



The American Botanical Council

T H E A B C
CLINICAL
G U I D E T O
ELDER BERRY



European Elder Berry

Sambucus nigra L.

Family: *Caprifoliaceae*



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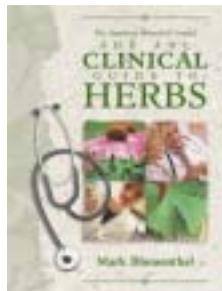
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THE ABC CLINICAL GUIDE TO HERBS is an excellent reference and provides national continuing education credit in 5 healthcare professions. Readers interested in what herbs and brands have been studied will find it here. Contains comprehensive, clinical-based information on the most popular herbs and proprietary herbal products. Each herb chapter discusses uses and safety information, and contains an extensively-referenced monograph, a table summarizing the most important clinical studies on that herb, a 2-page clinical overview, and a 1-page information sheet. 512pp.; hardcover; 2003.

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AMERICAN
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European Elder Berry

Sambucus nigra L.

Family: *Caprifoliaceae*

OVERVIEW

European elder fruit is a berry-like drupe, native to Europe, Northern Africa, and Western- and Central Asia with a long history of traditional use among European herbalists documented since ancient times in the writings of Hippocrates, Dioscorides, and Pliny the Elder. Elder berries have long been used for making preserves, wines, winter cordials, and for “adulterating,” i.e., adding flavor and color to other wines. In recent years, dietary supplements and other natural health products containing extracts, juices or syrups of European elder berry have become popular in the U.S. as remedies for treating cold and flu symptoms, marketed primarily through natural food stores alongside other popular herbal remedies used for treatment or prevention of upper respiratory tract infections and other symptoms associated with colds and flus.

PRIMARY USES

Common symptoms associated with:

- Influenza
- Colds
- Feverish conditions (as a diaphoretic)

OTHER POTENTIAL USES

- Diuretic (juice or tea; promotes renal elimination of water)

PHARMACOLOGICAL ACTIONS

In vitro: Significant antioxidant capacity as determined by oxygen radical absorbing capacity (ORAC), antiviral; inhibits viral replication, and immunoprotective or immunostimulatory; increases production of inflammatory and antiinflammatory cytokines.

Human: Elder berry extract increases hemagglutination inhibition titers to influenza B in the sera of flu patients.

DOSAGE AND ADMINISTRATION

Clinical trials on patients with influenza suggest using the standardized liquid extract for 3 to 5 days starting at the first sign of flu symptoms.

CRUDE PREPARATIONS

EXPRESSED JUICE: 1 glass (presumably 8 oz.; size not specified in original source) 2 times daily.

SYRUP: 1-2 tablespoons mixed with hot water.

TEA DECOCTION: 1 cup (made from 10 g dried berries) several times daily.



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STANDARDIZED PREPARATIONS*

SYRUP (contains 3.8 g standardized liquid extract (2:1) per 10 ml syrup):

For intensive use:

Adults: 2 teaspoons 4 times daily

Children: 1 teaspoon 4 times daily

For daily maintenance:

Adults: 2 teaspoons daily

Children: 1 teaspoon daily

LOZENGES (contains 130 mg standardized dry extract and 100 mg vitamin C):

For intensive use:

Adults: 2 lozenges 3 times daily

Children: 1 lozenge 4 times daily

For daily maintenance:

Adults: 1 lozenge 2 times daily

Children: 1 lozenge daily

[* The manufacturer states that it has standardized the elder berry extract used in all

Sambucol® preparations to its antiviral activity as measured in an in vitro bioassay, and that this quantified in vitro antiviral activity is consistent on a batch-to-batch basis.]

CONTRAINDICATIONS

None known.

PREGNANCY AND LACTATION: Although elder berry has been safely consumed in the diet of some cultures, at least one source suggests that elder berry should not be used when pregnant or lactating due to insufficient clinical data and potential risk of toxicity. However, there are no data suggesting that elder berry preparations would have an adverse effect on pregnancy or on nursing infants.

ADVERSE EFFECTS

No known reports (for properly prepared European elder berry preparations at therapeutic dosages). Unripe or insufficiently cooked elder berry preparations can induce toxic effects in humans (e.g., diarrhea, nausea, vomiting). There are reports of poisonings from the fresh juice of other *Sambucus* species, e.g., American elder (*S. canadensis*) and Mexican elder (*S. mexicana*). Also, in one study a small number of patients responded positively to skin prick test and/or RAST to an extract of elder pollen, flowers and berry.

DRUG INTERACTIONS

No known reports. One source suggests theoretical interactions based on speculative concerns that because elder berry may exhibit a diuretic and a laxative effect, caution should be exercised when taken concomitantly with diuretics or drugs that interact with diuretics, as well as with laxatives. There is a preliminary report of a potential beneficial interaction between elder berry preparations and decongestants and antibiotics.

CLINICAL REVIEW

Five small clinical studies on various elder berry preparations that included a total of 144 participants were reviewed, three of which were reported as part of the same study. Two randomized, double-blind, placebo-controlled (R, DB, PC) studies investigated the efficacy of a proprietary elder berry syrup (Sambucol®) for treating symptoms associated with influenza. In these studies, involving 27 and 60 patients respectively, patients treated with Sambucol® recovered significantly faster than patients in the control group. Three other trials, one of which was R, DB PC, investigated the effects of elder berry juice or an encapsulated spray-dried juice powder on components of cholesterol. In the R, DB, PC trial with encapsulated powdered juice, involving 34 subjects, a small, though non-significant, decrease in total cholesterol concentrations was measured in the treatment group. In a related crossover experiment involving 6 participants, a single, large dose (50 ml) of juice taken with a high-fat breakfast, showed no significant differences in postprandial triglyceride levels.

European Elder Berry

Sambucus nigra L.
[Fam. *Caprifoliaceae*]

OVERVIEW

European elder is a plant native to Europe, Northern Africa, and Western- and Central Asia. Its flowers and berries have a long history of use in traditional European medicine. Elder berries have also been used for making preserves, wines, winter cordials, and for adding flavor and color to other wines. Dietary supplements containing extracts, juices or syrups of European elder berry have become popular in the U.S. as remedies for treating cold and flu symptoms, sold mainly in natural food stores alongside other popular cold and flu herbal remedies.

USES

Treatment of cold and flu symptoms including aches and pains, coughing, nasal congestion, mucous discharge and fever; immune system stimulant.

DOSAGE

Clinical trials on patients with influenza suggest using the standardized extract for 3 to 5 days starting at the first sign of flu symptoms.

CRUDE PREPARATIONS

EXPRESSED JUICE: 1 glass (presumably 8 oz., size not specified in original source) 2 times daily.

SYRUP: 1-2 tablespoons mixed with hot water.

TEA DECOCTION: 1 cup (made from 10 g dried berries) several times daily.

STANDARDIZED PREPARATIONS*

SYRUP (contains 3.8 g standardized liquid extract (2:1) per 10 ml syrup):

For intensive use:

Adults: 2 teaspoons 4 times daily

Children: 1 teaspoon 4 times daily

Comments

When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of use. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement with care by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.



For daily maintenance:

Adults: 2 teaspoons daily

Children: 1 teaspoon daily

LOZENGES (contains 130 mg standardized dry extract and 100 mg vitamin C):

For intensive use:

Adults: 2 lozenges 3 times daily

Children: 1 lozenge 4 times daily

For daily maintenance:

Adults: 1 lozenge 2 times daily

Children: 1 lozenge daily

[*The manufacturer states that it has standardized the elder berry extract used in all Sambucol® preparations to its antiviral activity as measured in an in vitro bioassay, and that this quantified in vitro antiviral activity is consistent on a batch-to-batch basis.]

CONTRAINDICATIONS

None known.

Pregnancy And Lactation: There are no known restrictions although there are insufficient data to confirm safety during pregnancy or while breastfeeding.

ADVERSE EFFECTS

No reported side effects. Unripe elder berries or improperly prepared elder berry preparations can cause adverse side effects including diarrhea, nausea and vomiting.

DRUG INTERACTIONS

No confirmed drug interactions. Potential interactions with diuretics or drugs that interact with diuretics, as well as with laxatives have been speculated. A potential beneficial interaction between elder berry preparations and decongestants and antibiotics has also been speculated based on preliminary clinical observations.



The information contained on this sheet has been excerpted from *The ABC Clinical Guide to Elder Berry* © 2004 by the American Botanical Council, styled after *The ABC Clinical Guide to Herbs* © 2003 American Botanical Council (ABC). ABC is an independent member-based educational organization focusing on the medicinal use of herbs. For more detailed information about this herb please consult the healthcare provider who gave you this sheet. To order *The ABC Clinical Guide to Herbs* or become a member of ABC, visit their website at www.herbalgram.org.

European Elder Berry

Sambucus nigra L.

Family: *Caprifoliaceae*

OVERVIEW

Dating back to the fifth century BCE, the writings of Hippocrates, Dioscorides, and Pliny describe the use of medicines derived from the elder tree.¹ The common name elder is derived from the Anglo-Saxon word *æld*, meaning “fire” since blowing through the hollow stems of the young branches was a method for building up fires.² Elder was often referred to as the “medicine chest of the country people” and has a history of traditional use among Native Americans and herbalists of Europe.³ There is much European folklore associating the plant with life-enhancing effects such as increased longevity and vigor.^{3,4}

Much of the traditional use of elder and the modern research have focused on the flower, not the fruit; only recently in the past few decades have there been investigations into elder berry.



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(While elderberry is frequently written as one word, this monograph will employ the less common use of two words, e.g., elder berry, to eliminate as much as possible any confusion as to which plant part it is referring.) Numerous sources in the ethnobotanical and medical literature refer to historical, therapeutic, and toxicological information on “elder” without adequately documenting the plant part in question. Such ambiguities and lack of documentation can produce confusing data on the use and safety of preparations made from various parts of elder. In the information below, the authors and editors have made every best effort to ensure that the data relates specifically to preparations made from elder berry only.

References to the berry can be found in many pharmacopeias over the centuries, including the Italian, Dutch, Portuguese, Croat-Slovak, German, Austrian, Swiss and Hungarian.⁵ The medicinal uses of the berry are almost as numerous as those who reported them: Johann Bauhin (1541-1613) mentions their use by peasants for dysentery and diarrhea; Adam Lonicer (1528-1586) and Johann von Muralt (1638-1733) describe their use

for inducing perspiration to remove toxins; and Conrad von Megenberg (1309-1374) first mentioned elder berry juice to increase resistance to illness.⁵ The berries are regularly incorporated into food and condiments for coloring and flavor.^{2,6} They have long been used for making preserves, wines, winter cordials, and for “adulterating,” i.e., adding flavor and color to other wines.² Most of the elder berries in commerce are imported from the Russian Federation, Poland, Hungary, Portugal, and Bulgaria.⁷

DESCRIPTION

Elder, native to Europe, Northern Africa, and Western Asia, consists of over 20 species, many of which have similar chemical constituents.⁸ *Sambucus nigra* L., the species on which the majority of scientific research has been conducted, is a deciduous tree growing to 10 m (32 ft) with cream-white flowers and blue-black berries.⁹ The flowers, leaves, and berries all contain constituents of pharmacological importance including flavonoids, lectins, and anthocyanins.⁷ Elder berry preparations are made from either the fresh or dried fruit.⁶

PRIMARY USES

Elder berries are used to treat common symptoms associated with colds, feverish conditions (as a diaphoretic), and influenza.^{2,10,11}

OTHER POTENTIAL USES

- diuretic⁷

DOSAGE

Crude Preparations

SYRUP: 1-2 tablespoons mixed with hot water taken at night to promote perspiration and decongestion in cases of cough, cold or fever.² Simmer 5 lbs. of fresh, ripe berries with 1 lb. of sugar until the juice evaporates to the thickness of honey.

JUICE: 1 glass 2 times a day.^{10,12} Boil fresh berries in water for 2-3 minutes; express the juice, boil 10 parts juice with one part honey to preserve. (Amount of fresh berries and volume of water is not specified.)

TEA: One cup several times a day for treating feverish catarrhal afflictions or to act as a mild diuretic.⁷ Soak 10g of dried berries in cold water for several minutes, heat to boiling, decoct briefly, steep for 5-10 min, and decant.

STANDARDIZED PREPARATIONS

[Editors' Note: The manufacturer states that it has standardized the elder berry extract used in all Sambucol® preparations to its antiviral activity as measured in an in vitro bioassay, and that this quantified in vitro antiviral activity is consistent on a batch-to-batch basis.]¹³

Sambucol® syrup is a proprietary formula containing 38% black elder berry extract (2:1). The children's product is a proprietary formula containing 19% black elder berry extract. Per the

Sambucol® liquid formulations packages, the dosages are as follows:

For intensive use:

Adults: 2 teaspoons 4 times daily

Children: 1 teaspoon 4 times daily

For daily maintenance:

Adults: 2 teaspoons daily

Children: 1 teaspoon daily

Sambucol® lozenges:

For intensive use:

Adults: 2 lozenges 3 times daily

Children: 1 lozenge 4 times daily

For daily maintenance:

Adults: 1 lozenge 2 times daily

Children: 1 lozenge daily

DURATION OF ADMINISTRATION

Crude Preparations

None noted in the literature.

Standardized Preparations

Sambucol®: Clinical trials recommend 3 to 5 days within 48 hours of the onset of flu symptoms.^{14,15}

Clinical trials have shown Sambucol® was effective in shortening duration of flu and lessening its symptoms. Intensive Use dosage (see above) should start from onset of first flu symptoms and until symptoms resolve.^{14,15}

The daily maintenance dose as recommended by the manufacturer is based on in vitro studies that have shown Sambucol® to increase the activity of various immune system functions¹⁶⁻¹⁹; however, clinical trials have not yet been conducted to confirm an optimal duration for prophylactic effect.

CHEMISTRY

Elder berries are rich in flavonoids,^{4,20} vitamins C and P,¹⁰ and B1, B2, and B6.²¹ Elder berry contains the flavonoid glycosides, hyperoside, isoquercitrin, and rutin, and anthocyan glycosides chrysanthemine, sambucin, and sambucyanin.⁷ There is also approximately 0.01% essential oil containing 34 identified compounds. Present in the seeds are the cyanogenic glycosides, holo-calin, prunasin, sambunigrin, and zierin.⁷

PHARMACOLOGICAL ACTIONS

Crude Preparations

Human

None noted in the literature.

Animal

None noted in the literature. There are no data on animal research with elder berry in the available botanical and medical literature. A search on the Napralert database of 15 in vivo pharmacological studies on "Sambucus nigra" did not reveal any study that was specified to have been conducted with the "fruit" or "berry" of elder, most of the studies having been conducted on flowers, whole plant or other non-fruit preparations.

In Vitro

Four primary anthocyanins (cyanidin 3-sambubioside-5-glucoside, cyanidin 3,5-diglucoside, cyanidin 3-sambubioside, and cyanidin 3-glucoside) of elder berry were incorporated into the

plasma membrane and cytosol of endothelial cells following a 4-hour incubation with an extract.²² Human and animal endothelial cell enrichment with elder berry anthocyanins conferred significant protective effects against three oxidative stressors. In an additional experiment, an extract of elder berries (extraction process unspecified) were shown to exhibit oxygen radical absorbing capacity (ORAC) in an amount similar to cranberries (*Vaccinium macrocarpon* Aiton) and raspberry seeds (*Rubus idaeus*).²³

STANDARDIZED PREPARATIONS

Human

Increased hemagglutination inhibition titers to influenza B in the sera of flu patients who received Sambucol®.¹⁴

Animal

Disposition to acetic-acid induced colitis was decreased in rats fed a diet containing 4% elder berry (pomace) extract over a month.²⁴ Both macroscopic damage to the colon and myeloperoxidase activity were 50% lower in the treatment group compared with control diet group. Enhanced activity of lysosomal enzymes, considered to be an indicator of colonic mucosa integrity, was associated with the experimental group. Moreover, a lower level of primary products of lipoxygenation was also detected in the colon, liver, and erythrocytes of the experimental group.

Chimpanzees given Sambucol® orally, as either a prophylactic or as a symptom-dependent treatment experienced fewer flu-like, upper respiratory ailments than chimpanzees administered a placebo.²⁵ During the first fall and winter "flu season" of the study, five chimpanzees in an experimental group received 10 ml of Sambucol® daily, while five chimpanzees constituting a control group received sugar syrup. When chimpanzees in the experimental group exhibited flu-like symptoms, they received an increased dose of Sambucol®, 15 ml, twice daily. During the six months of the trial, the control group exhibited flu-like symptoms over a total of 39 days, whereas the experimental group had symptoms for a total of 12 days. During the second flu season, chimpanzees were strictly treated symptomatically with 15 ml of Sambucol® twice daily. Symptoms lasted for fewer than 24 hours in all animals treated symptomatically.

In Vitro

Reduced hemagglutination and inhibited replication of four type A human influenza viruses, three type B human influenza viruses, and three type A animal strains were demonstrated in Madin-Darby canine kidney cells incubated with Sambucol®.¹⁴ Inhibition of replication was dose dependent.

Production of four inflammatory cytokines (Interleukin-1 β , TNF- α , IL-6, IL-8) and one anti-inflammatory cytokine (IL-10) were significantly increased, compared to a control treatment, by the incubation of monocytes from healthy donors with different Sambucol® formulations, suggesting an immuno-stimulatory effect.¹⁶

Reduction in infectivity of HIV strains was reported when pre-incubated with Sambucol®.¹⁸ Replication of HSV-1 strains, including acyclovir resistant lines, was completely inhibited by Sambucol® elder berry extract.¹⁹

MECHANISM OF ACTION

Each of the following studies was done on a Sambucol® product unless specified otherwise.

- Elder berry extract inhibits hemagglutination produced by

the influenza viruses in humans.¹⁴

- Elder berry extract inhibits viral replication in humans and in vitro.^{14,19}
- Elder berry extract increases production of inflammatory and anti-inflammatory cytokines in humans.^{16,17}
- A 4% elder berry extract, extracted by 70% ethanol and vacuum-concentrated to 50-60% content dry matter enhances activity of lysosomal enzymes; reduces production of lipoxygenation products; reduces myeloperoxidase activity.²⁴
- An elder berry extract (per cent and extraction method unspecified) confers protection against oxidative stress.²²
- Elder berry extract exhibits oxygen radical absorbing capacity (ORAC) in vitro comparable to cranberry (*Vaccinium macrocarpon* Aiton) and raspberry seed (*Rubus idaeus*), but less than strawberry powder (*Fragaria* sp.), grape seed proanthocyanidin powder (*Vitis vinifera*), wild blueberry and blueberry extracts (*Vaccinium* spp.).²³

CONTRAINDICATIONS

None known. A review of the clinical, pharmacological and medical/scientific literature on elder berry has not produced any data that would constitute sufficient reasons for concerns about conditions that should be contraindicated with the use of elder berry preparations. One source suggests that persons with allergies to plants in the honeysuckle family (Caprifoliaceae) should avoid “elder” but no plant parts are distinguished or specified.²⁶ The same source acknowledges that there are no reports of allergy or hypersensitivity to elderberry or elderflower in the available literature.

PREGNANCY AND LACTATION: Although elder berry has been safely consumed in the diet of some cultures, at least one source suggests that elder berry should not be used when pregnant or lactating due to insufficient data and risk of toxicity.²⁶ The source notes a survey of pregnant women using dietary supplements in which one of the women reportedly experienced nausea and gastrointestinal discomfort when using an unspecified preparation of elder (plant part not noted).²⁷ However, there are no data suggesting that elder berry preparations would have an adverse effect on pregnancy or on nursing infants.

ADVERSE EFFECTS

Elder berry has no reported side effects. However, in one study a small number of patients responded positively to skin prick test and/or RAST to an extract of elder pollen, flowers and berry.²⁸ Improperly prepared elder preparations can induce toxic effects in humans through poisonous alkaloid and cyanogenic glycosides that are found in the roots, stems, leaves, bark, and unripe berries.²⁹⁻³¹ Effects of cyanide, also known as hydrocyanic acid (NCN), on humans include nausea, vomiting and diarrhea,^{30,31} as well as central nervous system and respiratory depression, and general lethargy.³² One report exists of poisoning cause by the ingestion of juice made from the berries of a different species of elder, *S. mexicana*, the elder tree indigenous to the western United States. Within 15 minutes of drinking the juice, pressed from leaves, stems, and berries, 11 people began to experience nausea and vomiting. Eight of these people were flown by helicopter to a hospital complaining of abdominal cramps, weakness, nausea, and vomiting. Some also complained of dizziness and numbness. One person who had ingested 5 glasses of the juice was hospitalized. All recovered quickly.³² There are anecdotal

reports of poisoning in children associated with an unnamed part (presumably the berry) of *S. canadensis*.²⁹

DRUG INTERACTIONS

Although there are no known confirmed drug interactions with elder berry, one source suggests some theoretical interactions.²⁶ The source notes that elder berry is associated with both a diuretic and a laxative effect; therefore, the authors of the cited report suggest caution be exercised when the berries and/or their preparations are taken in conjunction with diuretics or drugs that interact with diuretics, as well as caution with laxatives. However, based on current data, this caution appears to be strictly speculative.

Elder berry decoctions administered orally to laboratory rats before or simultaneously with subcutaneous injections of pentobarbitone caused a significant decrease of sleep induction time and increased sleeping time.³³ Berry decoctions administered orally 2 hours before subcutaneously injected morphine decreased the analgesic effect of morphine.³³ The relevance of the results of these studies to human oral use of elder berry preparations is difficult to establish.

One source states that there may be a beneficial interaction between elderberry preparations and decongestants like oxymetazoline (Afrin[®], manufactured by Schering-Plough HealthCare Canada Ltd), and antibiotics, as observed in “preliminary research” on patients, but there is no citation to such research.

AMERICAN HERBAL PRODUCTS ASSOCIATION (AHPA) SAFETY RATING

CLASS 1: Consumption of elder berry is safe when used appropriately (i.e., “Herbs which, when used appropriately, can be consumed safely without specific use restrictions.”).³⁰

REGULATORY STATUS

AUSTRALIA: Elder berry is a listable herbal entity under the Therapeutic Goods Act.³⁴

CANADA: Elder berry preparations with medicinal claims are regulated as Natural Health Products.³⁵

FRANCE: Elder berry is regulated as a traditional herbal medicine.³⁶

GERMANY: Elder fruit and its preparations were not evaluated by the German Commission E for safety and efficacy, although elder flower was reviewed and approved.³⁷

ISRAEL: In Israel, Sambucol[®] is regulated as a food supplement.³⁸

SWITZERLAND: The juice from the fruits is listed in the *Pharmacopoeia Helvetica V* as a purgative (large doses) and as a diuretic and diaphoretic.⁷

UNITED KINGDOM: Elder berry tablets are listed on the Veterinary Drugs General Sales List.⁷

UNITED STATES: Elder berry and elder berry products are regulated as dietary supplements.

CLINICAL REVIEW

There are 5 human trials (3 of which were reported as part of the same study) on various preparations derived from *S. nigra* berries that are summarized in the clinical studies table in this monograph. In general, the studies are mostly small. Two were randomized, double-blind, placebo-controlled studies investigating the efficacy of a proprietary elder berry syrup (Sambucol[®]) for treating symptoms associated with influenza.^{14,15} In these studies,

which involved 27 and 60 patients respectively, patients treated with Sambucol® recovered significantly faster than patients in the control group.

A placebo-controlled, double-blind study was conducted on 27 individuals with influenza (symptoms for ≤ 24 hours). Patients were randomized to receive either Sambucol® or placebo daily for 3 days. Children (5-11 years) received 2 tablespoons per day and adults (12 years and older) received 4 tablespoons per day for 3 days. A significant improvement in symptoms, including fever, was experienced by 93.3% of the elder berry group within 2 days. In contrast, 91.7% of the placebo group did not show similar improvement until day 6 ($P < 0.001$). Complete resolution (“cure”) was achieved within 2 to 3 days by approximately 90% of the elder berry group and within 6 days by the placebo group ($P < 0.001$). Immune system tests found a higher level of influenza antibodies in patients receiving elder berry than those receiving the placebo, suggesting enhanced immune activity.¹⁴

Another clinical trial with 60 adults also demonstrated the safety and efficacy of standardized elder berry syrup (Sambucol®) in the treatment of influenza and its symptoms.¹⁵ In this randomized, double-blind, placebo-controlled trial involving patients (18-54 years) with either influenza type A or type B, 15 ml of Sambucol® or a placebo was administered 4 times per day. Medication was initiated within 48 hours of the onset of symptoms (a potential weakness of this trial, as the elder preparation may have been even more effective with earlier intervention) and continued for 5 days. Study outcomes were determined from visual analogue scores (VAS) measuring flu symptoms (aches and pains, coughing frequency, quality of sleep, nasal congestion, and mucous discharge) and self-evaluation questionnaires. Baseline VAS values were not significantly different between the two groups. During treatment, VAS values were significantly higher (noting improvement) for the treatment group than for the control group ($P < 0.001$). Most VAS values in the elder berry group were close to 10 (pronounced improvement) after 3-4 days of treatment, whereas it took 7-8 days before the placebo group reached similar levels. Global evaluation scores (symptoms and overall wellness scores combined) for the elder berry group showed a pronounced improvement after a mean of 3.1 days compared to 7.1 days for the placebo group ($P < 0.001$). Moreover, a significantly larger number of patients in the control group resorted to “rescue medication,” such as an analgesic (i.e., paracetamol [acetaminophen]) or nasal spray, compared with the treatment group ($P < 0.001$).

BIOAVAILABILITY STUDIES ON ELDER BERRY

Four studies examined the bioavailability of elder berry anthocyanins. One study involved solely the investigator.³⁹ Two studies were conducted on 4 elderly, female volunteers.^{40,41} The fourth enrolled 8 men and 8 women in a cross-over design.²⁰ Results from these studies appear to support the idea that elder berry anthocyanins are bioavailable, though interpretations of results seem to differ from study to study. Mulleder et al. (2002) measured low concentrations of 2 anthocyanins (cyanidin 3-glucoside and cyanidin-3-sambubioside) in urine after oral consumption of elder berry concentrate high in anthocyanins (1.9 g). They concluded that, if bioavailable, these anthocyanins are available at low levels. Consumption of the same concentrate with the addition of 30 g sucrose resulted in reduced excretion of anthocyanins. Wu et al. (2002) found evidence of methylation of the same 2 anthocyanins in urine samples after administering elder berry extract (containing 720 mg anthocyanins), and also suggested that anthocyanins are absorbed and excreted at low rates

compared with other flavonoids. On the other hand, Cao and Prior (1999) and Milbury et al. (2002) reported the presence of the same anthocyanins, in their natural, unchanged state in urine and plasma samples after subjects consumed 1.5-1.9 g of elder berry anthocyanins, and claimed they are bioavailable.

A series of 3 trials, all reported by Murkovic et al. (2004), examined the effects of elder berry preparations on components of cholesterol.⁴² The trials varied in size from 6 to 34 subjects and in duration from 1 day to 3 weeks. The 2-week trial investigating the effects of elder berry on serum cholesterol was random and placebo-controlled with 20 men and 14 women (24-36 years of age). A small, though non-significant, decrease in total cholesterol concentrations was measured in treatment group (from 199 to 190 mg/dl) compared with control group (from 192 to 196 mg/dl) after subjects had consumed the equivalent of 5 ml elder berry juice (10% anthocyanin content) daily. Fourteen subjects (7 men, 7 women; 24-36 years of age) continued treatment for another week at which time LDL oxidation resistance was tested. There was no significant difference in resistance to induced oxidation between the treatment and control groups. Six subjects, in a cross-over experiment, consumed a high-fat breakfast with a single, large dose (50 ml) of elder berry juice. There was no difference in postprandial triglyceride levels.

BRANDED PRODUCTS

[Editors' note: This section contains some products that are not in the Clinical Overview section and the Clinical Studies Table. They are, however, mentioned in the Dosage section of this monograph and contain the same clinically-tested elder berry extract plus additional bioactive components.]

Sambucol®: Razei Bar / Manhat Technology Park, Bldg. 1, Flr. 1 / Jerusalem 91487 ISRAEL / Tel: (+972-2) 648-0577 / Fax: (+972-2) 648-0578 / Website: <http://www.sambucol.com> / Email: info@razeibar.com. Sambucol® Black Elderberry Extract contains 38% black elder berry extract with anthocyanins. Sambucol® Immune System Formula contains 4 g of a proprietary blend of 38% black elder berry extract with *Echinacea angustifolia* (root), *Echinacea purpurea* (stem, leaf and flower), and propolis, plus 100 mg Vitamin C (ascorbic acid) and 10 mg zinc (as zinc gluconate). Sambucol® For Kids contains a proprietary blend of 19% black elder berry extract with *Echinacea purpurea* (stem, leaf, and flower), *Echinacea angustifolia* (root), and propolis. Sambucol® Black Elderberry Extract Lozenge contains 130 mg of black elder berry extract and 100 mg Vitamin C. Sambucol® Immune System Formula Lozenge contains 90 mg of a proprietary blend of black elder berry extract and *Echinacea purpurea* (stem, leaf and flower), plus 100 mg Vitamin C and 5 mg zinc gluconate.

United States and Canada distribution through Nature's Way / 10 Mountain Springs Parkway / Springville, Utah 84663 / Tel: 801-489-1500 / Fax: 801-489-1700 / Email: info@naturesway.com. (www.naturesway.com).

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Clinical Studies on Elder Berry (*Sambucus nigra* L.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Zakay-Rones et al., 1995	Influenza treatment	DB, PC, R n=27 (children and adults)	3 days	2 tbs /day (children) 4 tbs/day (Adults)	Sambucol (38% black elderberry extract containing anthocyanins)	Treatment group recovered significantly faster (by days 2-3) than control group (by day 6) (P < 0.001). Enhanced immune activity detected in the treatment group.
Zakay-Rones et al., 2004	Influenza treatment	DB, PC, R n=60 (men and women, 18-54 years)	5 days	15 ml, 4 times a day	Sambucol (38% black elderberry extract containing anthocyanins)	Treatment group recovered 4 days earlier than control group. Nearly universal improvement in symptoms occurred after 3 days in treatment group, and after 7 days in control group (P < 0.001). Use of rescue medication (analgesic and nasal spray) was significantly lower in treatment group (P < 0.001).
Murkovic et al., 2004	Serum cholesterol	O, PC, R n=34 (20 men, 14 women)	2 weeks	400 mg	Spray-dried powder (equivalent to 5 ml elder berry juice; 10% anthocyanin content)	Small, non-significant decrease in cholesterol concentrations in treatment group (from 199 to 190 ml/dl) compared with control group (192 to 196 ml/dl).
Murkovic et al., 2004	Serum lipid	O n=6	1 day	50 ml	Elder berry juice	No difference in postprandial triglycerides with or without elder berry juice in subjects consuming a high fat breakfast.
Murkovic et al., 2004	LDL oxidation	O n=14 (7 men, 7 women)	3 weeks	400 mg	Spray-dried powder (equivalent to 5 ml elder berry juice; 10% anthocyanin content)	No significant effect on antioxidant status or resistance to oxidation of low-density lipoprotein

KEY: CO – crossover, DB – double-blind, n – number of patients, O – open, P – prospective, PC – placebo-controlled, R – randomized

Bioavailability Studies on Elder Berry (*Sambucus nigra* L.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Cao and Prior, 1999	Detection of anthocyanins in human plasma	n=1 healthy male (35 years)	1 day	25 g	Elder berry extract (containing 1.5 g anthocyanins)	Analysis of human plasma showed two spectral peaks matching those of anthocyanins in elder berry extract; evidence of in human body absorption.
Mulleder et al., 2002	Urinary excretion of cyanidin glycosides	O, CO n=16 (8 men, 8 women)	2 days	11 g	Elder berry concentrate (equivalent to 235 ml of fresh juice containing 1.9 g anthocyanins)	2 main anthocyanins of elder berry were detected unchanged in urine at low concentration. Ingestion of sucrose reduced excretion. Conclude limited bioavailability of anthocyanins in humans.
Milbury et al., 2002	Bioavailability of elder berry anthocyanins	O n=4 elderly women (63-71 years)	1 day	12 g	Elder berry extract (containing 720 mg anthocyanins) dissolved in water	Detection of 2 primary anthocyanins as glycosides in plasma and urine. Conclude anthocyanins bioavailable in unchanged glycosylated forms in humans.
Wu et al., 2002	Absorption and metabolism of anthocyanins	O n=4 elderly women (60-70 years)	1 day	12 g	Elder berry extract (containing 720 mg anthocyanins) dissolved in water	Evidence of methylation of 2 primary elder berry anthocyanins from urine samples. 4 metabolites were detected. Study suggests low rates of absorption and excretion of anthocyanins compared with other flavonoids.

KEY: CO – crossover, DB – double-blind, n – number of patients, O – open, P – prospective, PC – placebo-controlled, R – randomized

Standardized Elderberry Syrup Shortens the Severity and Duration of Influenza in Adults

by Donald J. Brown, N.D.

Reviewed: Zakay-Rones Z, Thom E, Wollan T, et al. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. *J International Med Res.* 2004;32:132–140.

Summary: In a randomized, double-blind, placebo controlled trial, 60 male and female patients (18-54 years old; mean 30 years old) were recruited from four primary care sites in Norway to study the efficacy of a standardized elderberry syrup for the treatment of influenza. Patients were screened for participation between December and February, when influenza infection is most prevalent. All volunteers selected for the study had a fever $\geq 38.0^{\circ}\text{C}$ (100.4°F) and at least one respiratory influenza symptom. Influenza type A virus was isolated from 54 patients and influenza type B from 6 patients. Patients were randomized to receive either a standardized black elder (*Sambucus nigra* L., Caprifoliaceae) berry syrup preparation (containing 38% elderberry extract plus small amounts of raspberry extract, glucose, citric acid, and honey; Sambucol[®], Razei Bar, Jerusalem, Israel) or a placebo syrup (same as above but with no elderberry). Patients were instructed to take 15 ml of elderberry or placebo 4 times per day. Study medication was started within 48 hours (mean 27.2 hours) of the onset of the influenza-like symptoms and continued for 5 days. Patients were also allowed to take a “rescue medication” (oral paracetamol and/or a dose-metered nasal spray [Otrivin[®], Novartis, Basel, Switzerland]) if necessary during the study. The primary study outcomes included visual analogue scores (VAS) for aches and pains, frequency of coughing, quality of sleep, mucus discharge in the respiratory tract, and nasal congestion. The VAS used a 10-point rating scale with 0 = no improvement and 10 = pronounced improvement. A self-evaluation score measuring overall personal well-being was also completed. Patients scored their symptoms on diary cards at baseline, four times a day during treatment, and twice daily for 5 days after the treatment had finished. Baseline VAS scores did not differ significantly between the elderberry and placebo groups. There was a significant difference ($p < 0.001$) between the two groups in the development of mean VAS scores. By days 3-4 of treatment, most of the VAS scores in the elderberry group were close to 10 (pronounced improvement), while the placebo group reached this level after 7-8 days. A significant difference ($p < 0.001$) in the global evaluation scores for the two groups was noted after a mean of 3.1 ± 1.3 days, while a similar score was obtained after 7.1 ± 2.5 days in the placebo group. Mean VAS scores for aches and pains, quality of sleep, mucus discharge in the respiratory tract, and nasal congestion were all greater than 9.0 by day 4 in the elderberry group and were ≤ 1.0 in the placebo group. The mean VAS score for aches and pains was 10.0 at day 5 in the elderberry group and at day 8 in the placebo group. Taking rescue medication was significantly less ($p < 0.001$) in the elderberry group (7 used paracetamol and 5 the nasal spray) versus the placebo group (26 and 21, respectively). Patients from both groups were fully recovered after 8 days. None of the patients reported any adverse events during the study.

Comments/Opinions: Sponsored by the makers of Sambucol, this

trial demonstrates the safety and efficacy of the standardized elderberry syrup for the treatment of influenza A in otherwise healthy adults. A previous Israeli trial with both adults and children showed similar efficacy in the treatment of influenza B/Panama.¹ In that trial, 27 subjects were randomized to receive Sambucol for 3 days at the onset of flu symptoms. Adults were instructed to take 4 tablespoons per day and children (under 12 years; the youngest was 5 years old) 2 tablespoons per day. A significant improvement of symptoms, including fever, was seen in 93.3% of the elderberry group within 2 days, compared to 91.7% of the placebo group not showing improvement until day 6 ($p < 0.001$). Complete resolution (“cure”) was achieved within 2 to 3 days in approximately 90% of the elderberry group and within 6 days in the placebo group ($p < 0.001$).

While the active constituents in this extract have not been clearly disclosed, it is thought that anthocyanins such as cyanidin 3-glucoside and cyanidin 3-sambuboside may be the key constituents in the extract.² Both are detectable in the plasma after oral ingestion of the extract.³ Possible mechanisms of action suggested for the extract include immunomodulatory actions as well as possible inhibition of viral adhesion to cell receptors. One ex vivo study found that incubation of human monocytes with Sambucol increased cytokine production—most notably tumor necrosis factor alpha (TNF- α) but also various interleukins (IL-1 β , IL-6, IL-8).⁴ An in vitro study found Sambucol inhibited the replication of common human and animal influenza A and B strains as well as prevention of viral adhesion to cell receptors.¹

Practice Implications: The results of this clinical trial support the use of a standardized elderberry syrup extract for the treatment of symptoms associated with influenza in otherwise healthy adults. Although based on small clinical trials, the data suggests a 50% reduction in both the severity and duration of symptoms in persons (adults and children) using the extract for 3 to 5 days. Based on the cost effectiveness of elderberry extract, future trials should focus on its potential value in preventing influenza and also its safety and efficacy in high risk populations such as immunocompromised patients, young children and infants, as well as the elderly. 🌿

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