dosage. In small dosages, bloodroot stimulates the heart, circulation, and digestive organs, and serves as a general tonic. In large doses, it stimulates the liver but sedates the heart, reduces the pulse, and causes nausea and expectoration. Toxic doses result in nausea, emesis, vertigo, and prostration. Bloodroot has been used medicinally to treat conditions such as inflammation, chronic hepatitis, atonic dyspepsia, catarrh, jaundice, headaches, rheumatism, dysentery, scrofula, amenorrhea, dysmenorrhea, hysteria, lung hemorrhage, general debility, impotence, bronchitis, laryngitis, sore throat, croup, asthma, whooping cough, pharyngitis, pneumonia, syphilis, eczema, ringworm, warts, carcinomata, ulcers, rhinitis, and nasal polyps. Various preparations are described.

Keywords: Chemical constituents, dosage, history, medicinal uses, preparations, toxicity.

Fern, K. 1997–2000. Plants for a future: the species database. http://www.ibiblio.org/pfaf/cgi-binarr_html?Sanguinaria+canadensis&CAN=LATIND. [Date accessed: May 24, 2004].

Provides information on common and scientific names, habitat, medicinal uses, cultivation, and propagation. Bloodroot grows in a variety of soil types, but prefers moist, well-drained, semishaded sites. Medicinal actions are cathartic, diuretic, emetic, emmenagogue, expectorant, febrifuge, homeopathic, odontalgic, sedative, stimulant, and tonic. Native Americans used bloodroot to treat fevers, rheumatism, and to induce vomiting. In modern medicine the herb is used internally as an expectorant, and as a treatment for bronchial, respiratory, and throat infections, migraines, and poor circulation. Bloodroot can be applied externally to treat skin diseases, warts, nasal polyps, and chilblains. Sanguinarine is extracted from the roots and added to dental products. Other uses include an insect repellent or red dye. The roots contain opium-like alkaloids and can be toxic in high doses. Rhizomes are harvested in the fall, dried, and stored away from moisture. Details for cultivating bloodroot in the garden are provided. Plants can be propagated by seed or by division of rhizomes.

Keywords: Cultivation, dental uses, dye uses, habitat, insect repellent, medicinal actions, medicinal uses, Native American uses, sanguinarine, soil requirements, toxicity.

Foster, S.; Duke, J.A. 2000. A field guide to medicinal plants and herbs of Eastern and Central North America. 2^d ed. The Peterson field guide series. National Audubon Society, National Wildlife Federation, and the Roger Tory Peterson Institute. New York: Houghton Mifflin Co. 411 p.

Provides information on bloodroot ecology, botany, and medicinal uses, with photographs. Plants flower from March through June, and are found in rich woods from Nova Scotia to Florida, west to east Texas and Manitoba. Small doses of the root are used to increase the appetite; large doses are used as a sedative. Native Americans used the roots to treat rheumatism, asthma, bronchitis, lung problems, laryngitis, and fevers. It was also used as a dye and love charm. Bloodroot contains the alkaloid sanguinarine, which has been shown to have antiseptic, anesthetic, and anticancerous properties. Sanguinarine has also been added to commercial dental products as an antiplaque agent. Roots can be toxic and should not be ingested.

Keywords: Dental uses, dye uses, habitat, love charm, medicinal uses, Native American uses, range, sanguinarine, toxicity.

Grieve, M. 1931. A modern herbal. Hypertext version by Botanical.com. 1995–2002. <http://www.botanical.com/botanical/mgmh/b/bloodr59.html>. [Date accessed: May 24, 2004].

Provides a botanical description and summary of medicinal uses. Chemical constituents include the alkaloids sanguinarine, chelerythrine, protopine, and B-homochelidonine as well as red resin and starch. Bloodroot has been used medicinally to treat dyspepsia, asthma, bronchitis, croup, scrofula, dysentery, heart disease, high pulse, ringworm, ulcers, eczema, and skin cancers. Toxic doses cause stomach burning, intense thirst, vomiting, faintness, vertigo, prostration, and dimness of eyesight. Roots have been used as a dye by both Native Americans and the French. Preparations and doses are listed.

Keywords: Alkaloids, chemical constituents, dye uses, history, medicinal uses, preparations, sanguinarine, toxicity.

Harding, A.R. 1936. Ginseng and other medicinal plants. Scanned version by M. Moore, 2002. <http://www.ibiblio.org/herbmed/eclectic/harding/sanguinaria.html>. [Date accessed: May 24, 2004].

Offers a thorough botanical description, with common names, harvest, and market information. A member of the Papaveraceae family, bloodroot is related to the opium poppy (*Papaver somniferum*). Bloodroot grows in open, wooded areas with rich soil. Rhizomes send up a single flower and leaf from each bud. Both the leaf and bud are smooth, and covered in a whitish bloom. Leaves grow on a stem 5 to 14 inches tall, and are palmate with five to nine cleft lobes and prominent veins. The leaves are only partially developed when the plant flowers, and continue to grow from 4 to 7 inches long and 6 to 12 inches across after the flowers fade. Flowers are 1 inch wide, and have numerous yellow stamens. Petals do not persist long; flowers quickly give way to oblong narrow seedpods. The rhizome is thick and fleshy, curved at the ends, 1 to 4 inches in length and 1/2- to 1-inch thick, with blood-red sap. Roots shrink considerably in drying, and break with a sharp fracture. Roots are harvested in autumn after the leaves die back, then dried and sold for 5 to 10 cents per pound. Bloodroot is listed in the U.S. Pharmacopoeia as a tonic, alterative, stimulant, and emetic. The red sap of the plant was used by Native Americans to dye baskets, weapons, and their own skin.

Keywords: Botanical description, dye uses, flowers, harvest, history, market prices, Native American uses, Papaveraceae family, rhizomes.

Houghton, C. 2001. Purple sage herb profiles. <http://www.purplesage.org.uk/profiles/bloodroot.htm>. [Date accessed: May 24, 2004].

Provides a botanical description, lists constituents and medicinal actions, and describes medicinal uses, combinations with other herbs, preparations, and doses. Medicinal actions are expectorant, spasmolytic, emetic, cathartic, antiseptic, cardioactive, uterine stimulant, topical irritant, escharotic, and antibacterial. Bloodroot is used to treat respiratory infections, colds, asthma, croup, laryngitis, poor circulation, migraines, nasal polyps, warts, and skin infections. It is also used in dental products to reduce plaque. Bloodroot can be poisonous and should not be used during pregnancy.

Keywords: Chemical constituents, medicinal actions, medicinal uses, preparations, toxicity.

Horticopia, Inc. 2001. *Sanguinaria canadensis*. Horticopia plant information. <http://www.horticopia.com/hortpix/html/pc4811.htm>. [Date accessed: May 24, 2004].

Summarizes bloodroot habitat information for gardeners. Bloodroot is a perennial that grows in hardiness zones 4A to 9A. Plants prefer full to partial shade and moist soil.

Keywords: Habitat, hardiness range, sun requirements, water requirements.

Jackson, D.; Shelton, K. 1997–2001. Alternative nature online herbal. <http://altnature.com/gallery/bloodroot.htm>. [Date accessed: May 24, 2004].

Offers a summary of medicinal uses and history. A brief botanical description is also provided. Roots are collected when flowers are in bloom, and dried for later use. The roots contain opium-like alkaloids and can be fatally poisonous; bloodroot is not edible and should not be used by pregnant women. Actions are anesthetic, cathartic, emetic, emmenagogue, expectorant, diuretic, febrifuge, sedative, stimulant, and tonic. Bloodroot is used in small doses to treat bronchial troubles, throat infections, heart problems, migraines, plaque, skin diseases, warts, and tumors. Native Americans used the roots as a dye.

Keywords: Alkaloids, dye uses, harvest, medicinal actions, medicinal uses, toxicity.

Ladanyi, P.A., inventor; Vipont Chemical Company, assignee. 1979.

USPTO patent full-text and image database. U.S. patent 4,145,412. <http://patft.uspto.gov/>. [Date accessed: March 10, 2004].

Patents the process for a special extract of bloodroot for use in various dental applications. Describes the process, summarizes the uses, and provides a history of previous patents for the medicinal use of bloodroot.

Keywords: Dental uses, patents.

Miller, R.A. 1988. Native plants of commercial importance. Grants Pass, OR: OAK, Inc. 343 p.

Includes information on ecology and growth range, botany, medicinal actions and use by Native Americans and eclectic physicians,¹ chemistry, marketing, prices for dried roots, and demand. Plants can be found growing in rich woods, bottomlands, and along shady streams from Nova Scotia south to Florida, and west to Manitoba and Oklahoma. This spring-blooming perennial produces one leaf and flower from each bud on the rhizome. Native Americans used the roots as a dye for skin and clothing, and to treat skin cancers. Other medicinal uses have included treatments for alcoholism, arthritis, asthma, breast tumors, bronchitis, cancer, catarrh, chest pains, colds, cough, croup, deafness, diphtheria, dysmenorrhea, dyspepsia, ear polyps, gleet, headache, influenza, liver problems, pharyngitis, pneumonia, rheumatism, nausea, and whooping cough. Constituents are listed, and their chemistry, particularly as related to dental uses, is discussed. Plants are occasionally used in ornamental landscaping. Instructions for collecting roots and dividing rhizomes for propagation and cultivation are presented. The domestic market is estimated at 200 tons and the world market at 2,000 tons. Plants are poisonous and should only be used by trained physicians.

Keywords: Chemical constituents, dye uses, habitat, market, medicinal uses, Native American uses, range.

Missouri Botanical Garden. 2002. Plant finder. <http://www.mobot.org/gardeninghelp/plantfinder/service.shtml>. [Date accessed: March 8, 2004].

Provides a summary of cultivation information useful to the gardener. Bloodroot is found in partial to full shade in moist, rich soil and is hardy in

¹ Eclectic physicians were doctors who treated patients with herbal medicines between the late 1800s and early 1900s.

zones 3 to 8. Plants grow 6 to 10 inches tall, spreading by an underground rhizome. A single leaf and flower emerge in early spring, the leaf curled around the bloom until it opens. The leaf continues to expand after the flower fades. Flowers are white, 2 inches wide, with 8 to 10 petals and numerous yellow stamens. Blooms open during the day and close at night. All parts of the plant have a bright-red sap that was once used by Native Americans as a dye. There are no serious pest or disease problems. Bloodroot is best suited for shaded woodlands, native plantings, and wildflower or rock gardens where the plants can naturalize.

Keywords: Botanical description, cultivation, disease, dye uses, flowers, habitat, hardiness range, landscape uses, pests.

Moerman, D. 1999. Native American ethnobotany database: foods, drugs, dyes, and fibers of native North American peoples. The University of Michigan-Dearborn. <http://herb.umd.umich.edu/>. [Date accessed: March 8, 2004].

Provides information on Native American uses of plants. Bloodroot was used by many Native American tribes, including the Algonquin, Cherokee, Chippewa, Delaware, Iroquois, Menominee, Meskwaki, Micmac, Mohegan, Ojibwa, Ponca, Potawatomi, Omaha, and Winnebago. Bloodroot was used medicinally as an abortifacient, tonic, emetic, blood purifier, and cough medicine. It was also used as a wash for ulcers and sores, a snuff for nasal polyps, and as a treatment for heart trouble, catarrh, stomach cramps, poison ivy, earaches, fevers, asthma, tuberculosis, gonorrhea, syphilis, piles, and rheumatism. The red juice from the roots was used to dye baskets, clothing, and skin. Several tribes also used bloodroot as a love charm.

Keywords: Dye uses, love charm, medicinal uses, Native American uses.

NatureServe Explorer. 2002. An online encyclopedia of life [Web application]. Version 1.6. Arlington, VA: NatureServe. <http://www.natureserve.org/explorer>. [Date accessed: March 10, 2004].

Provides details on bloodroot ecology, conservation status, market demand, and distribution. Bloodroot has a global heritage status rank of G5 and a national heritage status rank of N5 (abundant and secure). State heritage status ranks are provided for all States reporting bloodroot. Habitat loss and overcollection are contributing to declining populations rangewide. No monitoring is currently being done on wild populations. Poaching often takes place on public lands, particularly to supply a growing demand from the Chinese and Korean black markets, where roots sell for \$15 to \$30 per

pound. One herb dealer in the Southern Appalachians sold 40,000 to 55,000 pounds of bloodroot in 1999. Roots for the nursery industry are estimated to bring \$0.40 per bare-root plant. Prices per fluid ounce of bloodroot extract are estimated at \$9. Ecology and habitat are described.

Keywords: Conservation, distribution, global heritage status rank, habitat, market, national heritage status rank, poaching.

Petersen, F. 1905. *Materia medica and clinical therapeutics*. Scanned version by M. Moore, 2002. <http://www.ibiblio.org/herbmed/eclectic/petersen/sanguinaria.html>. [Date accessed: May 24, 2004].

Summarizes historical medicinal uses of bloodroot. Medicinal actions are stimulant, tonic, emmenagogue, and emetic. Bloodroot is used to treat relaxed and constricted larynx, pharynx, and bronchi with burning, uneasiness, and dryness; nasal catarrh with no discharge; and harsh, dry cough. Additional uses are listed along with preparations and dosage.

Keywords: History, medicinal actions, medicinal uses, preparations.

Plyler, S.C. 2001–2002. *Indian spring herbal encyclopedia*. <http://www.indianspringherbs.com/Bloodroot.htm>. [Date accessed: May 24, 2004].

Provides a general overview of bloodroot identification, history, medicinal uses, preparations, and dosage. A brief botanical and habitat description is provided. Constituents of the root include sanguinarine, sanguidimerine, cholerythrine, protopine, berberine, copticine, and red resin. Native Americans used bloodroot to treat rheumatism, asthma, bronchitis, laryngitis, fevers, and warts. The red juice was used as a dye and decorative skin stain. According to a legend from the Ponca Tribe, if a man rubbed bloodroot juice on his hands before shaking hands with the woman he wanted to wed, within 5 to 6 days she would be willing to marry him. Medicinal properties assigned to bloodroot include antiseptic, antispasmodic, cathartic, diuretic, emetic, emmenagogue, expectorant, febrifuge, sedative, stimulant, and tonic. The plant is used to treat bronchitis, asthma, croup, laryngitis, pharyngitis, poor circulation, and skin cancers. Bloodroot is poisonous and should be used carefully with the assistance of a trained herbalist or physician; large doses can cause low blood pressure, vertigo, tremors, vomiting, shock, and coma. Dosages are provided.

Keywords: Alkaloids, chemical constituents, dye uses, love charm, medicinal actions, medicinal uses, Native American uses, sanguinarine, toxicity.

Potter, S.O.L. 1902. A compend of materia medica, therapeutics, and prescription writing. Scanned version by H. Kress, 2000–2002. <http://www.ibiblio.org/herbmed/eclectic/potter-comp/sanguinaria.html>. [Date accessed: May 24, 2004].

Summarizes historical uses for bloodroot. Includes preparations, dosage, and physiological actions. Roots were used medicinally to treat chronic nasal catarrh, acute bronchitis and asthma, chronic bronchitis, atonic dyspepsia, impotence, amenorrhea, croup, pneumonia, scarlatina, nasal polyps, hypertrophy, ulcers, and syphilitic afflictions.

Keywords: History, medicinal uses.

Reed, D. 1999–2002. Wildflowers of the Southeastern United States. <http://2bnthewild.com>. [Date accessed: March 10, 2004].

Describes the botanical characteristics of bloodroot, with a brief summary of medicinal uses and folklore. Bloodroot is an herbaceous perennial with a single basal leaf that reaches 10 inches in height. A brief description of Native American usage and folklore is included. Bloodroot is used medicinally to treat skin afflictions such as ringworm, warts, polyps, fungal growths, and skin cancer; added to toothpastes to fight plaque and gingivitis; used to stimulate the digestive system; and as an emetic. The roots are poisonous and self-medication is not recommended.

Keywords: Botanical description, medicinal uses, toxicity.

Russell, A.B. 1997. Poisonous plants of North Carolina. North Carolina State University, Department of Horticultural Science. <http://www.ces.ncsu.edu/depts/hort/consumer/poison/Sanguca.htm>. [Date accessed: May 24, 2004].

Summarizes the toxic qualities of bloodroot. The isoquinoline alkaloids in the rhizomes are poisonous when ingested in large quantities. Symptoms of overdose include nausea, vomiting, faintness, dizziness, dilated pupils, fainting, diarrhea, and heart failure. This plant is highly toxic and can be fatal if ingested in large doses.

Keywords: Alkaloids, toxicity.

Sievers, A.F. 1930. The herb hunters guide. Misc. Publ. 77. Washington, DC: U.S. Department of Agriculture. Hypertext version. April 8, 1998. <http://www.hort.purdue.edu/newcrop/herbhunters/bloodroot.html>. [Date accessed: May 24, 2004].

Provides a description of the plant with common names, habitat and range, and harvest information. Common names for *Sanguinaria canadensis* include redroot, red puccoon, red Indian paint, puccoon root, coonroot, white puccoon, pauson, snakebite, sweet-slumber, and tetterwort. Plants emerge in early April, with a single leaf enclosing a flower bud, both covered with a smooth, whitish bloom. Leaves have five to nine lobes. After flowers die back, leaves mature to a size of 4 to 7 inches in length and 6 to 12 inches wide. The flowers are 1 inch across, waxy white in color, and fade to narrow oblong seedpods. The roots and stem contain blood-red colored sap. The roots, collected in the fall, are used medicinally.

Keywords: Botanical description, common names, flowers, harvest.

U.S. Department of Agriculture, Forest Service. 1993. Income opportunities in special forest products: self-help suggestions for rural enterprises. Agric. Inf. Bull. 666. Washington, DC. 206 p.

Estimates the domestic market for bloodroot at 200 tons and the world market at 2,000 tons.

Keywords: Market demand.

U.S. Department of Agriculture, Natural Resources Conservation Service. 2001. The PLANTS database. Version 3.1. Baton Rouge, LA: Plant Data Center. <http://plants.usda.gov/>. [Date accessed: March 15, 2004].

Summarizes bloodroot range and distribution, with maps for each State. Bloodroot is found in Arkansas, Connecticut, Florida, Georgia, Illinois, Iowa, Kansas, Kentucky, Maine, Massachusetts, Michigan, Missouri, New Hampshire, North Carolina, North Dakota, Rhode Island, South Carolina, South Dakota, Tennessee, Vermont, Virginia, West Virginia, and Wisconsin.

Keywords: Distribution, range.

United Plant Savers. [n.d.]. At risk plants. <http://www.plantsavers.org/>. [Date accessed: March 10, 2004].

Includes bloodroot on the “At-Risk” plant list. Plants on this list are considered to be significantly declining in numbers due to over harvest, loss of habitat, or innate sensitivity and rareness.

Keyword: Conservation.

Winterburn, G.W. 1882–1883. Transactions of the national eclectic medical association. Scanned version by M. Moore, 2001–2002. Vol. 10. <http://www.ibiblio.org/herbmed/eclectic/journals/nat-ecl-trans-1882.html>. [Date accessed: March 10, 2004].

Provides detailed information on the historical uses of bloodroot. The medicinal actions vary with the dosage. Small doses stimulate the heart, respiratory system, and act as a general tonic; whereas large doses decrease heart activity, paralyze the respiratory system, and cause emesis and lethargy. Bloodroot has strong actions upon the skin, mucus membranes, digestive system, respiratory organs, glandular structures, spinal system, muscular tissue, and female organs. Medicinal uses are listed with descriptions of specific case studies.

Keywords: Case studies, history, medicinal actions, medicinal uses.

Commercial Vendors

Note: The following list of vendors is included to provide access to current information about availability and prices. The authors do not intend to recommend these vendors over others not listed.

GardenMakers. [n.d.]. Bloodroot. <http://www.gardenmakers.com/>. [Date accessed: March 10, 2004].

Vendor of bloodroot plants for landscaping.

Keywords: Landscape uses, vendors.

Green Canyon. [n.d.]. Bloodroot. <http://www.greencanyon.com/products/c100390.htm>. [Date accessed: March 10, 2004].

Vendor of bloodroot for medicinal uses.

Keywords: Medicinal uses, vendors.

Herbal Wise. [n.d.]. Bloodroot. <http://herbalwise.com/bulklist.htm>. [Date accessed: March 10, 2004].

Vendor of bloodroot for medicinal uses.

Keywords: Medicinal uses, vendors.

HerbTrader. [n.d.]. Bloodroot. <http://www.herbtrader.com/bloodsancan.html>. [Date accessed: March 10, 2004].

Vendor of bloodroot for medicinal uses.

Keywords: Medicinal uses, vendors.

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Disclaimers

This annotated bibliography represents a comprehensive, but not exhaustive, review of the literature on bloodroot. The references included were identified through a detailed search of academic library-based databases, regional literature, government documents, Internet databases, as well as commercial Internet sites. Bibliographic references are organized into sections—Research Literature, Popular Press, Other Information Sources—to indicate their origins. Research Literature includes references to peer reviewed articles published in scientific journals, while the references in Popular Press are not scientifically reviewed, but are included to indicate popular knowledge and perceptions. Other Information Sources include technical bulletins, horticultural lists, historical documents, and Web sites.

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Predny, Mary L.; Chamberlain, James L. 2005. Bloodroot (*Sanguinaria canadensis*): an annotated bibliography. Gen. Tech. Rep. SRS-86. Asheville, NC: U.S. Department of Agriculture, Forest Service, Southern Research Station. 55 p.

Bloodroot (*Sanguinaria canadensis*) is a spring-blooming herbaceous perennial found mainly in rich woods throughout the Appalachian Mountain regions and across the Eastern United States. The common name bloodroot and scientific name *Sanguinaria* denote the blood-red sap found throughout the plant, particularly in the roots. This sap contains the alkaloids that make this plant so valuable. Native Americans used bloodroot as a dye, love charm, and medicine. European colonists adopted Native American medicinal uses to suit their own needs. Bloodroot was described in pharmacopoeias as early as the 1800s, with detailed descriptions of the plant, constituents, therapeutics, and case studies. The popular use of herbal remedies declined in the 1920s with the development of the pharmaceutical industry, though there has been a renewed interest in herbal medicine as research confirms the efficacy of some traditional uses. Bloodroot is still wildcrafted in the United States for domestic and international uses. This report describes the characteristics and growth habits of bloodroot, summarizes the various uses of the herb, reviews the global market and trade, examines the conservation status of the plant, and identifies needs for future research.

Keywords: Bloodroot, conservation, dental products, medicinal herbs, nontimber forest products, *Sanguinaria*.



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