

Elderberry as a Medicinal Plant

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Folk medicine has been around for millennia exploiting first wild then cultivated plants to prevent or cure a myriad of illnesses. Black elder have been used for centuries in Europe (French 1651), northern Africa, and some parts of Asia for such purposes as to keep the evil spirits away, to prevent or cure numerous ailments and health problems. Early settlers brought some of this knowledge to America where a closely related plant, the American elder, could easily be found in the wild. Native Americans also have a tradition of using elderberry for its healing properties (Borchers et al. 2000) and particularly to treat fever and rheumatism (Moerman 1986). While many of the reported effects lack adequate scientific validation, there are an increasing number of studies supporting important medicinal or therapeutic properties associated with American and black elders.

Despite this century old tradition, American elder remains relatively unknown to the public and the industry alike. In contrast, black elder production and processing are well established in Europe where an impressive array of food (pies, jellies, jams, wines...) and medicinal (supplements, extracts, syrups, lozenges...) products are available. The more extensive and ancient use of black elder is supported by a rich documentation; American elder has been much less studied. However, the taxonomic closeness of these two related plants is such that they share common properties and will be treated as one. Their alleged and demonstrated medicinal properties will be critically discussed in this paper. When necessary, significant differences will be stated.

BOTANY

American elder [*Sambucus nigra* sbsp. *canadensis* (L.) R. Bolli, Adoxaceae] is also known as elderberry and common elder. It is a close relative of black elder [*S. nigra* sbsp. *nigra* (L.) R. Bolli], a common plant in Europe. Bolli (1994) recently revised the genus *Sambucus* and reclassified American and black elders to the rank of subspecies. This distinction has not been widely applied yet and *S. canadensis* and *S. nigra* are still commonly used when referring to American elder and black elder, respectively. Donoghue (2003) concluded that the genus *Sambucus* belongs to the Adoxaceae instead of the Caprifoliaceae family, this correction is slowly being implemented. For a comprehensive description of black elder refer to Atkinson and Atkinson (2002).

American elder is native to eastern and central North America. It can be found from Nova Scotia (Canada) south to the state of Florida, and west to Manitoba (Canada) and the state of Texas (Small et al. 2004). It will grow on a wide range of types of soil and can tolerate occasional flooding; however spring floods are usually detrimental. Seed dispersal is mainly done by birds and mammals that feed on the berries. Seedlings hardly support any competition from faster growing weeds and new plants will preferably establish in open areas.

Elderberry is a deciduous multi-stemmed shrub with brittle branches that easily bent under the weight of its fruit clusters. Suckering from the roots and branching from the base of the main stems force the plant to form dense thickets. It can reach up to 9 m in height in the southern part of its distribution area but less than 4 m in the southern part of Canada (Small et al. 2004). Aging of the shrub is accompanied by the death of old branches, a process preventing the plant from reaching extreme heights.

Large (5–15 cm long) opposite pinnately compound leaves contain from 5 to 11 leaflets with sharply serrated margins. American elder is among the first shrubs to flush in early spring in Canada. In the northern part of its distribution range it blooms at the end of June independently of heat accumulation (Guilmette 2006). Blooming is synchronous for numerous cultivars of interest for the industry. Creamy-white flowers gather into large terminal clusters up to 35 cm across.



Fig. 1. Cluster of American elder berries (*Sambucus nigra* sbsp. *canadensis*, cv. York).

Wind rather than insects is the main vector for pollen distribution (unpubl. data). Fruit ripening happens over a 2-month period in northern latitudes. At maturity, small (5–9 mm in diameter) deep purple almost black berries (Fig. 1) hang up side down as the stem often bent under the weight. A single cluster can contain as many as 2000 berries. American elder should not be confused with red-berried elder (*S. racemosa* Michx. or *S. pubens* Michx.) which partly shares the same territory but blooms earlier and produces bright red berries.

HORTICULTURE

More than twenty different cultivars are available to consumers. While most were developed for their ornamental qualities, some such as Adams, Kent, Nova, Scotia, Victoria, and York, clearly offer high quality fruits with interesting commercial potential (Craig 1970). Elderberry is rather easy to grow. Hardwood cuttings, collected before bud break, and softwood cuttings, collected from July to August, should be transplanted on a raised bed over plastic mulch. Because there might be extensive dieback of terminal branches during winter, particularly in the northern part of its distribution, hardwood cuttings selection requires some training. Rooting reaches close to 100% provided that sufficient humidity was maintained. Production can be expected as early as the second year in the field with hardwood cuttings. Yield reaching 3 kg per plant the second year has been obtained in southern Quebec. By the fourth year, an average of 8 kg per plant can be expected at such latitude.

Since it competes poorly with neighboring vegetation, plastic mulch should be considered when establishing an orchard. However, once established elderberry can outgrow almost any competing weed and can survive severe mechanical damage. New canes can grow as much as 2 m in a single season. In production, height should be kept to less than 3 m to allow for manual harvest. Pruning will probably have to be considered around the fourth year as yield saturates or even decreases due to inner branches dieback. Mechanized pruning can be used by simply topping the plant about 75 cm from the ground.

Type of soil, yield, density, age of plants, and precipitation should all be considered when planning fertilization. As a rule of thumb, use 100 g of 10–10–10 per year of age per plant (Craig 1970). Planting density should be dictated by the full size of the plant at maturity and the kind of equipment that will be used to maintain the orchard. A distance no longer than 2 m between plants is sufficient to allow easy access to fruit clusters at harvest. Rows can be kept less than 4 m apart. Irrigation should be considered during the first year to insure proper development. Elderberry is relatively drought tolerant and probably won't require additional watering during an average summer and on heavy soil. Occasional irrigation might however be necessary in light soil or during dry summer. Proper drainage should be maintained under production conditions, particularly during spring thaw.

Harvest is done by hand and the plant can rapidly be stripped of its fruits. Mechanized harvest seems unlikely as some fruits are often buried within the plant. In the northern part of its distribution area, fruits can be harvested at the end of August over a 2 week period. As we go south, blooming and fruit maturation tend to be less synchronous (Easterday Patton and Judd 1988) which could complicate harvest. In order to preserve fruit quality, elder berries should be refrigerated as soon as possible. Processing can be delayed many months if fruits are kept frozen. Each berry contains 2 to 5 seeds. While a single plant can produce an impressive amount of seeds, they require a rather long stratification period (Brinkman 1974) and should not be considered as the best material for propagation.

The similarities between the American and European subspecies of *S. nigra* were insufficient to warrant the development of sustained production in North America. Over the last 50 years, only a few producers in the US managed to establish small orchards generally for local processing into pies, jams, jellies, and particularly wines. Elderberry wine production in the US and Canada probably started with the arrival of the first European settlers who brought this tradition from their homeland. It is not until the early 20th century that cultivar selection really took place in North America. Since the early 1990s, elderberry production is slowly picking up momentum in Canada with orchards being established in Ontario, Quebec, New Brunswick, Nova Scotia, and Newfoundland. This contrasts with black elder production in Europe where many countries, such as Denmark, Hungary, Poland, and Switzerland support both an important fruit production and processing industry. With an increasing demand for healthy food and the publication of numerous papers pointing at the health potential of small fruits, renewed interest in elderberry is expected both in Canada and the US.

MEDICINAL VALUES

Elderberry fruits are an excellent source of anthocyanins, vitamins A and C and a good source of calcium, iron and vitamin B6 (Table 1). They also contain sterols, tannins, and essential oils (Anon. 2005) and can readily be considered a healthy food. But more evidence is needed to really sustain any claim relative to their medicinal value.

Folk Medicine

In folk medicine, elder berries have been used for their diaphoretic, laxative and diuretic properties (Uncini Manganelli et al. 2005; Merica et al. 2006) and to treat various illnesses such as stomach ache, sinus congestion, constipation, diarrhea, sore throat, common cold, and rheumatism (Novelli 2003; Uncini Manganelli et al. 2005). The flowers are said to have diaphoretic, anti-catarthal, expectorant, circulatory stimulant, diuretic, and topical anti-inflammatory actions (Merica et al. 2006). Some of these properties seem justified since elderberry fruits contain tannins and viburnic acid, both known to have a positive effect on diarrhea, nasal congestion, and to improve respiration (Novelli 2003). Leaves and inner bark have also been used for their purgative, emetic, diuretic, laxative, topical emollient, expectorant, and diaphoretic action (Merica et al. 2006).

Indirect Evidence for Health Benefits

Elderberry medicinal potential comes from its antioxidant potential, a property shared by numerous phytochemicals. The human body is constantly under attack and uses free radicals to protect itself. Such mechanism can however lead to cascade effects that can be detrimental to the cells and even lead to cancer. Our body uses antioxidants from plant origins to neutralize harmful free radicals and elderberry total antioxidant capacity is one of the highest of all the small fruits. In one study including the black elder (Fig. 2), this species came third for its antioxidant capacity as measured with the FRAP method (Halvorsen et al. 2002). Using the ORAC technique to measure the antioxidant potential of various small fruits, Wu et al. (2004a,b) showed that the American elder had a much higher potential than cranberry and blueberry, two fruits praised for their high antioxidant capacity (Fig. 3). Such a high antioxidant potential in American elder berries has been confirmed in our laboratory (unpubl. data).

Polyphenols. Different definitions are proposed but despite the fact that they vary somehow, they all agree on the prevalence of these chemicals in plants. Many are however prudent when conferring medicinal properties to polyphenols. This reflects to some extent conflicting results found in the literature, a problem associated with the abundance of phenolic compounds found in nature.

Indeed, the polyphenolic profile of fruit juices, including elderberry, can be quite complex (Schwarz et al. 2001; Bermúdez-Soto and Tomás-Barberán 2004; Proestos et al. 2005) containing an array of compounds of which many are anthocyanins (Sanchez-Moreno et al. 2003). Other relatively common polyphenols are: flavonols, hydroxycinnamic acid derivatives, and flavan-3-ols. Elderberry juice is rich in total phenolics, anthocyanins, and flavonols; all these chemicals were shown to be highly correlated with their antioxidant capacity (Bermúdez-

Table 1. Chemical composition of various small fruits. Adapted from (Products and Services: Fruits and Fruits Juices, 2005).

Fruit	Water	Energy (kcal)	Iron (mg)	Phosphorous (mg)	Vitamin A (IU)	Vitamin B6 (mg)	Vitamin C (mg)
Blueberry	84	27	0.28	12	54	1.052	9.7
Cranberry	87	46	0.25	13	60	0.057	13.3
Elderberry	80	73	1.60	39	600	0.230	36.0
Grape	81	69	0.36	20	66	0.086	10.8
Mulberry	89	43	0.62	22	214	0.030	21.0
Raspberry	86	52	0.69	29	33	0.055	26.2
Strawberry	91	32	0.42	24	12	0.047	58.8

Soto and Tomás-Barberán 2004) ranking this species among the most interesting ones. Despite the prevalence of phenolic compounds in our diet, their absorption and bioavailability is still a matter of debate (Karakaya 2004). This author review on this subject is worth reading.

Flavonoids. Flavonoids are a subclass of polyphenols. These phytochemicals cannot be synthesized by humans (Peterson and Dwyer 1998). It was estimated that dietary intake varies between 23 and 1000 mg/day (Peterson and Dwyer 1998). They include, among others, anthocyanins (cyanidin, pelargonidin), flavanols (catechin, epicatechin), flavonols (quercetin, kaempferol), flavones (apigenin, luteolin), and flavanones (hesperetin, naringenin). While flavan-3-ols and flavonols are the most prevalent, it is probably the anthocyanidins that are the most abundant (Gebhardt et al. 2002). Various studies have demonstrated their antioxidant and antimutagenic activities and their possible implication in reducing the risks of cardiovascular disease and stroke (Peterson and Dwyer 1998). As it is for the other polyphenols, flavonoids absorption may vary between classes and much remain to be known about their absorption and metabolism (Peterson and Dwyer 1998).

Anthocyanins and Anthocyanidins. Anthocyanins are a large group of natural pigments responsible for the color of numerous fruits (Fossen et al. 1998). Natural anthocyanins occur as glycosides (i.e. attached to a sugar molecule) while anthocyanidins are aglycones of anthocyanins.

The most important polyphenols found in elderberry are anthocyanins, mainly cyanidin 3-glucoside and cyanidin 3-sambubioside (Gebhardt et al. 2002). The anthocyanin content of elderberries is one of the most important among common commodities (Clifford 2000). Interestingly, anthocyanins in American elderberries are acylated, thus more stable to light and heat than those found in black elder (Nakatani et al. 1995; Inami et al. 1996) which make them more suitable for processing.

Cyanidin. Cyanidin is one of the six anthocyanins aglycones (anthocyanidins) frequently found in common foods in the United States (Wu et al. 2006). According to these authors, cyanidin constitutes about 45% of total anthocyanins intake in the US.

Among various common plant-derived polyphenolic flavonoids, cyanidin has one of the highest antioxidant activities (Rice-Evans et al. 1995). The higher antioxidant potential of American elder compared to black elder is not surprising considering the findings of Stintzing et al. (2002) stating that acylation can increase the antioxidant activity of anthocyanins. Sterling (2001) proposed an interesting review about anthocyanins. More studies are needed since the extent of cyanidin 3-glucoside absorption, metabolism, and bioavailability are still unclear (Mülleder et al. 2002; Andlauer et al. 2003; Bitsch et al. 2004; Galvano et al. 2004).

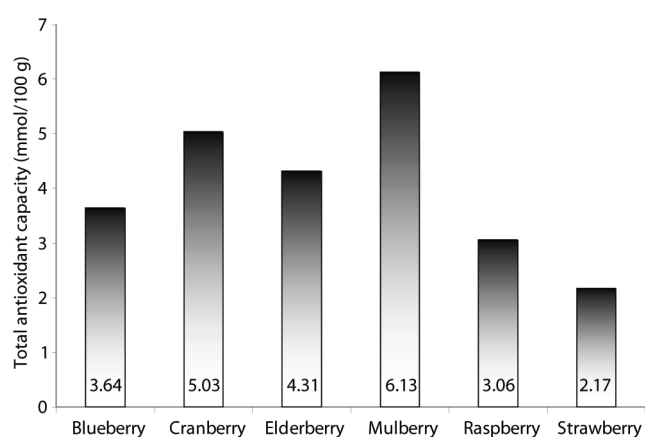


Fig. 2. Total antioxidant capacity of various small fruits as measured using the FRAP method. [FRAP = Ferric Reducing Antioxidant Potential]. In this example, elderberry is the European subspecies. Adapted from: (Halvorsen et al. 2002).

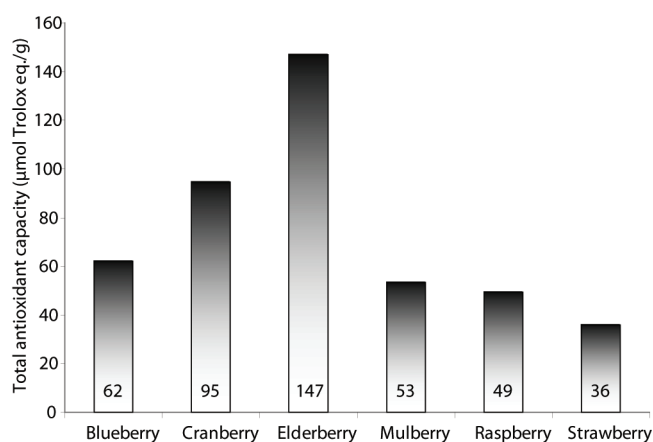


Fig. 3. Total antioxidant capacity of various small fruits as measured using the ORAC method. [ORAC = Oxygen Radical absorbance Capacity]. In this example, elderberry is the American subspecies. Adapted from: (Wu et al. 2004a).

Direct Evidence for Health Benefits

It is only recently that direct evidence has been provided showing that anthocyanins can be absorbed by humans (Cao and Prior 1999). These authors showed that after oral administration of elderberry extract, cyanidins are absorbed in their glycosidic forms. Despite these results, the exact form under which elderberry anthocyanins are absorbed by humans is still a matter of debate. More evidence showed that they are probably absorbed in their glycosidic forms (Cao et al. 2001; Murkovic et al. 2001; Milbury et al. 2002). The sugar moieties can alter their apparent absorption and metabolism (Wu et al. 2005). Absorption and excretion of anthocyanins were reported to be lower than other flavonoids (Wu et al. 2002). More evidence is available concerning anthocyanins absorption, including cyanidin 3-glucoside, by mammals (Talavéra et al. 2003, 2004; Felgines et al. 2006).

These reports have an important impact when considering possible health benefits from elderberry consumption since it is now demonstrated that anthocyanins are indeed absorbed (Cao and Prior 1999) and able to significantly increase plasma antioxidant capacity (Netzel et al. 2002). Once ingested, anthocyanins link themselves to free iron ions in the intestine. When the amount of free iron is insufficient, anthocyanins will reach the blood stream where they will link to free iron radicals (Sardi 2000). It is however not known if anthocyanins get into cells or appropriate subcellular compartments in an amount sufficient to affect metabolic processes (Prior 2003). Despite interesting progress, there is still a lot to be learned about the absorption, metabolism, and health effects of dietary anthocyanins (Netzel et al. 2002; He et al. 2006).

Probably the most interesting properties of elderberry extracts were reported by Zakay-Rones et al. (1995). Following earlier work done by Konlee (1998), these authors reported that a mixture containing elderberry extract had an inhibitory effect on haemagglutinin found in mycovirus. More work done by Barak et al. (2001, 2002) have shown that such a mixture could inhibit the replication of 11 strains of the influenza virus and increase cytokines production.

On a more general note, berry phenolics including anthocyanins have been proved to provide protection toward lipid and protein oxidation (Viljanen et al. 2004). Matsumoto et al. (2003) demonstrated the positive effects of cyanidin 3-glucoside on rhodopsin regeneration. In another study, Hecht et al. (2006) proposed that cyanidin 3-glucoside might play a chemopreventive role in animal models. Cyanidin was also found to be an effective inhibitor of human tumour cells in vitro (Meiers et al. 2001).

MARKET POTENTIAL AND FUTURE

Considering the market potential of American elder and the stability of its anthocyanins, that is superior to that of black elder pigments, it is difficult to understand why its production is so low in North America. In fact both the flowers and the berries are quite suitable for processing and close to 100 different products, mostly made from black elder, are proposed on the Internet. These products can be divided into two main categories: food and beverages, and health products.

Food and Beverages

In many aspects elderberries compare quite well with better known small fruit crops such as raspberry, cranberry, strawberry, blueberry, or even grape. They can be used to prepare jam, jelly, pie, salad dressing, sauce, snack, juice, soft drink, cordial, wine, port, and beer (Fig. 4). A very stable food colorant can be extracted from the berries and used in the food industry. Fresh and dried berries can be found in breakfast cereals, yogurt, and ice cream. To a lesser extent, elderberry flower can also serve to prepare fritters, wine, beer, and liquors. No information is available about fresh elder berries shelf life. The rather small size of these fruits prob-



Fig. 4. Common elderberry based products found in Canada.

ably makes them less appealing to consumers. This would explain why they are almost exclusively available as processed food.

Health Products

The high polyphenol content, including anthocyanins, of elderberry fruits has been recognized and exploited by the pharmaceutical and natural products industries. Shampoos and body lotions are proposed to consumers. There is also a full array of products including lozenges, syrups, herbal teas, extracts, and supplements, all capitalizing on various health benefits associated with specific components found in elderberry fruits or flowers. While commercial claims are sometimes over enthusiastic, there is now a sufficient amount of direct and indirect evidence to sustain most of them.

The Future

Results from various sources have shown that elderberry is rich in polyphenols, particularly cyanidin 3-glucoside, an anthocyanin. Its antioxidant capacity ranks high when compared to other well known fruits such as cranberry, mulberry, and blueberry (Fig. 2 and 3). Anthocyanin content of some cultivars is even higher than in the wild type (unpubl. data). Effort should be made to map North American elderberry ecotypes in order to select those with the highest pigment content and antioxidant potential. From an evolutionary standpoint, anthocyanins are produced in part to attract pollinators and animals that will feed on the fruits and disperse the seeds. They also protect the plants against the harmful effects of UV radiation and act as chemical weapons to protect the plant against oxidative stress associated with viral or fungal infection (Wrolstad 2004). As such, one could expect to find more pigments in fruits from plants growing closer to their northernmost limit where they are more likely to be subjected to stress. Validation of that assumption, in order to select elite specimens for breeding purposes as it has been proposed by McGhie et al. (2002), is then justified.

Since pigments from American elder are acylated, thus more suited for processing, it is to be expected that elderberry production in North America will benefit from an increasing demand from consumers for food with demonstrated health benefits. It was proposed that the intestinal absorption of the bioactive components from berry juices, including elderberry, may be superior to that from the fruit itself (Netzel et al. 2002). Vatten et al. (2005) also proposed that the properties of phytochemical components in whole foods, such as those found in elderberry flowers and fruits, would play a more effective role in maintaining human health than would isolated individual phenolics. While these statements are speculative, it is worth noting that elderberry reaches consumers in a much greater proportion as a processed product (juice or extract) than as fresh fruit. It would be interesting to compare the beneficial effects of fresh elderberry fruits with that of processed ones. It should be kept in mind that once extracted, anthocyanins stability is affected by numerous factors including pH, temperature, and light (Markakis 1974).

Mild symptoms of stomach ache and vomiting have been reported after the consumption of unripe elderberry fruit. But such cases are rare and these mild side effects are outweighed by the numerous medicinal uses they are known for, some of which are well documented.

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