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FILE: ▪ European Elderberry (*Sambucus nigra*)

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RE: Review of Pharmacology and Clinical Benefits of European Elderberry

Monograph. *Sambucus nigra* (Elderberry). *Altern Med Rev.* 2005;10(1):51-55.

European elder (*Sambucus nigra*) has been used historically as a diaphoretic, diuretic, astringent, laxative, and emetic. Berries are consumed in elderberry wine or pies and used as flavoring; traditionally, they were used in dyeing. Extracts of the berries are used currently as antiviral agents. Elderberry has also demonstrated immunomodulating, antioxidant, and insulin-stimulating effects. While the leaves, bark, and flowers have also been used in medications, most clinical studies have been conducted on the berry. [It should also be noted that American elderberry, formerly classified as *Sambucus canadensis* , is now classified as *S. nigra* var. c*anadensis.*]

Elderberry fruits have several active constituents, including flavonoids (quercetin and rutin), anthocyanins (cyanidin-3-glucoside and cyanidin-3-sambubioside), hemagglutinin protein *Sambucus nigra* agglutinin III (SNA-III), cyanogenic glycosides (including sambunigrin), viburnic acid, and vitamins A and C. The pharmacokinetics of many of these constituents are not completely understood. Research has focused on absorption and urinary excretion of the anthocyanins, which are absorbed and excreted intact, without first being hydrolyzed in the gastrointestinal tract.

Elderberry has mostly been studied for antiviral effects. Elderberry constituents were found to neutralize the activity of hemagglutinin spikes on the surface of several viruses, which are used to penetrate a host's cells in order to replicate. Based on these findings, Sambucol®, a syrup with 38% standardized extract of elderberry, was developed by Razei Bar Industries, Jerusalem, Israel. Sambucol has been used in numerous clinical studies. It has been found to neutralize and reduce the infectiousness of influenza viruses A and B, HIV strains, and *Herpes simplex* virus type 1 (HSV-1) strains and patient isolates. The complete inhibition of four strains of HSV-1 in human diploid fibroblasts warrants clinical trials. A formulation of elderberry flower extract, St. John's wort (*Hypericum perforatum*) and *Saponaria officinalis* also inhibited HSV-1 replication. Anecdotal evidence (6 case studies) and laboratory studies indicate that elderberry extract or elderberry combined with a thyme (*Thymus* spp.) extract (Thy-Mate™; ThymusPlus; Cumming, GA) may reduce viral load in people with HIV.

Elderberry extracts may also be immunomodulatory in healthy individuals as well as those with diseases characterized by immunosuppression. In vitro studies have demonstrated increased cytokine production (including tumor necrosis factor-alpha [TNF-*a*] and interleukins [IL] -1ß, -6, and -8) when blood-derived monocytes from healthy donors are exposed to various Sambucol preparations.

Anthocyanin flavonoids possess antioxidant properties. Low level concentrations (4 mcg/mL) of elderberry anthocyanins can efficiently regenerate *a*-tocopherol from *a*-tocopheroxyl radicals in models of copper-mediated low-density lipoprotein (LDL) oxidation. Also, human aortic endothelial cells incorporate elderberry anthocyanins into both membrane and cytosol, affording significantly enhanced resistance to reactive oxygen species, especially against H_2O_2-induced loss of cell viability. "[I]t is likely that supplementing with elderberry extracts containing anthocyanins provides significant antioxidant benefit."

Clinical indications for elderberry extracts are based on its demonstrated effects. Sambucol inhibits both influenza A and B strains when taken orally within 48 hours of onset of symptoms. Further studies on elderberry's ability to suppress other viruses are needed, but case studies on HIV patients, and elderberry's general safety, indicate that supplementation could provide a low-risk benefit. Similarly, with conditions associated with oxidative stress, such as cardiovascular diseases, cancer, neurodegenerative diseases, peripheral vascular disease, autoimmune disease, and multiple sclerosis, elderberry may be beneficial. Elderberry's ability to incorporate into endothelial cells may indicate a role in preventing vascular diseases.

Preliminary studies show that elderberry may cause a reduction in total cholesterol, as well as triglycerides and both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, thus making it potentially beneficial for individuals with elevated lipid levels. Furthermore, there is evidence that elder flower constituents can directly stimulate insulin secretion and glucose metabolism. Laboratory study investigating this effect was stimulated by the folk medicine belief that elder flower is a diabetes remedy. Clinical study is needed before elderberry can be recommended for these conditions, however.

There is no known drug interaction with elderberry. However, diabetics should monitor blood sugar closely if taking elder flower extracts, due to their ability to potentiate insulin release in vitro. Elderberry extracts generally have no side effects when used in recommended dosages; however, berries must be cooked before consumption. Raw berries or juice can cause vomiting or diarrhea. The leaves, stems, flowers and roots of elder contain toxic alkaloids. Also, a small percentage of the population has a type-1 allergy to elderberry. There are no known contraindications to using elderberry during pregnancy or lactation; however, as it is not well-researched under these conditions, it should be used by pregnant or nursing women only with caution.

Elderberry fruit syrups are most often standardized at 30-38% elderberry. Powdered extracts are taken at 500 mg 2-3 times daily for 3-4 days. Liquid syrups are taken at one tablespoonful (15 mL) three times daily. For acute viral infections, a course of treatment is at least three days.

— Mariann Garner-Wizard

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